MOTIVATION

The prevention of infectious disease transmission from human exposure to contaminated food, water, soil, and air remains a major task of environmental and public health professionals. There are numerous microbial hazards, including exposure via food, water, air, and malicious release of pathogens that may arise. Indeed, some have argued that the property of virulence of human pathogens is one which is favored by evolutionary interactions between pathogens and host populations and therefore will always be of important concern [1]. To make rational decisions in preparing, responding, and recovering from exposures to such hazards, a quantitative framework is of high benefit.

The objective of this book is to comprehensively set forth the methods for assessment of risk from infectious agents transmitted via these routes in a framework that is compatible with the framework for other risk assessments (e.g., for chemical agents) as set forth in standard protocols [2, 3].

In this chapter, information on the occurrence of infectious disease in broad categories will be presented, along with a historical background on prior methods for assessment of microbial safety of food, water, and air. This will be followed by an overview of key issues covered in this book.

PREVALENCE OF INFECTIOUS DISEASE

Outbreaks of infectious waterborne illness continue to occur, although it remains impossible to identify the infectious agent in all cases. For example, in 1991, a waterborne outbreak in Ireland resulting from sewage contamination of water supplies infected about 5000 persons. However, the infectious agent responsible for this outbreak could not be determined [4]. In the United States, it has been estimated that 38 million cases of foodborne infectious disease occur annually with unidentified agents [5].

In the United States, there have typically been three to five reported outbreaks per year in community drinking water systems involving infectious microorganisms, with perhaps up to 10,000 annual cases [6]. The 1994 Milwaukee *Cryptosporidium* outbreak with over 400,000 cases [7, 8] was a highly unusual event among these statistics. As shown in Figure 1.1, there has been an increasing ability to identify...
microorganisms responsible for waterborne diseases, and it is expected that with advances in molecular biology, this will increase.

There are substantially more outbreaks and cases of foodborne infectious diseases than are reported. Table 1.1 summarizes reports of U.S. cases of principal microbial infectious foodborne illnesses for two 5-year periods (1988–1992 and 1995–2006).

Figure 1.1 Percentages of outbreaks associated with public water systems (n = 680) by time period 1971–2006 that had unknown etiologies based on data from Ref. [6].

TABLE 1.1 Comparison of Five-Year Averages for Common Foodborne Reported Outbreaks

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases Outbreaks</td>
<td>Cases Outbreaks</td>
</tr>
<tr>
<td>Campylobacter</td>
<td>99.6 4.4</td>
<td>624 22</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>48.8 2.2</td>
<td>481&lt;sup&gt;a&lt;/sup&gt; 30&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Salmonella</td>
<td>4,235.4 109.8</td>
<td>3,475 144</td>
</tr>
<tr>
<td>Shigella</td>
<td>957.6 5</td>
<td>495 12</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>335.6 9.4</td>
<td>554 25</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>421.8 8.6</td>
<td>238 1</td>
</tr>
<tr>
<td>Listeria monocytogenes</td>
<td>0.4 0.2</td>
<td>22 2</td>
</tr>
<tr>
<td>Giardia</td>
<td>36.8 1.4</td>
<td>2 1</td>
</tr>
<tr>
<td>Norovirus</td>
<td>58.4 0.4</td>
<td>10,854 338</td>
</tr>
<tr>
<td>Vibrio (all)</td>
<td>11.4 1.8</td>
<td>114 5</td>
</tr>
<tr>
<td>Unknown etiologies</td>
<td>40,483 1,422</td>
<td>4,052 30</td>
</tr>
</tbody>
</table>

Source: From Refs. [9, 10].

<sup>a</sup>Include both Shiga toxigenic and enterotoxigenic.
There is a mix of causal agents, including bacteria, virus, and protozoa. It is noteworthy that (as in the case of waterborne outbreaks) the frequency of outbreaks of unknown etiology has dramatically decreased but the frequency of outbreaks associated with norovirus has dramatically increased. These changes are due in part to the ability to better identify causal agents (e.g., via molecular methods).

