3.1 Introduction

This chapter is primarily about the role of analytical techniques in the assessment of risk and specifically the value of water quality indicator parameters in this process. Assessment of risk in relation to drinking water supplies is undertaken for a number of reasons (Percival et al., 2000):

- To predict the burden of waterborne disease in the community, under outbreak and non-outbreak conditions. This is helpful in determining the impact of improvements in water supply on health and to act as a driver towards improvement.
- To help set microbial standards for drinking water supplies that will give tolerable levels of illness within the populations drinking that water.
- To identify the most cost-effective option to reduce microbial health risks to drinking water consumers.
- To help determine the optimum treatment of water to balance microbial risks against chemical risks from disinfection by-products.
- To provide a conceptual framework to help individuals and organisations understand the nature and risk to, and from, their water and how those risks can be minimised.

The focus of this chapter is to review the value of indicator parameters of water quality and other analyses in the context of three different approaches to the assessment of risk, namely:
• Epidemiological methods.
• Quantitative microbial risk assessment (QMRA).
• Qualitative risk assessment (including risk ranking).

3.2 What is risk?

Risk can be defined in the simplest form as ‘the possibility of loss, harm or injury’. This definition includes two separate concepts; the probability of an event and the severity of that event. These two concepts are illustrated in Figure 3.1, and this model helps the prioritisation of risks for any risk-reduction action. Clearly those risks that need most urgent action are high probability – high severity risks (upper right quadrant). Those that need little, if any, attention are low probability – low severity (lower left quadrant).

Figure 3.1. Two-dimensional classification of risk

<table>
<thead>
<tr>
<th>Severity of harm</th>
<th>Probability of occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low probability of severe harm (should be given intermediate priority attention)</td>
<td>High probability of severe harm (needs most urgent attention)</td>
</tr>
<tr>
<td>Low probability of mild harm (can probably be ignored or given low priority attention)</td>
<td>High probability of mild harm (should be given intermediate priority attention)</td>
</tr>
</tbody>
</table>

Despite the simplicity of this two-dimensional model, the processes that allow the calculation or quantification of risk differ. Indeed, many risk-based decisions are still subjective or semi-quantitative. Even where risk assessments are presented in an apparently objective, numerical manner these are often based on assumptions which are themselves subjective or semi-quantitative. One of the major problems with all forms of assessing risk is the quality and levels of uncertainty in much of the basic data (Macgill et al., 2001).

3.3 Types of evidence

Data used in the assessment of risk is obtained from experimental work on animals or volunteers and from epidemiological investigations. These epidemiological investigations may be conducted during an outbreak investigation or be done as part of planned research to investigate the causes and transmission of disease.
The most abundant source of epidemiological data on waterborne disease comes from outbreak investigations (Chapter 7), and outbreaks provide very valuable data for the assessment of risk. Particularly, outbreaks can provide clear evidence that a specific pathogen can be spread by the water route. Outbreak investigations also provide good information on what failures in the water supply and distribution chain led to the risk to health. This enables risk management strategies to focus on those stages in the water supply chain where failures are likely to occur. Outbreaks can also be the setting for epidemiological studies that provide useful information on what non-water-related factors affect risk of infection with the outbreak pathogen. However, outbreak data have their limitations (Andersson and Bohan, 2001). For any particular pathogen, it is rarely known what proportion of the burden of disease is due to sporadic spread by the water route. Nor is it known whether those factors responsible for failure leading to outbreaks are also those factors responsible for sporadic disease. Consequently information reliant only on outbreaks may not be applicable to the major proportion of waterborne disease. Also, epidemiological investigations of water-related disease may be biased by prior knowledge of cases and controls about the suspected cause of the outbreak (Hunter, 2000).

Targeted epidemiological studies can provide good data on the relationship between specific water quality parameters and disease in a population. Such studies can identify relationships between risk factors for all waterborne disease and not only that associated with outbreaks. Separating the waterborne fraction of gastrointestinal disease from the numerous other routes of infection is a challenge and the results from most epidemiological studies are presented as a level of association between drinking water and the parameter(s) under study. These studies are often subject to criticism as there are rarely clear-cut conclusions, and they are potentially subject to a number of biases and confounding factors.

Quantitative microbial risk assessment (QMRA) is an emerging field that has applications in specific situations and is discussed in more detail below. QMRA uses information on the distribution and concentration of specific pathogens in the water supply along with information on the infectivity of those pathogens to determine risk to public health.

Assessment of the quality of evidence is important yet rarely formally addressed in the assessment of risk (Macgill et al., 2001). Requirements for evidence related to demonstration of causality may be very different to that for dose response. In practice the overall body of evidence may include a number of studies each with strengths and weaknesses and employing often very different methods and approaches (Blumenthal et al., 2001; Haas and Eisenberg, 2001).
When assessing the risk of disease due to drinking water it is very important to consider the overall body of evidence, weighing each piece of evidence as to its quality. Given the uncertainty inherent in all epidemiological studies reliance on a single study, even an extremely well conducted one, may be misleading.

