

## Overview Review

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# Progress toward alleviating preventable waterborne diseases over the past 30 years

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## Abstract

Over the past several decades, there have been a number of national and international meetings on waterborne diseases. Conclusions from these meetings often seem remarkably similar and suggest little progress in the field of water and health. This is both a true and a false premise, as our ability to use molecular tools to describe microbial communities has advanced to the level at which whole genome sequencing is now a routine practice and can even be deployed in the field. This article seeks to illustrate both these advances and their limitations, especially for use in low-resourced settings. What remains clear is that for most of the world, basic hygiene and sanitation measures can do more for human health than any of our current advances in molecular biology. That is not to say that these advances are not remarkable and that they can undoubtedly revolutionize risk-based testing and surveillance. Although there are many factors that contribute to increased risks from waterborne diseases, climate change above all else is creating challenges that we are ill-prepared to meet. The biggest barrier to control of these diseases is not limitations in technology but has been and continues to be the lack of political will and economic incentives.

## Impact statement

The global burden of waterborne diseases has been and continues to be a major driver and impediment to human health, especially for low- and middle-income countries (LMICs). Many of these countries face the brunt of climate change due to lack of infrastructure and geographical location. For many, the fact that much of this burden is preventable is irrelevant without the tools, education, and political will. This article looks at some of our past knowledge about waterborne diseases and underscores our lack of progress in addressing a preventable area of human health that comes with significant global costs in terms of both human suffering and economics. Although we have some amazing new tools to detect the causative agents of disease, they do little or nothing to reduce this suffering. Disease continues to drive poverty, just as poverty drives disease and until we can educate decision-makers about these true costs to human development, we will make little progress.

## Introduction – Providing perspective

### *Past reviews and academy reports – Do we make progress?*

It is interesting to reflect that it is 28 years since one of us (TF) chaired one of the first American Academy of Microbiology's Scientific Colloquia in Guayaquil, Ecuador (April 1995). The report was on "A Global Decline in Microbiological Safety of Water: A Call for Action" (Ford and Colwell, 1996), and was, at least for a few years, the most frequently downloaded academy report (also translated into Spanish by Gary Toranzos, University of Puerto Rico). Subsequently, in 1999, TF published a review on the "Microbiological Safety of Drinking Water: United States and Global Perspectives" in *Environmental Health Perspectives* (Ford, 1999).

Both the review and the academy report concluded along similar lines, that we needed:

- Improved surveillance systems, risk assessment and predictive models, low-cost solutions for water treatment, and a better understanding of population susceptibility.
- Rapid assistance to communities and populations without regard for political boundaries during times of outbreak/epidemic disease.
- Education of policy-makers and the public about the social and economic burden of waterborne diseases – true valuation of water.

The review and the report emphasized the critical nature of new and resurgent disease, and the need to improve methods for detection using molecular tools.

TF was privileged to attend the next two academy colloquia with a focus on waterborne diseases. In 2001, we held a colloquium on "Reevaluation of Microbial Water Quality: Powerful

New Tools for Detection and Risk Assessment” (Rose and Grimes, 2000). Held in Amelia Island, Florida, in March 2000 and chaired by Joan Rose and Jay Grimes, this was a logical next step from the 1995 colloquium that focused on the advances achieved in genomics research.

We concluded that there was now an abundance of data showing that fecal coliform testing failed to detect many pathogens found in fecal and other wastes. Of course, this standard testing cannot indicate the presence of naturally occurring organisms that could be harmful, such as Harmful Algal Blooms (HABs) and the environmental pathogens that include *Legionella* and many of the non-tuberculous mycobacteria. Risk-based testing seems to be the way forward, but of course, that depends on the tools available to identify both old and new risks.

### Conclusions and recommendations show little change

In February 2002, TF had the pleasure of serving on the steering committee and attending “The Global Burden of Infectious Diseases through the Gastrointestinal Tract: A Critical Scientific Assessment of Exposure,” (Payment and Riley, 2002) in Galway, Ireland.

As before, a key conclusion was that “newer methods, especially molecular, genetic-based methods, should be employed to detect these (the ever-increasing list) pathogens.”

Among the usual recommendations about mandatory reporting, implementation of active surveillance, and improved risk assessment, this academy report also stressed education and communication, and the need to engage both political systems and the public in understanding both the social and economic implications of gastrointestinal diseases.

