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Epidemiology: Science as a Tool to Inform One Health Policy

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1.1 Introduction

Epidemiology is the study of disease dynamics in populations. It seeks to understand patterns of disease as a means of identifying potential prevention and control measures. It has been described as "an interesting and unique example of cross-fertilization between social and natural sciences" (Vineis, 2003). The basic principle of epidemiology is that disease is not a random event. Each individual in a population has a unique set of characteristics and exposures (risk factors) that determine his or her probability of disease. Clinical medicine is focused on the health of the individual while epidemiology and public health seek to apply assessment of risk factors at the community level. Understanding how those risk factors impact a community provides public health officials with the tools to develop policies and interventions for disease control and prevention in the community as a whole.

The One Health concept is coherent with the principles of epidemiology because risk factors for many diseases occur at the interface between humans, animals, and the environment. Failure to consider the interactions between them may result in public health policies that fail to effectively control disease and protect the environment. The One Health triad (Figure 1.1) of humans, animals, and the environment is analogous with the other triads that epidemiologists use to describe disease dynamics within a population:

- The host, agent, environment triad (Figure 1.2) is used to describe the interplay between these three key components of infectious disease transmission. Changes in any of these components alters the probability of disease.
- The three states of infectious disease status are illustrated by the susceptible, infected, removed (SIR) triad (Figure 1.3).
- Outbreaks of disease are characterized in terms of person or animal, place, and time as the first step of identifying the population at risk.
- Risk factors for disease causation are categorized as: necessary, sufficient, and component causes (Figure 1.4).

The goal of public health policy is to prevent transmission of disease agents to the susceptible segment of the population by controlling and treating disease among the infected and increasing the segment of the population that is removed (recovered or resistant). Identification and isolation of cases, quarantine of the exposed, and vaccination of the

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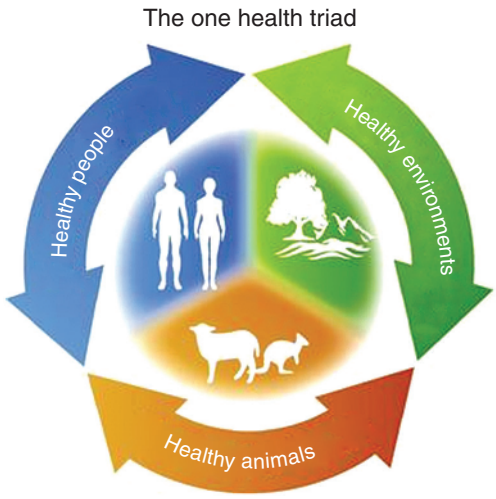

Figure 1.1 The One Health triad. *Source:* Thompson, 2013. Reproduced with permission of Elsevier.

susceptible are the primary tools employed by public health practitioners for infectious disease control. Development of effective programs to accomplish these goals requires an understanding of the:

1) Causes of disease (etiologic agent, pathophysiology, and risk factors.
2) Impact of the disease on the population (number of cases, ease of transmission, economic and social impact).
3) Natural course of the disease (reservoirs for the agents of disease, means of introduction of the agent into the population, period of infectivity, severity of disability, length of immunity, and potential for long-term sequelae) (Figure 1.5).

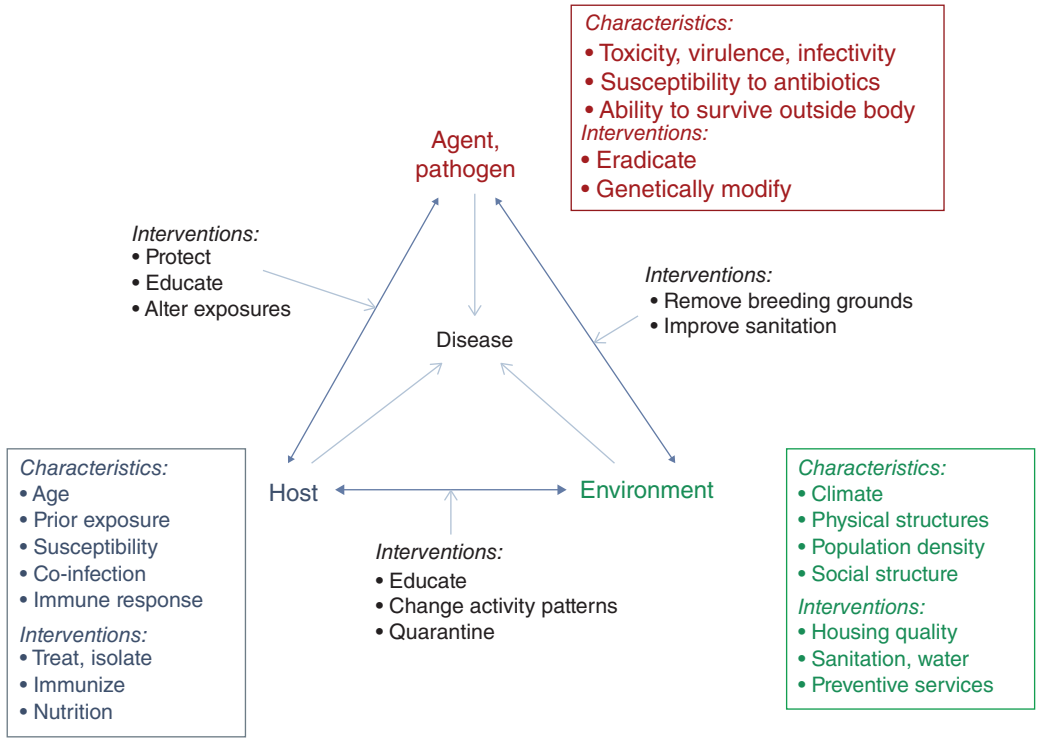

Figure 1.2 The "epidemiologic triad" of infectious disease summarizes the factors that influence an infection, and the measures you might take to combat the infection. *Source:* Used with permission from Ian McDowell (http://www.med.uottawa.ca/SIM/data/Pub_Infectious_e.htm#epi_triad).

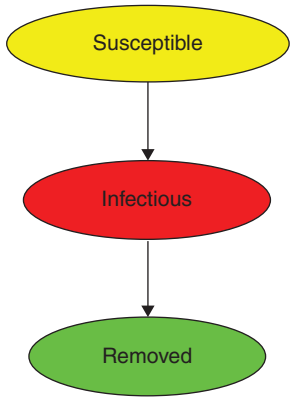

Figure 1.3 Infection modeling: the SIR model. **Susceptible** nodes – have not been infected yet and are therefore available for infection. They do not infect other nodes. **Infectious** nodes – have been infected and infect other nodes with a certain probability. **Removed** (recovered) nodes – have gone through an infectious period and cannot take part in further infection (neither actively nor passively). *Source:* Used with permission from Michael Jaros (http://mj1.at/articles/infection-modelling-the-sir-model/).

The goals of this chapter are to elucidate how epidemiology can 1) provide a tool for understanding the causes, impacts, and course of disease in human and animal populations within various ecosystems, and 2) form the basis for evidence-based health and environmental policy development.

1.2 Enhancing Our Understanding of Health and Disease

1.2.1 Causes of Disease

Epidemiology is unique among biomedical investigative approaches because of the observational nature of many of the study designs. Unlike laboratory studies, the epidemiologist often studies a naturally

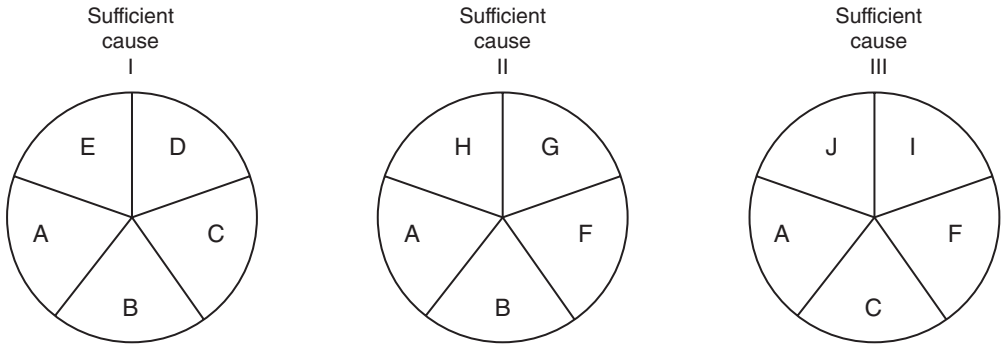

Figure 1.4 Necessary, sufficient, and component causes. The individual factors are called component causes. The complete pie (or causal pathway) is called a sufficient cause. A disease may have more than one sufficient cause. A component that appears in every pie or pathway is called a necessary cause, because without it, disease does not occur. *Source:* Rothman, 1976. Reproduced with permission of Oxford University Press.

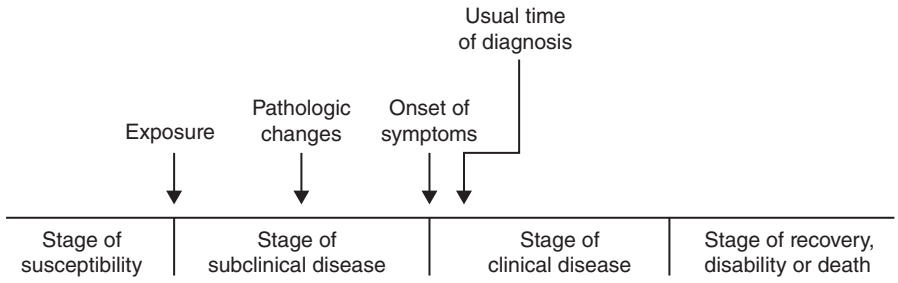

Figure 1.5 Natural history of disease timeline. *Source:* CDC, 1992.

occurring disease within a free-living population in which study subjects are not assigned to intervention groups (except in the case of clinical trials). Individuals may have a variety of independent exposures during the study period. Whether studying human or animal populations, the epidemiologist seeks to identify exposures that are associated with the probability of disease using statistical analysis of data from carefully documented exposures and outcomes. However, even if a statistically significant association between an exposure and disease outcome has been identified, that does not necessarily mean that a cause and effect relationship has been established. Much more rigorous standards have been set for establishing a causal relationship between a risk factor and the probability of disease.