It is generally recognized that reported outbreaks, either of water- or foodborne infectious disease, represent only a small fraction of the total population disease burden. However, particularly in the United States, voluntary reporting systems and the occurrence of mild cases (for which no medical attention is sought but nevertheless are frank cases of disease) have made it difficult to estimate the total caseload.

In the United Kingdom, comparisons between the number of confirmed cases in infectious disease outbreaks and total confirmed laboratory illnesses (occurring in England and Wales) have been made (Table 1.2). This suggests that the ratio of reported outbreak cases to total cases that may seek medical attention may be from 10 to 500:1, with some dependency on the particular agent.

Colford et al. [12] developed estimates for the total disease burden associated with acute gastroenteritis from drinking water. This relies on combining the reported outbreak data with interventional epidemiologic studies. Based on their analysis, the total U.S. disease burden is estimated to be 4.26–11.69 million cases per year in the United States, which is substantially in excess of the reported outbreaks. In the case of foodborne illness, there are an estimated 14 million cases per year [13].

Drinking water and food are by no means the only potential routes of exposure to infectious agents in the environment. Recreation in water (either natural or artificial pools) containing pathogens can produce illness [14].

Indoor air transmission can be a vehicle of infection. Legionella transmitted through indoor environments has been a concern since the 1970s [15]. The multinational epidemic of severe acute respiratory syndrome (SARS), caused by a coronavirus, was abetted at least in one location in Hong Kong by indoor aerosol transmission between apartments of infected individuals and susceptible individuals [16]. A broad spectrum of other respiratory pathogens including influenza, rhinoviruses, and mycobacteria can be transmitted by this route [17].

### Table 1.2 Comparison of Laboratory Isolations and Outbreak Cases in England and Wales, 1992–1994

<table>
<thead>
<tr>
<th>Agent</th>
<th>All Laboratory Reports</th>
<th>Confirmed Outbreak Cases</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campylobacter</td>
<td>122,250</td>
<td>240</td>
<td>509.4</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>47,463</td>
<td>127</td>
<td>373.7</td>
</tr>
<tr>
<td>S. sonnei</td>
<td>29,080</td>
<td>847</td>
<td>34.3</td>
</tr>
<tr>
<td>Salmonella</td>
<td>92,416</td>
<td>5,960</td>
<td>15.5</td>
</tr>
<tr>
<td>Cryptosporidium</td>
<td>14,454</td>
<td>1,066</td>
<td>13.6</td>
</tr>
<tr>
<td>E. coli O157</td>
<td>1,266</td>
<td>128</td>
<td>9.9</td>
</tr>
</tbody>
</table>

The deliberate release of *Bacillus anthracis* spores in 2001 (the “Amerithrax” incidents) brought widespread awareness to the potential for indoor releases (as well as releases in other venues) of bioterrorist agents to cause risk [18]. Therefore, of necessity, microbial risk assessors may need to consider the impact of malicious activity in certain applications.

**PRIOR APPROACHES**

Concerns for microbial quality of food, water, and other environmental media have long existed. In the early twentieth century, the use of indicator microorganisms was developed for the control and assessment of the hygienic quality of such media and the adequacy of disinfection and sterilization processes. The coliform group of organisms was perhaps first employed for this purpose [19–21]. Indicator techniques have also found utility in the food industry, such as the total count for milk and other more recent proposals [22]. Other indicator groups for food, water, or environmental media have been examined, such as *enterococci* [23–25], acid-fast bacteria [26], bacteriophage [27–29], and *Clostridia* spores [29–31].