### 3.4 Epidemiological approaches to risk

Epidemiology is the study of the incidence and transmission of disease in populations. Epidemiological investigations are central to the assessment of risk (Blumenthal et al., 2001), both in providing estimates of risk and in providing input data into risk assessment models. The epidemiological definitions of risk are distinct from definitions used more generally, and are defined in Table 3.1.

<table>
<thead>
<tr>
<th>Risk</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute risk</td>
<td>The number of new cases occurring within a certain sized population during a specified time period, usually referred to as incidence.</td>
</tr>
<tr>
<td>Attributable risk</td>
<td>The proportion of cases of a disease due to a particular risk factor.</td>
</tr>
<tr>
<td>Relative risk</td>
<td>The ratio between the incidence of disease in those members of the population exposed to a possible risk factor and those not exposed.</td>
</tr>
<tr>
<td>Odds ratio</td>
<td>The ratio between the probability that someone with a disease has experience of the potential environmental factor and the probability that a control has experience of the same factor. Provides an estimate of relative risk in case control studies.</td>
</tr>
</tbody>
</table>

Epidemiology relies on a limited range of methods and approaches to define risk (discussed in more detail elsewhere, e.g. Gordis, 2000). Most epidemiological studies can be classified as descriptive, analytical or intervention. Descriptive epidemiological studies set out to describe the distribution of cases of disease in time, place and person. Two types of descriptive study that have been used in relation to waterborne disease are the ecological study and the time series study. Analytical studies are generally of the case control or cohort type, in which individuals or groups are compared. Intervention studies are experimental studies that observe the impact of certain interventions (such as provision of point-of-use filters) on the risk of illness. The various types of study are described in Table 3.2.
Table 3.2. Types of epidemiological study that have been used in risk assessment of waterborne disease

<table>
<thead>
<tr>
<th>Study type</th>
<th>Description</th>
<th>Advantages and disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ecological study</td>
<td>Determining relationship between disease and risk factors by comparing the incidence of disease in different communities with varying exposure to risk factors.</td>
<td>Relatively inexpensive to carry out providing that disease rates and data on risk factors are already available. Because data is only available for groups, it is not known whether individuals with disease are exposed to risk factor. Good for generating hypotheses, but cannot be used as evidence of epidemiological proof.</td>
</tr>
<tr>
<td>Time series study</td>
<td>Determining relationship between disease incidence in a population and variation in a risk factor over time.</td>
<td>A type of ecological study and subject to the same advantages and disadvantages.</td>
</tr>
<tr>
<td>Case-control study</td>
<td>Determining relationship between disease and risk factors by comparing the incidence of disease in exposed individuals to matched controls.</td>
<td>Relatively inexpensive to carry out. Generates data on individuals exposed to the risk factors in comparison with healthy individuals.</td>
</tr>
<tr>
<td>Cohort study</td>
<td>Comparing rate of disease in two, or more, populations with different levels of exposure over a specific period of time on randomly selected individuals.</td>
<td>Relatively expensive to carry out. Generates data on the risk factors in populations by comparing groups of randomly selected individuals.</td>
</tr>
<tr>
<td>Intervention study</td>
<td>Comparing the rates of disease in two or more groups (cohorts) of randomly chosen individuals after intervening to change the level of exposure.</td>
<td>The gold standard for epidemiological proof, but can be time consuming and costly to carry out.</td>
</tr>
</tbody>
</table>

3.5 Studies linking ill health to indicators

While many microorganisms have been implicated as causative agents in outbreaks of various diseases, there is little epidemiological data on the endemic level of waterborne diseases and their aetiology. The association between many aetiological agents with a given route of exposure and their contribution to the total burden of disease is often uncertain. Studies that have attempted to define the burden of waterborne disease have targeted gastrointestinal illness, as it is the most frequent and easy to measure adverse outcome associated with drinking water (Prüss et al., 2002). This frequent outcome enables researchers to obtain information faster than with less common outcomes (e.g. hepatitis) or
outcomes that are less defined and are more difficult to link with specific exposures (e.g. malignant disease). However, use of gastrointestinal disease as an index of water-related disease impact has a number of limitations. Depending on how gastroenteritis is measured estimates of disease burden can vary substantially. Since the disease may be considered ‘mild’, especially amongst adults, relatively few people seek medical attention and even if they do they may not have faecal samples taken for laboratory investigation. Consequently, disease burden estimates based on national surveillance systems of laboratory reports can substantially underestimate disease burden (Wheeler et al., 1999). This has led to the use of self-reported gastroenteritis in several studies (discussed below). There are, however, problems with the use of self-reported gastroenteritis as a marker of disease, as depending on how gastroenteritis is defined rates can vary substantially. How the data is collected can also markedly affect estimates of disease burden. Retrospective studies, where individuals are asked whether they have had diarrhoea in the previous month can over-estimate illness by about three times when compared to prospective studies where volunteers maintain a daily health diary (Wheeler et al., 1999). This overestimate may be greater in outbreak settings (Hunter and Syed, 2001). Furthermore, since gastrointestinal disease is relatively common and may be transmitted by various means, it may be difficult to distinguish the waterborne contribution from the background ‘noise’.