1.2.1.1 Deterministic Models of Disease

Criteria for establishing causation for infectious disease have been described since the nineteenth century. Research by Robert Koch, Friedrich Loeffler, and Jakob Henle resulted in the Koch–Henle postulates published in 1882 (Sakula, 1983; Gradmann, 2014) (Figure 1.6). While this approach is useful when seeking to identify the etiologic agent responsible for an infectious disease, it has many limitations. The simplistic approach of a deterministic model for establishing disease causation is insufficient for identifying risk factors for chronic noninfectious diseases (such as type II diabetes) or even infectious diseases with a multifactorial etiology (such as new variant Creutzfeldt–Jakob disease, or CJD). In more recent years more complex

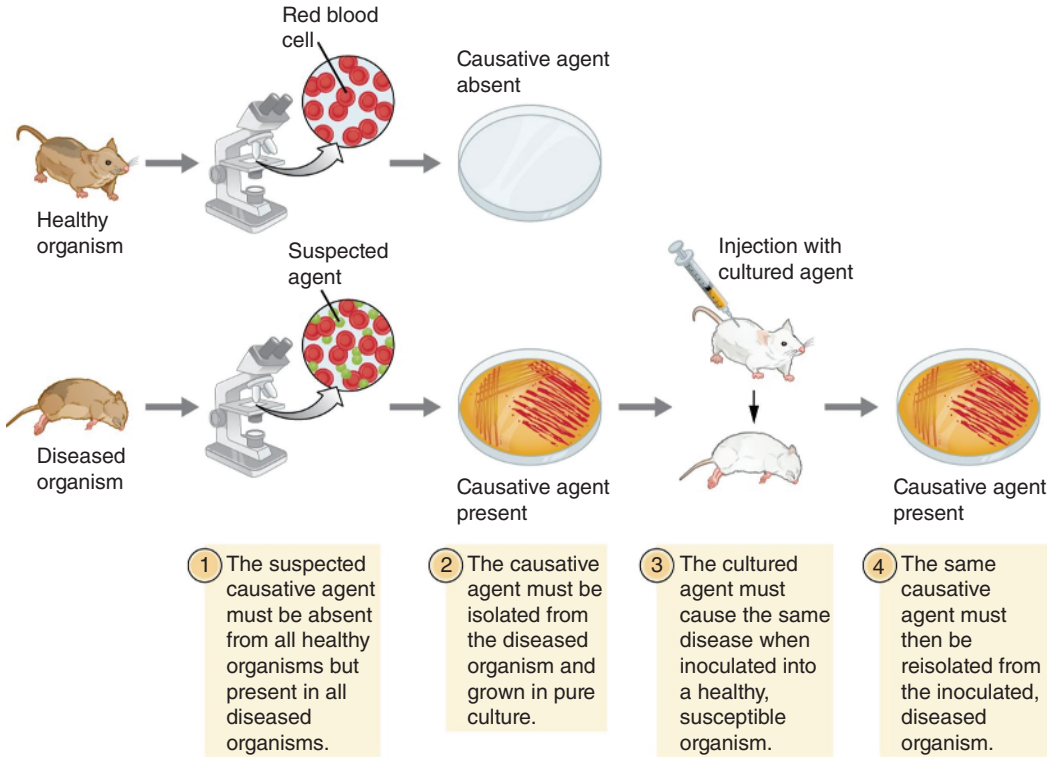

Figure 1.6 The steps for confirming that a pathogen is the cause of a particular disease using Koch's postulates.

models have been used to establish a causal relationship between a putative risk factor and disease.

1.2.1.2 Hill's Causal Criteria

Austin Bradford Hill published "The environment and disease: association or causation?" in 1965 (Hill, 1965). The manuscript describes nine criteria necessary for establishing a causal relationship between a risk factor and a disease:

1) *Strength of association:* the greater the magnitude of the association between the risk factor and the outcome, the more likely the relationship is to be causal.
2) *Temporality:* the risk factor must precede the onset of the disease.
3) *Consistency:* the same association should be observed in multiple studies with different populations.
4) *Theoretical plausibility:* the association should be biologically plausible and consistent with the pathophysiology of the disease.
5) *Coherence:* the association should be consistent with what is known about the disease.
6) *Specificity in the causes:* a risk factor should be associated with a single disease or outcome.
7) *Dose-response relationship:* as the dose of the risk factor is increased the probability and severity of the disease should increase in a linear fashion.
8) *Experimental evidence:* data from *in vitro* studies and animal models should support the causal association between the risk factor and the disease.
9) *Analogy:* similar causal relationships should be known.

The nature of these criteria makes it impossible for a single observational study to establish a causal relationship between an exposure and a disease outcome. The criterion of consistency requires that multiple studies, in different populations, show the same association. The criterion of temporality also requires that the association be demonstrated in prospective studies. Prospective study designs monitor the study population prior to the onset of disease and follow their exposures over time until the disease of interest occurs. However, as we learn more about the complexity of the interactions between hosts and their exposures, limitations of the Bradford Hill Causal Criteria have also been described (Rothman, 2012). Some of Hill's Causal Criteria have been challenged by known causal associations that are contradictory. Specificity of effect, dose-response gradient, and coherence are all criteria whose validity has been challenged.

The criterion of specificity fails to acknowledge the potential for a single exposure to cause a multiplicity of pathologic effects. One well-known example of this is seen with exposure to tobacco smoke, which is associated with lung cancer, chronic obstructive pulmonary disease, heart disease, stroke, asthma, impaired fertility, diabetes, premature/low birthweight babies, blindness, cataracts, age-related macular degeneration, and cancers of the colon, cervix, liver, stomach, and pancreas (American Lung Association, 2017).

Many disease-causing exposures fail to produce a linear dose-response gradient. Goldsmith and Kordysh (1993) reviewed the literature for examples of nonlinear dose-response relationships and concluded that nonlinear causal relationships are equally as common as linear associations. Their analysis of the literature concluded that dose-response relationships are often nonlinear when countervailing outcomes are likely. They cautioned against linear extrapolation of dose-response data to develop policies and regulations for the protection of human populations. Exposures such as ionizing radiation and vitamin toxicity have been reported to produce U- or J-shaped dose-response curves (May and Bigelow, 2005). Inadequate sample size in the research study, insufficient range in the exposure dosages, and variability in individual susceptibility are all factors that

impede the identification of these nonlinear dose-response causal relationships.

The criterion of coherence doesn't allow for paradigm shifts in models of disease causation. Identification of new mechanisms of disease pathogenesis may require elucidation of relationships that are not coherent with the current body of knowledge about the disease process. This is illustrated by the work of Marshall and Warren (1984) and their discovery of the role of *Helicobacter pylori* in the etiology of gastritis and peptic ulcers. Prior to their research, acid production was believed to be the key risk factor for the development of gastritis and peptic ulcers. Gastritis was thought to be a chronic inflammatory disease; the concept that it was actually due to a bacterial infection, was not coherent with the theory of the disease at the time of the findings by Marshall and Warren.

1.2.1.3 Multifactorial Models of Disease Causation

Krieger (1994) describes the transition in epidemiology from a focus on acute and infectious diseases to research focused on chronic disease. These more complex disease etiologies were first described as a "web of causation" in 1960. Multifactorial causes of disease have been framed as host-agent-environment models and social determinants of health. The public health application of these models is manifested as identification of the necessary component causes of disease and directing policies and interventions at those causes that are most amenable to alteration (see Figure 1.4).

In summary, epidemiology has evolved from a monocausal (deterministic) model to the multicausal concept of the "web of causation" (Vineis, 2003). The models that seek to describe disease causation continue to evolve. More recently, an "ecosocial framework" has been proposed as a more holistic, comprehensive approach to describing the how and why of disease occurrence (Krieger, 1994) (Figure 1.7). Unlike the web of causation, this model takes a One Health approach to understanding disease in human populations. Krieger concludes that "encouraging a social and ecologic point of view, this image also serves as a reminder that people are but one of the species that populates our planet; thus implies that the health of all organisms is interconnected."

1.2.1.4 Breaking the Chain of Transmission

The goal of epidemiology is to enhance the health of populations. The rationale for researching risk factors for disease is to identify policies and interventions that can be employed to prevent disease. One of the most important lessons of epidemiology is that disease can be controlled even when there is incomplete knowledge of the etiologic agent responsible for the disease. Louis Pasteur conducted research that led to the germ theory of disease between 1860 and 1864. Prior to this discovery, John Snow's classic work on the epidemiology of the 1854 cholera epidemic in London demonstrated that an infectious disease outbreak can be controlled by understanding risk factors for disease, even if the etiologic agent is unknown. In the 1854 outbreak, new cases of cholera were prevented by removing the handle from the Broad Street pump once the water source was identified as being the important exposure associated with cholera deaths in that part of London.

More recently, the first case of acquired immune deficiency syndrome (AIDS) was reported in 1981 and it wasn't until 1984 that the etiologic agent, human immunodeficiency virus (HIV), was discovered. However, in 1982, it was known that the disease was caused by a blood-borne or sexually transmitted virus and high-risk segments of the population had been identified. Even before the etiologic agent had been discovered, measures to prevent disease transmission were identified, including condom use and avoidance of needle-sharing among IV drug users (https://history.nih.gov/nihinownwords/docs/page_02.html) (Poundstone et al., 2004).