The use of indicator organisms was historically justified in because of difficulty in enumerating pathogens. However, with the increasing availability of modern microbial methods, for example, PCR, immunoassay, etc., for direct pathogen assessment, this justification has become less persuasive. In addition, in order to develop health-based standards from indicators, extensive epidemiologic surveillance is often necessary. The use of epidemiology has limitations with respect to detection limits (for an adverse effect) and is also quite expensive to conduct. Indicator methods are also limited in that many pathogens are more resistant to die off in receiving environments or source waters than indicators or have greater resistance to removal by treatment processes than indicators [26, 28, 29, 32]. Thus, the absence of indicators may not suffice to ensure the absence of pathogens. Even after a century of use, the indicator concept remains imperfect [33].

The use of quantitative microbial risk assessment (QMRA) will enable direct measurements of pathogens to be used to develop acceptance/rejection guidelines for food, water, and other vehicles that may be the source of microbial exposure to human populations. The objective of this book is to present these methods in a systematic and unified manner.

**SCOPE OF COVERAGE**

QMRA is the application of principles of risk assessment to the estimate of consequences from a planned or actual exposure to infectious microorganisms. In performing a QMRA, the risk assessor aims to bring the best available information to bear in understanding the nature of the potential effects from a microbial exposure. Since the information (such as dose–response relationships, exposure magnitudes) is almost invariably incomplete, it is also necessary to ascertain the potential error
involved in the risk assessment. With such information, necessary steps to mitigate, control, or defend against such exposures may be developed.

At the outset of performing a risk assessment, a scoping task should be undertaken. This task should set forth the objectives of the analysis and the principal issues to be addressed. Items such as consideration of secondary cases, individual versus population risk, agent or agents to be examined, exposure routes, and/or accident scenarios must be stipulated. However, this scoping may be changed during the course of a QMRA, to reflect the input derived from the risk manager(s) and other stakeholders.

**POTENTIAL OBJECTIVES OF A QMRA**

There may be diverse objectives for a QMRA. These objectives relate to the rationale for the performance of the assessment, as well as the methods to be employed. Broadly, the different objectives reflect different scales at which a risk assessment may be performed. The step of problem formulation is critical to any risk estimate [34]. It is necessary that the problem be formulated to meet the needs of the risk managers and stakeholders; indeed, it is now recognized that the successful practice of risk analysis requires frequent interchange with manager and stakeholders [3]. In general, the problems posed are of several types.

**Site-Specific Assessment**

The simplest type of QMRA that may be performed involves one site or exposure scenario. The following are typical of the questions that might be asked:

1. If a water treatment plant is designed in a certain way (with given removals of pathogens), then what is the risk that would be placed upon the population served?

2. A swimming outbreak (in a recreational lake) has just occurred. I believe that it resulted from a short-duration contamination event. What pathogen levels would be consistent with the observed attack rate?

3. Microbial sampling of a finished food product has found certain pathogens. What level of risk does this pose to consumers of the product?

4. A certain amount of infectious agent has been released into a room. What is the immediate danger to occupants, and how stringent should cleanup levels be?

Note that there are certain other contrasts in the objectives of the risk assessments to be posed. In (1) and (3), a before-the-fact computation is desired, while in (2) and (4), an after-the-fact computation is described. Also in (1), (3), and (4), pathogen levels are available (or somehow are estimated), while in (2), an inverse computation is needed given an observed attack rate.

In performing this risk assessment, the relationship between an exposure or technological metric and a risk measurement must be ascertained and then the particular point of correspondence determined (Fig. 1.2). In cases (1), (3), and (4), for a known (or assumed) exposure (on the x-axis), the corresponding range of risks
on the \( y \)-axis is sought. In cases (2), for known or assumed risks (on the \( y \)-axis), the corresponding range of exposures (or level of technological protection) is to be determined (on the \( x \)-axis).

**Ensemble of Sites**

A somewhat more complex situation occurs if the risk for a set of events or sites must be estimated. Basically, this now includes the necessity to incorporate site-to-site factors into the assessment. Some examples of this are as follows:

1. If I desire keeping the risk to a population served by multiple water treatment plants at a given level (or better), then what criteria should I use (microbial levels)?