The link between substandard drinking water and disease is relatively easy to demonstrate. Such a demonstration becomes more difficult to make as the quality of the water improves towards the current World Health Organization (WHO) Guidelines (WHO, 1993; 1996; 1997). Indeed, the link between highly treated drinking water meeting local regulations, as found in most industrialised countries, and microbial illness has only been reported relatively recently. For example, both waterborne Giardia and Cryptosporidium infection have clearly been linked to drinking water meeting or exceeding current standards, thereby challenging the value of the traditional microbial indicator parameters as well as the efficacy of treatment procedures (Gostin et al., 2000).

3.5.1 Untreated drinking waters

In developing countries there is abundant evidence that poor quality water containing indices of faecal pollution is the source of much disease in the population. There is, however, little data on the exact relationship between the two.

There is a substantial body of evidence that relates improvements in water supply and sanitation in general and in drinking water quality in particular, to
specific health outcomes (most frequently reductions in diarrhoeal disease). Many of the early studies had severe methodological flaws (Blum and Feachem, 1983), but two reviews of published studies have sought to identify better-conducted studies and assess the detected disease outcomes (Esrey et al., 1985; 1991). Most studies detected were from less-industrialized countries and a median reduction in diarrhoeal disease of 26 – 27% was reported. However, water quality was typically not assessed and in some cases opportunities for recontamination may have cast doubt on the actual intervention tested. In some more recent studies, far better characterisation of the intervention has been achieved with actual water quality measurements made (e.g. Quick et al., 1999 [E. coli] and Semenza et al., 1998 [chlorine residual]). Nevertheless, the absence of an estimate of exposure from most studies renders them unusable in formalised risk assessment requiring description of population dose-response.

3.5.2 Substandard drinking water

In France, Collin et al. (1981) prospectively studied gastrointestinal illnesses associated with the consumption of tap water, using reports from physicians, pharmacists and teachers. They reported five epidemics associated with poor quality water but they did not address the endemic level of gastrointestinal illnesses. The same group found a relationship between faecal streptococci and acute gastrointestinal disease (Ferley et al., 1986; Zmirou et al., 1987) in a study of 64 villages with sub-standard water. Thermotolerant coliforms, total coliforms and total bacteria made no independent contribution to disease. Zmirou et al. (1995) investigated the effect of chlorination alone, on water that did not satisfy microbiological criteria otherwise. The crude incidence of diarrhoea was 1.4 times more frequent in children from villages where water supplies had evidence of faecal pollution, even after chlorination. In Israel, Fattal et al. (1988) addressed the health effects of drinking water and did not show a relationship between health effects and total or thermotolerant (faecal) coliforms. Beaudeau et al. (1999) reported a relationship between the chlorine disinfection level and diarrhoeal illness in the population of Le Havre (France).

3.5.3 Drinking water meeting current regulations

In the USA, Batik et al. (1979) attempted to use cases of hepatitis A as an indicator of health risk, but could not establish a correlation with water quality nor, in a later study, did they find a correlation between traditional indicator parameters (coliforms) and the risk of waterborne outbreaks (Batik et al., 1983).
Craun *et al.* (1997) in the USA, evaluated the relationship between coliform compliance and outbreak occurrence. They found that coliforms were usually found in the water during an outbreak investigation but that during the previous months, coliforms were detected in only half of the systems and caused a violation in only a quarter of them. The violation rate was not different between community systems that experienced an outbreak and those that did not. In Namibia, Isaäckson and Sayed (1988) conducted a similar study and did not observe an increased risk of gastrointestinal illness associated with the consumption of recycled wastewater.

In Canada, two prospective studies have suggested that a very high proportion of gastrointestinal illnesses could still be attributable to tap water consumption, even when water (albeit from a degraded catchment) exceeded the current drinking water quality guidelines (Payment *et al.*, 1991; 1997).

Turbidity of treated drinking water has been linked to health effects in Milwaukee (MacKenzie *et al.*, 1994; Morris *et al.*, 1996), in Philadelphia (Schwartz *et al.*, 1997; 2000) and in Le Havre (Beaudeau *et al.*, 1999). It should be noted, however, that these studies of turbidity and adverse health outcome are ‘ecological’, in that they measure exposure of populations rather than of individuals and, as such, potentially suffer from bias due to the so called ‘ecological fallacy’ (Walter, 1991). While this does not mean that these studies are invalid, they cannot be taken as proof of an association in their own right.