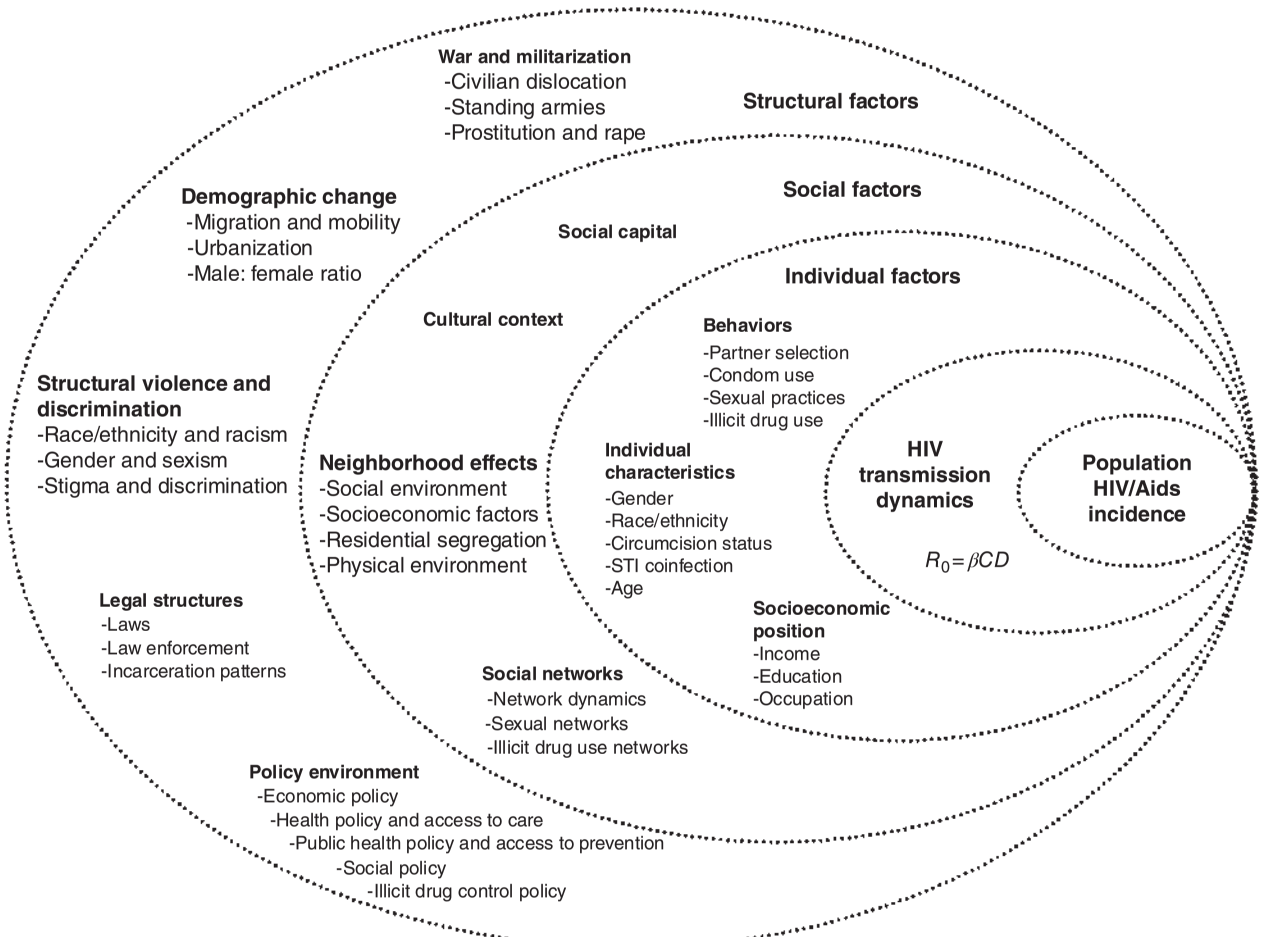

Figure 1.7 Ecosocial framework. An heuristic framework for the social epidemiology of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS). The dotted lines separating the levels illustrate the porous nature of the distinctions made between levels of analysis. In reality, there are extensive linkages between factors at all levels that give rise to observed epidemic patterns. STI, sexually transmitted infection. *Source:* Poundstone et al., 2004. Reproduced with permission of Oxford University Press.

1.2.2 Assessing the Impact of Disease

The foundation of assessing a population health problem is determining the impact of the disease on the population. How big is the problem? Answering this question requires establishing the:

- number of individuals in the population with the disease (prevalence);
- number of new cases of disease that will occur in a given period of time (incidence);
- ease with which the disease spreads within the population (infectiousness);
- severity of the illness (agent virulence); and
- cost of the disease to society.

The *prevalence* of disease is a measure of the number of cases of disease at a given point in time. Prevalence of disease includes both recently diagnosed cases and chronic cases that have lived with the disease for some time. Knowing the prevalence of a disease in a community allows public health personnel to determine the resources necessary to manage the disease in the community. The *incidence* of disease is focused only on those new cases of disease identified within a given time period. Incidence tells how frequently new cases of the disease are occurring.

Infectiousness is a description of how easily an agent is transmitted from one host to another. Some agents are inherently very infectious and can spread quickly and easily to multiple susceptible hosts. The basic reproduction number, or R_0, is a measure of infectiousness of an agent in a totally susceptible population. The R_0 is the number of new cases of disease a single case will generate during its infectious period. Examples of highly infectious pathogens include measles virus in humans and foot-and-mouth disease (FMD) virus in livestock. Measles has an R_0 of 12–18 (CDC and WHO, 2014) meaning that in an unvaccinated population, each case of measles can be expected to infect an additional 12 to 18 people. A recent study of FMD transmission in dairy cattle reported an R_0 of infinity for nonvaccinated dairy cattle in the same pen. In contrast, other agents are inherently less infectious. Estimates of infectiousness of the seasonal influenza virus report an R_0 of approximately 1.3 (Biggerstaff et al., 2014). R_0 is an inherent characteristic of an infectious agent. However, it is the interaction between the population, the environment, and the agent that best describes the spread of disease within a population. This is expressed by the effective reproduction number (R). "R" is the average number of new cases generated by a single case in a population that consists of both immune and nonimmune individuals. If R is less than 1.0, sustained transmission within a population cannot occur. As long as the R is greater than 1.0, meaning each case spreads the disease to more than one new case, the disease will continue to spread in the population. Without intervention the entire population will eventually get the disease.

The basic reproduction number (R_0) not only provides information about how likely an agent is to cause an epidemic, it also indicates the percentage of the susceptible population that must be vaccinated or be immune through natural infection to prevent disease transmission. This is referred to as *herd immunity* – a state in which enough members of the population are immune to the disease to prevent spread, thus protecting those who are not immune. So, for measles, 83–94% of the population must be vaccinated to achieve herd immunity (CDC and WHO, 2014), while for influenza it has been reported that only 13–40% (depending on the influenza strain) of the population needs to be vaccinated to establish herd immunity (Plans-Rubio, 2012).

The practical application of this information is that it can be used to direct public health interventions that have the potential to stop transmission. Vaccination programs reduce the number of individuals in the population who are susceptible to the disease, and the population can achieve a state of herd immunity if a sufficient percentage is vaccinated. Case finding efforts, combined with treatment and isolation of infectious

individuals, and education programs, such as hand washing and social distancing campaigns, can reduce the number of individuals in the population who are exposed to the agent, thereby preventing spread of the agent to new susceptible hosts.

The *virulence* of an agent is an indication of the severity of the illness it causes. Some pathogens cause mild, self-limited illnesses with few clinical signs, while more virulent agents result in debilitating disease or even death. Agent virulence is assessed using the *case-fatality rate* (CFR). The CFR is simply the rate of death due to a disease among all cases of the disease. The CFR for chickenpox in children (varicella) is 0.001% or 1 in 100 000 (Heymann, 2008). In comparison the CFR for rabies is 100% (WHO, 2017). Thus, the virus causing rabies in humans is much more virulent than that causing chickenpox.

In addition to considering the number of sick individuals, the rate of disease spread, and the severity of the illness, assessing the impact of a disease must also take into consideration the burden of the disease on society (Figure 1.8). Direct economic costs of disease include the cost to diagnose, treat, or prevent the disease. Indirect economic costs may include lost productivity due to absenteeism from work or losses due to declines in trade and tourism caused by fear of the disease, and so forth. Lastly the social disruption caused by the disease, or fear of the disease, can be more costly than the actual cases of disease. Remnants of this disruption may last years beyond the disease event.

It is easy to see how an outbreak of a high-incidence, rapidly spreading disease, caused by a very virulent agent, can have a huge economic and social impact on a community. This was apparent during the 2014–2016 West African Ebola virus disease outbreak in which there were an estimated 28 652 human cases and 11 325 deaths in 10 countries (CDC, 2016). The 2015 United Nations Development Group (UNDG) report on the socioeconomic impact of Ebola virus disease in West African countries indicates that the impact of the 2014–2015 Ebola outbreak was pervasive in the affected countries: labor markets shrank; access to food and the quality and quantity of food consumed was decreased; access to education declined for children, due both to mortalities among educators and school staff and to school closures; access to health services declined substantially; and there was an erosion of

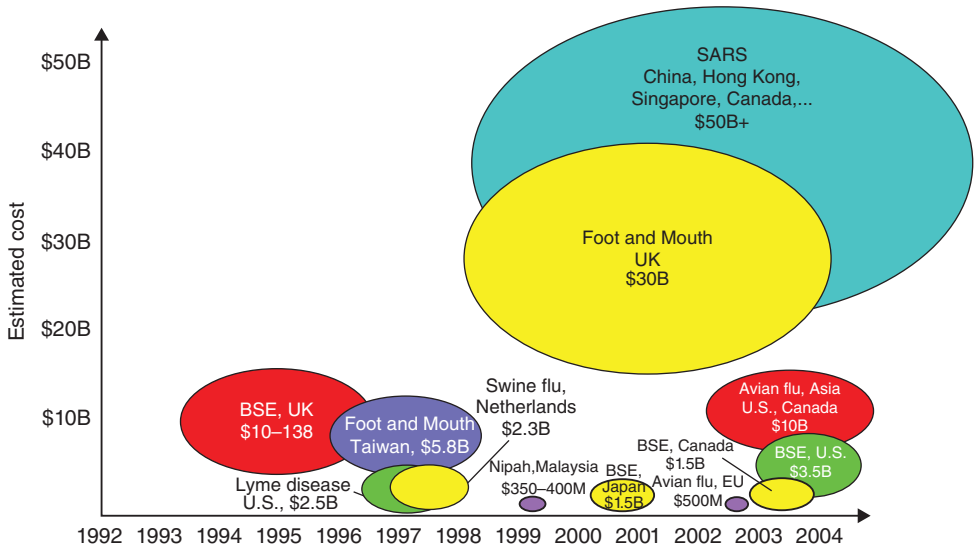

Figure 1.8 Economic impact of disease. *Source:* Karesh, 2007. Reprinted with permission from Bio-era.

communal cooperative behaviors and relationships (UNDG, 2015). Declines in gross domestic product (GDP) for the most severely impacted countries were estimated to range from 3.4% for Guinea to 13.7% for Liberia (UNDG, 2015). As a result, prior trends in poverty reduction are expected to slow or reverse in Guinea, Liberia, and Sierra Leone. In fact, the economic impact will be felt throughout the entire region. West Africa is expected to incur losses of approximately 3.6 billion US dollars per year for the period 2014–2017 (UNDG, 2015).

