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## *Section II*

# An introduction to emerging waterborne zoonoses and general control principles

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*J. Bartram and R. Carr*

Infectious diseases cause approximately 26% of all deaths worldwide and 31% of all disability. Water plays a role in the transmission of a significant number of these diseases. In the last 20 years, it has been recognized that many diseases are caused by emerging or re-emerging pathogens, 75% of which are zoonotic. Zoonoses can emerge in several ways — for example, as discrete events that lead to establishment of the pathogen in the human population and subsequent human-to-human transmission (e.g., human immunodeficiency virus) or as “spillover” events where the pathogen resides in animal reservoirs, which occasionally results in the transmission of the disease to humans. Chapter 2

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further explores some of the ways in which waterborne zoonoses emerge, especially with regard to how changing farming practices influence these events.

Chapter 3 provides a framework for determining what diseases are emerging, what diseases are waterborne, what diseases are zoonoses, or all of the above. The author also discusses pathogen properties that lead to environmental transmission and proposes a modification of the Bradley classification system of water-related diseases to include disease transmission through aerosols and the consumption of contaminated shellfish/seafood. Applying the proposed classification system to determine whether an organism is both waterborne and zoonotic, the author develops three case-studies to test the validity of the criteria.

Chapter 4 explores a variety of factors that influence the distribution and emergence of zoonoses. Many factors relating to the distribution and emergence of zoonoses are related to human activities, including migration, travel, urbanization, land development, changes in dietary practices, and the increasing use of antibiotics. The ability of pathogens to change characteristics, climate change, and the increase in the size of vulnerable human subpopulations also affect the impact and transmission of emerging waterborne zoonoses.

Many of the emerging waterborne zoonoses are difficult to manage. Chapter 5 explores the development of the concept of a control envelope for evaluating emerging pathogens against risks posed by better understood organisms. Effectively managing health risks from emerging waterborne diseases requires a cross-sectoral approach. A variety of risk management tools are available (e.g., quantitative microbial risk assessment, hazard analysis and critical control points, water safety plans, disease surveillance) but must be extended to encompass the entire spectrum of the control envelope to maximize the protection of human and animal health.

## 2

# Emerging zoonotic diseases and water

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*C. Bolin, C. Brown, and J. Rose*

### **2.1 FACTORS IN DISEASE EMERGENCE**

The global burden of infectious disease continues, despite landmark advances in the treatment and prevention of disease. In addition to the well described microbial and parasitic infections of humans and other animals, emerging infectious diseases have received increased attention in recent times. An infectious disease is considered to be emerging if it appears in populations of humans or other animals for the first time or has occurred previously but is increasing in incidence or expanding into new areas.

The emergence of an infectious disease is a complex process involving biological, social, and ecological factors. The Institute of Medicine (1992, 2003) has identified 13 factors key to the emergence of infectious diseases in humans:

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- microbial adaptation and change;
- human vulnerability;
- climate and weather;
- changing ecosystems;
- economic development and land use;
- human demographics and behaviour;
- technology and industry;
- international travel and commerce;
- breakdown of public health measures;
- poverty and social inequality;
- war and famine;
- lack of political will; and
- intent to harm.

We posit that many of these factors apply to the emergence of infections in domestic and wild animal populations as well.

With the inherent complexity of the biological and social systems involved in disease emergence, it is not possible to accurately predict the infectious agents destined to emerge. However, studies of infections that have emerged (Ewald 1996; Cleaveland *et al.* 2001; Taylor *et al.* 2001) in populations of humans and other animals have revealed the following:

- Viruses, prions, bacteria, and protozoa are more likely than fungi or helminths to be associated with emerging infections.
- Zoonotic pathogens comprise 75% of emerging infectious diseases.
- Pathogens that are subject to relatively frequent mutation or genomic reassortment events (e.g., RNA viruses and viruses with segmented genomes) are more likely to emerge.
- Pathogens that infect multiple hosts or pathogens that infect species that can harbour multiple closely related agents, providing an opportunity for reassortment or recombination (e.g., severe acute respiratory syndrome in cats), are likely to emerge.
- Agents transmissible by more than one route or by indirect contact (e.g., water, food, environmental contamination, vectors) are likely to emerge.

Zoonotic infections clearly play a central role in emerging infectious disease in humans. The exposure of humans to zoonoses follows two major epidemiological patterns. In some cases (e.g., human immunodeficiency virus), there is a point source of exposure of humans to the zoonotic agent, and then the disease is transmitted among, and often maintained in, humans. In other cases (e.g., Ebola

virus), animals serve as the reservoir for the agent, and the infection “spills over” to humans, with little transmission between humans. In this latter situation, the infection will die out in the human population without constant reintroduction from animal reservoirs.

Many emerging zoonotic diseases are transmitted by indirect contact — foods, water, environmental contamination, vectors, etc. — and are not reliant on direct contact between human and wild or domestic animal hosts for transmission. These same features may also be related to increased virulence of the pathogens (Ewald 1996, 1998). Analysis of these factors suggests that the interaction between animals (domesticated and free-ranging) and the water supply may be a rational area of concern for disease emergence. Some of these emerging infections may involve transmission of disease to humans through drinking-water or recreational water activities and the spread of infection to, and within, populations of animals.

## **2.2 ANIMAL AGRICULTURE AND POTENTIAL ENVIRONMENTAL IMPACT**

It is projected that the number of people in the world will be 7.7 billion by 2020 and 9.4 billion by 2050, with the largest increase coming from the developing world. Over the last 25 years, per capita meat consumption in developing countries grew at 3 times the rate in developed countries. If current trends continue, which is predicted, diets will continue to shift from plant-based to increased consumption of meat and dairy products. It is estimated that global livestock production will have to double by 2020 to supply needs. This demand-driven increase in animal agriculture has been termed the “livestock revolution” (Bradford *et al.* 1999; Delgado *et al.* 1999).

Traditional livestock systems are integrated, sustainable, low input, and “closed loop.” Historically, animal production in developing countries has been of this type. In traditional livestock rearing, manure is vital fertilizer, and animals return nutrients to the soil in forms that plants can readily use. In addition, in some areas, manure is a vital resource to be used as fuel or building materials. In most traditional systems, manure is effectively utilized and is not a disposal issue (Sherman 2001).

In comparison, modern or industrialized systems are high-input, open-loop systems. These industrialized systems provide significant efficiency in terms of economy of scale, consistency, and value to consumers. Industrialized systems began in the USA over 60 years ago with the poultry industry and have now become the norm for the swine industry also. It is more difficult to industrialize the cattle industries, largely because they are ruminants and benefit from grazing,

but beef feedlots and large dairies are examples of industrialization for this species as well (Sherman 2001). Animal agriculture in the developed world is almost entirely of this industrialized type, so that today, throughout the developed world, there are fewer farms managing larger numbers of animals. Manure produced in industrial systems is usually in excess of agronomic requirements and figures as a major disposal issue in all of these intensive animal production facilities.

Today, there are approximately 1.2 billion cattle, 800 million pigs, and 10 billion chickens in the world. Of the cattle and pigs, three-quarters are resident in the developing world, usually in traditional systems. With respect to chickens, industrialization has occurred more extensively even in the developing world, so that fully half of all the world's chickens are reared under conditions of intensive husbandry (Mason and Crawford 1993). Livestock numbers have been increasing while agricultural land has been decreasing, at a rate of 7% per decade, due to urbanization, commercial forces, and land degradation (Oldeman *et al.* 1991). Livestock densities in both the developed and developing worlds range between 5 and >6000 kg/km<sup>2</sup>, with the greatest concentrations in India, China, and Europe (AGA, undated).

The "livestock revolution" predicts that much of the increase in animal production will come from expansion of intensive systems of agriculture in the developing world (Bradford *et al.* 1999; Delgado *et al.* 1999). In fact, globally, the trend is clearly towards industrialization. Intensive systems of animal agriculture are increasing at the rate of 4.3% per year, with much of that increase happening in Asia, South America, and North Africa (Bradford *et al.* 1999; Delgado *et al.* 1999). As traditional systems are replaced by industrial agriculture, livestock density increases.

As mentioned above, manure disposal from industrialized facilities is problematic. Numerous systems have been developed to dispose of or recycle the manure, but many have environmental and health considerations.

Application to fields is the time-honoured manner of manure disposal, but it can cause considerable problems with nitrate leaching if the ground is frozen, there is excess rain, or the soil is very sandy. Runoff of manure into watersheds causes increased microbial proliferation, high biochemical oxygen demand, and altered aquatic microenvironments (Hooda *et al.* 2000). For pigs, 80% of waste is held in liquid storage systems for subsequent decontamination and application to land (De Haan *et al.* 1997). These earthen basins and lagoons work well as long as there are no significant compromises in integrity. Catastrophic events can ensue after natural disasters such as floods or earthquakes, or even because of faulty design. For broilers, virtually all waste goes into stacking pits. After three or four broods are raised in a house, the litter, which contains fibrous material, spilled feed, feathers, and bird excreta, is collected and held in a heat-generating pile for some weeks until pathogenic organisms are destroyed. This material is fed to

cattle, who consume it free-choice in self-feeders as a source of fibre and protein (Rankins *et al.* 2002). Beef and dairy faeces are usually collected as solids and later applied to land. There is an anaerobic slurry storage period, which is designed to decrease microbial content, but it has been shown that certain pathogenic organisms can survive beyond the designated period (Pell 1997; Hooda *et al.* 2000).

Industrialized systems of animal agriculture currently produce 7 billion tonnes of waste per year. As these intensive open-loop systems continue to grow by 4% per year, it is estimated that in 2020, there will be 18 billion tonnes of animal waste for disposal (De Haan 1997).

Some countries have become fairly aggressive in their policies regarding handling of manure. For instance, in the Netherlands in 2000, federal regulations were instituted for any farm housing at least 2.5 livestock units (LU) per hectare. This 2.5 LU is equivalent to the number of animals that excrete 102.5 kg of manure phosphate per year, or 2.5 dairy cattle, 13.9 growing pigs, or 427 broilers. There are 50 000 farms in the Netherlands that fell under this new restriction. Any farm exceeding the allowed production must pay a tax (Jongbloed and Lenis 1998). Over the next decades, industrialized production will increase dramatically in the developing world, where, historically, environmental regulations are much more relaxed.

Great strides have been made in the mapping of food consumption, human dimensions, and livestock-oriented production systems, as well as water use (Gerbens-Leenes *et al.* 2002; Kruska *et al.* 2003). While the tonnage of animal waste has been estimated based on nitrogen in animal excreta (Bouwman and van der Hoek 1997), little effort has been made to address the microbial and zoonotic infectious disease potential due to these changes associated with loading of manure onto land and water.

Faeces and urine from both humans and other animals are likely the largest source of environmental loading of pathogens associated with waterborne disease transmission (Figure 2.1). Loading, prevalence, concentrations, survival, and infectivity need to be compiled for the various pathogens associated with urine and faeces. We must also recognize that more than half the bacteria in the human intestine and more than 99% of environmental bacteria have not been cultured or characterized (Relman 1998; Kroes *et al.* 1999). This is almost certainly also true for the broad array of domestic and wild animals in our environment. Therefore, there is always a risk of the emergence of an as yet unrecognized agent of disease, representing a real challenge to public and animal health officials attempting to anticipate and prevent emerging infectious diseases.

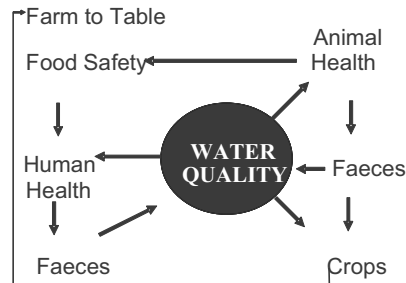


Figure 2.1. Interactions of humans and animals associated with faecal contamination of water.

### 2.3 RISK ASSESSMENT AND STRATEGIES

An analysis of the known factors that favour disease emergence indicates that zoonotic diseases with the potential to be waterborne are likely to be significant risks for the future. Therefore, assessment of risks and vulnerabilities of modern water treatment processes and also of the various aspects of water treatment processes around the world is essential and must be an ongoing, forward-thinking process. Our definition of “microbiologically safe water” is evolving from the utopian concept of pathogen-free water to a more realistic goal of providing drinking-water for human consumption (European Union Council Directive 98/83/EC and WHO guidelines as quoted by Szewzyk *et al.* 2000) to be “free from microorganisms and parasites ... which, in numbers or concentrations, constitute a potential danger to human health.” These statements must be interpreted along with a definition of acceptable risk. The US Environmental Protection Agency previously suggested (but has not concluded) that an acceptable risk of infection from potable water might be 1:10 000 per year, i.e., 1 case of the disease in 10 000 exposed persons per year (J. Cotruvo, personal communication, 2003). These types of guidance can be used to conduct mathematical modelling of the risk to the public and animal health of various agents. However, to conduct this risk assessment, key pieces of information are required to be known, or at least predictable, based on mathematical models: 1) the infectious dose–response of the pathogen of interest; 2) the concentration at which the agent can be found in water; and 3) the impact of various water treatment strategies on the reduction in infectivity of the pathogen of interest. While we have reasonable estimates of these factors for some traditional waterborne diseases, there are large gaps in our knowledge of the current and

future risks to the water supply in regards to emerging infectious diseases in general, and zoonotic diseases in particular.

Additional tools and strategies are needed to assess the biological impact of livestock and wildlife populations on the water supply (e.g., source tracking capability), the diversity of organisms in faeces and urine of humans and other animals, and what role on-farm manure handling procedures play in mitigating these risks. This information will help define changes in water treatment required to provide safe, potable water to a growing and increasingly stressed (nutritionally and immunologically) world population in the face of emerging infections and infections that are resistant to current practices. In some cases, this may require additional treatment of water coincident with ingestion by either humans or other animals. As we develop alternative strategies, careful attention must be paid to developing systems and safeguards that work in relatively underdeveloped environments as well as state-of-the-art water treatment facilities.

## 2.4 REFERENCES

- AGA (undated) *Livestock Atlas*. Animal Health and Production Division (AGA), Food and Agriculture Organization of the United Nations (<http://ergodd.zoo.ox.ac.uk/livat2/Livestock.htm>).
- Bouwman A.F. and van der Hoek, K.W. (1997) Scenarios of animal waste production and fertilizer use and associated ammonia emission for the developing countries. *Atmos. Environ.* **31**(24), 4095–4102.
- Bradford, E., Baldwin, R.L., Blackburn, H., Cassman, K.G., Crosson, P.R., Delgado, C.L., Fadel, J.G., Fitzhugh, H.A., Gill, M., Oltjen, J.W., Rosegrant, M.W., Vavra, M. and Wilson R.O. (1999) *Animal Agriculture and the Global Food Supply*. Council on Agriculture, Science and Technology, Ames, IA.
- Cleaveland, S., Laurenson, M.K. and Taylor, L.H. (2001) Diseases of humans and their domestic mammals: pathogen characteristics, host range, and risk of emergence. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **356**(1411), 991–999.
- De Haan, C. (1997) *Livestock Production and Sustainable Use of the Global Natural Resource Base*. Oral presentation to the Congress of the American Veterinary Medical Association, Reno, NV ([http://lnweb18.worldbank.org/ESSD/ardext.nsf/26ByDocName/LivestockproductionandsustainableuseoftheglobalnaturalresourcebaseInvitedPaper/\\$FILE/Livestockproductionandsustainable.pdf](http://lnweb18.worldbank.org/ESSD/ardext.nsf/26ByDocName/LivestockproductionandsustainableuseoftheglobalnaturalresourcebaseInvitedPaper/$FILE/Livestockproductionandsustainable.pdf)).
- De Haan, C., Steinfeld, H. and Blackburn H. (1997) *Livestock and the Environment, Finding a Balance — Issues and Options*. Food and Agriculture Organization of the United Nations, Rome.
- Delgado, C., Rosegrant, M., Steinfeld, H., Ehui, S. and Courbois, C. (1999) *Livestock to 2020: The Next Food Revolution*. Food, Agriculture, and the Environment Discussion Paper 28, International Food Policy Research Institute, Food and Agriculture

- Organization of the United Nations, and International Livestock Research Institute (<http://www.fao.org/waicent/faoinfo/agricult/AGA/agal/lvst2020/20201.pdf>).
- Ewald, P.W. (1996) Guarding against the most dangerous emerging pathogens. *Emerg. Infect. Dis.* **2**(4), 245–257.
- Ewald, P.W. (1998) The evolution of virulence and emerging diseases. *J. Urban Health* **75**(3), 480–491.
- Gerbens-Leenes, P.W., Nonhebel, S. and Ivens, W.P.M.F. (2002) A method to determine land requirements relating to food consumption patterns. *Agric. Ecosyst. Environ.* **90**, 47–58.
- Hooda, P.S., Edwards, A.C., Anderson, H.A. and Miller, A. (2000) A review of water quality concerns in livestock farming areas. *Sci. Total Environ.* **250**, 143–167.
- Institute of Medicine (1992) *Emerging Infections: Microbial Threats to Health in the United States* (ed. J. Lederberg, R.E. Shope, and S.C. Oaks), National Academy Press, Washington, DC.
- Institute of Medicine (2003) *Microbial Threats to Health: Emergence, Detection and Response* (ed. M.S. Smolinski, M.A. Hamburg, and J. Lederberg), National Academy Press, Washington, DC (<http://www.nap.edu>).
- Jongbloed, A.W. and Lenis, N.P. (1998) Environmental concerns about animal manure. *J. Anim. Sci.* **76**, 2641–2648.
- Kroes, I., Lepp, P.W. and Relman, D.A. (1999) Bacterial diversity within the human subgingival crevice. *Proc. Natl. Acad. Sci. U. S. A.* **96**, 14547–14552.
- Kruska, R.L., Reid, R.S., Thornton, P.K., Henninger, N. and Kristjanson, P.M. (2003) Mapping livestock-oriented agricultural production systems for the developing world. *Agric. Syst.* **77**, 39–63.
- Mason, I.L. and Crawford, R.D. (1993) Appendix A. Global status of livestock and poultry species. In *Managing Global Genetic Resources*, pp. 141–170, Board on Agriculture, National Research Council, National Academy Press, Washington, DC.
- Oldeman, L.R., Hakkeling, R.T.A. and Sombroek, W.G. (1991) *World Map of the Status of Human-induced Soil Degradation: Global Assessment of Soil Degradation*. International Soil Reference and Information Centre (ISRIC), Wageningen.
- Pell, A.N. (1997) Manure and microbes: public and animal health problems? *J. Dairy Sci.* **80**, 2673–2681.
- Rankins, D.L., Poore, M.H., Capucille, D.J. and Rogers, G.M. (2002) Recycled poultry bedding as cattle feed. *Vet. Clin. Food Anim. Pract.* **18**, 253–266.
- Relman, D.A. (1998) Detection and identification of previously unrecognized microbial pathogens. *Emerg. Infect. Dis.* **4**(3), 382–389.
- Sherman D. (2001) *Tending Animals in the Global Village: A Guide to International Veterinary Medicine*. Lippincott, Williams and Wilkins, Philadelphia, PA, 495 pp.
- Szewzyk, U., Szewzyk, R., Manz, W. and Schleifer, K.H. (2000) Microbiological safety of drinking water. *Annu. Rev. Microbiol.* **54**, 81–127.
- Taylor, L.H., Latham, S.M. and Woolhouse, E.J. (2001) Risk factors of human disease emergence. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **356**(1411), 983–989.

# 3

## What are the criteria for determining whether a disease is zoonotic and water related?

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*C.L. Moe*

### 3.1 INTRODUCTION

A number of new diseases have been recognized in the past quarter century. The term “emerging disease” was used in a seminal Institute of Medicine report in 1992 to describe infectious diseases whose incidence in humans has increased within the past two decades or threaten to increase in the near future (Lederberg *et al.* 1992). Even before the etiological agent in an emerging infectious disease can be identified or characterized, it is critical to understand the source of the agent and the likely and possible transmission routes so that effective prevention and control measures can be established as soon as possible.