### 3.5.4 The role of index/indicator parameters in assessing risk to health

During the course of the 20th century, the absence of traditional index/indicator parameters in drinking water was related to a significant reduction in waterborne outbreaks. This reflected the use of these organisms to indicate the presence of faecal contamination and through which valuable information on effectiveness and failure of interventions was progressively accumulated. More recently, occasional outbreaks and endemic disease have been linked to waterborne disease in the absence of the traditional indicator parameters. The causes are often failures in treatment or contamination of the treated product, but the coliform parameters (total, therotolerant or *E. coli*) cannot provide information on the removal and inactivation of pathogens that are several orders of magnitude more resistant to treatment. Hence, coliform parameters remain useful for specific purposes described elsewhere in this book, but future studies on waterborne disease should be targeted to additional indicator parameters (for instance, those described in Chapter 2). There is, however, no single direct measurement (including direct pathogen testing) available to predict health outcomes in a population. Turbidity and faecal
streptococci counts are the main indicator parameters that have been shown to have independent association with actual levels of disease in populations.

3.6 Quantitative microbial risk assessment (QMRA)

The QMRA approach to risk differs from epidemiological approaches in that the latter seeks to measure actual levels of disease in the population while the former attempts to calculate risk from what is known, or can be inferred, about the concentration of particular pathogens in the water supply and the infectivity of those pathogens to humans. The relative values of QMRA and epidemiology are strongly debated (Haas and Eisenberg, 2001).

3.6.1 The mathematical modelling of health risk

Establishing the exposure setting is the first step to the mathematical evaluation of microbial risk. The purpose is to determine the possible pathogens present, dose(s) consumed and the characteristics of the pathogen(s) that will define the outcome.

The quantitative approach to microbial risk assessment is based on the chemical risk assessment paradigm, and has been reviewed by Haas et al. (1999). As with chemical risk assessment, this is a formalised procedure involving four key steps (Table 3.3), each of which is briefly described below.

<table>
<thead>
<tr>
<th>Step</th>
<th>Aim</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Problem formalisation and hazard identification</td>
<td>To describe the overall environmental setting and relevant pathogens that may cause acute or chronic effects to human health.</td>
</tr>
<tr>
<td>2. Dose-response analysis</td>
<td>To find appropriate relationship(s) between pathogen exposure and infection or illness (from epidemiological studies).</td>
</tr>
<tr>
<td>3. Exposure assessment</td>
<td>To determine the size and nature of the populations exposed to each identified pathogen by route, amount and duration of the exposure.</td>
</tr>
<tr>
<td>4. Risk characterisation</td>
<td>To integrate the information from exposure and dose-response, to express public health outcomes, taking into account the variability and uncertainty of the estimations.</td>
</tr>
</tbody>
</table>

Table 3.3. Steps involved in quantitative microbial risk assessment

(Adapted from National Research Council, 1983)
While the conceptual framework for both chemical and microbial risk assessments is the same, pathogens differ from toxic chemicals in several key ways:

- The variability of different strains of the one pathogen to cause disease (differing virulence).
- Virulence can evolve as the pathogen passes through various infected individuals.
- Pathogens are generally not evenly suspended in water.
- Pathogens can be passed from one person to many (secondary spread), from either healthy but infected (asymptomatic) or ill (symptomatic) hosts.
- Whether a person becomes infected or ill depends not only on the health of the person, but also on their pre-existing immunity and pathogen dose.

### 3.6.2 Hazard identification (hazard assessment)

Pathogenic microorganisms are relatively well described in the scientific literature and, apart from emerging waterborne pathogens (LeChevallier et al., 1999a,b), data on their characteristics are generally available. Data needed for the risk assessment process include the severity of the outcome, susceptibility (long and short-term immunity), susceptible populations and secondary (person-to-person) disease transmission. The outcomes of the exposure include non-infection, asymptomatic infection and various levels of morbidity and mortality. Gender, age and some forms of susceptibility may also affect the outcome. Severe morbidity or mortality resulting from waterborne exposures are significant in developing countries, but are relatively rare in industrialised countries.

#### 3.6.2.1 Outbreaks

To properly conduct risk assessment, the hazard must be identified and outbreaks provide important data in microbial risk assessment. The pathogen responsible for the outbreak must be identified, the severity and contagiousness of the infection can be described, the patterns of transmission in the population can be studied and control measures can be evaluated. Waterborne disease outbreak surveillance is key to this evaluation, and identification of the aetiologic agent is dependent on the timely recognition of the outbreak, so that appropriate clinical and environment samples can be obtained. The interests and
expertise of investigators and the routine practices of local laboratories can also influence whether the aetiologic agent is identified (Frost *et al.*, 1996). Diarrhoeal stool specimens, for example, are generally examined for bacterial pathogens, but not for viruses. In most laboratories, testing for *Cryptosporidium* is only undertaken if requested and is not included in routine stool examinations for ova and other parasites. Hence, it is not surprising that even in the USA, with one of the most comprehensive registers of waterborne outbreaks, between 1992-1996 the causative organism was not identified in over 40% of investigations (*Levy et al.*, 1998).