In some cases, the devastating socioeconomic impact of a disease outbreak is caused by a combination of illness and death in both human and domestic animal populations. Rift Valley fever (RVF) is a mosquito-borne emerging viral disease that causes severe disease in human and animal populations. First reported in Kenya in 1930, outbreaks have been documented in several countries in sub-Saharan Africa. However, in the year 2000 a large outbreak of human cases was reported in Saudi Arabia and Yemen. A total of 516 human cases of severe RVF, with 87 deaths, were documented between August and November of 2000 (CDC, 2000). A 2007 outbreak of RVF in the Sudan was reported to have caused an estimated 75 000 human cases (Anyamba et al., 2010). Symptoms in human cases may range from mild febrile illness to vision loss, encephalitis, and hemorrhagic disease in 8–10% of cases (CDC, 2013). In cattle, sheep, goats, and camels, RVF causes abortion and perinatal mortality rates in excess of 95% (Hassan et al., 2011). Outbreaks of RVF in livestock result in reduced access to food, loss of income from livestock production, and loss of export markets due to trade bans, in addition to costs to the government for disease control, surveillance, and assistance to producers (Hassan et al., 2011). A 2007 RVF outbreak in Kenya was reported to cause US$32 million in losses (Rich and Wanyoike, 2010).

However, a relatively rare disease with few cases in any community can still place a huge burden on society in terms of the direct and indirect economic and social costs of the disease. The economic and social impact of diseases like severe acute respiratory syndrome (SARS) and bovine spongiform encephalopathy (BSE, or mad cow disease) illustrate that a limited number of human cases of disease can have huge social and economic consequences on the affected community and beyond (Figure 1.8). The SARS pandemic occurred from November 2002 through July 2003. During that period there were 8098 total cases of SARS with 774 deaths across 29 countries with an estimated economic impact of US$30–50 billion. Human exposure to the prion that causes BSE in cattle is a cause of variant Creutzfeldt–Jakob disease (vCJD) in humans. There were 178 human cases of vCJD in the UK between 1995 and 2016 (CDC, 2017), while concern that BSE may pose a human health risk resulted in losses of 740–980 million GBP in 1992 in the UK (Atkinson, 2014).

Even a disease outbreak in which only domestic animal health is at risk can have a substantial economic impact. From December of 2014 through June of 2015, the USA experienced its largest foreign animal disease outbreak in history. Only avian species were affected in this outbreak of highly pathogenic avian influenza, which spread across three migratory bird flyways and resulted in the death or euthanasia of more than 50 million birds on 232 premises (https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/animal-disease-information/avian-influenza-disease/sa_detections_by_states/hpai-2014-2015-confirmed-detections). Laying hens and turkeys were the predominant agricultural species impacted by the outbreak. Total economic losses associated with the outbreak were estimated to be US$3.3 billion (https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/animal-disease-information/avian-influenza-disease/sa_detections_by_states/hpai-2014-2015-confirmed-detections). In the UK, the 2001 outbreak of FMD was estimated to causes losses of 3.1 billion GBP to the food and agricultural segment alone, with additional losses to tourism that were similar in magnitude (Thompson et al., 2002). Over 10 million cows and sheep

were euthanized to get the outbreak under control. Although human health was not directly impacted by FMD, the outbreak response activities, which included the mass depopulation of livestock, restrictions in human movement, social isolation, and resultant job losses, took a heavy psychological toll on affected communities. As a result, increased rates of psychological morbidity were reported in affected areas, with morbidity rates in farmers correlated with the level of livestock culling and movement restrictions (Peck, 2005). These events highlight the inextricable connections between human, animal, and ecosystem health – demonstrating that events effecting one segment of the triad inevitably impact the others even if indirectly.

1.2.3 Natural Course of Disease

Each case of a disease in a population follows a progression from susceptible to recovery or death (see Figure 1.5). Interactions between the host, the agent, and the environment influence the rate of progression and the end result. *Susceptible* individuals are those at risk for becoming a case of the disease. Exposure to risk factors for the disease or to the infectious agent increases the probability of becoming a case only for those members of the population who are susceptible. Once a susceptible population member is exposed, the disease process may begin. This early phase of the disease often poses the greatest risk to the rest of the susceptible population because clinical signs of illness have not developed and the disease is difficult, if not impossible, to detect. For infectious diseases, this means that infected humans or animals may infect others in the population without showing clinical signs. The length of time from exposure to a disease-causing agent to the onset of clinical signs is referred to as the *incubation period*. Agents have different incubation periods, with some as short as a few minutes, while others may take decades before clinical signs develop (Table 1.1).

Once clinical signs appear, there is the possibility that the disease can be detected and steps taken to intervene and prevent transmission to other susceptible population members. Even if control measures or treatments are not implemented, the simple onset of signs can reduce contacts with noninfected susceptible population members. Animals that are clinically ill often distance themselves from the rest of the herd or flock (Lopes et al., 2016). In human populations, public health policies focused on social distancing have been shown to effectively reduce transmission of infectious disease (Glass et al., 2006).

The final stage of disease is also influenced by host and agent factors. As discussed earlier in this chapter, virulence of the agent influences severity of the illness, degree of disability, and the rate of death among cases. Agent *immunogenicity* reflects the host's ability to develop immunity to the disease upon recovery and the duration of this immunity. These agent characteristics also impact the ease with which effective vaccines can be developed to reduce the number of susceptible individuals in the population. The duration of the period of time from onset of clinical signs to the resolution of any secondary sequelae or long-term disability has a large potential impact on the economic and social costs of the disease.

1.2.3.1 Reservoirs of Disease

So far in this chapter, host factors and agent factors have been the focus of discussion. Where does the environment fit into this triad? Where does the infectious disease agent "live" when it is not infecting a host? In addition to understanding the agent and the susceptible hosts that it infects, breaking the chain of transmission requires understanding where that agent can be found in nature and how the host becomes exposed to it. The *reservoir* of a disease is the habitat in which the agent normally lives, grows, and multiplies (http://www.cdc.gov/ophss/csels/dsepd/ss1978/lesson1/section10.html). Humans, animals, and the environment are potential reservoirs for infectious disease agents and, in some cases, insects serve as vectors transmitting infectious disease agents to new hosts (Table 1.2). Identifying the reservoir and finding measures to control or eradicate

Table 1.1 Incubation periods of selected exposures and diseases.

Exposure	Clinical effect	Incubation/latency period
Saxitoxin and similar toxins from shellfish	Paralytic shellfish poisoning (tingling, numbness around lips and fingertips, giddiness, incoherent speech, respiratory paralysis, sometimes death)	Few minutes to 30 minutes
Organophosphorus ingestion	Nausea, vomiting, cramps, headache, nervousness, blurred vision, chest pain, confusion, twitching, convulsions	Few minutes to a few hours
Salmonella	Diarrhea, often with fever and cramps	Usually 6–48 hours
SARS-associated corona virus	Severe acute respiratory syndrome (SARS)	3–10 days, usually 4–6 days
Varicella-zoster virus	Chickenpox	10–21 days, usually 14–16 days
Treponema pallidum	Syphilis	10–90 days, usually 3 weeks
Hepatitis A virus	Hepatitis	14–50 days, average 4 weeks
Hepatitis B virus	Hepatitis	50–180 days, usually 2–3 months
Human immunodeficiency virus	AIDS	<1 to 15+ years
Atomic bomb radiation (Japan)	Leukemia	2–12 years
Radiation (Japan, Chernobyl)	Thyroid cancer	3–20+ years
Radium (watch dial painters)	Bone cancer	8–40 years

Source: Centers for Disease Control and Prevention (http://www.cdc.gov/OPHSS/CSELS/DSEPD/SS1978/Lesson1/Section9.html#_ref44).

the agent from that reservoir is a goal of epidemiology that often proves to be elusive.

1.2.3.2 Humans as a Reservoir

The best hope for disease eradication is found in those diseases in which humans are the only reservoir. In 1980 the world was declared free of smallpox. Stuart-Harris (1984) identified features of smallpox that facilitated eradication, including: characteristic rash, identifiability of virus location, lack of subclinical cases, absence of an animal reservoir, no vector, seasonality, no latency, only one serotype, and a stable vaccine. Poliomyelitis is considered by many to be the next disease in line for global eradication in part because it also lacks an animal reservoir or insect vector (Stuart-Harris, 1984; Kew et al., 2005). When an infectious disease is only transmitted from person to person and has an effective vaccine, there is the potential to achieve a global vaccination rate that induces herd immunity. As the number of susceptible individuals in the population declines over time, that disease may cease to exist.

1.2.3.3 Domestic Animal Reservoirs

Unfortunately, most emerging and re-emerging infectious diseases are *zoonotic*. That means they can be transmitted under natural conditions between animals and humans. Diseases with an animal reservoir are inherently more difficult to control effectively because control efforts must target both the animal and human susceptible populations. Although it is more challenging

Table 1.2 Important anthroponoses, zoonoses, and sapronoses.