Finally, in 2006, TF attended “Clean Water: What is Acceptable Microbial Risk?” (LeChevallier and Buckley, 2007). As with prior colloquia, key recommendations included the need for “rapid, inexpensive, easy to use, and easy to interpret analytical methods for specific pathogens or marker pathogens” and better risk communication.

The colloquia series have all been wonderful opportunities to think deeply about the implications – globally – of waterborne diseases, but they all suffer from the same conundrum. We must do so many things, but we really only ever scratch the surface when it comes to how these recommendations are implemented. We suspect that if we had asked John Snow what we should be doing about cholera in 1850, he would have said that we need new and better tools! It is no surprise that we have seen a resurgence in cholera in regions where the disease has been absent for more than 100 years. The breakdown of civil order through extreme weather events or civil unrest as we have seen for example in Haiti (Piarroux et al., 2011) and Yemen (Ng et al., 2020) provide ideal conditions for the spread of this disease.

One of the greatest challenges we face today with cities in both LMICs and wealthier countries is the dependence on vast networks of rapidly deteriorating distribution pipes. That is why TF, among others, engaged in discussions around 2010/2011 with Academy staff in Washington DC about holding a colloquium on the microbial ecology of water distribution systems, a key area of his (and SH’s) research interests (e.g., Ford, 1993; Egorov et al., 2002; Ford, 2006; Richards et al., 2018). Subsequently, in April 2012, a colloquium was held on “Microbes in Pipes (MIP): The Microbiology of the Water Distribution System” (Ingerson-Mahar and Reid, 2013). The attendee list included some of the top scientists in the field, and was no doubt a good conversation. The report does not appear to

add to solutions, emphasizing needs as in earlier reports. To summarize, these included a group effort to develop a research strategy that would engage stakeholders; establishing data needs and minimal sampling protocols (and tools); developing standards and data sharing plans; and building connections to funding agencies. All needs and no new solutions.

Most recently, the Academy convened a colloquium in 2021 on microbes and climate change (Microbes and Climate Change, 2021). As with many reports, it does a great job identifying risks from climate change including those related to water and health, but recommendations are very general and high-level and do not add to our knowledge base. It is interesting that if we revisit the first Academy Report from 1996, one of the first conclusions was to improve surveillance systems, and one of the key recommendations from this 2022 report is to “deploy increased surveillance and detection of zoonotic and vector-borne diseases.”

The last colloquium report with a primary focus on water systems was published 10 years ago, and although the World Health Organization and others continue to update us on the global burden of waterborne diseases, there remains a paucity of solutions.

### A perspective from history

In 2018 we published “a perspective on the global pandemic of waterborne disease” in *Microbial Ecology* (Ford and Hamner, 2018). We quoted the privately published journals of TF’s great x4 Grandfather, Jonathan Bell, in discussing a letter in the *Spectator* by Mr. F.C. Brown that discusses how the East India Company’s monopoly over salt (Brown, 1849) – and deprivation of the same was a primary reason for continuing cholera epidemics in India. Brown starts with the observation that:

With one solitary exception, in every country which the Asiatic cholera successively overran, its virulence seemed to wear itself out, and after a time more or less brief it abated, and in all of them its ravages altogether ceased. The remarkable exception to this rule is British India. In that devoted country the cholera never dies: it has never ceased to rage in some part, from the hour of its first appearance until the present time; and it is from British India, its perpetual seat.....that the pestilence has again radiated...

After arguments based on diet and blood composition that we will not repeat here, he discusses the fact that:

...The Asiatic cholera first broke out among the population of Jessore; an inland population subsisting almost wholly on vegetable food of local growth, which as human food is deprived of an essential organic constituent, and therefore rendered necessarily dependent upon receiving from an external source an abundant supply of common salt necessary for health and life. In such a population, a distemper of the character of cholera would be predicated to appear the more certainly, if the predisposition to engender it had been long and systematically induced by their being forcibly reduced to a privation of salt.

In Jessore, as throughout British India, inland and maritime salt is a strict monopoly of the East India Company, and a favourite resource for taxation. Any native detected in making a grain of salt for his own use is instantly seriously fined, or imprisoned for months.