The water quality data collected during and/or before the outbreak can be useful in identifying the causes of the outbreak and in preventing their reoccurrence. (Methods used for microbial water quality assessment are discussed in Chapter 8 and their use in outbreak investigation is described in Chapter 7). While background data on the level of faecal contamination, if not sewage pollution in water is very valuable, care is needed in interpreting data on finding or not finding pathogens. In particular, molecular epidemiology or similar typing methods are necessary to confirm if the species identified from water was also the agent present in the infected host (Chapter 7). There has been considerable controversy over a number of species of opportunistic bacterial pathogens with apparently non-pathogenic strains that may be found in drinking water, versus different strains (and presumably non-water sources) causing illness (*Edberg et al.*, 1986; *Havelaar et al.*, 1992; *Kühn et al.*, 1997).

3.6.2.2 ‘Emerging’ pathogens

As new pathogens are being described in the population or in the environment, their potential for being transmitted by the water route must be evaluated. Basic characteristics that allow a pathogen to be waterborne include:

- Excretion in the faeces and/or urine.
- An environmentally persistent stage.
- The ability to cause infection when inhaled or ingested.

Emerging pathogens include those that are increasingly being recognised as important contributors to waterborne disease as well as those that are newly discovered. As such, they include:
• Viruses: new enteroviruses, human caliciviruses (including Norwalk-like viruses), and hepatitis E.

• Parasitic protozoa: *Cyclospora cayetanensis*, various microsporidia and *Toxoplasma gondii*.

• Bacteria: Mycobacterium avium complex, *Helicobacter pylori*, pathogenic *Escherichia coli* and *Campylobacter jejuni* (LeChevallier et al., 1999a,b).

• Toxic cyanobacteria (Chorus and Bartram, 1999).

• Most faecal-oral pathogens are identified as causing acute gastrointestinal illnesses, with the major exceptions being hepatitis A and E viruses, *Helicobacter pylori*, *Salmonella typhi* and hookworm infection. However, it is important to note (as mentioned in Chapter 1) that some commonly recognised diseases (such as arthritis, type 1 diabetes mellitus, abortion, Guillain-Barré and Miller Fisher Syndrome) have been associated with, or are suspected to be caused by, infection with viral or bacterial pathogens excreted by humans or animals (Duim et al., 2000; Frisk et al., 1992; Gurgan and Diker, 1994; Havelaar et al., 2000; Maki-Ikola and Granfors, 1992; Niklasson et al., 1998).

### 3.6.3 Dose-response analysis

For QMRA, human dose-response studies are available for a few pathogens and can be used to estimate the effects of low level exposure to these microorganisms (Haas and Eisenberg, 2001). Two models of the infection process have been proposed: the exponential model (Equation 1) and the beta-Poisson model (Equation 2). These have been developed from biologically plausible assumptions about the infection process. Models may fit available data in a statistically acceptable sense and yet provide very different estimates for the risk at an extrapolated low dose; a situation that has frequently caused argument in chemical risk assessment. In QMRA, it may be possible to test the potential appropriateness of different dose-response functions by validating with outbreak data (Eisenberg et al., 1998).
Exponential model:

\[ \text{Probability}_{\text{infection}} = 1 - \exp(-rD) \]

*Equation 1*

Where \( D \) = pathogen dose; \( r \) = fraction of pathogens that survives to produce an infection.

Beta-Poisson model:

\[ \text{Probability}_{\text{infection}} = 1 - (1 + (D/ID_{50}))^{-\alpha} \]

*Equation 2*

Where \( D \) = pathogen dose; \( \alpha \) and \( ID_{50} \) are parameters of the beta-distribution used to describe variability in survival.

Given a set of dose-response data, *i.e.* exposure of populations to various doses of microorganisms and measurement of response (such as infection), the best fitting parameters of a dose-response relationship may be computed via standard maximum likelihood techniques. The method has been used for human viruses, parasitic protozoa and some bacterial pathogens (Haas *et al.*, 1999). Confidence limits to the parameters can then be estimated, and used as a basis for low-dose extrapolation (Kang *et al.*, 2000). It should be noted that, in general, dose-response studies have been conducted on healthy adults and may not reflect the response of the general population or of more susceptible population segments.

During an outbreak, individuals are exposed to different levels of the pathogen(s): the volume of water ingested may be coupled with data on the level of contamination of the water. These data can provide a dose-response relationship confirming volunteer studies. Furthermore, information on susceptible sub-populations (such as children and the immuno-compromised) may also be forthcoming. For example, waterborne outbreaks of cryptosporidiosis indicate that the general population may contract watery diarrhoea that lasts up to several days, whereas HIV-patients may be untreatable and die, thereby creating a much more significant health burden if the latter are included in a risk assessment (Perz *et al.*, 1998).