Category	Diseases
Anthroponoses	Measles*; rubella; mumps; influenza; common cold; viral hepatitis; poliomyelitis; AIDS*; infectious mononucleosis; herpes simplex; smallpox; trachoma; chlamydial pneumonia and cardiovascular disease*; mycoplasmal infections*; typhoid fever; cholera; peptic ulcer disease*; pneumococcal pneumonia; invasive group A streptococcal infections; vancomycin-resistant enterococcal disease*; meningococcal disease*; whooping cough*; diphtheria*; *Haemophilus* infections* (including Brazilian purpuric fever*); syphilis; gonorrhea; tuberculosis* (multidrug-resistant strains); candidiasis*; ringworm (*Trichophyton rubrum*); *Pneumocystis* pneumonia* (human genotype); microsporidial infections*; cryptosporidiosis* (human genotype); giardiasis* (human genotype); amebiasis; and trichomoniasis
Zoonoses transmitted by direct contact, alimentary (foodborne and waterborne), or aerogenic (airborne) routes	Rabies; hemorrhagic fever with renal syndrome*; hantavirus pulmonary syndrome*; Venezuelan*, Brazilian*, Argentinian, and Bolivian hemorrhagic fevers; Lassa, Marburg, and Ebola hemorrhagic fevers*; Hendra and Nipah hemorrhagic bronchopneumonia*; hepatitis E*; herpesvirus simiae B infection; human monkeypox*;Q fever; sennetsu fever; cat-scratch disease; psittacosis; mammalian chlamydiosis*; leptospirosis; zoonotic streptococcosis; listeriosis; erysipeloid; campylobacterosis*; salmonellosis*; hemorrhagic colitis*; hemolytic uremic syndrome*; yersiniosis; pseudotuberculosis; sodoku; Haverhill fever; brucellosis*; tularemia*; glanders; bovine and avian tuberculosis*; zoonotic ringworm; toxoplasmosis; and cryptosporidiosis* (calf genotype 2)
Zoonoses transmitted by hematophagous arthropods Hard ticks (*Ixodidae*)	Russian spring-summer encephalitis; Central European encephalitis; louping ill; Kyasanur Forest disease; Powassan; Crimean-Congo hemorrhagic fever*; Colorado tick fever; Rocky Mountain spotted fever; boutonneuse fever; African tick typhus*; other rickettsial fevers*; human granulocytic ehrlichiosis*; Lyme disease*; tularemia; and babesiosis
Soft ticks (Argasidae)	Tickborne relapsing fever
Mites (Trombiculidae, Dermanyssidae)	Scrub typhus; rickettsialpox
Lice (*Anoplura*)	Epidemic typhus; trench fever*; and epidemic relapsing fever
Triatomine bugs (Triatominae)	Chagas disease
Sandflies (Phlebotominae)	Sandfly fever; vesicular stomatitis; Oroya fever; and leishmaniasis
Mosquitoes (Culicidae)	Eastern, Western, and Venezuelan equine encephalomyelitides; Sindbis fever; Chikungunya and O'nyong nyong fevers*; Ross River epidemic polyarthritis*; Japanese encephalitis*; West Nile fever*; St Louis encephalitis; yellow fever; dengue/dengue hemorrhagic fever*; Murray Valley encephalitis; California encephalitis; Rift Valley fever*; and malaria*
Biting midges (Ceratopogonidae)	Oropouche fever; vesicular stomatitis
Tsetse flies (Glossinidae)	African trypanosomiasis
Fleas (Siphonaptera)	Murine typhus*; cat-scratch fever*; plague

(Continued)

Table 1.2 (Continued)

Category	Diseases
Sapronoses	Chlamydia-like pneumonia* (amoebic endosymbionts *Parachlamydia acanthamoebae* and other Parachlamydiaceae); tetanus; gas gangrene (*Clostridium perfringens*, *C. septicum*, *C. novyi*); intestinal clostridiosis* (*C. difficile*, *C. perfringens*); botulism; food poisoning* (*Bacillus cereus*); anthrax; vibrio gastroenteritis* or dermatitis (*Vibrio parahaemolyticus*, *V. vulnificus*); nosocomial *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* bacteremia* (including antibiotic-resistant strains); bacterial infections associated with cystic fibrosis* (*Burkholderia cepacia*; *Ralstonia* spp.); melioidosis* (*B. pseudomallei*); legionellosis* and Pontiac fever* (*Legionella pneumophila*, *L. micdadei*, and other spp.); atypical bacterial meningitis and sepsis* (*Chryseobacterium meningosepticum*); acinetobacter bacteremia* (*Acinetobacter calcoaceticus*, *A. baumannii*, *A. radioresistens*); corynebacterial endocarditis* (*Corynebacterium serosis*, *C. amycolatum*, and other nondiphtheriae corynebacteria); rhodococcosis* (*Rhodococcus equi*); possibly leprosy (some strains of *Mycobacterium leprae* were detected as living saprophytically in wet moss habitats); Buruli ulcer disease* (*Mycobacterium ulcerans*); mycobacterial diseases other than tuberculosis* (*M. kansasii*, *M. xenopi*, *M. marinum*, *M. haemophilum*, *M. fortuitum*, *M. scrofulaceum*, *M. abscessus*, and other spp.); nocardiosis (*Nocardia asteroides*, *N. brasiliensis*); actinomycetoma (*Actinomadura madurae*, *A. pelletieri*, *Streptomyces somaliensis*); dermatophytosis (*Microsporum gypseum*); histoplasmosis* (*Histoplasma capsulatum*, *H. duboisii*); blastomycosis (*Blastomyces dermatitidis*); emmonsiosis (*Emmonsia crescens*, *E. parva*); paracoccidioidomycosis (*Paracoccidioides brasiliensis*); coccidioidomycosis* (*Coccidioides immitis*); sporotrichosis (*Sporothrix schenckii*); cryptococcosis* (*Cryptococcus neoformans*); aspergillosis (*Aspergillus fumigatus*); mucormycosis (*Absidia corymbifera* and some other Mucorales); entomophthoromycosis (*Basidiobolus*, *Conidiobolus*, and *Entomophthora* spp.); maduromycetoma (*Madurella mycetomatis*, *M. grisea*, *Pseudoallescheria boydii*, *Leptosphaeria senegalensis*, *Neotestudina rosatii*); chromoblastomycosis (*Phialophora verrucosa*, *Exophiala jeanselmei*, *Fonsecaea compacta*, *F. pedrosoi*, *Cladosporium* carioni, *Rhinocladiella aquaspersa*); phaeohyphomycosis (*Wangiella dermatitidis*, *Dactylaria gallopava*, *Exophiala spinifera*); fusariosis* (*Fusarium oxysporum*, *F. solani*); primary amoebic meningoencephalitis* (*Naegleria fowleri*); and amoebic keratitis or chronic granulomatous amoebic meningoencephalitis* (*Acanthamoeba castellanii*, *A. polyphaga*)

Source: Centers for Disease Control and Prevention (https://wwwnc.cdc.gov/eid/article/9/3/02-0208-techapp1.pdf).
* Denotes emerging and re-emerging diseases.

than controlling a disease that is only present in human populations, it can be accomplished, especially if the susceptible animal population is a domestic animal species. Regulations requiring vaccination of pets or livestock, mandatory tests and slaughter programs for livestock, animal travel and trade restrictions, and requirements for health certifications can be enacted as public health policies to control zoonotic disease in animal populations and thereby enhance both animal and human health. The impact on human health of public health policies directed at animals can be seen in the effects of US

control efforts targeting rabies in dogs, and brucellosis and tuberculosis in cattle, on the rates of those diseases in the human population in the USA.

1.2.3.4 Wildlife Reservoirs

More challenging for disease control efforts is when the reservoir of disease is found in free-living wildlife. A variety of risk factors have been identified that may explain the emergence of new zoonotic infectious diseases into human populations in recent years. These phenomena are global in scope and not just an issue for developing countries. Population growth, civil unrest, population displacement, and urban/suburban sprawl contribute to humans now residing in previously pristine natural habitats where direct and indirect contact with wildlife is more likely to occur. Climate change and alteration of geographic home ranges of reservoir animals and insect vectors may result in the exposure of susceptible populations to new agents of infectious disease. Expansion of livestock and other agricultural production systems into new habitats can also result in increased exposure of domestic livestock and farm workers to wildlife reservoirs of disease. Global trade and travel also mean that a spillover event in one corner of the globe has the potential to move novel disease agents to any other area of the world in a matter of a few days. After its discovery in 1975, Lyme disease spread from deer, ticks, and humans in Connecticut to, in 2015, being the most commonly reported vector-borne illness in the USA (CDC, 2015). SARS traveled from Guangdong Province in southeast China to 29 countries in less than seven months, from November 2002 to July 2003. Nipah virus initially appeared in swine and swine farm workers in 1999 in Malaysia. There were 300 human cases of encephalitis associated with this outbreak, which resulted in 100 deaths. Over one million pigs were euthanized as a result. The reservoir was later determined to be fruit bats (*Pteropus* spp.) commonly known as flying foxes (http://www.searo.who.int/entity/emerging_diseases/links/nipah_virus_outbreaks_sear/en/). Since 2001, repeated outbreaks have been reported in Bangladesh and India resulting in a total of 280 cases and 211 deaths between 2001 and 2012. Person-to-person transmission in healthcare settings (*nosocomial infection*) has been a predominant feature in the outbreaks in India (Chadha et al., 2006). Cases in Bangladesh have been linked to the consumption of raw date palm sap contaminated by fruit bats (Islam et al., 2016).

One of the greatest challenges is identifying the wildlife reservoir of a new disease. When SARS appeared in 2002, the search began to find the wildlife reservoir that was the source of the spillover event. In 2003, it was reported that a SARS-like virus had been isolated from palm civets (Guan et al., 2003), triggering a province-wide effort to cull 10 000 palm civets in Guangdong Province.

1.2.3.5 Environmental Reservoirs

Lastly, the very environment itself can serve as a reservoir for infectious disease agents, with the potential to impact the health of humans, domestic animals, and wildlife. Air, water, and soil may be the site for disease agents to live, grow, and multiply.