This was certainly not the first nor the last time that global companies – and governments - have placed profits above human health.

Looking again at the *Spectator* article, Brown credits a Dr. Marden, M.R.I., Senior Surgeon to the London General Institution or Free Hospital, for the Cure of Malignant Diseases, etc., etc. for the use in 1832 of a combination of salts for the successful

treatment of cholera patients compared to seven other treatments (almost 70% recovery). In fact, in Marsden's, 1834 publication on "Symptoms of Treatment of Malignant Diarrhoea: Better Known by the name of Asiatic or Malignant Cholera" (Marsden, 1834) he presents remedies. These remedies for the "second stage" which he describes as follows:

Extreme prostration of strength; incessant vomiting and purging of limpid fluid; total suppression of urine; intolerable thirst; cold breath, and general coldness of body; sunken eyes; dark blue and corrugated appearance of the skin of the hands and feet, with violent spasms of the extremities and the bowels.

Dissolved in a small quantity of cold water and given frequently, he suggests:

For children up to the age of 4 years:

Common salt, one scruple.

Carbonate of soda, six grains.

Oxymuriate of Potash, 2 g – Mix for one dose.

He increases the amounts for older age groups.

It is interesting to look at today's oral rehydration therapy and see that they are a combination of sodium, glucose, potassium, and citrate – mixed with clean water. Although there has been some evolution, and in particular the addition of carbohydrates, usually in the form of glucose, this basic practice has been around for a long time. Marsden even discusses slow intravenous injection of these same ingredients (Marsden, 1834).

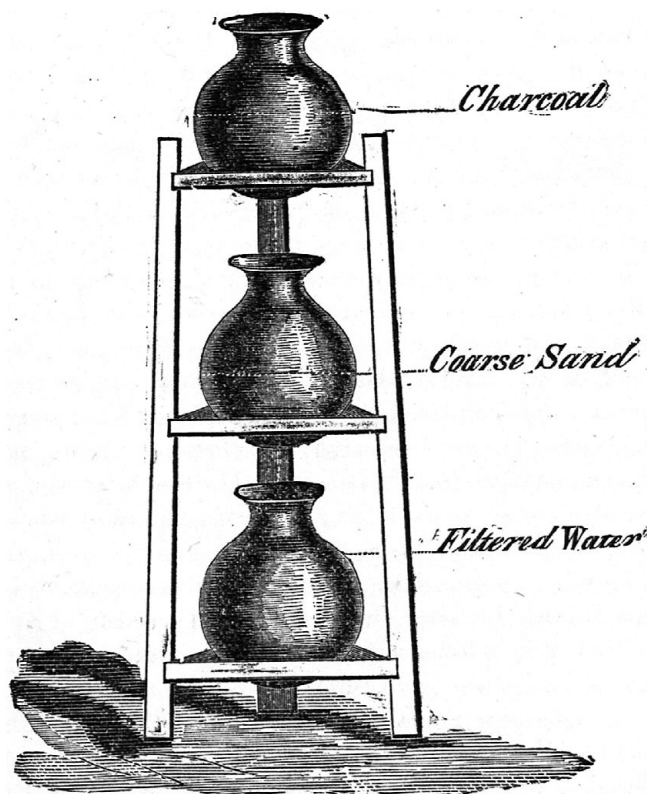
These old documents make fascinating reading in light of our not-so-modern attempts at reducing diarrheal disease and links to the full documents are provided in the references.

In the same *Microbial Ecology* (Ford and Hamner, 2018) paper we also highlighted Reginald Craufuird Sterndale (Ford's great  $\times 2$  grandfather), who both wrote about and illustrated the basic process of three-pot filtration in his 1881 publication on Municipal work in India (Sterndale, 1881). Sterndale recommended using "three ordinary porous earthenware culshis or jars", mounted vertically in a wooden stand with a small quantity of charcoal in the top jar and sand in the second jar (Figure 1). Of course, Sterndale did not invent the idea, and rudimentary water filtration to improve clarity, odor, and taste had been around for many centuries before his book. However, it is interesting to note that many similar technologies continue to be the only feasible water treatment options for impoverished areas of the world, and, indeed, can significantly reduce the incidence and mortality from waterborne disease. Sometimes the most simple solutions are best. Take for example sari cloth filtration and its effectiveness in reducing cholera morbidity and mortality in Bangladesh (Colwell et al., 2003; Huq et al., 2010).