Volunteer feeding studies have provided data on the dose-response curve for several pathogens (Haas *et al.*, 1999). It is, however, often difficult to obtain data on low doses as large numbers of volunteers would be needed to define the lower bounds of the dose-response curve. It is also difficult to extrapolate from a single strain to give a generalised model for a pathogen. Virulence differs from one strain to another and the outcomes are often very different (*e.g.* E. coli enteropathogenic versus non-enteropathogenic strains). The debate around the human health significance of exposure to human versus animal strains of *Cryptosporidium parvum* is another example. Feeding trials with three different
bovine strains of *C. parvum* have generated 50% infective doses (ID$_{50}$) for oocysts in healthy human volunteers ranging between 9 and 1,042 (Okhuysen et al., 1999). Such a wide range is potentially problematic as the ID$_{50}$ is the parameter defining the slope of the dose-response curve in the beta-Poisson model. A further complication is that pre-existing immunity may provide protection from infection and illness at low oocyst doses (Chappell et al., 1999), thereby changing the low dose-response extrapolation in a manner not accounted for by any current model.

Relatively few data points are used to generate the curve and the degree of uncertainty over the position of each data point is high. Each data point is a sample mean of the probability of illness for people exposed to a set dose of pathogen. The confidence intervals for each sample mean will be wide. It is unlikely that all the measured points exactly correspond with the true population means for each dose. In such circumstances it is impossible to be certain about what dose-response model would best fit the actual curve (as opposed to the curve of the sample means). There is, therefore, considerable uncertainty in which model best fits the actual dose response curve and what its parameters should be (Coleman and Marks, 1998). The impact of these uncertainties is most marked at low doses (i.e., at the dose that will most frequently be experienced in real life). Therefore, the predicted number of illnesses following low dose exposure can vary by several orders of magnitude (Holcomb et al., 1999).

### 3.6.4 Exposure assessment

The actual dose consumed by an individual is generally unknown and difficult to estimate. Methods for the detection of some pathogens are not even available, and most pathogens occur at very low levels in treated water (generally below detection). The general level of some pathogens (e.g., enteroviruses, *Giardia*, *Cryptosporidium*), however, are available for sewage and untreated water. These raw water values can be used, along with the proportion of surrogate removed by treatment, to indirectly estimate the level of individual pathogens after treatment, thereby providing an estimate of the ‘dose’ in the water. The possible uses of surrogates and indicators are further discussed below.

For drinking waters, the volume ingested per ‘exposure’ is relatively well defined after several studies in a number of countries (e.g., Roseberry and Burmaster, 1992). A volume of two litres per person per day is often used to estimate drinking water exposure, but this does not reflect the fact that only a fraction of that volume is consumed unmodified (especially unboiled). This is important for QMRA as microorganisms are inactivated by heat; therefore water
consumed in hot drinks or used in the preparation of cooked food would not be a risk factor.

Viruses and parasites have been detected in drinking water, which was otherwise apparently safe, without any detectable health effect being seen in the receiving population (Bouchier, 1998). Possible reasons for this include false positive detections, the presence of non-infective pathogens and the pathogen is present in a concentration below that which would be expected to cause detectable disease in the population. On the other hand, unrealistically large volumes of drinking water would need to be sampled for example to meet the USEPA’s level of acceptable waterborne risk ($<10^{-5}$ infections per annum – see 1.5.1). Translating this for Cryptosporidium parvum would mean that 500 samples of 2 000 litres each would be needed to make a reasonably accurate estimation of the allowed concentration ($7 \times 10^{-6}$ per litre) (Teunis et al., 1996). Furthermore, depending on the detection method used, an unknown proportion of pathogens isolated from the environment may be incapable of causing infection. Therefore, alternative strategies are recommended to estimate pathogen concentrations.

The applications of coliform bacteria to index the pollution of source water, or as an indicator of water treatment efficacy or recontamination of treated water have provided little information on health effects in developed regions. Nonetheless, these organisms can play an important part in estimating pathogen numbers for a screening-level or first tier of a QMRA. For example, direct measurement of viral, parasitic protozoa and bacterial pathogens is possible for sewage effluents, as is the estimation of pathogen prevalence data for the faeces of some domestic animals. Hence, predictions of pathogens in source waters can be made if the relative proportion of human and animal faecal load is determined by, say, the analysis of faecal sterols (Leeming et al., 1998). For environments where sewage is the primary faecal contaminant, then pathogen dilutions in source waters can be estimated directly by the dilution of thermotolerant coliforms (index for bacterial pathogen contamination) and spores of Clostridium perfringens (index for the hardier viral and protozoan pathogens) (Medema et al., 1997).

For physical treatment barriers, such as sand or membrane filters, and for disinfection by chlorine, ozone or UV, surrogates for pathogen removal are also generally accepted. Total aerobic spores or spores of C. perfringens are reasonable surrogates for the cysts and oocysts of parasitic protozoa and coliphages may also be appropriate for human enteric viruses (Facile et al., 2000; Hijnen et al., 2000; Ndiongue et al., 2000; Owens et al., 2000). Note that while coliphages make good models for human virus removal by physical means, that may not be the case for mixed oxidants (Casteel et al., 2000).
3.6.5 Infectious disease models and risk characterisation

As outlined in the previous sections, attempts to provide a quantitative assessment of human health risks associated with the ingestion of waterborne pathogens have generally focused on static models that calculate the probability of individual infection or disease as a result of a single exposure event. They do not address the properties that are unique to infectious disease transmission such as secondary transmission, immunity and population dynamics (Haas and Eisenberg, 2001). To understand the role that water plays in the transmission of enteric pathogens and to estimate the risk of disease due to drinking water within a defined population it is important to study the complete disease transmission system, as illustrated in Figure 3.2. It is also important to recognise the additional pathways that describe the natural history of enteric pathogens: animal-to-environment-person, person-to-environment-to-person, and person-to-person (Eisenberg et al., 2001).