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There are a number of newly recognized infectious agents that have been associated with outbreaks of water-related disease or appear to have the potential for waterborne transmission. How did we know that these diseases were water-related? There has been a recent surge in the number of new zoonoses and new forms of existing zoonoses that have been identified (Mahy and Brown 2000). How did we know that these infections were zoonotic? The knowledge that a newly recognized disease is water related and zoonotic is critical for planning public health protection measures. In order to better understand these classifications of “water related” and “zoonotic,” it is useful to start with the definitions of these terms and examine the infections that are commonly accepted to fall within these definitions. We can then propose criteria for determining what is a water-related zoonotic disease and test these criteria on newly recognized diseases to see how well they work.

### 3.2 ZOONOSES

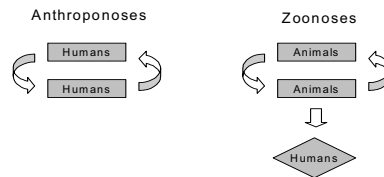
Zoonoses have been defined as “those diseases and infections (the agents of) which are naturally transmitted between vertebrate animals and man” (WHO/FAO 1959). Examples of zoonotic infections have been recognized among all the major groups of infectious agents: prions, viruses, bacteria, protozoa, and helminths. Some of these agents may infect only one type of animal and humans. Others may infect several types of animals as well as humans.

Wilson (2001) explained that there are two types of zoonoses: direct and indirect. In direct zoonoses, an infection is transmitted from animals to humans by direct contact with the animal via a bite, ingestion of animal tissue, or skin contact with an animal (Figure 3.1a). Examples of direct zoonoses are rabies, trichinellosis, and tularaemia. Indirect zoonoses (Figure 3.1b) involve transmission of the infectious agent from animals to humans via a vector or vehicle. Examples of indirect zoonoses include cryptosporidiosis, the plague (*Yersinia pestis*), ehrlichiosis (*Ehrlichia chaffeensis*), West Nile virus, and leptospirosis (*Leptospira interrogans*). Some infections, such as tularaemia, can be transmitted both directly via animal contact and indirectly via water ingestion or inhalation of infectious aerosols. For some zoonoses — avian influenza, Hendra and Nipah viruses, human immunodeficiency viruses HIV-1 and HIV-2, and Ebola virus — it is not clear how the agent was transmitted from animals to humans (Mahy and Brown 2000).

Another key differentiating factor between zoonoses is whether humans are a “dead-end host” (e.g., rabies virus) or whether subsequent human-to-human transmission can occur (e.g., HIV-1 and HIV-2 and cryptosporidiosis). In direct zoonoses, the pathogen is normally transmitted between animals only and is accidentally spread to humans. Because humans are not part of the normal

transmission cycle, we become a “dead-end host” (Wilson 2001). In some cases, transmission may be from the natural animal reservoir to another animal species and then to humans. One indication that the intermediate animal host may not be the true natural reservoir of the infectious agent is if the disease is often fatal in the animal — as in the case of Marburg virus in monkeys or Hendra virus in horses (Mahy and Brown 2000). Some zoonoses emerge when there is a host that is co-infected with human and animal strains of an infectious agent and a new reassortant strain is produced — such as avian influenza viruses that have surface antigens (haemagglutinin subtype H5 or H9) that are new to the human population and to which we have little or no immunity. In this example, pigs can be infected with both human and avian influenza viruses in addition to swine influenza and may serve as the host where reassortant virus strains are created. For some organisms, such as *Cryptosporidium*, it is difficult to differentiate between zoonotic and anthroponotic strains. The origin of some *Cryptosporidium* strains is predicted by molecular typing to be zoonotic, but the epidemiological evidence indicates that the predominant transmission is anthroponotic (Leoni *et al.* 2003).

**a. Direct Transmission**



**b. Indirect Transmission**

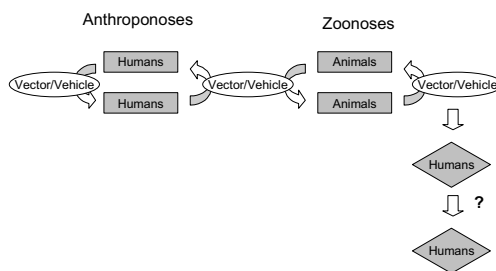


Figure 3.1. Direct (a) and indirect (b) transmission of infectious agents (from Wilson 2001).

### 3.3 WATER-RELATED DISEASE

#### 3.3.1 Environmental transmission of infectious agents

Many factors affect the ability of an infectious agent to be transmitted through the environment (Figure 3.2) (Feachem *et al.* 1983). First, the infectious agent must enter the environment. For most water-related pathogens, the organism enters the environment via human or animal faeces deposited on land or in water. Some organisms enter the environment via human or animal urine (*Leptospira* and schistosomes). Other organisms may be directly discharged into water, such as guinea worm larvae, which exit via the skin. Some organisms live within mosquitos that must breed near water. It is not always known whether there is transovarial transmission and the organism is actually within the mosquito eggs that are deposited in water. The load of organisms entering the environment depends on the prevalence of the infection in the population of humans or animals, the concentration of the infectious agent in the faeces or urine, and how long an infected individual will shed the organism.

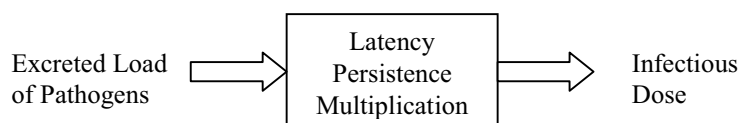


Figure 3.2. Environmental transmission of infectious agents (from Feachem *et al.* 1983).

Once the agent is in the environment, several factors affect the ability of the organism to be transmitted to a human host:

- (1) The organism may require time in the environment to undergo further development before it becomes infectious. Latency is the time between the excretion of the pathogen and the time that it is infective to a new host. Most enteric viruses, bacteria, and protozoa have no latent period and are immediately infectious after excretion. Other organisms, such as helminths, typically require time in the environment to develop into an infectious stage and may pass through one or more intermediate hosts (e.g., schistosomiasis).
- (2) The ability of the organism to persist in the environment is critical to its transmissibility. The longer an organism can persist, the more likely it is to have the opportunity to come into contact with a

susceptible host. Survival time in water depends on many physical factors (pH, temperature, sunlight) as well as characteristics of the organism. The survival times of water-related pathogens in water range from hours to years. Some pathogens, such as *Salmonella*, *Campylobacter*, and *Vibrio cholerae*, are capable of entering a dormant state described as “viable but non-culturable,” which allows them to survive longer under adverse conditions in the aquatic environment and yet maintain their pathogenicity (Hunter 1997). Other pathogens have a stage in their life cycle, such as a spore or oocyst, that is environmentally resistant. *Vibrio cholerae* colonizes the surface of zooplankton, which permits prolonged survival in environmental waters between seasonal epidemics (Tamplin *et al.* 1990). The fate of the organism in wastewater and water treatment processes is also a key element in understanding the risk of waterborne transmission.

- (3) The ability of the organism to replicate in the environment is also important. Under favourable conditions, some water-related pathogens can multiply in the aquatic environment. This is not possible for viruses and protozoa that are obligate parasites. However, some enteric and all aquatic bacterial pathogens can multiply in the environment and may reach high concentrations. Some water-related helminth pathogens may be amplified within an intermediate aquatic host.

The final element in this transmission process is the infectious dose or degree of water exposure necessary to transmit the infection. Infectious dose varies widely among environmentally transmitted organisms and is difficult to measure. Limited data on dose–response come from human challenge studies with healthy adult volunteers. The dose that induces infection in 50% of exposed individuals, described as the median infectious dose (ID<sub>50</sub>), can range from about 10<sup>9</sup> colony-forming units of *Salmonella pullorum* (Teunis *et al.* 1996) to 10–1000 *Cryptosporidium* oocysts (Teunis *et al.* 2002). The ID<sub>50</sub> can vary by the strain of microorganism and by the host population, depending on age and immune status.

### 3.3.2 Bradley’s classification of water-related diseases

The classification of water-related diseases by Bradley (1977) provides a valuable framework for understanding the relationship between infectious disease transmission and water. This classification system’s advantage is that it facilitates planning effective prevention and control measures for a variety

of water-related diseases, depending on the type of agent and transmission route. Bradley (1977) described four main categories of water-related infections: “water-borne infections,” “water-washed infections,” “water-based infections,” and “infections with water-related insect vectors.” Some infections may fit into more than one of these categories, and often water is not the only transmission route or even the major transmission route for some of these infections.

The “water-borne infections” are those classically recognized as waterborne disease, such as typhoid and cholera, where an enteric microorganism enters the water source through faecal contamination and transmission occurs by ingestion of contaminated water. Transmission by this route depends on 1) the amount of faecal contamination in the water, the concentration of pathogens in the faecal contamination (determined by the number of infected persons or animals in the environment), and the survival of the pathogenic organism in water; 2) the infectivity of the organism; and 3) individual ingestion of (exposure to) the contaminated water. Control of these infections is generally through improvement of microbiological water quality, either through water treatment or source protection.

“Water-washed infections” are diseases due to poor personal and/or domestic hygiene. These diseases are not due to the presence of infectious agents in water but rather to the lack of readily accessible water. This limits washing of contaminated hands and utensils and thus permits transmission of infectious agents, such as *Shigella* spp. Transmission is again related to the presence of faeces from an infected individual, infectivity of the organism, amount of faecal contamination on the hand or surface, and the persistence of the organism on surfaces. Lack of water for bathing also facilitates the spread of diseases that affect the eyes and skin, such as trachoma, conjunctivitis, and scabies. Control of these diseases is through provision of greater quantities of water, closer, easier access to water, and education to improve personal and domestic hygiene.

“Water-based infections” are worm infections in which the pathogen must spend a part of its life cycle in the aquatic environment. This category is further subdivided into diseases acquired by ingestion of water and diseases acquired by contact with water. The prototype infections in this category are dracunculiasis, due to ingestion of water contaminated with guinea worm (*Dracunculus medinensis*), and schistosomiasis, which is transmitted by contact with water contaminated with species of the trematode genus *Schistosoma*. The original source of the guinea worm is larvae discharged from the female worm that lies in a vesicle, usually on the lower leg or foot of an infected human. The larvae are discharged when the vesicle is immersed in water and are then ingested by a copepod (genus *Cyclops*), where they

develop into the infective stage. Humans become infected when they ingest water containing the copepods (Bradley 1977). Typically, the eggs of schistosome worms enter the aquatic environment from the urine or faeces of an infected human. However, dogs, cats, pigs, cattle, water buffalo, horses, and wild rodents may serve as the reservoir of *Schistosoma japonicum*, which is found in East Asia (Chin 2000). The eggs hatch in the water to produce miracidia, which infect snails, develop into the infective stage, and are shed by snails into the water over a period of months. Humans become infected when the free-swimming infective larvae penetrate the skin during water contact (Bradley 1977). Control of dracunculiasis and schistosomiasis is through protection of the water source and the user by limiting skin contact with water and by eradication of intermediate hosts.

The types of water contact diseases most frequently encountered in industrialized countries are those associated with recreational exposure to contaminated marine water, freshwater lakes, ponds, creeks, or rivers, and occasionally treated water in swimming pools, wave pools, hot tubs, and whirlpools. In developing countries, risk of water contact diseases may be from bathing or doing laundry in contaminated surface waters. Water contact diseases are also often associated with occupational exposure to waters. While many water contact diseases are associated with enteric organisms and ingestion of water with faecal contamination, there are some diseases of the ear, eye, and skin that are associated with actual water contact and systemic illnesses associated with penetration of a pathogen through an open wound or abrasion. Reported recreational water outbreaks have involved *Giardia*, *Cryptosporidium*, *Shigella sonnei*, and *Escherichia coli* O157:H7 that presumably entered the gastrointestinal tract via ingestion. Other recreational water outbreaks have involved ingestion of, contact with, or inhalation of indigenous aquatic organisms such as *Naegleria*, *Pseudomonas*, *Legionella* (Lee *et al.* 2002), several *Vibrio* species, and several *Mycobacterium* species (Dufour 1986). Epidemiological/microbiological studies indicate that *Staphylococcus aureus* skin and ear infections are often associated with recreational use of water, and the source of these organisms may be other bathers or the water (Charoencra and Fujioka 1995). *Vibrio vulnificus* can cause serious wound infections when a skin injury occurs in marine water or from contact of pre-existing wounds with marine water (Klontz *et al.* 1988). Cyanobacterial toxins have been associated with contact irritation after bathing in marine or fresh waters (Codd *et al.* 1989). An additional cause of water contact infections is the *Leptospira* species that are neither enteric organisms nor aquatic organisms, but enter water via the urine of infected domestic and wild animals (Dufour 1986). Leptospirosis is probably the most widespread zoonosis worldwide and occurs in urban and rural areas of both

developed and developing countries. Because of the non-specific symptoms of leptospirosis, it is believed to often be misdiagnosed and under-reported (WHO 2003c).

“Infections with water-related insect vectors” are those transmitted by insects that breed in water, such as mosquito vectors of malaria, or insects that bite near water, like the tsetse flies that transmit sleeping sickness. Control of these infections is through the application of pesticides, destruction of breeding grounds, and construction of piped water supplies.

### 3.3.3 Other water-related transmission routes

Two additional water-related modes of transmission of infectious agents are transmission by inhalation of water aerosols and transmission by the consumption of raw or undercooked shellfish or contaminated fish. The major pathogens associated with aerosol transmission are *Legionella* spp., especially *L. pneumophila*, the etiologic agent of Legionnaire’s disease and Pontiac fever. *Legionella* are ubiquitous in water and soil and are capable of prolonged survival and reproduction in the aquatic environment. Growth within free-living amoebae appears to enhance survival and provide protection from routine disinfection (Winn 1995). Outbreaks of legionellosis have been associated with aerosols from cooling towers and evaporative condensers of large buildings or with hot and cold water systems in hospitals, hotels, and other institutions. *Legionella* can proliferate in hot water tanks maintained at 30–54 °C (Wadowsky *et al.* 1982), and exposure to aerosols from showerheads can occur. These infections are controlled through minimizing exposure to contaminated aerosols and routine cleaning and disinfection of water systems with adequate doses of chlorine, chloramines, or ozone (Muraca *et al.* 1990; Winn 1995). Water quality guidelines generally include limits on *Legionella*.

The potential for aerosol transmission of *Mycobacterium avium* and other non-tuberculous mycobacteria and the risk to the immunocompromised population continue to be a concern. Like *Legionella*, these organisms are frequently isolated in environmental and treated water systems and are able to colonize and propagate within water distribution systems (Jenkins 1991). Wendt *et al.* (1980) reported the isolation of non-tuberculous mycobacteria from aerosol samples near the James River in Virginia, USA. The isolates (mostly *M. intracellulare*) were biochemically similar to those recovered from human clinical specimens, suggesting that airborne mycobacteria derived from fresh water might be a significant source of infection. Non-tuberculous mycobacteria have also been isolated from hot water systems, and, like *Legionella*, they can survive in co-culture with protozoa (Ford 1999).

Bivalve molluscan shellfish serve as vehicles of enteric disease transmission because of their ability to concentrate enteric organisms from faecally contaminated water in their tissues. Numerous outbreaks have been attributed to the consumption of raw or undercooked oysters, clams, and mussels (Morse *et al.* 1986). Many pathogens, including hepatitis A and E viruses, human caliciviruses (Norwalk-like viruses), pathogenic *E. coli*, *Salmonella typhi*, and species of *Shigella*, *Vibrio*, *Plesiomonas*, and *Aeromonas*, have been implicated in shellfish-borne disease (Hackney and Potter 1994a, 1994b). Shellfish and some species of fish may also serve as vehicles for algal toxins. Toxic species of *Gonyaulax* and *Gymnodinium* are concentrated by filter-feeding molluscs and can cause paralytic shellfish poisoning among shellfish consumers (Carmichael *et al.* 1985). Reef-feeding fish can concentrate toxic dinoflagellates of the genus *Gambierdiscus*, which cause ciguatera seafood poisoning among consumers (Carmichael *et al.* 1985). Paragonimiasis is a trematode disease involving the lungs (Chin 2000). Infection is from consumption of raw, pickled, or partially cooked freshwater crabs or crayfish containing infective larvae. In humans, the larvae excyst, move through the intestinal tract to the lungs, and develop into egg-producing adult worms. Eggs expectorated into the sputum are swallowed and excreted in faeces. Faecal contamination of fresh water allows the larvae to hatch, penetrate snails and undergo a cycle of development, and emerge and penetrate crabs and crayfish.

### 3.4 CRITERIA FOR ZONOTIC WATER-RELATED DISEASE

Given these characteristics of zoonotic diseases and water-related diseases, what criteria are useful for determining whether a disease is both zoonotic and water related? Do we limit these criteria only to “infections,” or should they also apply to intoxications and other adverse health effects associated with zoonotic organisms? How do these criteria apply to organisms with complex life cycles that involve multiple stages, such as schistosomiasis? The following draft criteria seem to be a reasonable starting point:

- (1) *The pathogen must spend part of its life cycle within one or more animal species.* It should be able to replicate or undergo development within an animal host and within a human host. However, the organism may not always cause symptomatic disease in either the animal or human host. The stringency of this criterion rests on the definition of “animal.” Should

organisms that infect aquatic animals or fish or those that invade copepods or snails be included?

- (2) *Within the life cycle of the pathogen, it is probable or conceivable that some life stage will enter water* — via faeces, urine, or tissue of an infected animal or human, because it is originally an aquatic organism, or possibly within the eggs of an insect vector. The organism must be able to persist in water for at least a few hours or days in order to be transmitted by exposure to water. Replication in water is not necessary. It is recognized that the predominant life stage in water may be different from the predominant life stage in the animal or human host. A stringent form of this criterion would be that there must be evidence that the organism can be detected in water.
- (3) *Transmission of the pathogen (or toxin produced by the organism) from animal source to human must be through a water-related route:*
  - water ingestion;
  - water contact;
  - inhalation of water or wastewater aerosols;
  - consumption of shellfish or other seafood harvested from waters impacted by animals or animal waste; and
  - consumption of seafood infected with a pathogenic organism.

These initial criteria are quite broad and encompass organisms with very different life cycles and transmission pathways, especially if one includes vector-borne water-related infections. It is arguable whether water-washed infections associated with poor hygiene and lack of adequate water and infections associated with water-based or water-related vectors should be included in these criteria, because one could also classify these infections as person-to-person transmission or vector-borne transmission. However, the case can be made that water management decisions will affect the transmission of these diseases, so they could be considered water related. For specific areas of interest, such as faecal–oral water-related zoonotic disease, the criteria can be narrowed to include only those organisms that 1) infect the enteric tract of animals and humans, 2) are shed in faeces, and 3) are transmitted via water ingestion or consumption of seafood from harvest waters contaminated with animal faeces.

Using these criteria, one can apply a modification of the Bradley classification system to water-related zoonotic diseases, as illustrated in Table 3.1.

### **3.5 APPLICATION TO SELECTED EXAMPLES**

The purpose of these criteria is to help identify emerging water-related zoonotic diseases and provide some insight into how to control and prevent these diseases

using public health experience with other diseases. In order to test their usefulness, we will apply them to three examples of emerging diseases.

Table 3.1. Classification of water-related zoonotic diseases

Category	Zoonotic examples	Relevant control strategies
Waterborne via drinking-water	Salmonellosis, <i>E. coli</i> O157:H7, cryptosporidiosis, giardiasis, campylobacteriosis, microsporidiosis, toxoplasmosis, balantidiasis, yersiniosis, tularaemia, cysticercosis	Improve microbiological water quality through water treatment; protect drinking-water sources from contamination by animal faeces
Waterborne via recreational water contact	Leptospirosis, cryptosporidiosis, giardiasis	Protect water source from animal contamination
Water-washed	Cryptosporidiosis, giardiasis, balantidiasis, hepatitis E virus?	Increase water quantity to improve hygiene; promote hand washing
Water-based	Schistosomiasis ( <i>Schistosoma japonicum</i> )	Protect user, control aquatic hosts, surface water management
Water-related insect vectors	West Nile virus, Rift Valley fever virus, yellow fever virus, sleeping sickness (African trypanosomiasis)	Protect user, control vector, surface water management
Inhalation of water/wastewater aerosols	Mycobacteria	Protect individuals who have occupational exposure; limit human exposure to geographic areas impacted by aerosols
Aquatic food	Paragonimiasis	Avoid ingestion of raw or undercooked crustaceans; prevent faecal contamination of freshwater crab and crayfish habitats, control snails by molluscicides

### 3.5.1 Severe acute respiratory syndrome (SARS)

Severe acute respiratory syndrome (SARS) is an example of an emerging disease where many questions about zoonotic reservoirs and water-related transmission are still unanswered. In the Guangdong Province of China, cases of an unknown respiratory illness with high fever, dry cough, dyspnoea, myalgia, and sometimes diarrhoea began to appear in November 2002 (Wu 2003). These cases were not reported to the World Health Organization (WHO) and did not receive much official attention until an outbreak occurred in Hong Kong in

February 2003. The disease quickly spread to more than 30 countries, including Vietnam, Singapore, Canada, Ireland, the USA, and Taiwan (Wu 2003). WHO issued a global alert about SARS on 12 March 2003. Understanding the transmission, identifying the etiological agent, and enacting effective control measures have occupied much of the public health community since that alert. In retrospect, it is impressive how quickly the causative agent (SARS coronavirus) was identified, cloned, and sequenced. Although there were more than 8400 estimated cases and 900 estimated deaths attributed to SARS by early August 2003 (WHO 2003a), the epidemic seems to have slowed, and control efforts seem successful.