## More recent directions and challenges

### GeneChips™ to whole genome sequencing and metagenomics

In the early 2000s, there was much anticipation around the development of gene arrays. The Affymetrix GeneChip™, in particular was going to revolutionize the field of environmental detection. In simplistic terms, we had the thought that it would not be too long before we could automate these arrays to "light up" when specific pathogens "flowed by" and hybridized to gene probes fixed to these arrays. Dip one in a glass of water and we would have pathogen detection in real time. In fact, the technology was very exciting – we were awarded an



**Figure 1.** Copy of an original drawing of a three-pot vertical filtration system from Sterndale (1881). Also reproduced in Ford and Hamner (2018).

NSF MRI to purchase an Affymetrix system at Montana State University in the early 2000s. There were companies at the time working to develop arrays that could be used in environmental detection, including drinking water, but to my knowledge, they never reached the commercial level. PCR was beginning to revolutionize our ability to detect *Escherichia coli* and specific pathogens, something we used extensively for source tracking in the Ganges, Little Bighorn, and Animas Rivers (Hamner et al., 2007, 2014, 2020). At the same time, whole genome sequencing was becoming cheaper and simpler. Still not the answer, but metagenomics offers a new way to start thinking about both environmental (and clinical) diagnostics that we will examine later. It is important to note that metagenomics fails to identify infectivity, particularly relevant in relation to infectious viruses. We can, however, look at and identify certain virulence genes (and antimicrobial resistance genes (AMR)) and hence establish a possible level of risk (e.g., Seo et al., 2023).

In theory, the application to polymicrobial contamination of the environment, together with the ability to detect specific AMR and virulence genes, has huge implications for water quality assessment (Bibby et al., 2019; Hamner et al., 2019; Hong et al., 2020; Acharya et al., 2020; Martin et al., 2021; Santiago-Rodriguez and Hollister, 2023; and others). Barriers are not so much in the technologies themselves, but rather in our inability to reproducibly isolate and purify DNA and RNA from complex environmental samples, especially in the field and in under-resourced settings.

### Business and governments – The problem not the solution?

Methods and technologies have largely been developed for use in the wealthiest countries. In general, they are unsuitable for use in

remote regions that lack the resources to purchase reagents, lack access to supply chains, cold storage, electricity, internet, basic laboratory facilities, safety equipment, etc. There are parallels here with vaccine development, in that massive resources were put into developing mRNA vaccines after the emergence of coronavirus disease-2019 (COVID-19). However, at least in the beginning, these vaccines required the cold chain for delivery, something that made them very difficult to access from LMICs and impossible for remote regions of the world. Do not get us wrong, the science was extraordinary but at the same time, it established global inequities – something Ford and colleague Charles Schweik argued in a Conversation Piece back in January 2021 (Ford and Schweik, 2021). We have done the same for safe drinking water.

The bulk of private funding has gone into producing sophisticated technologies for providing clean water for the wealthier nations, where company profits are the driving force. When the occasional company establishes more advanced treatment in an LMIC, or even fairly basic water filtration and disinfection, it seldom if ever comes with training and annual maintenance costs. Those costs can run to several hundred thousand dollars/year depending on capacity (Statistique Canada, 2011) and are beyond the reach of most LMICs. The world is littered with well-intended solutions to provide clean water that fail through lack of maintenance, training, or community participation (Nelson et al., 2021). Some notable failures include the catastrophic effects of World Bank and UNICEF funding for shallow tube wells to provide clean drinking water in Bangladesh and West Bengal - resulting in mass arsenic poisonings (Chakraborti et al., 2015). On a smaller but oft-repeated scale, broken pumps and storage tanks sit idle in many LMICs due to lack of community funds, expertise, and parts to fix them (Agence France-Presse, 2014). The Guardian put out an excellent and evocative YouTube video on the Yamuna River in 2017 that in one part illustrates the problem of a non-functioning water tank and filter (The Guardian, 2017). The authors' own experience is that pit latrines installed by International Agencies in one Indian city were never used by children as they were dark, smelly and cost a rupee. Open defecation remained far more preferable (personal communication).