A fundamental concept in disease transmission models is the reproduction number, \( R_0 \), which is defined as the number of infections that result from the introduction of one index case into a population of susceptible individuals. Therefore, \( R_0 \) is a measure of the ability of a pathogen to move through a population. An \( R_0 >1 \) suggests that the pathogen is multiplying within a community and that prevalence is increasing, whereas an \( R_0 <1 \) suggests that the disease is dying out of the population. An \( R_0 \) that is on average equal to 1 suggests that the disease is endemic in the population. There are various methods to estimate \( R_0 \) for different pathogens and in different environmental settings (Dietz, 1993). Measles, for example, is a highly infectious respiratory transmitted disease and has been estimated to have an \( R_0 \) of approximately 14. Polio, on the other hand, a waterborne pathogen has an \( R_0 \) of approximately 6.
Figure 3.2. Conceptual model for rotavirus infection pathways

(from Haas and Eisenberg, 2001)


Summarising the previous sections, the individual daily dose of pathogenic microorganisms via some particular product may be calculated as (Teunis et al., 1996):

\[ Dose = C \times \frac{1}{R} \times I \times 10^{-DR} \times V \]

Equation 3

\( C \) = Concentration of pathogenic microorganisms in raw (source) materials (or partially processed products, if data are available).

\( R \) = Recovery of the detection method.

\( I \) = Fraction of the detected pathogens that is capable of infection (viability).

\( DR \) = Removal or inactivation efficiency of the treatment process, expressed as its Decimal Reduction factor (DR = 0 when concentrations in the finished product are available).

\( V \) = Daily individual consumption of the considered product.
In many cases, risk evaluations start from the assumption that the dose-response relationship is approximately linear at low doses. Therefore, at very low doses, calculation of the risk of infection simply consists of multiplying the dose estimate with the slope of the dose-response relationship. Estimates of daily risk may be extrapolated to yearly risk. When $P_1^*$ and $P_n^*$ are the probabilities of infection after a single (e.g. daily) exposure and after repeated exposures (n times a daily exposure) respectively:

$$P_n^* = 1 - (1 - P_1^*)^n \approx n \times P_1^*$$  \hspace{1cm} \text{Equation 4}

The latter simplification is valid as long as $P_1^* << 1$ (Haas et al., 1999).

From the above discussions it would seem that microbial data, whether relating to indicator parameters or pathogens, have most relevance to the exposure assessment phase of QMRA. These provide estimates of actual levels of pathogens in water or the likelihood that water is exposed to faecal pollution. However, caution must be exercised in assuming a direct relationship between this level and risk to health. Despite the use of numbers and mathematical equations, QMRA is not yet an exact science.

3.7 Qualitative risk assessment

Qualitative methods for analysing microbial hazards and managing risks are commonplace within the food industry. They are applied as part of a systematic process including Hazard Analysis Critical Control Points (HACCP) (Coleman and Marks, 1999), which has recently been taken up by the water industry (Havelaar, 1994; Barry et al., 1998; Deere and Davison, 1998; Gray and Morain, 2000; Deere et al., 2001; Dewettinck et al., 2001; Davison et al., 2002).

Although hazard identification and exposure assessment are common issues across qualitative and quantitative methods, dose-response models and risk characterisation steps (Table 3.3), are usually replaced with risk rankings in qualitative assessments. These rankings are generally derived from expert opinion summarising:

- Likelihood of possible risk pathways.
- Severity of outcome from each pathway.
- Numbers of people that may be impacted.
Water agencies are now focusing on the whole system approach, as illustrated in Figure 3.3, which includes an assessment of all types of physical, chemical and microbiological risks. Possible ranking schemes are numerous, but follow the generic structure indicated in Table 3.4, with Table 3.5 illustrating a simple risk scoring table.

**Table 3.4. Possible qualitative risk assessment approach to rank or scale hazardous scenarios**

<table>
<thead>
<tr>
<th>Step</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Hazard scenario</td>
<td>Identification of hazardous scenarios, such as massive rainfall-induced contamination of source water, filter breakthrough or loss/breakdown of chemical disinfection system (i.e. not necessarily limited to a single pathogen).</td>
</tr>
<tr>
<td>2. Likelihood</td>
<td>Ranking or scaling of how likely the event is (e.g. # events per year).</td>
</tr>
<tr>
<td>3. Consequence</td>
<td>Ranking or scaling of the consequence (e.g. short-term injury or ill-health through to permanent disability or death).</td>
</tr>
<tr>
<td>4. Scale of effect</td>
<td>Consideration of the number of people affected by the hazard scenario.</td>
</tr>
<tr>
<td>5. Risk score</td>
<td>Different weightings may be given to (2) to (3) and multiplied to give a value for each hazard scenario.</td>
</tr>
<tr>
<td>6. Rank</td>
<td>Each hazard scenario is then ranked, to provide a priority list for risk management.</td>
</tr>
</tbody>
</table>