Airborne transmission of infectious disease is illustrated by *Coxiella burnetii,* the agent that causes Q fever in several species, including humans. *C. burnetii* is a hardy agent that can travel long distances on dust particles and remain infectious for years outside of a living host. Infection of humans usually occurs by inhalation of these organisms from air that contains airborne barnyard dust contaminated by dried placental material, birth fluids, and excreta of infected animals (https://www.cdc.gov/qfever/stats/index.html). The acute phase of the disease causes flu-like signs. Sequelae associated with Q fever may include pneumonia, inflammation of the heart and liver, and central nervous system complications. Pregnant women are at increased risk for pre-term delivery or miscarriage. In 1983 a large outbreak of Q fever was reported in Switzerland in which there were 415 confirmed human cases (Dupuis et al., 1987). Epidemiologic

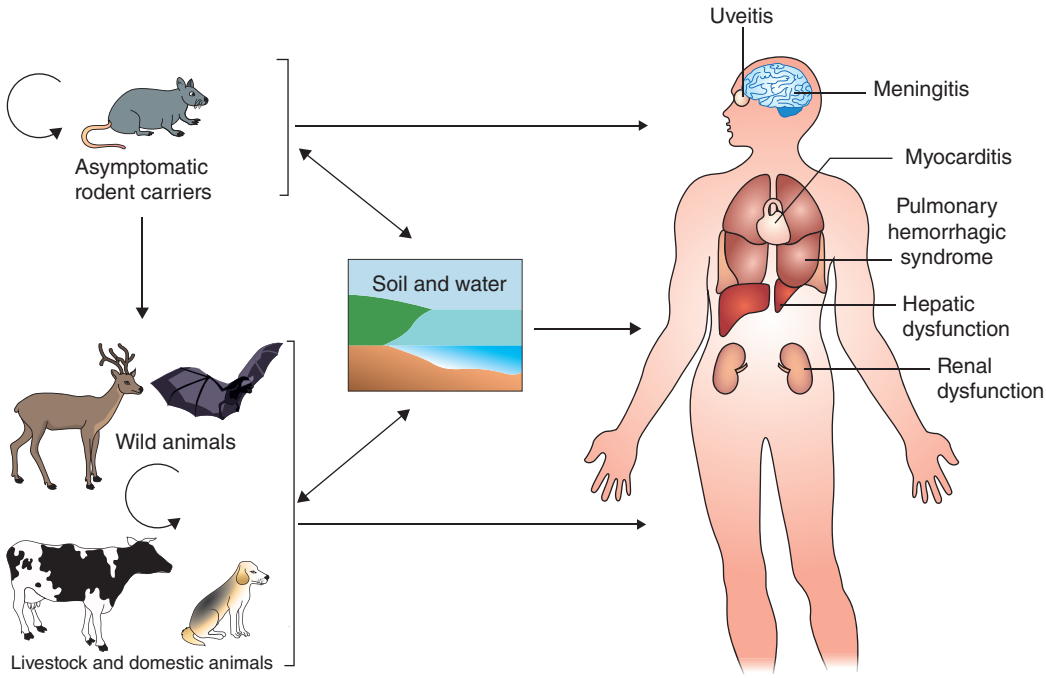

Figure 1.9 Leptospirosis reservoirs and transmission to humans. *Source*: Ko et al., 2009. Reproduced with permission of Nature Publishing Group.

investigation revealed that the outbreak was associated with 12 flocks of sheep returning to the valley from Alpine pastures. Those who resided near roads traveled by the sheep were at increased risk of becoming ill. The agent was also isolated from sheep on several facilities in the region. The authors concluded that better collaborations between physicians and veterinarians could prevent such outbreaks in the future (Dupuis et al., 1987).

Leptospirosis is one of the most common bacterial zoonotic diseases globally (Pappas et al., 2008). In humans, leptospirosis may begin with flu-like symptoms, vomiting, and diarrhea. A second phase of the disease may then occur, manifested by meningitis or liver and kidney failure. It is treatable with antibiotics (https://www.cdc.gov/leptospirosis/symptoms/index.html) but must be diagnosed correctly. Water contaminated with urine from infected animals is the most frequent means of human exposure (Figure 1.9). It has been classified as a re-emerging infectious disease since outbreaks are occurring with increasing frequency in several parts of the world. Extreme weather events, such as flooding, typhoons, and hurricanes, associated with the ecological effects of climate change, have been associated with an increase in human cases of leptospirosis (Lau et al., 2010). Studies have reported that the Caribbean, Latin America, India, Southeast Asia, Oceania, and eastern sub-Saharan Africa are regions with the highest morbidity and mortality due to leptospirosis (Pappas et al., 2008, Costa et al., 2015). This is consistent with reports of an outbreak of leptospirosis in Mumbai, India, in the summer of 2015 with 54 cases and an unusually high case-fatality rate of one-third (Herriman, 2015). In addition, studies have documented a substantial increase in the number of leptospirosis-positive dogs in the USA (Moore et al., 2006; Alton et al., 2009).

Figure 1.10 A Nenets herder in a malitsa with his reindeer-drawn sledge on the Yamal Peninsula in the Siberian Arctic in winter. Yamal Peninsula, Yamalo-Nenets, Russia (2014). *Source:* Image by Nick Mayo/RemoteAsiaPhoto.

Soil has been identified as the reservoir for three outbreaks of anthrax reported in Siberia during the summer of 2016. These outbreaks offer additional illustrations of the interdependent relationships between humans, animals, and the environment. Record high temperatures in the region, attributed to climate change, have resulted in the thawing of deep layers of permafrost. Underneath that permafrost was soil harboring the bacterium that causes anthrax (*Bacillus anthracis*), believed to be from a reindeer carcass of a previous anthrax outbreak in the region. As a result, 1500 reindeer died from the disease, thousands were euthanized, and 100 human cases, including one death, have been reported (Guarino, 2016). To control the spread of the disease, Russian officials are reported to have planned to euthanize 250 000 deer by the end of 2016 (Doucleff, 2016). Concerns have been raised that the disease and the control efforts may threaten the future of the Nenets, pastoralists who herd and raise the reindeer in the traditional nomadic manner (Doucleff, 2016) (Figure 1.10).

1.3 From Understanding Epidemiology to Public Policy

The previous sections of this chapter have discussed how epidemiology provides the tools for understanding the causes, impacts, and course of disease in human and animal populations within various ecosystems. Figure 1.11 illustrates the role of epidemiology research in prevention and control of infectious disease. Epidemiology is routinely used to inform health policies and standards of care at both the individual patient and the population levels. Here are examples of the application of the principles of epidemiology for use in clinical and public health decision making. Many of these concepts introduced in this chapter form the basis of the discussions in the subsequent chapters of this text.

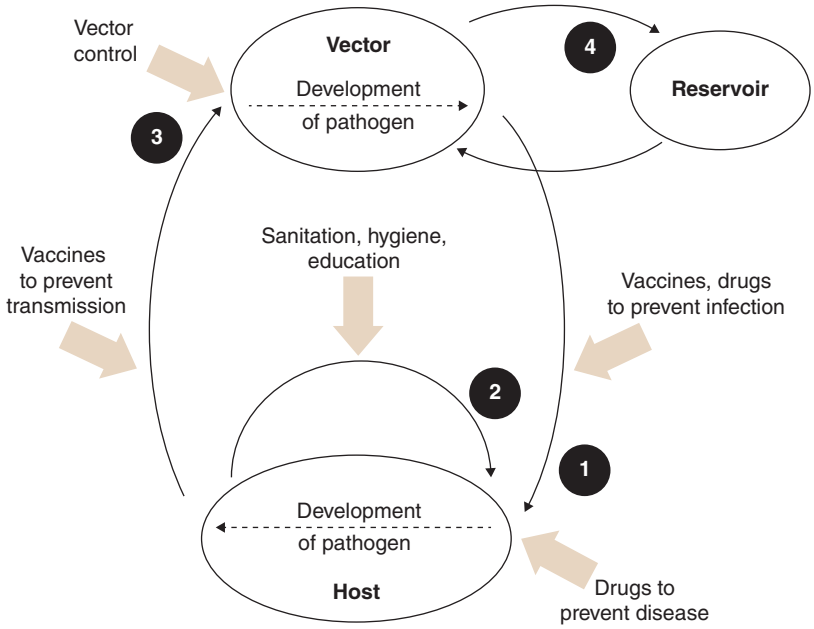

Figure 1.11 Role of epidemiology research in prevention and control of infectious disease. The black arrows illustrate a generalized infectious cycle; the shaded arrows indicate points where infectious diseases can be prevented. (1) A host is infected by the reservoir or a vector for the pathogen. This individual may infect (2) other hosts in a population or (3) new vectors. (4) The pathogen also may cycle between the vector and a reservoir. *Source:* Reproduced with permission of the National Institute of Medical Science.

1.3.1 Assessments of Diagnostic Test Reliability

When a physician or veterinarian conducts a diagnostic test on a patient, how certain are we that the results are valid? Epidemiologists assess the validity of diagnostic tests by determining their sensitivity and specificity. *Sensitivity* is defined as the ability of the test to correctly identify those who have the disease, and *specificity* is defined as the ability of the test to correctly identify those who do not have the disease (Gordis, 2014). These characteristics, which are inherent to the particular diagnostic test, are important especially when screening a population for a disease. However, at the level of the individual patient, predictive value is more informative. The *positive predictive value* is the probability of disease in an individual patient with a positive test result. It answers the question, "What are my chances of having the disease when my test result is positive?" Conversely, *negative predictive value* is the probability of being free of the disease given a negative test result. Predictive value incorporates the sensitivity and specificity of the test and the prevalence of the disease in the population from which the patient originates. Interpreting a diagnostic test in an individual patient requires epidemiologic data on the prevalence of the disease in the patient population. A diagnostic test that is very sensitive and specific may still have a low positive predictive value in an individual patient if he or she is from a population with a very low prevalence of the disease in question.

1.3.2 Determination of Safety and Effectiveness of New Treatments and Vaccines

The clinical trial is the primary method employed by epidemiologists to assess the safety and effectiveness of new treatments

and vaccines. It is a research study conducted in the population for which the intervention is intended, as opposed to a laboratory study in a model animal species. Humans or animals at risk of a disease may participate in a clinical trial to assess the safety and effectiveness of a new vaccine intended to prevent the disease in that population. Patients with a disease may participate in a clinical trial to determine the safety and effectiveness of a new treatment for the disease. Clinical trials produce the best data available for healthcare decision making (https://www.nhlbi.nih.gov/studies/clinicaltrials). By standardizing the treatment approach and the subjects participating in the clinical trial, researchers are able to make unbiased assessments of how well the intervention performed, which types of patients were best suited for the intervention, and if there were negative side effects attributable to the intervention.

1.3.3 Assessing Health at the Level of the Individual, Community, or Ecosystem and Establishing Standards of Care for Prevention and Treatment Protocols/Programs

In addition to clinical trials for assessing the safety and effectiveness of vaccine and treatments, epidemiologists use three observational study designs to identify both risk factors for disease and preventive measures: the *cross-sectional*, *case-control*, and *cohort* studies. Due to the observational nature of these studies, conducted within the population of interest, data generated can be used by health policy makers to establish real world standards of care for prevention and treatment protocols, assess the effectiveness of public health programs, recommend vaccination schedules, and even assess environmental and ecosystem health.