We were struck by an excellent publication from the World Health Organization in 2008 that calculated that nearly 10% of the global burden of disease could be prevented by clean water, basic hygiene, and sanitation. The point the authors made was clear, that most waterborne diseases are preventable and the economic savings are vast (Prüss-Üstün et al., 2008).

In fact, according to the website, NGOsource, billions of dollars are spent each year on water, sanitation, and hygiene. This money supports pumps and infrastructure of which 40% are estimated to break down within 3 years and only a small percentage of those that survive produce good quality water (<20%) (White, 2014). In a March 2009 briefing for the International Institute for Environment and Development (IIEDO) (Skinner, 2009), Skinner estimated that in rural Africa, an estimated 50,000 water supply points were effectively dead and that in some regions 80% of wells do not function. The author suggests this is a failed investment of anything from US\$215–360 million. The tragedy here is of course the cost to human health, but it is also sobering to think about the scale of resources that could achieve so much with proper management and oversight.

### *The global burden of disease project – Help or hindrance?*

In teaching water and health through the years, a question that often comes up is whether the global burden of disease project has

helped or hindered the distribution of resources to address the largely diarrheal burden of waterborne diseases in developing countries (Behera and Mishra, 2022). The concept is undoubtedly useful for including years living with disabilities as a metric of the burden of disease, but this would tend to favor the more developed countries, where the likelihood of developing chronic diseases is much greater than in the poorest nations. Of course, the burden of chronic disease in developing countries has been increasing for some time (Nugent, 2008), but it still remains that in the poorest regions of the world, life expectancy is such that many people never reach an age when many chronic diseases tend to develop. When we started teaching about water and health in the late 1980s, the burden of diarrheal disease cases had been reported as an annual rate of about 4 billion for many years. At the time, this was close to the global population, so the ludicrous assumption was that there was one bout of diarrhea/person/year caused by infectious agents. We say ludicrous when you consider that there are parts of the world where persistent diarrhea (PD), defined as lasting for more than 2 weeks, is still a significant problem and cause of mortality in children under 5, due primarily to polymicrobial infections and/or intestinal parasites (Abba et al., 2009; Dupont, 2016; Bandsma et al., 2019). Anecdotally, we have been told of children who had never had a solid bowel movement. Is PD a single or a multiple case? Our estimations are certainly more fact-based today, but they are still very much estimations and it is widely acknowledged that they dramatically underestimate the actual incidence of diarrhea as many cases and indeed, deaths, go unreported. Our own work in India and Russia has suggested that incidence of gastrointestinal disease is orders of magnitude greater than officially reported numbers (Mohanty et al., 2002; Egorov et al., 2003; Hamner et al., 2006).

We have been reminded through the thoughtfulness of one reviewer that the inequities in water and health we discuss are not simply a problem for LMIC. The obvious case in point is the extreme inequities faced in Flint, Michigan among lower-income neighborhoods due to lead exposure (e.g., Campbell et al., 2016). Unfortunately, other examples abound and are more often than not the result of systemic racism and a history of racist policies within societies (Brown et al., 2023; Lee et al., 2023).

### *Water security – A persistent and expanding challenge*

Waterborne disease continues to pose serious public health challenges for vulnerable communities where the need for basic sewage collection and sanitation has not been adequately addressed. Traditionally, one important aspect of the study of waterborne pathogens has been to determine the prevalence and distribution of pathogens in natural and manmade settings and their role in causing waterborne diseases such as diarrhea and related gastrointestinal illnesses. It has recently been posited that even in resource-rich communities, the rapidly expanding need and use of water, combined with new and more complex means of using water, are leading to waterborne pathogens being implicated in contributing to a much wider range of diseases, including “respiratory illnesses, neurological illnesses, skin problems... and bloodstream infections (CDC, 2023).” Increasing human population and the expansion of high-density/high-rise housing and buildings (including hospitals, industrial and office structures) have driven the increased need for both water as well as increasing complex distribution and piping systems (CDC, 2023). In the face of such changes, it is increasingly challenging to maintain safe water supplies to protect public health.