**Table 3.5. Simple risk scoring table for prioritising risks**

(Davison et al., 2002)

<table>
<thead>
<tr>
<th>Likelihood</th>
<th>Severity of consequences</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Insignificant</td>
</tr>
<tr>
<td>Almost certain</td>
<td>5</td>
</tr>
<tr>
<td>Likely</td>
<td>4</td>
</tr>
<tr>
<td>Moderate</td>
<td>3</td>
</tr>
<tr>
<td>Unlikely</td>
<td>2</td>
</tr>
<tr>
<td>Rare</td>
<td>1</td>
</tr>
</tbody>
</table>

The risk score for a particular hazard = likelihood × severity of consequences.

An example of the descriptive terms that can be used to rate the likelihood and severity for calculation of the risk score is given in Table 3.6.
Figure 3.3. Generic flow diagram for sources of microbial risk in a drinking water context

(Adapted from Stevens et al., 1995)
Table 3.6. Example descriptive terms for risk score calculation (Davison et al., 2002)

<table>
<thead>
<tr>
<th>Item</th>
<th>Definition</th>
<th>Weighting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Almost certain</td>
<td>Once a day</td>
<td>5</td>
</tr>
<tr>
<td>Likely</td>
<td>Once per week</td>
<td>4</td>
</tr>
<tr>
<td>Moderate</td>
<td>Once per month</td>
<td>3</td>
</tr>
<tr>
<td>Unlikely</td>
<td>Once per year</td>
<td>2</td>
</tr>
<tr>
<td>Rare</td>
<td>Once every five years</td>
<td>1</td>
</tr>
<tr>
<td>Catastrophic</td>
<td>Potentially lethal to large population</td>
<td>5</td>
</tr>
<tr>
<td>Major</td>
<td>Potentially lethal to small population</td>
<td>4</td>
</tr>
<tr>
<td>Moderate</td>
<td>Potentially harmful to large population</td>
<td>3</td>
</tr>
<tr>
<td>Minor</td>
<td>Potentially harmful to small population</td>
<td>2</td>
</tr>
<tr>
<td>Insignificant</td>
<td>No impact or not detectable</td>
<td>1</td>
</tr>
</tbody>
</table>

Compared to both epidemiological and quantitative microbial risk assessment, this approach does not seek to determine actual levels of disease associated with a supply. As such, criticisms cannot be made that the conclusions are imprecise compared with reality. The other advantage that this approach has over other methods is that out of the process itself solutions to minimise risk will present themselves. On the other hand, reliance on ‘expert opinion’ does not always produce the correct answer as experts’ opinions and models of the world are often subject to bias and inaccuracies as with any other source of data (Hunter and Fewtrell, 2001).

3.7.1 Indicators and qualitative microbial risk assessment

Microbial and other indicator analyses will be a major source of evidence at several stages of qualitative risk assessment. The role of such information in conducting assessments of source water quality, treatment efficacy and integrity of the distribution system are discussed in more details in Chapters 4–6.

As will be seen, studies on the presence of indicator organisms frequently provide more useful information for qualitative risk assessment than do studies on enumeration of specific pathogens. Nevertheless, well-designed studies of specific pathogens can also be of great value in certain situation. For example, the detection of *E. coli*, faecal streptococci or sulphite-reducing *Clostridia* in source water all indicate that the water is subject to contamination from human or animal faeces. Detection and typing of *Cryptosporidium* in source water will
give a better understanding of the risk to the water supply system and the sources of contamination.

Coliform bacteria in treated water may give an indication that water treatment systems are not operating satisfactorily or that water is becoming contaminated within the distribution system. However, coliform bacteria alone are not good indicators of risk from chlorine-resistant pathogens such as *Cryptosporidium*. Some indicator organisms may be naturally present in the source water or can be deliberately seeded into the inlet to a water treatment works and monitored at various stages in the treatment and distribution in order to demonstrate the effectiveness of the whole system.

### 3.8 Summary

Microbial and other indicator parameters play an essential role in all the models used in the assessment of risk discussed in this chapter. However, the exact relationship between these indicator parameters and risk to health is still far from clear. Although studies have shown that turbidity and faecal streptococci are independent indicators of health risk there is no clear-cut predictive relationship. Even where information on pathogens in potable water is available, current quantitative risk assessment models have considerable uncertainty in their calculated risk. Perhaps the real value of such indicator parameters is in qualitative risk assessment where they can be used for identifying where failures may occur in the water extraction, treatment and distribution system.
REFERENCES


Esrey, S.A., Potash, J.B., Roberts, L. and Schiff, C. (1991) Effects of improved water supply and sanitation on ascariasis, diarrhoea, dracunculiasis,