Some epidemiological observations raised questions about the origins of the SARS virus and a possible animal reservoir early in the investigation of the epidemic. A WHO team reviewing the histories of the early cases in Guangdong noticed that a relatively high proportion of the cases had some connection with the food industry and that people who lived near markets were also more likely to be cases. Also, animal market workers, but not the general population, were found to have antibodies to the SARS virus (Normile and Enserink 2003). There appeared to be no link between SARS and eating specific foods. Once the sequence of the SARS virus was known, it was evident that it was different from the coronaviruses commonly found in domestic animals (pigs, cattle, chickens) and may have evolved in an isolated reservoir for some time before jumping to humans.

A study from the University of Hong Kong and the Shenzhen Center for Disease Control focused on exotic animals available in markets in Guangdong and reported the detection of a SARS-like coronavirus from six masked palm civets and also from a racoon dog (Normile and Enserink 2003). However, another research team from the China Agriculture University in Beijing was not able to detect SARS virus in any samples from civets or dozens of other species that were sampled. Neither research group felt that civets were the primary reservoir for the SARS virus, but rather that the civets may have become infected from contact with another animal reservoir in the wild or in the market holding facilities (Normile and Enserink 2003). Four international research teams are starting further studies of domestic and wild animals to seek animal reservoirs for the SARS virus. Other laboratory studies are attempting to infect different animal species with the SARS virus. The ban on civets and 53 other wild animal species from the markets of Guangdong was lifted in August 2003 (Normile and Yimin 2003).

Evidence that the SARS virus could be spread by wastewater or faecally contaminated water is mixed. Transmission of the virus by aerosolized wastewater was suspected during the investigation of the SARS outbreak at Amoy Gardens in Hong Kong (Hong Kong Department of Health 2003). This is

a large housing estate built in 1981 with approximately 20 000 residents. An index SARS case visited a relative in Block E building in March 2003 and experienced diarrhoea during his visit. By mid-April, there were 321 SARS cases in Amoy Gardens, and 41% of the cases were concentrated in Block E. The surrounding buildings (B, C, and D) also had much higher SARS incidence rates than the other 11 buildings. Cases appeared earlier in Block E than in the other blocks, and the timing of these cases suggested a point source exposure. Survey data indicated that 66% of these cases had diarrhoea. Laboratory studies have shown that many SARS cases excrete coronavirus in their stools.

Environmental investigations (Hong Kong Department of Health 2003) indicated that the U-trap in the bathroom floor drains were usually dry and that there was a cracked sewer vent pipe in Block E. Tests with oil droplets suggested that aerosols travelled upwards in the light wells (utility channels) between each floor and that droplets could enter a bathroom through the floor drain because of negative pressure generated by exhaust fans when the bathroom door was closed. The investigators hypothesized that a virus in the faeces of the index SARS case was transmitted to a few other residents in Block E. These cases then caused greater contamination of the sewage system in Block E and transmission to other residents. Residents in nearby buildings became infected via person-to-person contact with their neighbours and perhaps from other environmental contamination. However, environmental samples of air and water in the Amoy Gardens were negative for the SARS virus.

Given that the SARS virus is excreted in faeces and these results, it seems possible that SARS could have been transmitted through wastewater droplets. However, one would have expected to have seen more examples of SARS transmission via exposure to wastewater in the various other settings where the epidemic spread. Possibly, this transmission route did contribute to SARS in other countries but was not recognized due to inadequate investigation; it is also possible that the Amoy Gardens buildings provided a unique environment that allowed the virus to accumulate to unusually high levels and expose residents to a high dose.

To date, the SARS coronavirus has been detected in animals and humans, is likely to enter water via faeces of infected persons, and *may* be transmitted via wastewater aerosols. It is not clear that SARS coronavirus causes disease in animals, and it has not yet been detected in water or wastewater.

### **3.5.2 *Pfiesteria* species**

*Pfiesteria*, a genus of dinoflagellates, was first described in laboratory studies of fish mortality (Noga *et al.* 1993) and in association with major fish kills in North Carolina, USA (Burkholder *et al.* 1992). *Pfiesteria* spp. have been

detected in waters with fish kills from the mid-Atlantic to the Gulf Coast. Laboratory studies indicate that these organisms have a complex life cycle, including a toxic stage (Burkholder 1999). Ulcerative lesions, narcosis, erratic behaviour, and death have been observed in several fish species exposed to active cultures of *Pfiesteria* and *Pfiesteria*-like organisms (Burkholder and Glasgow 1997).

Public concern about possible human health hazards posed by *Pfiesteria* spp. began in 1995, when adverse health effects were reported among investigators working with this organism in the laboratory (Glasgow *et al.* 1995). Glasgow *et al.* (1995) described three laboratory workers with exposure to *Pfiesteria* cultures via direct contact with hands and arms and potential inhalation of aerosols from open aquaria. The exposed persons experienced various combinations of symptoms, which included numbness and tingling in hands and feet, skin lesions, respiratory and eye irritation, headaches, abdominal cramps, difficulties with mental concentration and memory, and personality changes. Most of the prominent symptoms subsided after cessation of exposure, although resolution of some symptoms took several months.

In August 1997, a fish kill occurred on the Pocomoke River in Maryland, USA, which triggered a study of 24 individuals with varying degrees of exposure to the Pocomoke waters and other estuaries in the Chesapeake Bay and 8 unexposed waterworkers (Grattan *et al.* 1998). Subjects were asked about water exposure and health symptoms, examined by a medical team, and tested with a neuropsychological screening battery. Individuals who reported high exposure (6–8 h per day in affected waterways with extensive skin contact and exposure to aerosolized spray) were significantly more likely than occupationally matched controls to complain of neuropsychological symptoms, headache, skin lesions, or a burning sensation of skin on contact with water. Nineteen study subjects exposed to affected waters had significantly reduced scores compared with 19 non-exposed subjects (matched on age, gender, education, and occupation) on three neuropsychological tests that indicated difficulty with learning and higher cognitive function. The investigators reported a dose–response effect and that study subjects who reported the greatest exposure to the affected waters had the lowest scores on selected neuropsychological tests. No consistent abnormalities were detected in the physical examinations or laboratory assessments of the study subjects. As with the reported cases among laboratory workers, the major neurocognitive problems appeared to be transitory, and the test scores for all study subjects returned to within normal ranges by 3–6 months after cessation of exposure. However, pre-exposure cognitive test performance for these individuals is not known, and some study subjects complained of persistent symptoms for a longer period of time. This study is the first systematic investigation of human health

effects after exposure to a fish kill associated with *Pfiesteria*. However, the study was limited by the small number of subjects and the facts that they were largely self-selected, exposure status was self-reported and may have been affected by recall bias, and the medical team was not blinded to the exposure status of the subjects during the medical and neuropsychological evaluations.

In response to concerns about *Pfiesteria* and human health and the many different types of health problems that were claimed to be associated with *Pfiesteria* exposure, the US Centers for Disease Control and Prevention and a panel of experts drafted criteria for “possible estuary-associated syndrome” (PEAS) to describe the adverse consequences of exposure to *Pfiesteria* and related organisms (Centers for Disease Control and Prevention 1999). The key criteria included in the definition were 1) exposure to estuarine water with a fish kill or fish with lesions consistent with *Pfiesteria* or *Pfiesteria*-like organisms, 2) symptoms of memory loss and confusion, 3) three or more other symptoms from a list of clinical features that have been reported in previous incidents of *Pfiesteria* exposure, 4) symptoms developing within 2 weeks of exposure to estuarine water and persisting for 2 weeks or longer, and 5) inability of the health care provider to identify another cause for the symptoms. Using these criteria, three prospective cohort studies of fishers and other waterworkers were launched in North Carolina, Virginia, and Maryland to explore the health risks of estuary exposure (Moe *et al.* 2001).

There is still controversy about whether *Pfiesteria* spp. are a primary causative agent of fish mortality or only a contributing factor, as well as about the presence and characteristics of the toxin and the health risks to persons who are exposed to waters with *Pfiesteria* spp. in the natural environment. Based on current knowledge, *Pfiesteria* spp. have been detected in the tissues of diseased fish (but not in humans), have been detected in water, and *may* cause adverse human health effects via exposure through water contact or water aerosols to a toxin. Whether *Pfiesteria* spp. fit the proposed criteria for a water-related zoonotic disease depends on whether 1) fish are considered to be “animals,” 2) there is sufficient evidence that there is a toxic form of the organism that causes adverse health effects in fish and humans, and 3) there is sufficient evidence that exposure to the toxin occurs via either water contact or inhalation of water aerosols. If PEAS is a water-related zoonotic disease, the risks of adverse health outcomes associated with *Pfiesteria* spp. may be significant only at intense exposures similar to those experienced by the laboratory workers.

### **3.5.3 Bovine spongiform encephalopathy (BSE)**

Bovine spongiform encephalopathy (BSE) is a transmissible, neurodegenerative, fatal brain disease of cattle. It has a long incubation period of 4–5 years; once

symptoms appear, however, the duration of the disease is weeks to months. Between November 1986 and November 2002, 181 376 confirmed cases were reported in the United Kingdom. There have been an additional 3286 cases reported in other European countries since 1989 (WHO 2003b). The etiologic agent is believed to be a prion — an infectious, self-replicating, mutated protein. Although the exact nature of the etiologic agent is still being debated, it is clear that the agent is highly stable and resists freezing, drying, and high temperatures. The disease appears to be transmitted between cattle by animal feed (meat and bone meal) that contains tissue from BSE-infected cows or scrapie-infected sheep.

Variante Creutzfeldt-Jakob disease (vCJD) is a rare, fatal degenerative brain disease of humans. It is important to note that vCJD is different from the classic form of CJD that is endemic throughout the world and affects older adults. The first vCJD cases were reported in 1996; through November 2002, 139 cases have been reported (WHO 2003b). The majority of these cases (129) were in the United Kingdom, and the average age at death was 29 years (WHO 2003b). The similarities in the human disease and cattle disease, long incubation period, similar symptoms, and similar morphology of infected brain tissue suggest that these diseases are both caused by the same agent. Transmission from cattle to humans is believed to occur through ingestion of beef and beef products from BSE-infected cattle. Human susceptibility to the disease is also likely to involve host genetic factors (McCormack *et al.* 2002).

When evaluating BSE as a candidate for a water-related zoonotic disease, several unknowns exist. The BSE agent clearly causes disease in cattle, and strong evidence suggests that the same agent is also responsible for a similar disease in humans. It is conceivable that the BSE agent could enter water if tissue from infected cattle (slaughterhouse waste or landfill leachate) enters water. There have been several incidents of public concern about the possibility of BSE-contaminated water (WaterTech Online 2000). However, Gale (1998) suggested that the likely concentration of BSE prions in the environment would be too low to pose a significant risk, even after a lifetime of exposure to contaminated water. The survival of the agent in water is unknown, although the agent is believed to be very stable in general. Currently, there are no reports of the detection of BSE agent in water, but it is likely that no methods exist to test water samples for this agent. There has been concern about the possible threat to groundwater supplies in the United Kingdom from buried carcasses of infected cattle.

### 3.6 SUMMARY

There has been a recent surge in the number of newly recognized zoonotic diseases, some of which have water-related transmission routes. There is striking variety in the species and life cycles of water-related zoonotic organisms and how these organisms can move from animals to humans. A set of broad criteria has been proposed to help determine whether a disease is both zoonotic and water related. The application of these criteria to different emerging diseases identifies the critical gaps in our understanding of these diseases. The control of the diseases that meet these criteria involves water management strategies. However, many of these organisms can be transmitted to humans by more than one route, and water may not be the dominant transmission route. Therefore, control of water-related transmission may be necessary but not always sufficient to prevent these diseases. The stringency of the criteria proposed here can be adjusted to examine specific types of diseases and specific types of water-related transmission, depending on the application.

### 3.7 REFERENCES

- Bradley, D. (1977) Health aspects of water supplies in tropical countries. In *Water, Wastes and Health in Hot Climates* (ed. R. Feachem, M. McGarry, and D. Mara), pp. 3–17, John Wiley & Sons, London.
- Burkholder, J.M. (1999) The lurking perils of *Pfiesteria*. *Sci. Am.* **218**, 42–49.
- Burkholder, J.M. and Glasgow, H.B. (1997) Trophic controls on stage transformations of a toxic ambush-predator dinoflagellate. *J. Eukaryotic Microbiol.* **144**, 200–205.
- Burkholder, J.M., Noga, E.J., Hobbs, C.H. and Glasgow, H.B. (1992) New “phantom” dinoflagellate is the causative agent of major estuarine fish kills. *Nature* **358**, 407–410.
- Carmichael, W., Jones, C., Mahmood, N. and Theiss, W. (1985) Algal toxins and water-based diseases. *Crit. Rev. Environ. Control* **15**, 175–313.
- Centers for Disease Control and Prevention (1999) Possible estuary-associated syndrome. *Morbid. Mortal. Wkly. Rep.* **48**, 381–383.
- Charoenc, N. and Fujioka, R. (1995) Association of staphylococcal skin infections and swimming. *Water Sci. Technol.* **31**, 11–17.
- Chin, J., ed. (2000) *Control of Communicable Diseases Manual: An Official Report of the American Public Health Association*, 17th edn. American Public Health Association, Washington, DC.
- Codd, G., Bell, S. and Brooks, W. (1989) Cyanobacterial toxins in water. *Water Sci. Technol.* **21**, 1–13.
- Dufour, A. (1986) Diseases caused by water contact. In *Waterborne Diseases in the United States* (ed. G. Craun), pp. 23–41, CRC Press, Boca Raton, FL.
- Feachem, R.G., Bradley, D.J., Garelick, H. and Mara, D.D. (1983) *Sanitation and Disease: Health Aspects of Excreta and Wastewater Management*. pp. 23–51, Wiley, Chichester.
- Ford, T.E. (1999) Microbiological safety of drinking water: United States and global perspectives. *Environ. Health Perspect.* **107**(Suppl. 1), 191–206.

- Gale, P. (1998) Quantitative BSE risk assessment: relating exposures to risk. *Lett. Appl. Microbiol.* **27**, 239–242.
- Glasgow, H.B., Burkholder, J.M., Schmechel, D.E., Tester, P.A. and Rublee, P.A. (1995) Insidious effects of a toxic estuarine dinoflagellate on fish survival and human health. *J. Toxicol. Environ. Health* **46**, 501–522.
- Grattan, L.M., Oldach, D., Perl, T.M., Lowitt, M.H., Matuszak, D.L., Dickson, C., Parrott, C., Shoemaker, C., Kauffman, C.L., Wasserman, M.P., Hebel, J.R., Charache, P. and Morris, J.G., Jr. (1998) Learning and memory difficulties after environmental exposure to waterways containing toxin-producing *Pfiesteria* or *Pfiesteria*-like dinoflagellates. *Lancet* **352**, 532–539.
- Hackney, C. and Potter, M. (1994a) Animal-associated and terrestrial bacterial pathogens. In *Environmental Indicators and Shellfish Safety* (ed. C. Hackney and M. Pierson), pp. 172–209, Chapman and Hall, New York.
- Hackney, C. and Potter, M. (1994b) Human-associated bacterial pathogens. In *Environmental Indicators and Shellfish Safety* (ed. C. Hackney and M. Pierson), pp. 154–171, Chapman and Hall, New York.
- Hong Kong Department of Health (2003) *Outbreak of Severe Acute Respiratory Syndrome (SARS) at Amoy Gardens, Kowloon Bay, Hong Kong. Main Findings of the Investigation* ([http://www.info.gov.hk/info/ap/pdf/amoy\\_e.pdf](http://www.info.gov.hk/info/ap/pdf/amoy_e.pdf)).
- Hunter, P.R. (1997) *Waterborne Disease: Epidemiology and Ecology*. John Wiley, Chichester.
- Jenkins, P.A. (1991) Mycobacteria in the environment. *J. Appl. Bacteriol.* **70**, 137S–141S.
- Klontz, K., Lieb, S., Schreiber, M., Janowski, H., Baldy, L. and Gunn, R. (1988) Syndromes of *Vibrio vulnificus* infections: clinical and epidemiologic features in Florida cases, 1981–1987. *Ann. Intern. Med.* **109**, 318–323.
- Lederberg, J., Shope, R.E. and Oaks, S.C., ed. (1992) *Emerging Infections: Microbial Threats to Health in the United States*. Institute of Medicine, National Academy Press, Washington, DC.
- Lee, S.H., Levy, D.A., Craun, G.F., Beach, M.J. and Calderon, R.L. (2002) Surveillance for waterborne-disease outbreaks — United States, 1999–2000. *Morbidity and Mortality Weekly Report* **51**(SS-8).
- Leoni, F., Gallimore, C.I., Green, J. and McLauchlin, J. (2003) Molecular epidemiological analysis of *Cryptosporidium* isolates from humans and animals by using a heteroduplex mobility assay and nucleic acid sequencing based on a small double-stranded RNA element. *J. Clin. Microbiol.* **41**(3), 981–992.
- Mahy, B.W.J. and Brown, C.C. (2000) Emerging zoonoses: crossing the species barrier. *Rev. Sci. Tech. Int. Off. Epizoot.* **19**(1), 33–40.
- McCormack, J.E., Baybutt, H.N., Everington, D., Will, R.G., Ironside, J.W. and Manson, J.C. (2002) PRNP contains both intronic and upstream regulatory regions that may influence susceptibility to Creutzfeldt-Jakob disease. *Gene* **288**, 139–146.
- Moe, C.L., Turf, E., Oldach, D., Bell, P., Hutton, S., Savitz, D., Koltai, D., Turf, M., Ingsrisawang, L., Hart, R., Ball, J.D., Stutts, M., McCarter, L., Wilson, L., Haselow, D., Grattan, L., Morris, J.G. and Weber, D.J. (2001) Cohort studies of health effects among people exposed to estuarine waters: North Carolina, Virginia and Maryland. *Environ. Health Perspect.* **109**(Suppl. 5), 781–786.
- Morse, D., Guzewich, J., Hanrahan, J., Stricof, R., Shayegani, M., Deibel, R., Grabau, J., Nowak, N., Herrmann, J., Cukor, G. and Blacklow, N. (1986) Widespread outbreaks of

- clam- and oyster-associated gastroenteritis: role of Norwalk virus. *N. Engl. J. Med.* **314**, 678–681.
- Muraca, P., Yu, V. and Goetz, A. (1990) Disinfection of water distribution systems for *Legionella*: a review of application procedures and methodologies. *Infect. Control Hosp. Epidemiol.* **11**, 79–88.
- Noga, E.J., Smith, S.A., Burkholder, J.M., Hobbs, C. and Bullis, R.A. (1993) A new ichthyotoxic dinoflagellate: cause of acute mortality in aquarium fishes. *Vet. Rec.* **133**, 48–49.
- Normile, D. and Enserink, M. (2003) Tracking the roots of a killer. *Science* **301**, 297–299.
- Normile, D. and Yimin, D. (2003) Civets back on China's menu. *Science* **301**, 1031.
- Tamplin, M.L., Gauzens, A.L., Huq, A., Sack, D.A. and Colwell, R.R. (1990) Attachment of *Vibrio cholerae* serogroup O1 to zooplankton and phytoplankton of Bangladesh waters. *Appl. Environ. Microbiol.* **56**, 1977–1980.
- Teunis, P.F.M., van der Heijden, O.G., van der Giessen, J.W.B. and Havelaar, A.H. (1996) *The Dose-Response Relation in Human Volunteers for Gastro-intestinal Pathogens*. Report No. 284550002, National Institute of Public Health and the Environment (RIVM), Bilthoven.
- Teunis, P.F.M., Chappell, C.L. and Okhuysen, P.C. (2002) *Cryptosporidium* dose response studies: variation between isolates. *Risk Anal.* **22**, 175–183.
- Wadowsky, R., Yee, R., Mezmar, L., Wing, E. and Dowling, J. (1982) Hot water systems as sources of *Legionella pneumophila* in hospital and nonhospital plumbing fixtures. *Appl. Environ. Microbiol.* **43**, 1104–1110.
- WaterTech Online (2000) *Mad Cow Scare Hits Drinking Water Supply*. 14 December 2000 ([http://www.watertechonline.com/News.asp?mode=4&N\\_ID=19009](http://www.watertechonline.com/News.asp?mode=4&N_ID=19009)).
- Wendt, S., George, K., Parker, B., Graft, H. and Falkinham, J. (1980) Epidemiology of infection by nontuberculous mycobacteria. *Am. Rev. Respir. Dis.* **122**, 259–263.
- Wilson, M.L. (2001) Ecology and infectious disease. In *Ecosystem Change and Public Health: A Global Perspective* (ed. J.L. Aron and J.A. Patz), pp. 283–324, The Johns Hopkins Univ. Press, Baltimore, MD.
- Winn, W. (1995) *Legionella*. In *Manual of Clinical Microbiology*, 6th edn (ed. P. Murray, E. Baron, M. Pfaller, F. Tenover, and R. Tenover), pp. 533–544, ASM Press, Washington, DC.
- WHO (2003a) *Summary Table of SARS Cases by Country, 1 November 2002 – 7 August 2003*. World Health Organization, Geneva ([http://www.who.int/csr/sars/country/en/country2003\\_08\\_15.pdf](http://www.who.int/csr/sars/country/en/country2003_08_15.pdf)).
- WHO (2003b) *Bovine Spongiform Encephalopathy*. Fact Sheet No. 113, World Health Organization, Geneva (<http://www.who.int/mediacentre/factsheets/fs113/en/>).
- WHO (2003c) *Human Leptospirosis: Guidance for Diagnosis, Surveillance and Control*. World Health Organization, Geneva (<http://www.med.monash.edu.au/microbiology/staff/adler/LeptoGuidelines2003.pdf>).
- WHO/FAO (1959) *Second Report of the Joint WHO/FAO Expert Committee on Zoonoses*. WHO Technical Report Series No. 169, World Health Organization, Geneva.
- Wu, J.-C. (2003) Severe acute respiratory syndrome (SARS), a zoonotic infection with rapid spread: are we ready for the coming ones? *J. Chin. Med. Assoc.* **66**, 315–317.