### Climate change, the water cycle, and infectious disease

Climate change is closely associated with water availability and water safety. Climate change is driving changes in temperature and precipitation patterns and more extreme weather events. Increases in the temperature of the atmosphere and of bodies of water cause water to evaporate more quickly, which in turn forces water to move more rapidly and carry increased energy through the water cycle (Olmedo et al., 2022). Although much more complicated in reality, in simple terms, the water cycle can be defined as the evaporation of water from the earth's surface, movement of water vapor into the atmosphere, condensation in the atmosphere, followed by precipitation as rain and snow. As this cycle of evaporation, condensation, and precipitation speeds up, extreme weather events become more likely, including severe storms and flooding that can threaten wastewater and water treatment and infrastructure and curtail safe water supplies (Wang et al., 2022). Flooding has been associated with increased pathogen contamination of ground water and private wells with a greater likelihood of transmission of waterborne disease (Andrade et al., 2018; Musacchio et al., 2021). Water and wastewater treatment infrastructure designed to withstand milder weather extremes of the past are more likely to be incapacitated by increasingly severe storms and flooding that occur with greater frequency, necessitating reevaluation of current operations and infrastructure to ensure greater resilience in providing safe water supplies (Beller-Simms et al., 2014).

Very recently, an increase in catastrophic weather events and flooding worldwide has garnered great attention in media reporting, due to the impact on human suffering and disease, and mounting economic costs (NBC News, 2023; Munich, 2023; Washington Post, 2023). With the warming of coastal temperatures in the US, for example, there has been an alarming uptick of infections caused by *Vibrio vulnificus* resulting in at least 12 deaths during 2023 (CDC Health Alert Network, 2023; USA Today, 2023).

### Conveying the message and urgency of addressing climate change and water protections to the public and to political leadership

With changing temperature and precipitation patterns, climate change is altering the incidence and intensity not only of rainfall but also of droughts, and the popular press and news services are increasingly taking note (Galindo et al., 2022; O'Malley, 2023). Although it is widely acknowledged that education is crucial in coaxing the public to begin to understand and be concerned about climate change (UN, 2023), it is also acknowledged that concern alone is not easily translated into meaningful actions adopted by governments and policy-makers (NRC, 2011; Li et al., 2023). Despite surveys indicating that citizens worldwide are concerned about climate change, the political will to seriously address this challenge is still lacking (Williams et al., 2021; Grobusch and Grobusch, 2022). This may be due to the complexity of understanding: (1) the problem of climate change and its widespread ramifications, including challenges to public health and access to safe drinking water, (2) the causes of climate change, and (3) how to effectively address and adapt to climate change (it may simply be too overwhelming to most citizens and policy-makers alike, unless they are directly affected and moved to action) (Kamarck, 2019). At least in high-income countries, this ignorance among politicians is a clear indication of the failure of science education at all levels (Dillon and Avraamidou,

2021). Additionally, and in the United States in particular, it is particularly alarming how politicized the topic of climate change has become and remains (Kamarck, 2021). A political tug-of-war gridlock has ensued. As a case in point, the federal Clean Water Rule of 2015 clarified and strengthened provisions of the 1972 Clean Water Act, intended to safeguard source waters for drinking (public health) and recreation, and protect wetlands important for wildlife habitat, flood protection, and the ecological service of filtration as water moves through the water cycle on land (Federal Register, 2015). Conversely, during the next presidential administration in the US, a repeal of many environmental and water protections ensued (Popovich et al., 2020). Notably, the Navigable Waters Protection Rule of 2020 rescinded many of the protections of the Clean Water Rule of 2015. With political leadership again changing in the White House through the election of 2020, the current administration has reestablished protections of water quality and aquatic ecosystems and provisions of the 2015 Clean Water Rule through the Revised Definition of "Waters of the United States" (Federal Register, 2023).