The *cross-sectional* study uses a representative sample of the population to determine the approximate prevalence of disease and to identify behaviors and characteristics that are associated with having the disease. Individuals are sampled at a single point in time to determine whether or not they have the disease in question and to determine their exposure status to risk factors believed to be associated with disease occurrence. The odds of exposure among cases is compared with the odds of exposure among noncases. The cross-sectional study is useful for determining the scope of the problem for a common disease in a population and provides data for making a rapid assessment of potentially important exposures. However, no attribution of causality can be applied since there is no way to determine if a potential risk factor occurred prior to an outcome of interest. When the disease is rare or it is not feasible to get a representative sample of the population, the case-control study design is often employed.

The *case-control* study begins with a set of cases (subjects with the disease of interest) identified by the researchers and a set of controls (similar subjects who do not have the disease of interest). Since the participants are not part of a representative sample of the population, disease prevalence is not determined. However, this approach does allow for assessment of associated exposures in rare diseases. As with the cross-sectional study design, case and control subjects are assessed for exposure to potential risk factors and the odds of exposure among cases and controls are compared.

The *cohort* design is the third observational study design. A cohort is simply a group of individuals with something in common. The cohort study sets inclusion and exclusion criteria for the group of individuals and then observes that group over time, recording exposures and occurrence of disease. The key to the cohort study is the criterion that cohort members must be free of the disease of interest at the start of the observation period. Subjects are monitored over time and the risk of disease in the exposed is compared to the risk of disease in the unexposed.

The cross-sectional and case-control study designs are limited by the retrospective

nature of exposure assessment inherent in their design. In both approaches the onset of disease begins prior to the onset of data collection. Thus, it is not always possible to clearly establish whether exposure preceded onset of disease. The criterion of temporality is essential in the establishment of a causal association. The cohort study design is unique for its potential to demonstrate a temporal association between the exposure and the disease of interest.

1.3.4 Establishing Disease Response Regulations and Control Standards

In addition to providing data for intervention recommendations, epidemiology provides a tool for directed action in the face of an epidemic. Several types of exposures may contribute to disease outbreaks including exposure to infected humans, domestic animals, and wildlife; consumption of contaminated food or water; and contact with contaminated surfaces. The case-control study design and retrospective cohort design are used to investigate outbreaks of disease with the goal of determining the source. An outbreak of a disease is defined as more cases than anticipated in a given time and place. Establishing that an outbreak is occurring requires some knowledge of the anticipated baseline disease level (incidence or prevalence). Once it has been determined that there is a true increase in disease, epidemiologists use case-control and retrospective cohort studies to identify exposures associated with cases of the disease.

Applying the multifactorial web of causation approach may lead to several types of risk factors identified as associated with cases of the disease. They may be factors intrinsic to the host, such as age, sex, or physiological state; or extrinsic, such as dietary, lifestyle, or occupational risk factors. They may be characteristics inherent to the agent, as in mutations altering infectiousness or virulence, or environmental influences, such as temperature, relative humidity, or UV radiation. When the outbreak is caused by the introduction of a disease into a new geographic region or host, the outbreak investigation can result in the identification of human or animal movements associated with disease introduction.

In response to the identification of risk factors for disease, health and regulatory agencies can implement interventions to break the chain of transmission, stop the current outbreak, and prevent future outbreaks. Control measures such as isolation, quarantine, and movement restrictions for humans and animals that are known or suspected cases of infectious disease can be effective outbreak response measures when epidemiologic evidence supports that such activities are associated with disease spread.

The primary goal of food safety regulations is to prevent future outbreaks of food-borne disease. When food handling and processing procedures are identified as risk factors in a food-borne disease outbreak, evidence-based food safety regulations can be developed to improve the safety of the food supply. Similarly, if wildlife species are identified as disease reservoirs, epidemiologic data about the magnitude and distribution of disease in the wildlife population is vital for the establishment of policies for wildlife disease surveillance and control policies. Wildlife disease surveillance and ecosystem health data are also crucial for setting guidelines and monitoring safety standards in environmental health policy.

Knowledge attained through outbreak investigations provides the data to support disease control initiatives such as: vaccine development or modification; public education programs for behavioral changes to enhance personal hygiene, food handling, and social distancing; and introduction of new occupational and food safety standards to prevent disease transmission.

The next section details real world examples of public health challenges posed by zoonotic infectious diseases and the application of epidemiologic data to develop a One Health approach to policy measures undertaken to address those challenges.

1.4 Examples of the Benefits of Using a One Health Approach

One Health is generally viewed as incorporating: 1) animal health (including domestic and wildlife), 2) human health, and 3) environment/ecosystem health. Interwoven within these three is a fourth pillar: 4) food and water security (Katz et al., 2013). Cross-cutting these four pillars are communication and policy considerations. Epidemiology serves as a critical tool in connecting the four pillars and in providing opportunity to generate results that can be used to design intervention strategies and policy actions. Two real life examples will illustrate benefits of applying a One Health approach in two major zoonotic diseases, brucellosis (Box 1.1) and tuberculosis (Box 1.2).

Box 1.1 A One Health approach to conduct brucellosis outbreak investigations in Uganda, East Africa

Brucellosis is a zoonotic disease that affects humans and many animal species. While there are more than eight species of *Brucella*, five species of brucellosis (*B. abortus*, *B. melitensis*, *B. suis*, *B. ovis*, and *B. canis*) cause abortions, arthritis, and orchitis in animals. In humans, the disease causes undulating fever, neurological disease, endocarditis, and arthritis. It is commonly misdiagnosed as malaria in developing countries. Brucellosis is both a public health and economic concern in many countries of the world. We will illustrate One Health approaches used in conducting outbreak investigations and research in Uganda.

Outbreak investigation in Western Uganda – 2013

An apparent increase in the number of human cases of brucellosis was reported in two health centers within two districts (Figure 1.12). Medical officers interviewed reported that the normal incidence was two to three cases per month. During the same period, increased abortions in cattle were reported in the districts. The District Veterinary Office (DVO) indicated that, in the district, usually 10–15 abortions were reported per month. However, they were now receiving 30–50 cases per month. Therefore, it was decided to conduct a One Health-based outbreak investigation to get at the root of the problem using the following phases.

Planning

At the university level, the College of Veterinary Medicine and the School of Public Health at Makerere University were involved. At the governmental level, the Ministry of Agriculture, Animal Industry, Fisheries and Wildlife and the Ministry of Health were involved. From the aforementioned institutions and governmental agencies, an interdisciplinary Outbreak Investigation Team (OIT) was formed. The team consisted of epidemiologists, microbiologists, veterinary pathologists, wildlife ecologists, physicians, veterinarians, laboratory technologists, and media specialists. A communication strategy was determined ahead of time, and a single person was to be in charge of communication within the outbreak investigation team. Communication to the media was to be done jointly by animal health and public health authorities, and laboratory protocols for sample collection, preservation, transport, and processing were jointly developed, well as data collection instruments, data analysis, and interpretation.

Training

Prior to starting the investigation, a short training session was held, which lasted 3 days. The first day covered the principles of outbreak investigation and ethical conduct of research. The second

(Continued)

Box 1.1 (Continued)

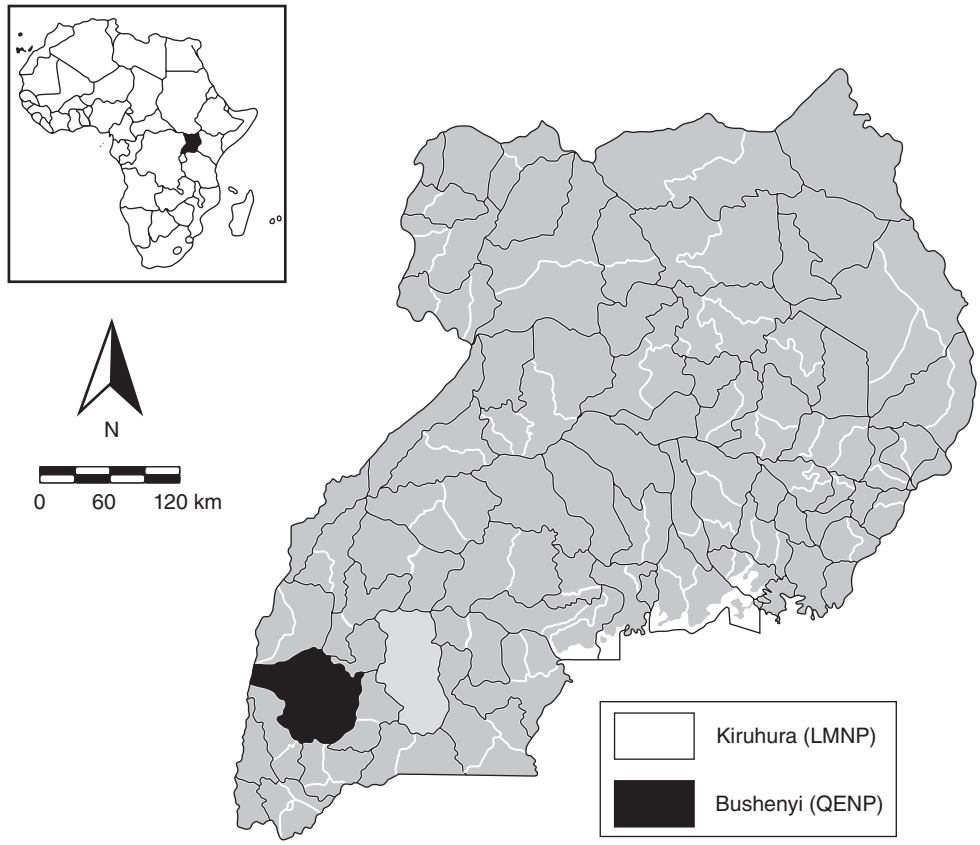

Figure 1.12 Districts in Western Uganda where brucellosis outbreak investigations were conducted 2013.

covered the type of questionnaires and different ways of administering them. The two questionnaires (one for human subjects and the other for livestock) that were going to be used were discussed, and because they were going to be administered in person, professional and cultural sensitivities were discussed in detail. The third day was devoted to how to assemble a team and preparation of the supplies needed. The individuals who were going to collect blood from humans were nurses and laboratory technologists familiar with blood collection. Individuals who were going to collect blood and milk from cattle and goats were veterinarians and veterinary technicians familiar with collection of the samples. A total of 24 individuals were trained.