# 4

## Impacts of anthropogenic and environmental factors on the distribution of zoonoses

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### 4.1 INTRODUCTION

The geographical distribution of diseases has shown major changes over human history. With the improvement of urban sanitation, the development of antibiotics, and the development of vaccines, as well as improved individual hygiene behaviour and a higher standard of living, there has been a considerable decrease in infectious diseases since the end of the 19th century in developed countries that made the transition to modern industrial societies.

Since the 1980s, an increase in epidemics has occurred worldwide — for example, the return of diphtheria and tuberculosis in Russia (Müller 2000),

© World Health Organization (WHO). *Waterborne Zoonoses: Identification, Causes and Control*. Edited by J.A. Cotruvo, A. Dufour, G. Rees, J. Bartram, R. Carr, D.O. Cliver, G.F. Craun, R. Fayer, and V.P.J. Gannon. Published by IWA Publishing, London, UK. ISBN: 1 84339 058 2.

bovine spongiform encephalopathy in Great Britain (Kurth 1997), cholera in South America (Chin 2000), and Ebola in South Africa (Kurth 1997). Infectious diseases remain among the most frequent causes of death globally.

The question arises as to the cause of the increase in infectious diseases, including water-transmittable diseases, and whether further increases would be expected. Numerous risk factors that can influence the occurrence and spreading of infectious diseases are discussed in the technical literature. These include geographical aspects, environmental changes, socioeconomic factors, and pathogen-specific factors, as well as individual behaviour. Internal and external migration, population growth, lack of living space, impoverishment, military actions, uncontrolled and rapid urban growth, environmental changes as a result of changes in land use, air pollution and climate change, construction of irrigation systems, dams, de- and reforestation, the development of mass tourism, mass production in the food industry, as well as an increase in international trade are only some of the risk factors to be mentioned (Haggett 1994; Kurth 1997; Kovats *et al.* 1999; Githeko *et al.* 2000; Patz *et al.* 2000; WHO 2002a; Woolhouse 2002). Some risk factors contributing to the increased occurrence of zoonoses in the Mediterranean region are, according to Mantovani and Prosperi (1995), the changing patterns of migration of people and animals, the densities of human populations, domestic animals, and wild animals, types of farming, pig-rearing, the presence of stray dogs, slaughtering methods, food and living patterns, and trade.

Human activities have profound effects on the environment. Table 4.1 summarizes the impact of some anthropogenic factors on the distribution of zoonotic diseases.

## 4.2 PATHOGEN RESERVOIRS AND MOBILITY

Human migration has been the main source of epidemics throughout recorded history. Trade caravans, religious pilgrimages, and military conflicts facilitated the spread of many diseases, including plagues and smallpox (Wilson 1995).

The mobility of people continues to increase due to social, economic, and political factors. Worldwide, about 125 million people are migrant workers, immigrants, or refugees searching for education, employment, or safety, making them vulnerable to infectious diseases that are not endemic in their home countries (Theron and Cloete 2002). Furthermore, natural hazards such as flooding, earthquakes, and hurricanes often force people to search for new settlement areas. The increasing number of military conflicts brings soldiers into new environments. Large numbers of troops from mid-latitude countries operate in tropical and subtropical climates (Haggett 1994).

The consequences of mobility are that people carry pathogens, insect vectors, immunity due to past infections, vulnerability, genetic material, cultural preferences, behavioural patterns, and technology to new environments, which influence their risk for infection and their capacity to introduce diseases in the new region (Wilson 1995).

Table 4.1. Impact of human activities

Cause	Effect
Mobility due to population growth, urbanization, social inequality, stress	Migration movements (e.g., into slums of large cities)
	Spatial proximity to waste disposal, sewage, and contaminated rodents or other roaming animals
	Collapse of the public health infrastructure
	Invasion of a non-immune population by an infectious agent
Mobility due to national and international conflicts	Exposure of soldiers and refugees to a range of diseases not encountered in their home region or country
	Lack of medical care, hygiene, safe drinking-water
Mobility due to travel	Increased potential for disease spread due to air travel
	Decreasing travel times
	Increasing size of aircraft
Trade, transboundary animal transport, import of exotic animals	Deficient surveillance for infected animals
Agricultural practices	Land use, manure deposits, manure application, livestock, dairy farming, drained areas, mass production of food and animals
Water control, irrigation projects	Change of ecology of large regions
	Surface water serves as breeding site
	Increased soil salinity
Human habits	Changing consumption patterns
	Eating raw or undercooked fish or meat
	Pet-keeping
	Close contact with (infected) animals
	Colonization of new environments
	Lack of knowledge of self-protective lifestyles
Infrastructure changes	Development of technical systems
	Water supply distribution network
	Cooling towers
	Air conditioning
Demographic factors	Increase of risk groups
	Aged population
	Immunocompromised patients

Cause	Effect
Pathogen-specific factors	Decrease or increase of pathogenicity Antibiotic-resistant pathogens
Climate change	Increasing warm winters benefit the proliferation of infectious agents Changes in the geographical range of pathogens, vectors, and reservoirs Increased seasonality in rainfall Storm frequency increases Floods, prolonged droughts

#### 4.2.1 Population growth and urbanization

The world population will grow from the current 6.3 billion to an estimated 8.9 billion people by the year 2050. Nearly all of the 2.6 billion increase will be in the developing countries of Africa, Asia, and Latin America (UNFPA 2003). Due to social, economic, and political factors, there is an increasing shift of populations to urban areas. Nearly half of the world population now lives in urban settlements. The number of large cities increased sharply during the last several decades (Moore *et al.* 2003). Current data indicate 18 cities with populations greater than 10 million (UNPD 2003).

Urbanization is often associated with rapid and unplanned growth, poverty, and environmental degradation. Substandard housing, crowding, air pollution, water pollution, overusage of water sources, and inadequate sanitation facilities and services are mostly related to rapid urban growth (Moore *et al.* 2003).

Negative effects on human health evolve from a higher risk of disease contacts through crowding and pollution (Haggett 1994). Crompton and Savioli (1993) showed that in developing countries, high rates of intestinal parasitic infections occur where rural/urban migration results in poor periurban settlements. Furthermore, the aggregation of human populations into high-density urban regions has important effects in providing host reservoirs for maintaining infection chains (Haggett 1994). Disease vectors, such as rodents and insects, find new habitats within the changing urban landscape and may come into close contact with people.

The poor population in urban areas often does not have access to the municipal water supply. The people often depend on common pumps or surface water sources, which are often faecally contaminated due to inadequate solid waste collection (Moore *et al.* 2003). Municipal supplies are also often unreliable.

In industrialized countries, heavy faecal contamination of surface waters can occur as a result of the introduction of treated or untreated sewage.

Characteristic sources are municipal or private sewage discharges, industrial effluents, and recreational activities. Enteric viruses, for example, are predominantly found in rivers or seawater polluted by discharges from densely populated and industrial areas (Johl *et al.* 1991; Van Olphen *et al.* 1991; Payment and Franco 1993).

The increasing growth of populations with the extension of settlement areas, as well as the extension of agricultural areas into new environments and up to catchment areas of drinking-water resources, must be seen as risky environmental changes.

#### **4.2.2 International and national conflicts**

Increasing numbers of cross-boundary military conflicts bring soldiers into new environments. Large numbers of troops from mid-latitude countries operate in tropical and subtropical climates, where they come into contact with a different spectrum of infectious diseases (Haggett 1994).

Thousands of people abandon their villages and cities as a consequence of military actions. Severe water-associated outbreaks occur due to the lack of medical care, hygiene, drinking-water, and healthful behaviour among refugees.

#### **4.2.3 Travel**

Travel patterns of tourists have changed over several decades. Bradley (1988) showed that over the last four generations, the spatial range of travel has increased 10-fold. In particular, air travel has increased the potential for spread of disease, not only through decreasing travel times, but also due to the increasing size of aircraft (Haggett 1994). Important aspects of these problems include the transmission of foodborne and waterborne diseases, the translocation of insect vectors, the rapid transport of people with subclinical infections as well as direct transmission while in the aircraft, and the transmission of zoonoses through animal transport (Royal and McCoubrey 1989).

With the rising popularity of international travel to exotic locations, travellers are often exposed to pathogenic agents that are not endemic in their countries. This could result in an invasion of a non-immune population by the infectious agents, which often leads to a more severe manifestation of diseases (Wilson 1995).

Problems of water supply in many developing countries arise from insufficient technology with regard to well heads, water treatment, supply systems, and hygienic behaviour. Water resources have been polluted over the years due to inadequate protection of surface reservoirs and groundwater from faecal and toxic wastes. Travellers from countries with high standards of water

supply have higher risks of acquiring waterborne diseases than the indigenous population, because the residents have developed immunity to many of the local waterborne pathogens.

Shigellosis (bacillary dysentery), typhus, and paratyphus are typical diseases of travellers, which are of minimal importance as endemic diseases in developed countries (RKI 2000). Hepatitis A also often occurs in travellers. For residents of countries with low sero-prevalence levels, such as Sweden, vaccination is recommended before travel to countries where the disease is endemic (Bottiger and Christenson 1998).

### 4.3 TRADE

A huge volume of plants, animals, and other materials is transported all over the world. The globalization of markets brings fresh fruits and vegetables over long distances to places where they are not grown. A consequence of shipping the goods is the unintended transfer of microorganisms from and to different ecosystems and populations (Wilson 1995).

Millions of calves and cattle are transported across, from, and to Europe every year. Most of these animals are going to slaughterhouses in the respective countries or in another community state or coming or going abroad. These transports can cause severe stress in animals, entailing poor welfare. Furthermore, they increase risks of spreading infectious diseases over large distances. According to Hartung *et al.* (2003), "Existing legislation does not provide enough protection to transported animals especially over long distances largely because considerable parts of the regulations are not sufficiently based on scientific evidence."

Worldwide, over 50 species of helminth parasites from fish, crabs, crayfish, snails, and bivalves are known to cause human infections. Some of the zoonotic diseases are more prevalent than others and can pose serious health hazards. The majority of seafood zoonoses occur along coastal regions where seafood products are commonly consumed. However, improvements in transportation technology and food handling allow fresh seafood to be distributed throughout the world. Thus, the potential to acquire parasitic infections from seafood is not limited to coastal populations.

Global food trade is expected to increase due to increases in global income levels, improved transportation networks, including improved refrigeration, and the fact that the growing population requires larger quantities of nutrition and safe food (Buzby 2001). There has been a remarkable increase in the consumption of animal products in countries such as Brazil and China, although the levels are still below the levels of consumption in North America and most other industrialized countries (WHO 2002a).

#### 4.4 AGRICULTURAL AND HUSBANDRY PRACTICES

The contamination of the environment with enteric pathogens from agriculture depends upon the number of infected non-human hosts, the number of transmissible stages excreted, host behaviour, and agricultural practices. Enteric pathogens may enter the environment via storage and spread of farmyard manure, on-farm discharge of faecally polluted water to land or to watercourses, runoff from pastureland into water bodies, or the disposal of faecally contaminated waste from abattoirs (Slifko *et al.* 2000).

Several studies have shown that the most frequent association for *Cryptosporidia* and *Giardia* is between surface water sources and the presence of a high density of domestic and wild animals. *Cryptosporidia* occurrence has been frequently correlated with dairy farming and density of fallow deer in the catchment area, whereas *Giardia* cysts were predominately associated with the presence of urban sewage (LeChevallier *et al.* 1997; Atherholt *et al.* 1998; Hsu *et al.* 1999; Payment *et al.* 2000; Kistemann *et al.* 2002). Adenoviruses and enteroviruses were found in lakes and rivers whose catchment areas were influenced by poultry and sheep farming (Till *et al.* 2000).

In many countries — for example, in Southeast Asian countries — untreated night soil is used as a fertilizer in agriculture or as food in aquaculture (Bo *et al.* 1993). Contamination with pathogens and eggs of parasites affects soil, groundwater and surface water, vegetables, and fish. This poses health risks to workers and farmers and to consumers eating raw fish taken from ponds fertilized with night soil. In a province in south China where the cultural preference is to consume raw fish, the infection rate with *Clonorchis sinensis* reached 100% in some areas (Bo *et al.* 1993).

Modern animal husbandry has tended to increase the number of animals raised per unit area. Feeding and watering of animals are automated, and the use of antibiotics supports animal growth rates. These changes have introduced some new risks. In particular, the increased concentration of animal excreta can be hazardous to human health and the environment (Cole *et al.* 1999).

Numerous wastes are produced by intensive swine production. They are associated not only with potentially transferable antimicrobial resistance patterns, but also with several infectious agents that can be pathogenic to humans (Cole *et al.* 2000). Hepatitis E, for example, is thought to be transmissible through swine (Worm *et al.* 2002).

Bacterial enteric diseases due to *Salmonella enteritis* and *Escherichia coli* O157:H7 (enterohaemorrhagic *E. coli* [EHEC]) are examples of diseases associated with changing farming practices and consumer habits (Meslin 1992). Cattle are asymptomatic natural reservoirs of *E. coli* O157:H7. It has been reported that about 30%, and as high as 80%, of all cattle are carriers of this

pathogen. High-producing dairy cattle are fed large grain rations in order to increase feed efficiency. This is thought to be correlated to higher shedding of EHEC than using a forage diet (Callaway *et al.* 2003). Other reservoirs of EHEC are sheep, goats, red deer, horses, dogs, birds, and flies. The bacteria can survive in liquid manure, non-liquid manure, and drinking troughs. Foods that are irrigated, washed, or prepared with polluted water are also a common cause of infection (Doyle 1990).

*Campylobacter* spp. are common in poultry, particular chickens. In production systems, poultry flocks can be infected through the environment, overcrowded conditions, and their low immune status (Sahin *et al.* 2002). Tully and Shane (1996) indicated that newly introduced birds (ostriches, emus, rheas) may contaminate soil and water with pathogens such as *Mycobacterium* spp. and *Salmonella* spp. Mass production of animals, development of large meat factories, and international trade of meat products and animals are believed to be the reasons for the increased prevalence of yersiniosis in humans (Neubauer *et al.* 2001).

#### **4.5 WATER CONTROL AND IRRIGATION**

Large water projects have caused social and environmental disasters. Malaria, bilharzia, and other tropical diseases have been caused in numerous cases by dam construction and development of new irrigation systems. Such projects can expand habitats for mosquitos, aquatic snails, and flies, which spread disease among resettled agricultural populations. Excess irrigation and poor drainage can cause increased salinization of soils. High salt concentrations can adversely affect vegetation, wildlife, and cultivated crops (Jobin 1999).

World population growth means that more dams and irrigation systems will be needed for survival in Africa and other dry areas. Efficient use of water resources and sustainable designs and proper operation must be implemented more widely (Jobin 1999).

The use of inadequately treated wastewater in irrigation and faecal sludge in soil amendment and fertilization is often associated with an elevated prevalence of intestinal helminth infections and diarrhoeal diseases in both workers and food consumers (Mara and Cairncross 1989).

#### **4.6 CHANGING HUMAN BEHAVIOUR**

The preparation and consumption of meat or fish are associated with specific cultural preferences. In recent years, globalization of the food supply has changed consumer habits. As a consequence, some foodborne diseases have shifted to new areas.

Previously, the majority of seafood zoonoses occurred along coastal regions where seafood products are commonly consumed. Through the improvement of transportation facilities, seafood is now available worldwide. Changing consumption habits — such as eating raw seafood dishes (e.g., sushi and sashimi) and the tendency to reduce cooking times when preparing seafood products — have increased the risk of fish-borne parasitic zoonoses in areas where the products were previously not common (Deardorff 1991).

Foodborne zoonoses may also occur due to inadequate preparation of meat, vegetables, and fruits. People now more frequently eat raw, undercooked, smoked, salted, pickled, or air-dried meat, which may have a higher risk of infection (Slifko *et al.* 2000).

The highest biodiversity of all terrestrial ecosystems is to be found in tropical forests. The invasion into formerly untouched areas by hunters, villagers, tourists, and others has led to intensified contacts with free-living animals. Increased contacts between people and animals in tropical forests and high population densities of humans and domestic animals pose a high risk for the emergence of new diseases (Ludwig *et al.* 2003). Construction of roads in previously forested areas provides access for non-immune, non-protected populations (road workers, tourists, miners, etc.) into new environments (Patz *et al.* 2000).

Deforestation is mostly connected to conversion of the area into grazing land for cattle and agricultural or settlement areas. With the introduction of new animal or plant species, new habitats for parasites or vectors can be created. The replacement of former forests by agricultural land use attracts new settlers and migrants who frequently have a lack of immunity to the endemic zoonoses and also lack of knowledge of protective hygienic habits (Patz *et al.* 2000).

#### **4.7 INFRASTRUCTURE CHANGES**

Legionnaires' disease is a classic example of the fact that an ecological milieu for pathogens that does not constitute a danger for human beings in their natural environment can be created by infrastructure changes. The development of new technologies is usually associated with improvements in the quality of life, but it also can create new problems. With the extended use of water in large constructed systems, like drinking-water distribution systems, warm-water plumbing systems, air conditioning systems, cooling towers, etc., the risk of Legionnaires' disease has increased in the last decades (McDade 2002).