2. For a food product subject to contamination by pathogens, what would be an acceptable treatment specification (e.g., heating time, holding period) to ensure microbial acceptability?

3. I am designing a water quality standard for recreational bathing waters. If a uniform (e.g., national) standard is to be developed, what standard would ensure that average risk was acceptable with keeping the risk of a large “cluster” of illnesses low?

In addition to incorporating a measure of ensemble average risk, in general, it is also desired to ensure that no single member of the ensemble be unacceptably extreme. For example, consider the evaluation of three options of disease control among three communities, as indicated in Table 1.3.

This table indicates the number of cases, and the rate, among the three communities. The three policy options yield the same number of expected cases. However, there are differences in the allocation of risk among the communities of different sizes. In option A, all communities have an identical level of estimated risk. In option B, the risk increases as community size decreases, while in option C, the risk increases as community size increases. This distribution of risk among affected subsets of the
ensemble being considered adds an additional dimension for consideration by a risk manager—which may be termed risk equity.

SECONDARY TRANSMISSION

Infectious microbial diseases are different in terms of risk to a population than are chemical agents in that an individual who may become infected (with or without illness) can then proceed to infect additional individuals. These secondary (tertiary, quaternary, etc.) cases may be persons who had no direct contact with the initial vehicle of exposure, but nevertheless in fairly accounting for the public health impact, they should be considered.

Secondary cases may arise by a variety of mechanisms. Particularly among close family members, household secondary cases can arise by direct or indirect (e.g., surface contamination) contact; this is particularly so when the primary case or one household secondary case is a child [35–37]. Table 1.4 summarizes secondary case statistics obtained from a variety of outbreaks. As will be discussed in Chapter 10, the secondary case rate is a complex factor involving (among other things) the nature of the venue and contact patterns when infected and susceptible individuals intermingle.

Presumably, secondary cases may also arise from close contact with an asymptomatic individual (in the “carrier” state). This is well known for highly acute and (now) uncommon illnesses (such as typhoid). Excretion of Norwalk virus following recovery (and resulting in additional cases) has been documented to occur for as long as 48 h post recovery [44].

OUTBREAKS VERSUS ENDEMIC CASES

As noted previously, there may be a substantial difference between reported outbreak cases and total disease burden in a community. In order for a disease case to receive recognition by the public health authorities, the following specific and sequential steps must occur [47]:
1. An ill person must seek medical care.
2. Appropriate clinical tests (e.g., blood, stool) must be ordered by the attending physician.
3. The patient must comply with obtaining the sample.
4. The laboratory must be capable of detecting the relevant pathogens.
5. The clinical test must be positive.
6. The test result must be reported to the health agency in a timely manner.

If any of the links in this sequential chain are broken, then a disease case will not enter the records maintained by health authorities. For example, with increasing controls on