### Surveillance and detection of waterborne pathogens using molecular biology

The need to safeguard freshwater ecosystems that protect and purify water supplies was impressed upon us by our microbial source tracking study of the Little Bighorn River in Montana (Hamner et al., 2014). Testing of the river in the town of Crow Agency revealed several potentially pathogenic serotypes of *E. coli*. Community concern expressed by members of the Crow Environmental Health Steering Committee (Cummins et al., 2010) led to a source tracking study of the potential impact on the river of a large cattle ranch upstream of Crow Agency close to the Wyoming state border. A drainage ditch running downslope from a concentrated animal feed operation (CAFO) on the ranch directly to a small wetland bordering the Little Bighorn River was identified as a likely conduit for cattle manure runoff into the river. Out of 167 isolates of *E. coli* obtained from sampling cattle manure from the CAFO, 23% tested positive for the intimin gene characteristic of enteropathogenic and enterohemorrhagic *E. coli*. Nineteen isolates of atypical enteropathogenic *E. coli* serotype O156:H8 were identified among manure isolates, matching an O156:H8 strain obtained nearby in the river. DNA fingerprinting using repetitive element sequence-based PCR (repPCR) was also conducted for a total of 589 *E. coli* isolates; in addition to the CAFO feedlot manure isolates, *E. coli* strains were also obtained from sampling of the drainage ditch running downslope of the CAFO feedlots, water flowing in the wetland area fed by the drainage ditch, and nearby sites along the river. Analysis of the 589 fingerprints identified 24 pairs that were matches between a feedlot manure isolate and a river isolate, a manure isolate and a drainage ditch isolate, or a drainage ditch isolate and a river isolate - all evidence for the migration of *E. coli* from the CAFO feedlot into the river (Hamner et al., 2014). A poignant anecdote about these findings was that in a conversation with one of the ranch employees, the employee expressed surprise at our study and findings, saying that the river water appeared so clean and clear flowing in the vicinity of the ranch office where she worked, not having considered the impact that manure drainage could be having in releasing large amounts of runoff with potentially pathogenic bacteria into the river (Hamner, personal recollection).

### Moving forward: Metagenomics and enhanced identification of microbial pathogens

Targeted approaches to testing for presence or absence of a given microbial pathogen are now being partially supplanted by metagenomics technology. Metagenomics represents a non-targeted approach by potentially identifying all DNA sequences (and microbial species, both culturable and non-culturable) in a sample being tested. In a subsequent investigation of the prevalence of microbial pathogens in the Little Bighorn River, we conducted a metagenomics analysis of DNA obtained from water collected in July 2017 from a swim hole site in Crow Agency frequented by children (Hamner et al., 2019). *E. coli* counts of 66 colony-forming units per 100 ml river water were obtained using the m-coliBlue 24 method, a concentration deemed acceptable by the EPA guideline that recreational water for swimming should not contain more than 126 CFU/100 ml (USEPA, 2012). Genomic DNA was prepared directly from river water as well as from one of the filter disks that was used to selectively grow *E. coli* and other coliforms using m-coliBlue24 during the colony count procedure. Metagenomics analysis of total DNA processed directly from river water identified several eukaryotic genera of concern to human health, but only a few potentially pathogenic prokaryotic genera, *Acidovorax* and *Aeromonas*. Surprisingly, no *E. coli* sequences were identified in this preparation of DNA directly from water, despite there being an *E. coli* colony count of 66 cfu/ml. This was presumably due to there being an overwhelming number of other DNA signatures from non-*E. coli* microbes that masked the presence of *E. coli* sequences that might have been identified if the Oxford Nanopore Minion platform could have generated sequencing data indefinitely. When DNA was prepared and sequenced from colonies growing overnight in selective medium for *E. coli* enumeration, several bacterial species including important human pathogens were identified, including toxigenic *E. coli* (serotypes O157:H7, O104:H4), *Shigella* spp. and *Vibrio cholerae*. Several bacteriophage, antimicrobial resistance markers, and virulence gene sequences relevant to human disease were also noted. Virulence gene sequences indicative of enterohemorrhagic *E. coli* (e.g., serotype O157:H7) were identified, suggesting the continued presence of this important human pathogen in the river. The presence of O157:H7 is particularly troubling, given that the infectious dose for humans may be as low as 1–10 cells. Our approach in choosing to perform metagenomics on both river water microbial DNA as well as on selectively grown coliforms (using m-coliBlue24) was fortunate in that it revealed the presence of important pathogens despite the concentration of *E. coli* measured being well under the limit of the EPA guideline for recreational water. With increasingly severe and unpredictable weather patterns and flooding, as well as continued, unaddressed microbial pollution of our freshwater resources, it may be necessary to revise the methodology and guidelines used to define what constitutes safe use of water for drinking and recreation. Metagenomics technology may well be suitable for routine surveillance of freshwater resources if it can be adapted for automated and affordable testing, especially in remote locations. Of course, “affordable testing” is very much a relative term for communities where routine coliform testing would be considered both too expensive and impractical due to lack of resources (training and supplies).