Only since the 1980s has it been recognized that proliferation of microorganisms in treated drinking-water without particular nutrients is possible (Christian and Pipes 1983). This regrowth of heterotrophic organisms usually does not involve bacteria from animal or human faeces but instead involves

organisms that occur naturally in the aquatic environment and the soil (Botzenhart and Hahn 1989). These organisms reach the drinking-water via the raw intake water or during pipe construction and repair. They have the capability to multiply in water systems in which they are both nourished and protected by biofilms from physical removal, disinfectants, and temporarily high temperatures. Examples of hygienically relevant microorganisms are *Legionella pneumophila*, *Pseudomonas aeruginosa*, *Aeromonas*, *Mycobacterium*, and *Acinetobacter* (Szewzyk *et al.* 2000). Some microorganisms of faecal origin have the ability to survive and be transported in the drinking-water supply network. These include *E. coli*, *Cryptosporidium*, *Giardia*, and enteroviruses (Flemming 1998).

Most of the heterotrophic organisms that proliferate in water systems are not pathogenic, but some pathogens can be harboured in biofilms. Biofilms form from a matrix of extracellular polymer substances. The biofilms serve as habitat for the microorganisms. Depending on the nutrient supply, they can multiply and can access the water. The formation of biofilms in the pipe system is encouraged or limited by certain factors. The colonization is dependent on the pipe material used, the age of the pipe system, corrosion phenomena, stagnation conditions in the system, temperature, pressure, disinfectant residuals, nutrients, and pH. Furthermore, the tolerance of biofilms to disinfection agents is of importance to drinking-water supply systems (Flemming 1998).

Infrastructures in water supply are subject to a generally long-term planning perspective, and correspondingly the capacities of the pipe systems are only slowly adapted to new trends. Pump stations, conduits, and storage systems are closely connected. Problems in the pipe system can be caused by overhead traffic, underground displacement, corrosion, frost, and construction work. Leakage and breaks lead to losses of water as well as to impairments in the drinking-water quality.

Recontamination in primarily clean drinking-water can be associated with home plumbing that has not been installed and maintained appropriately or that is out of date. Sites at particularly high risk are hospitals, nursing homes, day care centres, and other public institutions where high-risk populations may reside.

#### **4.8 DEMOGRAPHIC CHANGES**

Particular health risks arise in populations whose resistance against a pathogenic microorganism has been reduced. These groups of people are an environment that can support proliferation of some pathogens. For example, the course of gastrointestinal infections is often more severe in young people, especially

infants, and in the aged, rather than in healthy adults. Severe health complications can also arise as a result of dehydration (Chin 2000).

In the USA, the portion of high-risk groups in the total population is approximately 20% (Gerba *et al.* 1996). High standards of living and progress in medical science have led to an increasing life expectancy and a higher portion of older people, who are more vulnerable to infections. The fatality risk from bacterial gastroenteritis outbreaks is up to 10 times higher in nursing homes than in the general population. Intestinal diseases can have grave complications in immunocompromised patients. As a result of chemotherapies or after organ transplantation, patients are very vulnerable to viral infections of the gastrointestinal tract. Cryptosporidiosis often appears in patients with acquired immunodeficiency syndrome (AIDS) (Gerba *et al.* 1996), and clinical treatment is generally not effective.

An additional at-risk group is the increasing number of patients in home nursing, which can be seen in Europe, due to attempts to reduce costs in health care. The occurrence of at-risk groups in several European countries is shown in Table 4.2. It can be assumed that the ratio of the population at risk (i.e., with an increased risk of infection) to the normal European population is 1:6 (Exner and Kistemann 2003).

Table 4.2. Occurrence of “at-risk” populations in different European countries (adapted from Exner and Kistemann 2003)

	UK	Germany	The Netherlands
Total population	60 million	82 million	16 million
Over 65 years old	9 million	13 million	2 million
Under 1 year old	600 000	800 000	100 000
People living with cancer	1 million	– <sup>a</sup>	160 000
Discharged from hospital within previous 2 weeks	200 000	–	60 000
Hospital outpatients at home	–	1 270 000	–
AIDS cases	15 000	–	91
Total at-risk persons	>1 in 6	>1 in 5.6	>1 in 6.3

<sup>a</sup> No data.

Worldwide, nearly half of all people are under the age of 25 (UNFPA 2003), out of which about 617 million are children under the age of 5 (UNPD 2003). More than 10 million children die each year, most from preventable causes, and almost all in developing countries. Key issues include malnutrition and deaths due to infectious diseases and poor general sanitation (Black *et al.* 2003).

Gastrointestinal infections are one of the principal causes of morbidity and mortality among children. For children under 5 years of age in developing

countries, a median of 3.2 episodes of diarrhoea per child-year was calculated. Estimates of mortality revealed that 4.9 children per 1000 per year in these areas die as a result of diarrhoeal illnesses in the first 5 years of life (Kosek *et al.* 2003).

About 41% of child deaths occur in sub-Saharan Africa, and another 34% in south Asia. Most of the children live in rural areas, but poor periurban populations also have high mortality rates. Unhygienic and unsafe environments, including ingestion of unsafe water, inadequate availability of hygiene, and lack of access to sanitation, cause 88% of child deaths from diarrhoea (Black *et al.* 2003).

## 4.9 PATHOGEN CHARACTERISTICS

### 4.9.1 Genetic mutations

The ability of an infectious agent to cross the species barrier is a complex multifactorial process. New types of pathogens or new forms of adaptation of microorganisms can be explained by mutations for the most part. The mechanisms of the microbial evolution can either decrease or increase the pathogenicity or virulence of a pathogen. In addition, microorganisms can leave their natural host and become endemic in a new species (Kurth 1997).

RNA viruses — for example, human immunodeficiency virus (HIV) and influenza viruses — show extremely high mutation rates. As a result, RNA virus populations consist of a dynamic swarm of mutants, even within a single host individual. Maintaining such a genetically highly diverse population allows rapid adaptation to a new environment and host (Ludwig *et al.* 2003).

The recent outbreak of severe acute respiratory syndrome (SARS) demonstrated the capacity of viruses to change their hosts. The SARS agent was identified as belonging to the family of coronaviruses. It is believed that within an animal host, the coronaviruses developed unique genome sequences that have crossed over to people in rural areas of a southern Chinese province (Pearson *et al.* 2003). Even though the outbreak was stopped, the infectious disease may return. As with the influenza viruses, development of mutations may be favoured by immunity in people and the use of antiviral drugs (Pearson *et al.* 2003).

Another prominent example is the formation of pathogenic *E. coli* strains that may have taken up virulence by genetic diversification. In contrast to the harmless *E. coli*, five variations of the species are of human pathogenic importance: EHEC, EIEC (enteroinvasive *E. coli*), ETEC (enterotoxigenic *E. coli*), EPEC (enteropathogenic *E. coli*), and EAEC (enteroadherent *E. coli*) (Eisenstein and Zaleznik 2000). EHEC is currently one of the most important

strains of waterborne pathogens, even though it is easily eliminated by basic water treatment. In 2000, in the town of Walkerton, Ontario, Canada, an estimated 2300 people became ill and 7 died from exposure to EHEC-contaminated drinking-water (Hrudey 2003), which was not adequately disinfected.

#### 4.9.2 Drug resistance

Antibiotics inhibit bacterial growth by interfering with vital cell functions such as protein synthesis. Every time an antibiotic is used, there is selective pressure to allow the growth of resistant organisms, because the antibiotics selectively kill or reduce the viability of only the sensitive bacteria. This leaves the resistant ones with the opportunity to proliferate more in the host or environment. Through the process of natural selection, the resistant bacteria very rapidly become the dominant variants in the population (Levy 1998). In addition, pathogens can acquire new antibiotic-resistant genes from other species in the environment (Woolhouse 2002).

The selection of antibiotic-resistant and drug-resistant pathogens has become more frequent through massive and increasing use of antimicrobial drugs in humans, food animals, and fruits and vegetables. Drug-resistant infections in humans are often associated with prolonged hospital stays, and they increase the risk of complications and death.

According to McGeer (1998), nearly half of the antimicrobial drug use in North America is in agriculture, out of which the majority is given to animals to promote growth rather than to treat any existing infections. The main risk to humans from agricultural antibiotics is that the drugs used in animals are similar to those used in humans. As a result, resistance mechanisms developed in agricultural settings may be effective against both human and animal antibiotics (McGeer 1998).

In the last decade, for example, there has been a worldwide increase in the *Salmonella typhimurium* phage type DT104. It is common in cows and pigs and is also often isolated in humans with *Salmonella* infections. The phage type DT104 seems to have increased virulence, and it is additionally associated with multiple resistance to antibiotics (FVO 2001).

#### 4.10 THE IMPACT OF CLIMATE CHANGE

In recent years, there is stronger scientific evidence that climate is changing on a wide range of temporal and spatial scales due to both natural variability and external (e.g., anthropogenic) factors.

The 20th century has experienced an increase in precipitation of 0.5–1% over most mid- and high latitudes of the continents in the northern hemisphere, accompanied by an increase in the frequency of heavy precipitation events. It is likely that the global average water vapour concentration and precipitation will increase further during the 21st century. In areas where an increase in mean precipitation is anticipated, larger year-to-year variations in precipitation are very likely to occur (IPCC 2001).

The regional effects of climatic changes have, in fact, not been sufficiently analysed. An increasing occurrence of extreme weather conditions has also been registered in temperate zones — for example, the flooding events of the Rhine, Meuse, Oder, Danube, and Elbe in the 1990s and early 21st century (WHO 2002b). In general, it is likely that for many mid- and high-latitude areas, primarily in the northern hemisphere, statistically significant increases have occurred in the proportion of total annual precipitation derived from heavy and extreme precipitation events. It is likely that there has been a 2–4% increase in the frequency of heavy precipitation events over the second half of the 20th century (IPCC 2001).

By the year 2100, the mean sea level is projected to rise by 9–88 cm on a global scale. More than half of the world's population now lives within 60 km of the sea (WHO 2001). According to the WHO (2001), some of the most vulnerable regions are the “Nile delta in Egypt, the Ganges-Brahmaputra delta in Bangladesh, and many small islands including the Marshall Islands and the Maldives.”

The links between climate change and human health are still very poorly understood. However, climate change, together with other ecological and demographic changes, can have adverse effects on human health. This hypothesis may be supported by the concurrence of ongoing changes in patterns of human disease and the advent of climate changes (Kovats *et al.* 1999).

#### **4.10.1 Seasonality**

Seasonality in some disease incidence is closely connected to weather patterns. Vector-borne diseases in particular show a strong correlation to seasonal weather changes. For example, the death rate from malaria is highest at the end of the rainy season (Patz and Lindsay 1999).

Climatic cycling also seems to have a strong influence on the pattern of the emergence of diarrhoeal diseases. Several studies show a direct correlation between seasonal precipitation patterns and the occurrence of gastrointestinal diseases (Atherholt *et al.* 1998; Curriero *et al.* 2001). In some areas, weather patterns are changing also, with more prolonged droughts. Falling water levels and reduced river runoff increase the risk of cyanobacterial blooms and also

make water treatment more difficult, as the levels of sediments and organic material increase (Leder *et al.* 2002).

Apart from natural seasonal variability, climate is also influenced by other factors that may have an influence on weather events in several parts of the world at the same time. The El Niño Southern Oscillation is a complex climate phenomenon that can be detected every 2–7 years. The El Niño changes the oceanic currents and thereby the weather in many parts of the world. The regions where the phenomenon has a strong effect on climate are southern Africa, East Africa, Peru, and Southeast Asia (WHO 2001).

The El Niño effect forces warm equatorial Pacific water to flow from the western to the eastern Pacific, bringing heavy rainfall to some regions, while others suffer from drought (Patz and Lindsay 1999). Correlations could be found between the occurrence of the El Niño phenomenon and cumulative outbreaks of malaria, rodent-borne hantavirus, or Rift Valley fever in certain countries, especially during the strong El Niño years 1997 and 1998 (Patz and Lindsay 1999).

#### **4.10.2 Heavy rainfall and floods**

High rainfall and storms change the drainage conditions of flowing waters. The straightened courses of rivers and creeks, which result in improvement of land for cultivation by means of irrigation, drainage, or soil conservation, can also contribute to extreme flood situations. Microorganisms become mobile through dispersion of sediments. The avulsion of the surface of the soil and high discharge of settlement sewage increase the microbial burden, which can be transported over long distances as a result of the high flow rate of the water. Curriero *et al.* (2001) proved that outbreaks due to surface water contamination showed the statistically strongest association with extreme precipitation during the months of disease outbreaks. It is estimated that about 50% of waterborne outbreaks occur as a consequence of heavy rainfall events (Curriero *et al.* 2001). In a study on microbial loads of flowing waters during heavy rainfall, an increase of the concentrations of parasites was especially found in water samples that were taken parallel to the flood wave at 2-h intervals. It was determined that between 0.31% and 0.77% of the mean expected annual discharge can enter the waters during heavy rainfall events (Kistemann *et al.* 2002).

Indirect effects of floods on human health include damage of water supply systems, disruption of pipes, damage to sewage disposal systems, and insufficient supply of safe drinking-water. Standing water and migration of rodents or other host animals may expand the range of vector habitats, which

may lead to an increase in zoonotic and waterborne infectious diseases (WHO 2002b).

#### **4.10.3 Temperature**

The accumulation of greenhouse gases in the lower atmosphere due to human activities has led to a reduction of the efficiency with which the Earth's surface radiates heat to space. As a consequence, the global average surface temperature (the average of near surface air temperature over land and sea surface temperature) has increased since 1861, and scientists of the Intergovernmental Panel on Climate Change (IPCC) forecast an increase in average global temperature of 1–3.5 °C by the year 2100 (IPCC 2001).

During the 20th century, the average surface temperature experienced an increase of  $0.6 \pm 0.2$  °C. The decade from 1990 to 2000 was the warmest decade and 1998 the warmest year in the instrumental record since 1861. This increase in temperature is likely to have been the largest of any century during the past 1000 years (IPCC 2001).

The global rise in the mean annual temperature will facilitate spreading of tropical and subtropical diseases, such as malaria and leishmaniasis, to moderate latitudes (Haggett 1994). The extent of the rise in temperature and its spatial manifestation are, however, still speculative.

The 10 °C annual isotherms, which are regarded as the approximate northern boundary for the occurrence of leishmaniasis and its vectors in the Mediterranean area (Piekarski 1952), are moving farther north. These tendencies are already observable today, as sandflies have been identified in northern France and southern Switzerland (Ashford and Bettini 1987) and, in 1999, for the first time in Germany (Naucke and Pesson 2000).

### **4.11 SUMMARY AND CONCLUSION**

Anthropogenic and ecological factors influence the transmission of zoonoses. In this chapter, old and new risk factors for the emergence of these diseases were discussed in the framework of environmental and climate changes and human factors. Although it is still difficult to forecast the future impact of geographical and ecological effects on the distribution of infectious diseases, there is a greater awareness of this potential problem among policymakers, researchers, and others.

Increased risks for the transmission of waterborne and zoonotic diseases can be related to the mobility of populations, high density and close proximity of domestic and feral animal and human populations, agricultural practices, heavy rainfall events, and demographic factors. Improved surveillance and monitoring

and greater commitments to sanitation and water management are needed to detect global and ecological changes and to ensure protection from associated re-emerging and emerging infectious diseases.

#### 4.12 REFERENCES

- Ashford, R.W. and Bettini, S. (1987) Ecology and epidemiology: Old World. In *The Leishmaniasis* (ed. W. Peters and R. Killick-Kendrick), vol. I, pp. 366–414, Academic Press, London.
- Atherholt, T.B., LeChevallier, M.W., Norton, W.D. and Rosen, J.S. (1998) Effect of rainfall on *Giardia* and crypto. *J. Am. Water Works Assoc.* **90**, 66–80.
- Black, R.E., Morris, S.S. and Bryce, J. (2003) Where and when are 10 million children dying each year? *Lancet* **361**, 2226–2234.
- Bo, L., Ting-xin, D., Zhi-ping, L., Lou-wei, M., Zhu-xuen, W. and An-xiu, Y. (1993) Use of night soil in agriculture and fish farming. *World Health Forum* **14**, 67–70.
- Bottiger, M. and Christenson, B. (1998) [First study of hepatitis occurrence in Sweden: low immunity is associated with susceptibility to infection.] *Lakartidningen* **95**(16), 1801–1804 (in Swedish).
- Botzenhart, K. and Hahn, T. (1989) Vermehrung von Krankheitserregern im Wasserinstallationssystem. *GWF-Wasser/Abwasser* **130**, 432–439.
- Bradley, D.J. (1988) The scope of travel medicine. In *Proceedings of the 1st Conference on International Travel Medicine*, April, Zürich, pp. 1–9, Springer, Berlin.
- Buzby, J.C. (2001) Effects of food-safety perceptions on food demand and global trade. In *Changing Structure of Global Food Consumption and Trade*, pp. 55–66, Economic Research Service, US Department of Agriculture, Washington, DC.
- Callaway, T.R., Elder, R.O., Keen, J.E., Anderson, R.C. and Nisbet, D.J. (2003) Forage feeding to reduce preharvest *Escherichia coli* populations in cattle, a review. *J. Dairy Sci.* **86**(3), 852–860.
- Chin, J. (2000) *Control of Communicable Diseases — Manual*. American Public Health Association, Washington, DC.
- Christian, R.R. and Pipes, W.O. (1983) Frequency distribution of coliforms in water distribution systems. *Appl. Environ. Microbiol.* **45**, 603–609.
- Cole D.J., Hill, V.R., Humenik, F.J. and Sobsey, M.D. (1999) Health, safety and environmental concerns of farm animal waste. *Occup. Med.* **14**(2), 423–448.
- Cole D., Todd, L. and Wing, S. (2000) Concentrated swine feeding operations and public health: a review of occupational and community health effects. *Environ. Health Perspect.* **108**(8), 685–699.
- Crompton, D.W. and Savioli, L. (1993) Intestinal parasitic infections and urbanization. *Bull W. H. O.* **71**, 1–7.
- Curriero, F.C., Patz, J.A., Rose, J.B. and Lele, S. (2001) The association between extreme precipitation and waterborne disease outbreaks in the United States, 1948–1994. *Am. J. Public Health* **91**, 1194–1199.
- Deardorff, T.L. (1991) Epidemiology of marine fish-borne parasitic zoonoses. *Southeast Asian J. Trop. Med. Public Health* **22**, 146–149.
- Doyle, M.P. (1990) Pathogenic *Escherichia coli*, *Yersinia enterocolitica*, and *Vibrio parahaemolyticus*. *Lancet* **336**(8723), 1111–1115.