### TABLE 1.4 Summary of Secondary Case Data in Outbreak Situations

<table>
<thead>
<tr>
<th>Organism</th>
<th>Secondary Attack Ratio</th>
<th>Secondary Prevalence in Households</th>
<th>Remarks</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryptosporidium parvum</td>
<td>0.33</td>
<td>0.33</td>
<td>Outbreak in contaminated apple cider</td>
<td>[38]</td>
</tr>
<tr>
<td>C. parvum</td>
<td>N/A</td>
<td>0.042</td>
<td>Drinking water outbreak (Milwaukee)</td>
<td>[37]</td>
</tr>
<tr>
<td>Shigella</td>
<td>0.28</td>
<td>0.26</td>
<td>Day-care center outbreaks in children</td>
<td>[39]</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>0.42</td>
<td>0.15</td>
<td>Day-care center outbreaks in children</td>
<td>[30]</td>
</tr>
<tr>
<td>Giardia lamblia</td>
<td>1.33</td>
<td>0.17</td>
<td>Day-care center outbreaks in children</td>
<td>[39]</td>
</tr>
<tr>
<td>Viral gastroenteritis</td>
<td>0.22</td>
<td>0.11ª</td>
<td>Drinking waterborne outbreak</td>
<td>[40]</td>
</tr>
<tr>
<td>Viral gastroenteritis</td>
<td>0.56</td>
<td>N/A</td>
<td>Drinking water outbreak (Denmark)</td>
<td>[41]</td>
</tr>
<tr>
<td>Norovirus</td>
<td>0.5–1.0</td>
<td>0.19</td>
<td>Swimming outbreak</td>
<td>[42]</td>
</tr>
<tr>
<td>Norovirus</td>
<td>1.1</td>
<td>0.29</td>
<td>Swimming outbreak</td>
<td>[43]</td>
</tr>
<tr>
<td>Norovirus</td>
<td>N/A</td>
<td>0.44</td>
<td>Foodborne outbreak</td>
<td>[36]</td>
</tr>
<tr>
<td>Norovirus</td>
<td>0.4</td>
<td>N/A</td>
<td>Foodborne outbreak</td>
<td>[44]</td>
</tr>
<tr>
<td>E. coli O157:H7</td>
<td>N/A</td>
<td>0.18ª</td>
<td>Day-care center outbreak in children</td>
<td>[45]</td>
</tr>
<tr>
<td>Unidentified day-care diarrheal diseases</td>
<td>1.38</td>
<td>0.09ª</td>
<td></td>
<td>[46]</td>
</tr>
</tbody>
</table>

N/A, information not available.

ª Ratio of secondary cases to primary cases.

ª Proportion of households with one or more primary cases who have one or more secondary cases.

ª Proportion of persons in contact with one or more primary cases who have a secondary case.
medical care, stool samples may not be obtained from mild cases of illness. Some organisms may only be present sporadically, or may be difficult to test, in stool or blood sample. Patients may not seek medical attention for mild cases of illness. Furthermore, in the United States in particular, the surveillance of environmentally induced disease is done on a passive basis, and hence, the number of actual illness clusters that are actually compiled into recorded statistics is only a small fraction of such clusters of illness that occur [47].

From a more fundamental point of view, an outbreak of illness is generally defined as occurrence of the illness at a level greater than normal or anticipated. This definition recognizes that there is a level of illness (endemic) that may exist under usual circumstances. The detection of such outbreaks poses a particular challenge. The problem is illustrated conceptually in Figure 1.3.

Additional complications arise from the different patterns of illness in a community, including definite periodicities, as well as temporal trends, and from the presence of reporting lags associated with laboratory analysis and time for patients to seek medical attention. Figure 1.4 illustrates the different patterns of illness in the case of six pathogens for England and Wales [48].

In the case of waterborne and foodborne illnesses, it is highly likely that the level of such endemic illnesses is substantially greater than those occurring during outbreaks (even accounting for unrecognized outbreaks).

As a result, there are often many cases of environmentally caused (water, air, food) infectious disease that are unrecognized. One example of this is *Campylobacter*. There has been an average of about 200 cases per year of water- and foodborne illness in outbreaks of this organism, and yet estimates of the disease burden suggest about 2,100,000 cases per year, that is, approximately 10,000 cases per case of detectable outbreak illness. Therefore, it will be important to assess the factors that may influence outbreak detection. These issues will be discussed in subsequent chapters.

![Figure 1.3 Schematic of disease occurrence in a hypothetical community (Modified from Ref. [47]).](image-url)
REFERENCES


Figure 1.4 Weekly count of reported organism isolations in England and Wales: (a) rotavirus, (b) *Clostridium difficile*, (c) *Salmonella derby*, (d) *Shigella sonnei*, (e) influenza B, and (f) *Salmonella typhimurium* DT 104 (From Ref. [48]).
REFERENCES