### Moving forward: Education?

Back in the 1990s, Ford was a member of Harvard’s Center for Health and the Global Environment that, under the visionary leadership of Dr. Eric Chivian, was focused on educating policy-makers through

writings, congressional briefings, and courses – on all topics related to global change. Ford chaired two of these briefings in Washington DC on “Increased Flooding Events and Climate Change” (1998) and “Water, Population and Human Health” (1999). We even emphasized the importance of providing global education to physicians in a letter to the *Lancet* (Chivian et al., 2002) – a topic of increasing importance at a time when pandemic disease has become a reality. It is sad to reflect that these and many other activities seem to have failed to change the discourse over climate change in any real, solution-focused sense.

At the time of this writing in early 2023, despite the ongoing global stresses of: (1) a continuing COVID pandemic, (2) a continued war in Ukraine, and (3) mounting concern from scientists and activists about the threats of climate change to life as we know it, it is as important as ever to work to protect the availability and safety of water resources, both to support life itself, agriculture and industrial processes, and to address the threat of waterborne disease. How can we improve our efforts to safeguard this most fundamental requirement for life, water? Although the science is slowly moving forward to understand and adapt to the threats to global water security posed by climate change and a steadily increasing human population needing more water, efforts to educate the public and political leaders on these topics seem paramount. But, is education on climate change itself the key? Alarming, “climate change has become a highly politicized topic in the policy arena and in education, and people’s willingness to be educated or to learn depends on their attitude toward the issue itself” (NRC, 2011). In other words, if people have already decided that they do not believe in climate change, they are highly unlikely to make an effort to study and understand it. It is likely that other approaches to address climate change will need to be taken. Local concerns (rather than a global outlook) may need to be addressed for a local audience. For example, reducing carbon emissions may be attractive to people and businesses, and politicians for economic reasons, to simply save money; others may be won over by a concern for national security (NRC, 2011).

Kamarck (2021) proposes a three pronged approach to addressing climate change (which is closely tied to water security): (1) pursue technological remedies supported both by private and public investment; (2) improve scientific literacy in general in schools; and (3) as laws and policies are implemented to address the climate and water security, ensure that regulatory jurisdiction is backed by accountability.

### Conclusion and final thoughts

#### Should we end this article the way we began?

- “We need to improve surveillance systems, risk assessment, and predictive models, provide low-cost solutions for water treatment and a develop a better understanding of population susceptibility.
- We need rapid assistance to communities and populations without regard for political boundaries during times of outbreak/epidemic disease.
- We need to educate policy makers and the public about the social and economic burden of waterborne diseases – true valuation of water.
- We need to improve methods for detection.”

Yes and no. We suspect the above will always apply, but we have made remarkable progress in a number of areas. We think it is fair to say that a risk-based approach to water quality makes sense, especially in more developed countries with the luxury of multi-

barrier approaches to protect water quality (watershed protection, adequate treatment and distribution system maintenance (Morris and Ford, 1998; Ford, 1999). For this approach, we need pathogen-specific detection and our advances in molecular biology place us close to real-time detection systems, although there is certainly more work to be done.

The bottom line remains that the bulk of waterborne diseases occur in LMIC and are preventable. Low-cost solutions exist, but are not deployed and implemented primarily through economic and political barriers. Future solutions must focus on the political discourse. We've even made extraordinary advances in basic water quality monitoring for use in remote regions of LMIC. Colilert™ and the Compartment Bag Test (CBT) (Stauber et al., 2014) are remarkable achievements, both developed in University labs where profits were not the only driving force. It is ironic that when Stephen C Edberg was working on a defined substrate method for detection of coliforms and *E. coli* at Yale in the 1980s (Edberg et al., 1989, 1990, 1988), one of us (Ford) was a postdoc at Harvard at the time and was asked if he was interested in evaluating the technology. Unfortunately, he saw no future in the method and declined (mind you, he was also highly skeptical of molecular approaches to microbiology, preferring plate cultures and membrane filtration!). He could not have been more wrong, and today promotes both Colilert™ and CBT (also a defined substrate-based test) whenever possible for use in low-resourced settings. Today, both Ford and Hamner also focus on metagenomics to define microbial communities in a variety of different settings.

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