- Eisenstein, B.I. and Zaleznik, D.F. (2000) Enterobacteriaceae. In *Principles and Practice of Infectious Diseases* (ed. G.L. Mandell, J.E. Bennett, and R.D. Dolin), vol. 2, pp. 2294–2310, Churchill Livingstone, Philadelphia, PA.
- Exner, M. and Kistemann, T. (2003) Is there a need for better drinking-water quality management? In *Water Safety. Conference Abstracts*, pp. 11–18, Federal Environmental Agency, Berlin.
- Flemming, H.C. (1998) Biofilme in Trinkwassersystemen - Teil I: Übersicht. *GWF-Wasser/Abwasser* **139**, 65–71.
- FVO (2001) Food safety, antibiotic resistance, zoonosis report and more. *FVO Magazine*. Swiss Federal Veterinary Office, Bern ([www.foodsafety.ch](http://www.foodsafety.ch)).
- Gerba, C.P., Rose, J.B. and Haas, C.N. (1996) Sensitive populations: who is at the greatest risk? *Int. J. Food Microbiol.* **30**, 113–123.
- Githeko, A.K., Lindsay, S.W., Confalonieri, U.E. and Patz, J.A. (2000) Climate change and vector-borne diseases: a regional analysis. *Bull. W. H. O.* **78**, 1136–1147.
- Haggett, P. (1994) Geographical aspects of the emergence of infectious diseases. *Geogr. Ann., Ser. B* **76**(2), 91–104.
- Hartung, J., Marahrens, M. and von Holleben, K. (2003) Recommendations for future development in cattle transport in Europe. *Dtsch. Tierarztl. Wochenschr.* **110**(3), 128–130.
- Hrudey, S.E., Payment, P., Huck, P.M., Gillham, R.W. and Hrudey, E.J. (2003) A fatal waterborne disease epidemic in Walkerton, Ontario: comparison with other waterborne outbreaks in the developed world. *Water Sci. Technol.* **47**(3), 7–14.
- Hsu, B.M., Huang, C., Jiang, G.Y. and Hsu, C.L. (1999) The prevalence of *Giardia* and *Cryptosporidium* in Taiwan water supplies. *J. Toxicol. Environ. Health A* **57**, 149–160.
- IPCC (2001) *Third Assessment Report — Climate Change 2001: The Scientific Basis*. Contribution of Working Group I, Intergovernmental Panel on Climate Change, University Press, Cambridge (<http://www.ipcc.ch>).
- Jobin, W. (1999) *Dams and Disease*. E&FN Spon, London.
- Johl, M., Kerkmann, M.-L., Kramer, U. and Walter, R. (1991) Virological investigation of the river Elbe. *Water Sci. Technol.* **24**, 205–208.
- Kistemann, T., Classen, T., Koch, C., Dangendorf, F., Fischeder, R., Gebel, J., Vacata, V. and Exner, M. (2002) Microbial load of drinking water reservoir tributaries during extreme rainfall and runoff. *Appl. Environ. Microbiol.* **68**, 2188–2197.
- Kosek, M., Bern, C. and Guerrant, R.L. (2003) The global burden of diarrhoeal disease, as estimated from studies published between 1992 and 2000. *Bull. W. H. O.* **81**(3), 197–204.
- Kovats, R.S., Haines, A., Stanwell-Smith, R., Martens, P., Menne, B. and Bertollini, R. (1999) Climate change and human health in Europe. *Br. Med. J.* **318**, 1682–1685.
- Kurth, R. (1997) Infektionskrankheiten im Wandel. *Spektrum Wiss. Doss. Seuchen* **3**, 22–27.
- LeChevallier, M.W., Norton, W.D. and Atherholt, T.B. (1997) Protozoa in open reservoirs. *J. Am. Water Works Assoc.* **89**, 84–96.
- Leder, K., Sinclair, M.I. and McNeil, J.J. (2002) Water and the environment: a natural resource or a limited luxury? *Med. J. Aust.* **177**, 609–613.
- Levy, S.B. (1998) The challenge of antibiotic resistance. *Sci. Am.* **278**(3), 32–39.
- Ludwig, B., Kraus, F.B., Allwinn, R., Doerr, H.W. and Preiser, W. (2003) Viral zoonoses — a threat under control? *Intervirology* **46**, 71–78.
- Mantovani, M. and Prosperi, B. (1995) The Mediterranean and zoonoses. In *Information Circular*, vol. 1, pp. 2–13, World Health Organization/Mediterranean Zoonoses Control Centre, Geneva.

- Mara, D. and Cairncross, S. (1989) *Guidelines for the Safe Use of Wastewater and Excreta in Agriculture and Aquaculture*. World Health Organization, Geneva.
- McDade, J. (2002) Legionnaires' disease 25 years later: lessons learned. In *Legionella* (ed. R. Marre, Y.A. Kweik, C. Barlett, N.P. Cianciotto, B.S. Fields, M. Frosch, J. Hacker, and P.C. Lück), pp. 1–10, ASM Press, Washington, DC.
- McGeer, A.J. (1998) Agricultural antibiotics and resistance in human pathogens: Villain or scapegoat. *Can. Med. Assoc.* **159**(9), 1119–1120.
- Meslin F.X. (1992) Surveillance and control of emerging zoonoses. *World Health Stat. Rep.* **45**(2–3), 200–207.
- Moore, M., Gould, P. and Keary, B.S. (2003) Global urbanization and impact on health. *Int. J. Hyg. Health* **206**, 269–278.
- Müller, O. (2000) Russland - Vormarsch der Seuchen. *Dtsch. Arzt.* **97**, 2222–2224.
- Naucke, T.J. and Pesson, B. (2000) Presence of *Phlebotomus* (Transphlebotomus) *mascittii* Grassi, 1908 (Diptera: Phlebotomidae) in Germany. *Parasitol. Res.* **86**(4), 335–336.
- Neubauer, H., Sprague, L.D., Scholz, H. and Hensel, A. (2001) [*Yersinia enterocolitidis* infections: 2. Impact on human health.] *Berl. Munch. Tierarztl. Wochenschr.* **114**(3–4), 81–87 (in German).
- Patz, J.A. and Lindsay, S.W. (1999) New challenges, new tools: the impact of climate change on infectious diseases. *Curr. Opin. Microbiol.* **2**(4), 445–451.
- Patz, J.A., Graczyk, T.K., Geller, N. and Vittor, A.Y. (2000) Effects of environmental change on emerging parasitic diseases. *Int. J. Parasitol.* **30**, 1395–1405.
- Payment, P. and Franco, E. (1993) *Clostridium perfringens* and somatic coliphages as indicators of the efficiency of drinking water treatment for viruses and protozoan cysts. *Appl. Environ. Microbiol.* **59**, 2418–2424.
- Payment, P., Berte, A., Prevost, M., Menard, B. and Barbeau, B. (2000) Occurrence of pathogenic microorganisms in the Saint Lawrence River (Canada) and comparison of health risks for populations using it as their source of drinking water. *Can. J. Microbiol.* **46**, 565–576.
- Pearson, H., Clarke, T., Abbott, A., Knight, J. and Cyranoski, D. (2003) SARS: what have we learned? *Nature* **424**, 121–126.
- Piekarski, G. (1952) Begleittext zu Karte 31. In *Die geographische Verbreitung der Leishmaniasen und der Phlebotomen als ihrer Überträger im Mittelmeerraum 1906-1950*, pp. 97–102, Weltseuchen-Atlas I, Hamburg.
- RKI (2000) Wichtige Infektionskrankheiten in Deutschland - zur Situation im Jahr 1999, Teil 1: Darminfektionen (Gastroenteritiden) - 1. Folge. *Epidemiol. Bull.* **23**, 183–187.
- Royal, L. and McCoubrey, I. (1989) International spread of disease by air travel. *Am. Fam. Physician* **40**(5), 129–136.
- Sahin, O., Morishita, T.Y. and Zhang, Q. (2002) *Campylobacter* colonization in poultry: sources of infection and modes of transmission. *Anim. Health Res. Rev.* **3**(2), 95–105.
- Slifko, T.R., Smith, H.V. and Rose, J.B. (2000) Emerging parasite zoonoses associated with water and food. *Int. J. Parasitol.* **30**, 1379–1393.
- Szewzyk, U., Szewzyk, R., Manz, W. and Schleifer, K.H. (2000) Microbiological safety of drinking water. *Annu. Rev. Microbiol.* **54**, 81–127.
- Theron, J. and Cloete, T.E. (2002) Emerging waterborne infections: contributing factors, agents, and detection tools. *Crit. Rev. Microbiol.* **28**, 1–26.
- Till, D.G., McBride, G.B., Ball, A., Taylor, K. and Pyle, E. (2000) *Pathogens and indicators in New Zealand recreational freshwaters*. Poster abstract, First World Water Congress, Paris.

- Tully, D.N. and Shane, S.M. (1996) Husbandry practices as related to infectious and parasitic diseases of farmed ruminants. *Rev. Sci. Technol.* **15**(1), 73–89.
- UNFPA (2003) *The State of World Population 2003*. United Nations Population Fund, New York (<http://www.unfpa.org/swp/swpmain.htm>).
- UNPD (2003) *World Population Prospects: The 2002 Revision Population Database*. United Nations Population Division (<http://esa.un.org/unpp>).
- Van Olphen, M., de Bruin, H.A.M., Havelaar, A.H. and Schijven, J.F. (1991) The virological quality of recreational waters in the Netherlands. *Water Sci. Technol.* **24**(2), 209–211.
- WHO (2001) *Climate and Health*. Factsheet No. 266, World Health Organization, Geneva (<http://www.who.int/inf-fs/en/fact266.html>).
- WHO (2002a) *Diet, Nutrition and the Prevention of Chronic Diseases*. Report of a Joint WHO/FAO Expert Consultation, WHO Technical Report Series 916, World Health Organization, Geneva.
- WHO (2002b) *Floods: Climate Change and Adaptation Strategies for Human Health*. Report on a WHO Meeting, WHO Regional Office for Europe, World Health Organization, Copenhagen.
- Wilson, M.E. (1995) Travel and the emergence of infectious diseases. *Emerg. Infect. Dis.* **1**(2), 39–46.
- Woolhouse, M.E. (2002) Population biology of emerging and re-emerging pathogens. *Trends Microbiol.* **10**, 3–7.
- Worm, H.C., Schlauder, G.G. and Brandstatter, G. (2002) Hepatitis E and its emergence in non-endemic areas. *Wien. Klin. Wochenschr.* **114**, 663–670.

# 5

## The control envelope and risk management

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*R. Carr and J. Bartram*

### 5.1 INTRODUCTION

As discussed in chapter 1, emerging waterborne zoonoses will continue to pose new challenges to public health. As time passes, the spectrum of pathogens changes in response to pathogen evolution, environmental change, progressive technological developments, increasing scientific capacities, and changes in human behaviour and the vulnerability of populations (WHO 2003a). The foodborne and waterborne pathogens that currently pose the greatest threat to public health are also frequently the most recently identified (at least in developed countries) (Tauxe 2002). As the routes of transmission for an emerging/(re)emerging pathogen become known, strategies for controlling the pathogen are developed, and the threat from the pathogen is significantly reduced, bringing other pathogens to higher visibility (Tauxe 2002).

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This chapter explores different factors that are associated with the transmission of waterborne zoonotic diseases and evaluates the ability of current disease management strategies to effectively manage the risks they pose. It introduces the concept of a “control envelope,” which provides a framework for evaluating the threats from different pathogens against threats from well known benchmark organisms. Using the control envelope, emerging waterborne zoonotic pathogens can be assessed as being (a) firmly within the control envelope and thus do not pose unique management challenges; (b) on the edge of the control envelope, i.e., of concern but should be manageable with the right strategies; or (c) outside of the envelope and will require new approaches for managing associated health risks. The control envelope concept provides a useful starting point for developing risk management strategies, such as hazard analysis and critical control points (HACCP) and water safety plans (WSPs).

## 5.2 CONTROL ENVELOPE

Most emerging pathogens will have some similarities to existing pathogens and thus may be adequately controlled by current management strategies, technologies, and/or infrastructure. This package of interventions, henceforth referred to as the control envelope, includes the severity of health outcomes and the technological and organizational responses that may be used to control the disease. The control envelope offers a starting point for screening emerging waterborne pathogens against known properties of other pathogens (e.g., disease severity) and the effectiveness of current disease control measures. The concept of the control envelope provides a useful tool for predicting under which conditions certain pathogens will pose the greatest threats (see Table 5.1). A pathogen that is likely to exceed any one of the control envelope parameters could be flagged as a potential threat and management interventions introduced accordingly.

For example, in cases where inadequate water treatment or short-term under-performance leads to pathogen breakthrough, it is of much greater concern if the organism causes a severe illness (e.g., *Escherichia coli* O157:H7) than if the pathogen causes a mild self-limiting illness (e.g., norovirus) (see Table 5.1). Of course, if the pathogen causes a severe illness in a special subpopulation, such as individuals infected with human immunodeficiency virus (HIV), then the consequences can also be grave. *Cryptosporidium* causes a mild self-limiting illness in most individuals; in immunocompromised individuals, however, the illness may persist indefinitely (this is exacerbated by the fact that, until recently, there was no effective chemotherapy). In the 1993 *Cryptosporidium* outbreak in

Milwaukee, USA, of the 54 associated deaths, 85% of the victims were infected with HIV (Hoxie *et al.* 1997).

Table 5.1. Examples of known waterborne zoonotic pathogens and exceedances of control envelope parameters (from Mas-Coma *et al.* 1999; Hermon-Taylor and El-Zaatari 2004; WHO 2004)

Pathogen	Control envelope parameter of concern
<i>Cryptosporidium parvum</i>	Widespread domestic and wild animal reservoirs Environmentally persistent Resistant to treatment processes Low infectious dose Limited immune response Vaccine development unlikely Severe outcomes in immunocompromised populations No effective treatment
<i>Toxoplasma gondii</i>	Widespread domestic and wild animal reservoirs Severe outcomes in immunocompromised and fetuses Environmentally persistent Resistant to treatment processes
<i>Campylobacter jejuni</i>	Widespread domestic and wild animal reservoirs Antibiotic-resistant strains Severe outcomes in immunocompromised and delayed sequelae Low infectious dose
<i>Escherichia coli</i> O157:H7	Widespread in domestic animal reservoirs Severe outcomes in children Low infectious dose Persistent in certain environments Resistant to antibiotics
<i>Mycobacterium avium</i> ssp. <i>paratuberculosis</i>	Causes severe illnesses in susceptible individuals Infects a wide range of animal hosts, both domestic and wild, and is widespread in various regions Difficult to isolate, culture, and identify Evades the immune system by surviving in macrophages Can be carried asymptotically for years Environmentally persistent Resistant to heat and chlorination and can survive in biofilms and distribution systems Has multiple transmission routes, including drinking-water, recreational water contact, and the inhalation of aerosols Resistant to a number of antibiotics and may reappear after treatment is completed

Pathogen	Control envelope parameter of concern
Hepatitis E virus (HEV)	Geographic spread and frequency of infection of animal reservoirs unknown Severe outcomes in pregnant women Low infectious dose Detection and cultivation difficult Thought to be environmentally persistent Thought to be resistant to treatment processes No medical treatment available
<i>Fasciola hepatica</i>	Widespread in domestic and wild animals in certain regions Disease of moderate to high severity Low infectious dose Limited immune response Environmentally persistent Resistant to treatment processes Can infect a variety of snail intermediate hosts in a wide range of habitats Can develop drug resistance Human variant has novel properties that facilitate the transmission through drinking-water

The control envelope will differ significantly from country to country and will depend on many different factors, including climate, level of technological development, access to water supply and sanitation, farming practices, etc. For example, waterborne zoonotic pathogens such as certain strains of *E. coli* (non-enterotoxigenic) or *Salmonella* will pose little threat to people with access to well managed water supplies where disinfection is routinely practised, but could contribute to a significant burden of waterborne disease in situations where drinking-water is not adequately disinfected.

Each of the following subsections looks at key areas for the control of emerging waterborne diseases, including livestock and animal management; source water protection; water storage, treatment, and distribution; and point of use/household. For each key area, pathogen–human factors, technological/management interventions, and examples of factors that might lead to a breach in the control envelope are discussed. In addition, some relevant pathogen properties and human characteristics are briefly considered at the end of the section.

### 5.2.1 Livestock and animal management

Livestock and animal management is a key component of the control envelope because it involves prevention of pollution at the source. Table 5.2 gives an overview of some important disease management considerations. Chapters 24 and 25 provide more details on livestock and animal management strategies to reduce the transmission of waterborne zoonoses.

Table 5.2. Control envelope for livestock/animal management

Pathogen–human factors	Technological/management interventions	Examples of factors that might lead to a breach in the control envelope
Wide range of zoonotic reservoirs (domestic/wild)	Vaccination of domestic animals	Use of antibiotics as growth promoters has led to the creation of multiple drug-resistant pathogens and in some cases may have led to the transfer of virulence genes to other pathogens <i>C. jejuni</i> rapidly spread to other chickens in a flock through non-disinfected water Infected livestock introduced into a country due to improper quarantine procedures Pregnant women contracting toxoplasmosis from handling cat litter boxes
Geographic range of zoonotic reservoirs	Hygienic rearing conditions for animals	
Proximity to human populations	Adopting water quality and food quality standards for livestock	
Exposure to antibiotics	Treatment of animal wastes at source	
	Exclusion of animals from catchment basins	
	Chemotherapy for livestock (only as necessary)	
	Stop use of antibiotics as growth promoters	
	Develop probiotics to exclude pathogens or reduce shedding from the intestinal tracts of domestic livestock	
	Controlling the international trade of livestock and exotic pets	

#### 5.2.1.1 Pathogen–human factors

Important control envelope considerations for livestock and animal management include the host specificity of the pathogen, i.e., can it infect a wide range of both domestic and wild animals or just a few. Likewise, the geographic spread of animal reservoirs in the catchment basin is a key factor. The exposure of domestic animals to antibiotics can select for antibiotic-resistant pathogen strains and in some cases may promote the transfer of

virulence genes from one bacterial species or strain to another (Tauxe 2002). The proximity of humans to animal reservoirs will increase the potential for human exposure to emerging waterborne (and other) zoonoses. Other examples of important considerations are presented in Table 5.2.

### *5.2.1.2 Technology/management interventions*

For livestock/animal management, a number of technologies and interventions to control disease transmission are available. The interventions fall roughly into two categories: 1) preventing or treating infections in animals (e.g., vaccination, adopting water and food quality standards for livestock, hygienic rearing conditions, chemotherapy of infected animals); and 2) preventing pathogens from entering water sources (e.g., waste treatment at source, exclusion of animals from catchment basins, establishing vegetative buffer zones, regulating the international trade in livestock and exotic pets). For example, in the 1980s, *Salmonella* Enteritidis swept through chickens worldwide, but Australia and New Zealand managed to avoid this, at least in part through strict quarantine procedures (Crump *et al.* 2001).

### *5.2.1.3 Examples of factors that might lead to a breach in the control envelope*

Antibiotic-resistant strains of *Campylobacter jejuni* infecting humans in the USA have been directly linked back to poultry (CDC 2002). *Campylobacter jejuni* has been observed to be rapidly transmitted through a flock of chickens by contaminated, non-disinfected water, and *E. coli* O157:H7 may be transmitted to other cattle through contaminated water troughs (Tauxe 2002). *Mycobacterium avium* (ssp. *paratuberculosis*) (MAP), thought to be a cause of Crohn's disease in humans, was introduced into sheep, cattle, and possibly humans in Iceland by the importation of infected sheep (see Box 5.1) (Hermon-Taylor and El-Zaatari 2004).

## **5.2.2 Source water protection**

Table 5.3 describes some elements associated with the control envelope for source water protection. Chapter 26 includes more information on catchment protection from livestock and other animals.

### *5.2.2.1 Pathogen–human factors*

Some of the factors that influence disease transmission in animals/livestock are also relevant to source water protection — e.g., the prevalence and geographic spread of infected animals in the catchment basin. For example, in

a study in the United Kingdom, Chapman (2000) found that 16% of the cattle in herds were infected with *E. coli* O157:H7. Other studies have indicated that from 1 to 10% of cattle in North America and Europe are infected with *E. coli* O157:H7. *Escherichia coli* O157:H7 has been found to infect cattle, sheep, deer, and chicks (Armstrong *et al.* 1996). A significant percentage of livestock herds in Europe and North America test positive for MAP, and MAP has been found to infect a wide range of both domestic and wild animals (Hermon-Taylor and El-Zaatari 2004). Pathogens that are environmentally persistent and resistant to treatment processes will generally pose management challenges (e.g., *Cryptosporidium*, *Giardia*, *Fasciola hepatica*).

Box 5.1. Introduction of MAP-infected sheep and association with Crohn's disease in Iceland

In the 1930s, 20 sheep were imported into Iceland from Germany. Although the sheep appeared healthy, at least some of them were asymptotically infected with *Mycobacterium avium* ssp. *paratuberculosis* (MAP). The sheep were distributed to 14 farms. In 1938, at five of the original farms, sheep were diagnosed with Johne's disease (a disease in livestock that has symptoms similar to those of Crohn's disease in humans and is caused by MAP). The disease eventually spread to cattle on the same farms and slowly spread throughout all of Iceland's sheep population (Hermon-Taylor and El-Zaatari 2004).

MAP has been reported as a probable cause of Crohn's disease in humans and is frequently identified in patients with Crohn's disease (Hermon-Taylor *et al.* 1998; Sechi *et al.* 2001). Prior to the 1930s, Crohn's disease had never been recognized in Iceland; subsequently, the increase in the disease in human populations has mirrored the spread of MAP throughout livestock on the island (Hermon-Taylor and El-Zaatari 2004). In Iceland, Crohn's disease increased from 0.4 cases per 10<sup>5</sup> population in the 1950s to 5.6 cases per 10<sup>5</sup> population in the 1990s — a 1300% increase (Bjornsson 1989; Bjornsson *et al.* 1998; Bjornsson and Johannsson 2000; Hermon-Taylor and El-Zaatari 2004).

MAP is a pathogen that would not easily be managed within the current control envelope (see Table 5.1). For more information concerning MAP and its association with Crohn's disease, see Hermon-Taylor and El-Zaatari (2004).

### 5.2.2.2 Technological/management factors

Strategies for source water protection incorporate both management interventions and technological solutions. Management can include animal exclusion from catchments and establishing vegetative buffer zones. Technological solutions include installing wastewater treatment facilities (or

upgrading old ones), repairing leaking sanitation systems, and covering water storage reservoirs.

Table 5.3. Control envelope for source water protection

Pathogen–human factors	Technological/management interventions	Examples of factors that might lead to a breach in the control envelope
Proximity of zoonotic reservoirs to water sources	Exclusion of animals from vulnerable areas (fencing)	Heavy rainfall events often precede disease outbreaks
Ubiquity of animal reservoirs in catchment basin	Human/animal waste treatment at source	Failure of animal waste storage lagoons during severe storm events
Human and animal waste treatment	Wastewater treatment	Failure to site or protect wells adequately
Soil runoff potential	Buffer zones	Lack of vegetative buffer zones
Integrity of sanitation systems	Protection of wells/springs, groundwater	Animals allowed access to riparian zones
Use of human/animal wastes as fertilizers	Reduction of soil erosion	
Environmental persistence	Repair of leaking sanitation systems	
Resistance to treatment processes	Covering drinking-water reservoirs	
	Treatment of animal/human wastes prior to use as fertilizers	

### 5.2.2.3 *Examples of factors that might lead to a breach in the control envelope*

Heavy rainfall events wash large amounts of contaminants, including animal faeces, into watersheds. These severe weather events often precede waterborne disease outbreaks. Curriero *et al.* (2001) analysed disease outbreak data in the USA and compared the data with rainfall events from the period 1948–1994. Sixty-eight per cent of the disease outbreaks were significantly associated with heavy rainfall (above the 80th percentile for severity of rainfall). Outbreaks associated with groundwater sources occurred 2 months after severe rainfall events. Among the contributing factors in the 2000 outbreak of *E. coli* O157:H7 in Walkerton, Canada, was a failure to protect groundwater from animal runoff. Additionally, the well was shallow (5–8 m in depth) and located an insufficient distance (less than 100 m) from sources of animal manure (Hrudey 2003). A 1996 US Environmental Protection Agency (EPA) survey of rural wells found 40% contaminated with *E. coli* (not necessarily O157:H7) (Tenenbaum 2002).

### 5.2.3 Water storage, treatment, and distribution

Water storage, treatment, and distribution form the core components of the traditional water supply industry and have always been considered as key elements for protecting public health. Examples of important control envelope considerations for these processes are presented in Table 5.4. Treatment technologies for both animal and human wastes are discussed in more detail in chapters 25 and 26.

Table 5.4. Control envelope for water storage, treatment, and distribution

Pathogen–human factors	Technological/management interventions	Examples of factors that might lead to a breach in the control envelope
Environmental persistence	Sanitary surveys to identify sources of contaminants	Severe storm events that overload or incapacitate treatment facilities
Resistance to treatment processes	Cover water storage reservoirs or store in confined aquifers	Animal access to storage reservoirs (e.g., birds)
Ability to grow in environment	Change treatment technologies	Normal fluctuations in treatment processes
	Change disinfectants	Over-reliance on microbial indicators
	Optimize treatment processes	Ingress of contaminants into distribution system
	Process monitoring to complement indicator organism monitoring	Loss of pressure in distribution system
	Repair distribution systems	
	Manage water distribution systems to reduce development of biofilms	
	Repair leaking sewers	

#### 5.2.3.1 Pathogen–human factors

Environmental persistence and resistance to treatment processes are important pathogen characteristics in water storage, treatment, and distribution. *Cryptosporidium* and *Giardia* are both persistent environmentally and extremely resistant to chlorine. *Escherichia coli* has been found to survive in biofilms in distribution systems even when high residual chloramine concentrations are present (Williams and Braun-Howland 2003). *Mycobacterium avium* complex (MAC) is also resistant to chlorine and can grow in biofilms (AWWA 1999). Pathogens that have more severe outcomes are important because short-term under-performance can lead to pathogen breakthrough.

### 5.2.3.2 *Technological/management interventions*

Prevention of disease transmission through water storage, treatment, and distribution is to some extent a function of system design. The supply of safe water requires a multi-barrier approach that compensates for short-term treatment performance fluctuations. Conducting sanitary surveys is an important procedure for identifying potential sources of contamination. Optimizing water treatment performance through process and indicator organism monitoring and selecting appropriate treatment processes are also necessary. Covering reservoirs or using confined aquifers for water storage can reduce contaminant ingress. Water distribution systems should be adequately maintained and kept under positive pressure. Distribution systems should be managed to control biofilm formation.

### 5.2.3.3 *Examples of factors that might lead to a breach in the control envelope*

Even in well managed water treatment systems and settings where health care infrastructure is adequate, risk management strategies will occasionally fail. For example, the efficiency of water treatment processes varies over time and spatially through the treatment system (Gale and Stanfield 2000). Events such as heavy rainfall, system overloading, short-circuiting, membrane failures, or inadvertent recycling of filter backwash can cause pathogen breakthroughs. The May 2000 *E. coli* O157:H7 outbreak in Walkerton, Canada, that affected over 2000 people was a result of the failure to protect drinking-water supplies from farm runoff, a failure in the water disinfection processes, and a failure to communicate laboratory results to local public health officials (Kondro 2000; WHO 2004).

Moreover, monitoring for pathogens or indicator organisms is not conducted on a real-time basis, and thus contamination is already through the system before it has been detected. Even where routine monitoring is in place, contamination slugs can be missed. Gale and Stanfield (2000) modelled *Cryptosporidium* breakthrough events and demonstrated that a significant proportion (33%) of random 100-litre spot samples would detect zero oocysts, but that a very small percentage of samples would contain hundreds or even thousands of oocysts. The high-concentration samples could easily be missed by the monitoring process. This was the case for the 1993 *Cryptosporidium* outbreak in Milwaukee, USA, that affected 403 000 people (MacKenzie *et al.* 1994). Similarly, *Cryptosporidium* was detected in 26% of filtered drinking-water samples taken from 82 different treatment plants in one survey (Aboytes and LeChevallier 2003).

Friedman *et al.* (2003) demonstrated that significant volumes of water could enter the distribution system through small leaks when pressure in the system was not maintained. Also, Kirmeyer *et al.* (2001) showed that soil and water in close proximity to distribution systems often contained evidence of faecal contamination, including the presence of enteric viruses, and thus posed a potential contamination risk during low-pressure events.

#### 5.2.4 Point of use/household

The point of water use and the household represent another element of the control envelope. Poor conditions of water, sanitation, and hygiene (personal, domestic, and food) can affect the transmission of waterborne zoonoses at the point of water use (including in hospitals and other facilities). Table 5.5 presents examples of important point-of-use considerations in the transmission of waterborne zoonoses.

Table 5.5. Control envelope for point of use/household

Pathogen–human factors	Technological/management interventions	Examples of factors that might lead to a breach in the control envelope
Transmission through poor personal, domestic, or food hygiene	Point-of-use water treatment Improve personal, domestic, and food hygiene	Poorly designed sanitation systems or cross-connections Pregnant women handling litter boxes
High probability of secondary or person-to-person transmission	Access to adequate household sanitation Access to improved water supply Prevent cross-connections	Unsanitary conditions that lead to exposure to diseases transmitted by rats (e.g., leptospirosis, HEV)
Reservoirs include domestic animals or exotic animals kept as pets	Regulate the keeping of exotic pets Vaccination/chemotherapy of household pets	Poor personal, domestic, and food hygiene
Vaccination	Protect household water/food supply from animals	
Immune status	Risk communication to sensitive subpopulations	

##### 5.2.4.1 Pathogen–human factors

Pathogens that infect household pets (e.g., toxoplasmosis in cats) or other animals that might be found in living spaces (e.g., *Leptospira* or HEV, which can infect rats) pose a threat. Diseases that have high secondary infection rates

through person-to-person spread (e.g., *E. coli* O157:H7) are also of concern. People that do not have access to adequate water supply and sanitation and/or practise poor hygiene habits will be at increased risk. A number of human factors will also be important at this point, including immune status (normal or immunocompromised), vaccination, and a number of other factors that will be further discussed in section 5.2.6.

#### 5.2.4.2 *Technological/management interventions*

Hygiene education and increasing access to improved water supply and sanitation will impact the household transmission of waterborne zoonoses (and other waterborne diseases as well). Designing sanitation systems and identification and removal of household cross-connections are also important interventions. Risk communication targeted to vulnerable populations (e.g., pregnant women, immunocompromised individuals) has been effective for helping to control health risks in some cases. For example, pregnant women could be advised about the dangers of handling cat litter boxes. People suffering from chronic liver diseases could be discouraged from eating raw oysters.

#### 5.2.4.3 *Examples of factors that might lead to a breach in the control envelope*

Many cats are infected with *Toxoplasmosa gondii* and can transmit this disease to humans, mainly through contact with litter boxes, but possibly also through contaminated water in contact with food (e.g., in the garden) or by being consumed directly (e.g., if a household well is poorly protected). Pregnant women and HIV-infected individuals are at increased risk from toxoplasmosis because the consequences are much more severe (CDC 2003). In the 2003 severe acute respiratory syndrome (SARS) outbreak, a proportion of victims in one apartment block were thought to have been exposed to the SARS virus by inhalation of faecal droplets. People were exposed to faecal droplets containing the SARS virus through a combination of a poorly designed sanitation system and a ventilation system that pulled the faecal droplets into their apartments (SHWF 2003).

### 5.2.5 **Pathogen properties that influence the control envelope**

Pathogen properties will have a great impact on various parameters of the control envelope. Table 5.6 describes some pathogen factors and how they influence the control envelope. Characteristics of specific bacteria, viruses, protozoa, fungi, and helminths are described in more detail in Section V.

A number of pathogen properties impact the way in which they can be managed within the current control envelope. Pathogen virulence and infectivity can differ by orders of magnitude between different strains. Many of the recently emerged pathogens have very low infectious doses (ID) (Tauxe 2002). For example, *E. coli* O157:H7 may have an ID of 50 or less according to the study of an outbreak associated with the consumption of dry cured salami in the USA (CDC 1995). Other pathogenic strains of *E. coli* have much higher IDs, in the order of 100 000–1 000 000 organisms (Teunis *et al.* 1996). Part of this difference may be attributed to the acquisition of a new characteristic — for example, the transfer of a virulence gene from another organism or the ability to survive in low-pH environments. *Escherichia coli* O157:H7 can survive under certain circumstances at pHs as low as 2 (Conner and Kotrola 1995) and can thus be transmitted in acidic foods, such as apple cider (Miller and Kaspar 1994).

Table 5.6. Pathogen properties and how they impact the control envelope

Properties	Examples of potential control strategies
Virulence/infectivity	Surveillance of immunocompromised populations
Severity of outcome	
Epidemic potential	Surveillance of human and animal populations for infection and disease
Environmental survival/growth	
Resistance to water treatment processes	Development of isolation, identification, and culture techniques/technologies
Lack of host specificity	Research on pathogen virulence/transmission factors
Ability to develop new characteristics (e.g., antibiotic resistance)	Vaccine/chemotherapy development
Susceptibility to host immune response	Elimination of non-essential use of antibiotics
Susceptibility to chemotherapeutic agents	Research on treatment trains and pathogen removal

The ability of an organism to change is an important characteristic. Some pathogens can rapidly develop new characteristics, such as new surface proteins, to evade host immune responses (e.g., *Plasmodium falciparum* or HIV) or develop antibiotic resistance. For example, one study demonstrated that *C. jejuni* in chickens were converted from 100% sarafloxacin-susceptible strains to 100% sarafloxacin-resistant strains within days of first being exposed to the antibiotic (McDermott *et al.* 2001). There is also some evidence to suggest that sublethal doses of antibiotics increase the transfer of virulence genes between different strains of bacteria, potentially leading to the development of new serotypes — possibly even *E. coli* O157:H7 (Zhang *et al.* 2000; Tauxe 2002).

Interventions to control the disease risks from emerging waterborne zoonoses will often need to be tailored to the specific organism and may include:

- the development of rapid and simple isolation, identification, and/or culture techniques/technologies;
- improved human and animal surveillance to identify emerging pathogens of possible concern;
- reducing the use of antibiotics for growth promoters in livestock;
- research on vaccines and medicine for both humans and animals; and
- research on effective treatment trains and pathogen inactivation.

### 5.2.6 Human characteristics and their impact on the control envelope

Human characteristics, including genetic, socioeconomic, and behavioural factors, are all likely to have a profound impact on the transmission of waterborne zoonoses. Table 5.7 gives examples of some human characteristics and how they affect the control envelope.

Table 5.7. Human characteristics and their impact on the control envelope

Human characteristics	Technological/management interventions
Immune status	Education of public, especially high-risk populations
Age	Identifying high-risk populations
Pregnancy	Improvement of hygiene practices
Medications taken	Vaccination
Presence of other diseases	Research into new vaccines/chemotherapeutic agents
High-circulation vs. low-circulation environments	Increasing access to improved water supply and sanitation
Genetic susceptibility	Increasing the distance between animals and humans
Malnutrition	Behaviour modification (e.g., cooking food thoroughly)
Access to improved water supply and sanitation	Point-of-use water treatment
Personal, domestic, and food hygiene behaviour	
Proximity to animal reservoirs	

Pathogen properties and human characteristics interact to determine disease transmission. Human immune status is a key factor and can be altered in several ways, depending on the environment. In conditions where there is high circulation of pathogens (i.e., sanitary standards are low), early exposure to a pathogen such as hepatitis A virus (HAV) may lead to a mild self-limiting

illness and lifelong immunity. The same virus can cause a relatively serious disease in people that are infected as adults (i.e., in low pathogen circulation environments). Other diseases can cause acute illnesses (e.g., *E. coli* O157:H7) or chronic infections in children in the same environments, potentially leading to serious health consequences (e.g., hepatitis B virus [HBV]).

Human immune status can be affected by diseases (HIV, cancer), age, drugs, pregnancy, malnutrition, genetics, etc. According to Exner and Kistemann (2003), approximately one out of six people in the United Kingdom, Germany, and the Netherlands fits the definition of immunocompromised. The simple act of taking an antacid tablet for indigestion can make an individual more susceptible to infection with a pathogen that would not normally survive in the acidic environment of the stomach. Behaviour also plays a very important role with regard to disease susceptibility. For example, people that eat inadequately cooked meat or seafood — especially shellfish — increase their risks of contracting an infection.

Important interventions to address human dimensions of the control envelope largely focus on improving access to water supply and sanitation, risk communication, vaccine/medicine development, and behaviour modification. These interventions have been discussed elsewhere in this chapter in more detail.

### 5.3 RISK MANAGEMENT

Risk management strategies include HACCP-like approaches that identify control points and use data from epidemiological studies (where they exist), microbiological evaluations of water or food products, and quantitative microbial risk assessment (QMRA) to develop WSPs that are based on the multi-barrier principle.

The control envelope not only covers interventions from farm to fork but goes beyond, because it can also include altering human and animal immunity through vaccination and other processes. Effective management strategies will require a vast range of expertise, including veterinarians, range management experts, farmers, water resource managers, hydrogeologists, civil engineers, health professionals, and others. Prevention of pollution at the source is the most effective solution, and thus management strategies that focus on reducing the pathogens in animal reservoirs or treating waste that contains the pathogens before it reaches water sources are likely to have the greatest impact on health protection.

### 5.3.1 HACCP

HACCP is a systematic approach to the identification, assessment, and control of hazards (Codex Alimentarius Commission 1997) during production, processing, manufacturing, preparation, and use of food, water, or other substances to ensure that the food, water, or other substances are safe when consumed or used. The HACCP system incorporates safety control into the design of the whole process rather than relying solely on end-product testing. The HACCP approach provides a preventive and thus a cost-effective method for ensuring product safety. Initially created for the food processing industry, HACCP has subsequently been applied to a number of different processes, including drinking-water treatment, aquaculture production, and the use of sewage sludge in agriculture (Havelaar 1994; Garrett *et al.* 1997; Godfree 2000).

Application of HACCP systems in many different manufacturing or treatment processes has led to more efficient prevention of adverse health effects associated with the consumption or use of the products. For example, the implementation of an industry-wide HACCP programme for seafood processors in the USA is thought to have averted 20–60% of the normal number of seafood-borne illnesses (Birley and Lock 1998). A similar programme for the prevention of foodborne listeriosis in the USA reduced the incidence and mortality of this disease by 44% and 49%, respectively, over a period of 4 years (Billy 1997).

Limited evidence suggests that implementation of HACCP-like processes into a water quality assurance framework (WSP) will also reduce water-related disease incidence and outbreaks. For example, in the USA, disease outbreaks associated with drinking-water supplied from surface water decreased from 31.8% of all drinking-water outbreaks in 1995–1996 to 11.8% in 1997–1998 (Barwick *et al.* 2000). Much of this reduction was attributed to a partnership between the US EPA and drinking-water agencies to implement HACCP-like preventive procedures designed to optimize water treatment at their facilities (Barwick *et al.* 2000; Godfree 2000). The US EPA Interim Enhanced Surface Water Treatment Rule (US EPA 1998) also includes HACCP-like strategies for reducing drinking-water-related disease (Godfree 2000). In north-west England, the implementation of a HACCP-like process to protect the watershed has at least partially contributed to a lack of *Cryptosporidium* outbreaks in the catchment basin since 2000 and a general decline in the background incidence rate from 1400 cases per year to approximately 400 per year in each of 2001 and 2002 (Godfree 2003). It is likely that further use of these programmes in water treatment, water supply, and water reuse processes will have similar results.

Deere *et al.* (2001) outlined the development of a HACCP system for drinking-water and presented some case-studies for identifying critical control points.

### 5.3.2 Epidemiological evidence and QMRA

Epidemiological studies are needed to determine the actual disease transmission due to a specific exposure. Data from epidemiological studies are crucial for determining actual health risks, but studies must be large enough to capture significant differences in levels of disease due to a specific exposure. Additionally, epidemiological studies can be expensive.

QMRA (further discussed in chapter 29) provides an alternative or supplementary framework to epidemiology for identifying potential excess risk for defined pathways of particular pathogens from source to recipient. QMRA translates the environmental occurrence of pathogens into the probability of infection (microbial risk) following the paradigm used for chemical risk assessment and has the potential to provide much greater sensitivity in identifying risk. The usefulness of QMRA, however, is dependent upon the quality and appropriate use of available data for describing the occurrence, persistence, and human dose–response of pathogens in the environment (Petterson and Ashbolt 2003).

For emerging pathogens, data on their environmental occurrence may be very limited. Before QMRA can be effectively used as a tool to manage risk, techniques and technologies for identifying, quantifying, and assessing the viability of pathogens need to be developed (see Section VI for further information). Similarly, research on identifying appropriate indicator organisms for emerging waterborne zoonoses or other key parameters for monitoring (e.g., particle counts, turbidity) needs to be conducted.

Given the vagaries in data on immune status and variability, QMRA can only predict potential excess risks for specific pathogens and pathways. Further, limited dose–response data are available, especially for potential animal reservoirs, and in some cases these data vary by more than 1000-fold for different strains of the same pathogen. For the time being, therefore, QMRA should not be seen as directly comparable to epidemiological data, but rather as a tool to assess the sensitivity of changes in performance of (treatment) elements and to identify major risk groups and pathways (Petterson and Ashbolt 2003).

### 5.3.3 Water safety plans

WSPs are used to develop a systematic programme for protecting water quality from catchment to tap. In the case of waterborne zoonoses, important elements of the plan will include managing animal disease reservoirs outside what

normally might be considered the responsibilities of a water supplier. This aspect of pollution prevention is critical, as large percentages of animals may be carriers of pathogens. Similarly, infected animals may be widespread within the catchment basin. For example, *Cryptosporidium*, MAP, *C. jejuni*, and *F. hepatica* can infect a wide range of both domestic and wild animals and may infect animals throughout the catchment basin. WSPs could be expanded to include the delivery of appropriate quality water to livestock.

Both HACCP and WSPs should include analysis of the health impacts that might be associated with infrequent catastrophic system failures (e.g., flooding of a treatment facility or sabotage) and develop management strategies for such events to control health impacts. For example, WSPs should include procedures for informing health authorities in emergencies and alerting the public in the case of a boil water notice.

For water supply services, water quality management is critical. The detection of waterborne zoonotic pathogens in both raw water and water delivered to consumers is often slow, complex, and costly, which limits early warning capability and affordability. Reliance on water quality determination alone is insufficient to protect public health (UNESCO-WWAP 2003).

The most effective and protective means of consistently ensuring a supply of acceptably safe water is the application of a preventive “quality assurance” framework. A preventive framework, developed to manage water quality, works in an iterative cycle, encompassing assessment of public health concerns, risk assessment, establishing health-based water quality targets, and risk management. Feeding into this cycle are the determination of environmental exposure levels for both humans and animals and the estimation of what constitutes a tolerable risk (see chapter 28) (UNESCO-WWAP 2003; WHO 2004).

According to UNESCO-WWAP (2003), water quality management may be through a combination of protection of water sources, control of treatment processes, and management of the distribution and handling of water. It has five key components:

- (1) water quality targets based on critical evaluation of health concerns (both human and animal health);
- (2) system assessment to determine whether the water supply chain (up to the point of consumption/use) as a whole can deliver water of a quality that meets the above targets;
- (3) monitoring of the control points in the supply chain, which are of particular importance in securing water safety;

- (4) management plans documenting the system assessment and monitoring and describing actions to be taken under normal and incident conditions (this includes documentation and communication); and
- (5) a system of independent surveillance that verifies that the above are operating properly.

It is important that water quality targets, defined by the relevant national health authority, are realistic under local operating conditions and are set to protect and improve public health. Formal water supply agencies have a basic responsibility to provide safe water and would be expected to develop and implement management plans to address points 2–4 above (UNESCO-WWAP 2003).

The management plans, or WSPs, developed by water suppliers should address all aspects of the water supply and focus on the control of water production, treatment, and delivery of drinking-water. The control of the microbial quality of drinking-water requires the development of WSPs that, when implemented, provide the basis for process control to ensure that pathogen loads are acceptable. Implicit within this process is that a tolerable disease burden has been defined at national and local levels and that water quality targets, which have been established to improve public health, are achievable (UNESCO-WWAP 2003).

#### **5.3.4 Disease surveillance and targeted studies**

Surveillance of public health status and trends is a very important tool for risk management. As the disease transmission characteristics of pathogens become better known, then methods for their control can be developed. Similarly, surveillance facilitates the prioritization of risk management by putting disease risks into the context of the overall burden of waterborne disease within a society (see chapter 28).

Surveillance can be used to answer a number of questions. First, is the disease (or severe outcome) present in the population (immunocompetent or immunocompromised populations)? If the disease or severe outcome exists in the population, is there evidence of transmission through water? Another important consideration is the ability of the surveillance system to detect emerging diseases, and at what level.

Routine surveillance of currently known waterborne zoonoses, including *Cryptosporidium*, *E. coli* O157:H7, etc., is important. However, to identify emerging threats, Tauxe (2002) suggests that increased surveillance efforts be directed towards pathogens that cause severe disease in immunocompromised

individuals and further investigation of organisms that cause asymptomatic infections in various animals.

In some ways, immunocompromised individuals are the sentinels of emerging zoonotic infections. Evidence that humans are being exposed to emerging or re-emerging pathogens will first appear in these individuals. Severe illnesses will be more common in these subpopulations, increasing the probability that the pathogen will be identified/isolated from blood or other normally sterile tissues rather than in food or faeces, where there are large numbers of other organisms (Tauxe 2002). For example, *C. jejuni* was first recognized as a cause of bacteraemia in children with leukaemia (King 1962). It was only after selective isolation procedures were developed that the organism could be identified in the faeces of children with diarrhoea (Tauxe 2002).

According to Tauxe (2002), many of the emerging zoonoses identified in recent years share similar features, including the following:

- cause asymptomatic infections in their animal hosts;
- animal hosts act as long-term carriers of the organism;
- cause infections in humans in relatively low doses; and
- are transmitted through products, such as water or foods, that are not cooked before consumption.

Therefore, closer surveillance of asymptomatic infections in animals may yield important clues for managing emerging zoonotic pathogens.

Targeted studies of populations looking for serological evidence of infection can also be useful. For example, cryptosporidiosis was often thought to be largely a developed country problem. However, when studies started to look at serological evidence of *Cryptosporidium* infection in various developing countries, they found it at very high levels. In Anhui, China, over half of the children by age 5 demonstrated antibodies to *Cryptosporidium*. In a poor area of Brazil, over 90% of the children developed antibodies to *Cryptosporidium* by the age of 1 (Ungar *et al.* 1988; Zu *et al.* 1994).

### 5.3.5 International networks

The international trade in food products and the general growth in international travel make it increasingly important to develop international networks to monitor the spread of both known and emerging pathogens. Products grown with contaminated water may cause health effects at both the local and international levels, and international trade in agricultural products across regions is growing. Exports of contaminated fresh produce from different geographical regions can facilitate the spread of both known pathogens and

strains with new virulence characteristics into areas where the pathogens are not normally found or have been absent for many years (Beuchat 1998). Infected livestock (see Box 5.1) and exotic pets may also introduce emerging pathogens into new regions.

Modern processing methods for meat products also facilitate the spread of pathogens across regions. Large packing/processing plants process meat from various regions. In a 1993 *E. coli* O157:H7 outbreak in the USA, the source trace-back showed that beef used in the product had come from several suppliers and three different countries. Armstrong *et al.* (1996) estimated that one infected cow used to produce ground beef could contaminate up to 8 tonnes of meat. Moreover, pathogens may be introduced into areas where natural immunity is absent, resulting in more severe health consequences.

SARS also provides an example of how fast a disease can cross the globe in the era of modern travel. All of this illustrates the need for international surveillance networks that can facilitate cooperation to control the transport of waterborne and other emerging zoonoses into new regions. For example, the World Health Organization and an international network of national governments have established a network of 148 laboratories to monitor polio eradication efforts. Reported cases of polio are evaluated quickly, and necessary actions can be taken to prevent outbreaks from growing. Because of these efforts, wild polio strains currently exist in only a handful of countries, and the disease is scheduled to be completely eradicated by 2005 (WHO 2003b). Similar cooperative efforts will be needed in the future to prevent the dissemination of emerging waterborne zoonoses.

## 5.4 CONCLUSION

Many of the emerging waterborne zoonoses are difficult to manage. Developing the concept of a control envelope provides a framework for evaluating emerging pathogens against risks posed by better understood organisms. The control envelope is defined broadly and may require professionals to consider risk management strategies outside of their areas of expertise (e.g., water supply and distribution). Effective management of emerging waterborne zoonoses thus requires cooperation across a broad range of disciplines. A variety of risk management tools are available (e.g., QMRA, HACCP, WSP, disease surveillance) but must be extended to encompass the entire spectrum of the control envelope to effectively manage many of the newly emerging waterborne zoonoses.

## 5.5 REFERENCES

- Aboytes R. and LeChevallier, M.W. (2003) Detection of infectious *Cryptosporidium* in filtered drinking water. In *Proceedings of the American Water Works Association Annual Conference and Exposition, Anaheim, CA, 16–19 June*, American Water Works Association, Denver, CO.
- Armstrong, G.L., Hollingsworth, J. and Morris J.G. (1996) Emerging foodborne pathogens: *Escherichia coli* O157:H7 as a model of entry of a new pathogen into the food supply of the developed world. *Epidemiol. Rev.* **18**(1), 29–51.
- AWWA (1999) Committee Report: Emerging pathogens — bacteria. *J. Am. Water Works Assoc.* **91**(9), 101–109.
- Barwick, R.S., Levy, D.A., Craun, G.F., Beach, M.J. and Calderon, R.L. (2000) Surveillance for waterborne-disease outbreaks — United States, 1997–1998. *Morbid. Mortal. Wkly. Rep.* **49**(SS-4), 1–35.
- Beuchat, L.R. (1998) *Food Safety Issues, Surface Decontamination of Fruits and Vegetables Eaten Raw: A Review*. World Health Organization, Geneva.
- Billy, T.J. (1997) *HACCP and Food Safety — Application in a Mandatory Environment*. Remarks delivered before the World Congress on Meat and Poultry Inspection, 10 June, Sint Michielsgestel. Food Safety and Inspection Service, US Department of Agriculture, Washington, DC (<http://www.fsis.usda.gov/oa/speeches/1997/world.htm>).
- Birley, M.H. and Lock, K. (1998) *The Health Impacts of Peri-urban Natural Resource Development*. Liverpool School of Tropical Medicine, Liverpool.
- Bjornsson, S. (1989) Inflammatory bowel disease in Iceland during a 30 year period, 1950–1979. *Scand. J. Gastroenterol.*, **24**(Suppl. 170), 47–49.
- Bjornsson, S. and Johannsson, J.H. (2000) Inflammatory bowel disease in Iceland, 1990–1994: a prospective, nationwide, epidemiological study. *Eur. J. Gastroenterol. Hepatol.* **12**, 31–38.
- Bjornsson, S., Johannsson, J.H. and Oddsson, E. (1998) Inflammatory bowel disease in Iceland, 1980–89. *Scand. J. Gastroenterol.* **33**, 71–77.
- CDC (1995) *Escherichia coli* O157:H7 outbreak linked to commercially distributed dry-cured salami — Washington and California, 1994. *Morbid. Mortal. Wkly. Rep.* **44**, 157–160.
- CDC (2002) *National Antimicrobial Resistance Monitoring System for Enteric Bacteria — Annual Report for 2000*. Centers for Disease Control and Prevention, Atlanta, GA (<http://www.cdc.gov/ncidod/dbmd/narms/>).
- CDC (2003) *Fact Sheet: Toxoplasmosis*. Division of Parasitic Diseases, Centers for Disease Control and Prevention, Atlanta, GA ([http://www.cdc.gov/ncidod/dpd/parasites/toxoplasmosis/factsht\\_toxoplasmosis.htm#4](http://www.cdc.gov/ncidod/dpd/parasites/toxoplasmosis/factsht_toxoplasmosis.htm#4)).
- Chapman, P.A. (2000) Sources of *Escherichia coli* O157 and experiences over the past 15 years in Sheffield, UK. *J. Appl. Microbiol. (Symp. Suppl.)* **88**, 51S–60S.
- Codex Alimentarius Commission (1997) *Hazard Analysis and Critical Control Point (HACCP) System and Guidelines for Its Application*. Annex to CAC/RCP 1-1969, Rev. 3, Food and Agriculture Organization of the United Nations, Rome.
- Conner, D.E. and Kotrola, J.S. (1995) Growth and survival of *Escherichia coli* O157:H7 under acidic conditions. *Appl. Environ. Microbiol.* **61**, 382–385.
- Crump, J.A., Murdoch, D.R. and Baker, M.G. (2001) Emerging infectious diseases in an island ecosystem: the New Zealand perspective. *Emerg. Infect. Dis.* **7**, 767–772.

- Curriero, F.C., Patz, J.A., Rose, J.B. and Lele, S. (2001) The association between extreme precipitation and waterborne disease outbreaks in the United States, 1948–1994. *Am. J. Public Health* **91**(8), 1194–1199.
- Deere, D., Stevens, M., Davison, A., Helm, G. and Dufour, A. (2001) Management strategies. In *Water Quality: Guidelines, Standards for Health; Assessment of Risk and Risk Management for Water-related Infectious Disease* (ed. L. Fewtrell and J. Bartram), IWA Publishing, London, for the World Health Organization, Geneva.
- Exner, M. and Kistemann, T. (2003) Is there a need for a better drinking-water quality management? In *Water Safety Conference (Berlin, 28–30 April) Abstracts* (ed. O. Schmoll and I. Chorus), German Federal Environmental Agency (Umweltbundesamt), Berlin.
- Friedman, M.J., Radder, L., Harrison, S., Howie, D., Britton, M., Boyd, G., Wang, H., Gullick, R., LeChevallier, M., Funck, J. and Wood, D. (2003) *Verification and Control of Low Pressure Transients in Distribution Systems*. AWWA Research Foundation and American Water Works Association, Denver, CO.
- Gale, P. and Stanfield, G. (2000) *Cryptosporidium* during a simulated outbreak. *J. Am. Water Works Assoc.* **92**(9), 105–116.
- Garrett, E.S., Lima dos Santos, C. and Jahncke, M.L. (1997) Public, animal, and environmental health implications of aquaculture. *Emerg. Infect. Dis.* **3**(4), 1–6.
- Godfree, A.F. (2000) Assuring microbiologically safe drinking water. In *Proceedings of the American Water Works Association Water Quality Technology Conference*, 5–9 November, Salt Lake City, UT.
- Godree, A. (2003) Adoption of HACCP principles for water safety with particular reference to *Cryptosporidium*. In *Water Safety Conference (Berlin, 28–30 April) Abstracts* (ed. O. Schmoll and I. Chorus), German Federal Environmental Agency (Umweltbundesamt), Berlin.
- Havelaar, A. (1994) Application of HACCP to drinking water supply. *Food Control* **5**(3), 145–152.
- Hermon-Taylor, J. and El-Zaatari, F.A.K. (2004) The *Mycobacterium avium* subspecies *paratuberculosis* (MAP) problem, and its relation to the causation of Crohn's disease. In *Pathogenic Mycobacteria in Water*, IWA Publishing, London, on behalf of the World Health Organization, Geneva.
- Hermon-Taylor, J., Barnes, N., Clarke, C. and Finlayson, C. (1998) *Mycobacterium paratuberculosis* cervical lymphadenitis, followed five years later by terminal ileitis similar to Crohn's disease. *Br. Med. J.* **316**, 449–453.
- Hoxie, N.J., Davis, J.P., Vergeront, J.M., Nashold, R.D. and Blair, K.A. (1997) Cryptosporidiosis-associated mortality following a massive waterborne outbreak in Milwaukee, Wisconsin. *Am. J. Public Health* **87**(12), 2032–2035.
- Hrudey, S.E. (2003) Basis for the quality management recommendations from the Walkerton Inquiry. In *Water Safety Conference (Berlin, 28–30 April) Abstracts* (ed. O. Schmoll and I. Chorus), German Federal Environmental Agency (Umweltbundesamt), Berlin.
- King, E.O. (1962) The laboratory recognition of *Vibrio fetus* and closely related *Vibrio* species isolated from cases of human vibriosis. *Ann. N. Y. Acad. Sci.* **98**, 700–711.
- Kirmeyer, G.J., Friedman, M., Martel, K., Howie, D., LeChevallier, M., Abbaszadegan, M., Karim, M., Funk, J. and Harbour, J. (2001) *Pathogen Intrusion into the Distribution System*. AWWA Research Foundation and American Water Works Association, Denver, CO.
- Kondro, W. (2000) *E. coli* outbreak deaths spark judicial inquiry in Canada. *Lancet* **355**(9220), 2058.

- LeChevallier, M.W. and Norton, W.D. (1995) Plant optimization using particle counting for treatment of *Giardia* and *Cryptosporidium*. In *Protozoan Parasites and Water* (ed. W.B. Betts, D. Casemore, C. Fricker, H. Smith, and J. Watkins), Royal Society of Chemistry, Cambridge.
- MacKenzie, W.R., Hoxie, N.J., Proctor, M.E., Gradus, M.S., Blair, K.A., Peterson, D.E., Kazmierczak, J.J., Addiss, D.G., Fox, K.R., Rose, J.B. and Davis, J.P. (1994) A massive outbreak in Milwaukee of *Cryptosporidium* infection transmitted through the public water supply. *N. Engl. J. Med.* **331**(3), 161–167.
- Mas-Coma, S., Esteban, J.G. and Bargues, M.D. (1999) Epidemiology of human fascioliasis: a review and proposed new classification. *Bull. W. H. O.* **77**(4), 340–346.
- McDermott, P.E., Bodeis, S.M., English, L.L., White, D.G. and Wagner, D.D. (2001) High-level ciprofloxacin MICs develop rapidly in *Campylobacter jejuni* following treatment of chickens with sarafloxacin. In *Proceedings of the 101st Annual Meeting of the American Society for Microbiology, Orlando, FL*, Abstract Z-20, p. 742, ASM Press, Washington, DC.
- Miller, L.G. and Kaspar, C.W. (1994) *Escherichia coli* O157:H7 acid tolerance and survival in apple cider. *J. Food Prot.* **57**, 460–464.
- Pettersson, S.A. and Ashbolt, N.J. (2003) *WHO Guidelines for the Safe Use of Wastewater and Excreta in Agriculture: Microbial Risk Assessment Section*. Unpublished document prepared for the World Health Organization, Geneva, 36 pp.
- Sechi, L.A., Mura, M., Tanda, F., Lissia, A., Solinas, A., Fadda, G. and Zanetti, S. (2001) Identification of *Mycobacterium avium* subsp. *paratuberculosis* in biopsy specimens from patients with Crohn's disease identified by *in situ* hybridization. *J. Clin. Microbiol.* **39**, 4514–4517.
- SHWF (2003) *Press Release: Transcript of Secretary for Health, Welfare and Food on the Findings of an Investigation of Severe Acute Respiratory Syndrome Outbreak at Amoy Gardens (Parts 1 and 2), 17 April*. Ministry of Health, Welfare and Food, Hong Kong Special Administrative Region (<http://www.info.gov.hk/gia/general/200304/17/0417290.htm> and <http://www.info.gov.hk/gia/general/200304/17/0417308.htm>).
- Tauxe, R.V. (2002) Emerging foodborne pathogens. *Int. J. Food Microbiol.* **78**(2002), 31–41.
- Tenenbaum, D.J. (2002) Overpowering manure. *Environ. Health Perspect.* **110**(4), 1–2 (<http://ehpnet1.niehs.nih.gov/docs/2002/110-4/forum.html>).
- Teunis, P.F.M., van der Heijden, O.G., van der Giessen, J.W.B. and Havelaar, A.H. (1996) *The Dose–Response Relation in Human Volunteers for Gastro-intestinal Pathogens*. RIVM Report No. 284550002, Rijksinstituut voor Volksgezondheid en Milieu (National Institute for Public Health and the Environment), Bilthoven.
- UNESCO-WWAP (2003) Basic needs and the right to health. In *Water for People, Water for Life*, published for the United Nations Educational, Scientific and Cultural Organization (UNESCO) and the World Water Assessment Programme (WWAP) by Berghahn Books, Barcelona.
- Ungar, B.L., Gilman, R.H., Lanata, C.F. and Peres-Schael, I. (1988) Seroepidemiology of *Cryptosporidium* infection in two Latin American populations. *J. Infect. Dis.* **157**, 551–556.
- US EPA (1998) 40 CFR Parts 9, 141, and 142. National primary drinking water regulations: interim enhanced surface water treatment; final rule. US Environmental Protection Agency. *Fed. Regist.* **63**(241), 69478–69521.
- WHO (1996) *Guidelines for Drinking-water Quality*, 2nd edn, vol. 2, *Health Criteria and Other Supporting Information*. World Health Organization, Geneva.

- WHO (2003a) *Emerging Issues in Water and Infectious Disease*. World Health Organization, Geneva.
- WHO (2003b) *Polio Eradication*. World Health Organization, Geneva (<http://www.polioeradication.org/>).
- WHO (2004) *Guidelines for Drinking Water Quality*, 3rd edn. World Health Organization, Geneva.
- Williams, M.H. and Braun-Howland, E.B. (2003) Growth of *Escherichia coli* in model distribution system biofilms exposed to hypochlorous acid or monochloramine. *Appl. Environ. Microbiol.* **69**(9), 5463–5471.
- Zhang, X., McDaniel, A.D., Wolf, L.E., Keusch, G.T., Waldor, M.K. and Acheson, D.W.K. (2000) Quinolone antibiotics induce Shiga toxin-encoding bacteriophages, toxin production, and death in mice. *J. Infect. Dis.* **181**, 664–670.
- Zu, S.-X., Li, J.-F., Barrett, L.J., Fayer, R., Zhu, S.-Y., McAuliffe, J.F., Roche, J.K. and Guerrant, R.L. (1994) Seroepidemiologic study of *Cryptosporidium* infection in children from rural communities of Anhui, China. *Am. J. Trop. Med. Hyg.* **51**, 1–10.