Implementation

Fifteen livestock farms that reported abortions were identified, and the OIT visited them together and administered two simple questionnaires. The first questionnaire (human) was administered to 136 persons on the farms who came in contact with animals. The second questionnaire (animal) was administered to one person who was in charge of the livestock. From the available 168 cattle and 131 goats, blood and milk (where appropriate) were collected, and blood was collected from the 136 humans on the farms. The collected specimens were taken to a single regional laboratory for testing. The rose Bengal plate test (RBPT) with *B. abortus* and *B. melitensis* and the milk ring test were used to test for evidence of *Brucella* spp. exposure in cattle and goats. The Brucella micro-agglutination test (BMAT) and the lateral flow assay (LFA) for IgG and IgM were used on samples from humans. The outbreak investigation showed evidence of brucellosis in humans, cattle, goats, and milk. The seroprevalence was

Box 1.1 (Continued)

14% for cattle, 17% for goats, and 11% for humans from the outbreak investigation.

Communication of results
Communication of results to the public was accomplished jointly by representatives of the Ministry of Health and Ministry of Agriculture, Animal Industry, Fisheries and Wildlife.

Benefits of a One Health approach

The major benefits of a One Health approach that were realized in this example include: 1) shared facilities (lab) and activities, such as driving to the farms together to collect samples and needed data; 2) coordination of activities and responses, and communication to the public and policy makers; 3) education of farmers regarding how to reduce transmission of brucellosis within herds and between herds, transmission risk to humans through consumption of raw milk and dairy products, and handling livestock birth materials from infected animals; and 4) cost savings as a result of reduced time spent on the investigation, and sharing of resources (see Table 1.3 for illustration of monetary savings from applying a One Health approach). No follow-up data are available to assess whether this approach reduced human morbidity and mortality, but subjective information from the medical officers in the district suggests that there have been reduced cases of brucellosis in the district. Livestock and wildlife officials in the area have used the information in their outreach programs to the industry. In addition, there has been increased awareness of the disease in both the Ministry of Health and Ministry of Agriculture, and it has served as a catalyst for the use of a One Health approach in dealing with a zoonotic disease.

Table 1.3 Illustration of savings in US dollars as a result of applying a One Health approach to a brucellosis outbreak investigation and response in Western Uganda 2013.

	Supplies	Personnel	Others	Total
Animal health	600	2980	3005	6585
Public health	1098	3368	3877	8343
Animal and public health	1560	4295	3776	9631
Savings				5297

1.4.1 Overall Summary of Practical Experiences Applying a One Health Approach

The value of the One Health approach in dealing with zoonotic diseases, such as brucellosis and tuberculosis, would be:

1) Developing integrated approaches that will consider the role of humans, domesticated animals, wildlife, and the environment in the epidemiology of the disease.
2) Opportunities for shared resources; such as data and information, facilities, and personnel.
3) Increased efficiency and effectiveness.

Outbreak investigations and surveillance programs are often limited by funding in both resource-limited and high-income countries. Having public health, livestock, and wildlife agencies work together creates a strong voice to the policy makers of the need for continued funding. This is particularly true in Michigan, where the message to the policy makers has stressed both the economic and public health benefits of controlling and eradicating tuberculosis.

Box 1.2 A One Health approach for controlling *Mycobacterium bovis* in cattle, deer, and humans in Michigan, USA

In 1994, after a white-tailed deer (*Odocoileus virginianus*) with *M. bovis* was reported in the state of Michigan, surveillance programs were initiated in wildlife, livestock, captive cervid farms, and humans. Since 1994, cases of *M. bovis* have been reported in deer, followed by reports in cattle in 1998, and in humans in 2002 and 2004. To date, 52 beef herds, 15 dairy herds, four beef lots, four captive cervid herds, and one bison herd have been identified as infected with bovine tuberculosis (bTB) in Michigan (Figure 1.13), and the disease has cost millions of US dollars in surveillance and the testing and removal of infected animals. Bovine tuberculosis has a complex epidemiology with multiple, susceptible hosts and routes of transmission, and with ecosytems influencing host interaction and survival of the pathogen. Due to the complex epidemiology associated with this disease in the state of Michigan, multiple governmental agencies have had to use a One Health approach to work together to control the disease involving multiple disciplines. The One Health approach used in Michigan involves three pillars: 1) TB State Advisory Committee, 2) TB Interdisciplinary Technical Team, and 3) engagement of joint TB activities.

TB State Advisory Committee (TBAC)

A State Advisory Committee, whose responsibility was to advise the state on all matters relating to TB in livestock, wildlife, and humans, was formed in 1998. The committee is composed of individuals from all the relevant government departments in the state (Michigan Department of Agriculture & Rural Development, Michigan Department of Natural Resources, and Michigan Department of Community Health), federal agencies (USDA & CDC), Michigan State University (MSU), the livestock industries (dairy and beef), Michigan Farm Bureau, and deer hunting groups. The committee addresses policy issues, including surveillance strategies, outbreak investigation, and communication to the industries and the public at large.

TB Interdisciplinary Technical Team

An Interdisciplinary Technical Team was formed, composed of practicing veterinarians, TB epidemiologists, a TB program officer, deer ecologists, epidemiologists, pathologists, microbiologists, agricultural economists, sociologists, and extension specialists. The team addresses technical matters relating to strategies for control and eradication of TB, research, teaching, and communication of the problem and strategies for dealing with the disease.

Joint TB activities

Common TB activities handled in a One Health approach include: sharing of data between agencies, sharing of laboratory facilities, training of students, interdisciplinary research for new control strategies, and joint outbreak investigations of TB on a livestock farms. Examples of such investigations have been reported (Kaneene et al., 2002, 2014; Bruning-Fann et al., 2017).

Benefits

There are several benefits of applying a One Health approach in dealing with diseases. A specific example of such benefit in Michigan can be illustrated by the joint investigation of suspected bovine TB on a cattle farm. An earlier approach to investigating a suspected herd involved the different key government departments and the university going onto the farm separately. This approach was costly and caused a lot of stress and anxiety to the farmers affected. It was estimated (2015) that a single visit to each farm by a One Health team would cost US$3675, and would get just as much needed information. In contrast, multiple single visits by different agencies would cost US$5100. The other

Box 1.2 (Continued)

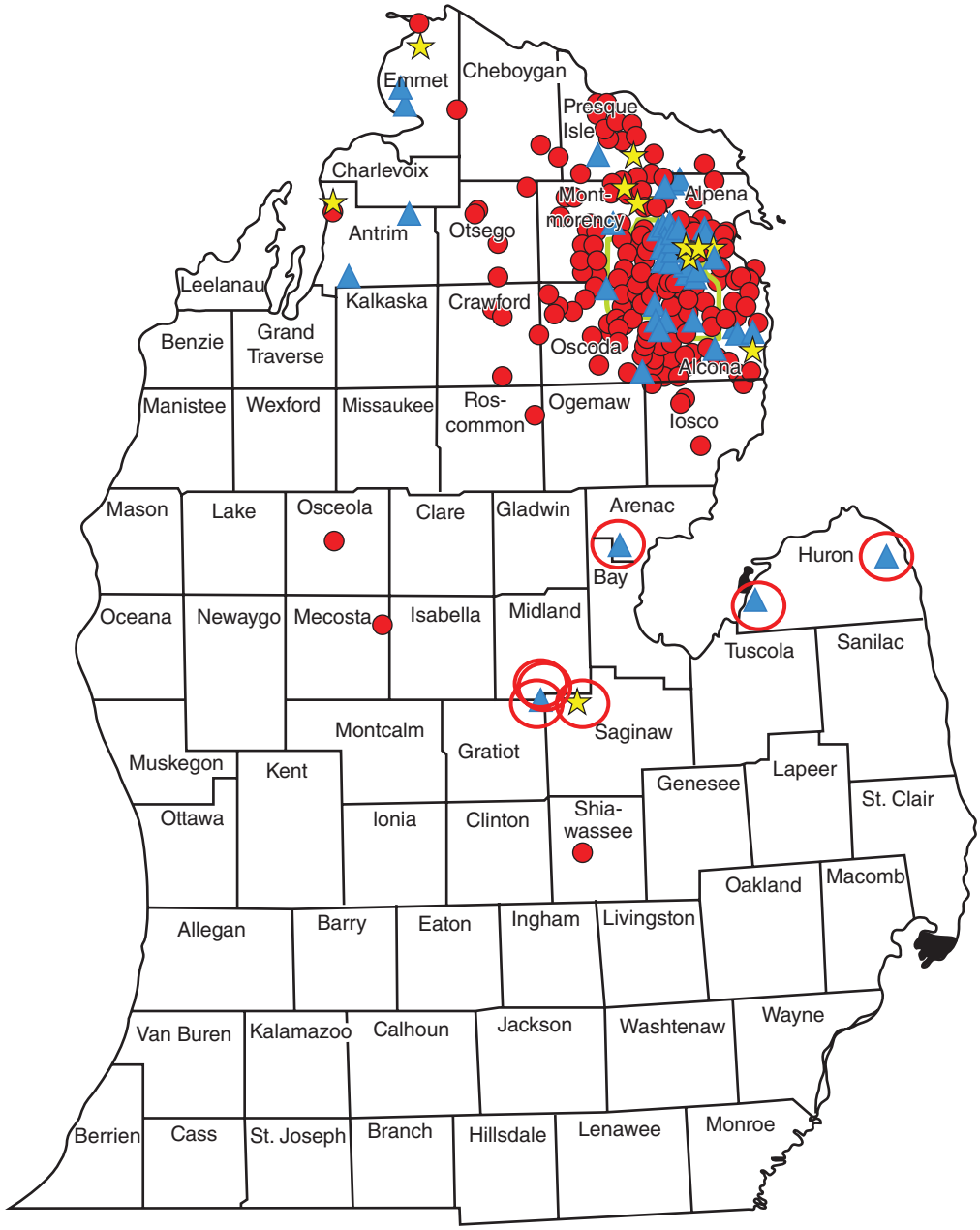

Figure 1.13 County map of the lower peninsula of Michigan depicting locations where *Mycobacterium bovis*-infected deer and *M. bovis*-affected beef and dairy herds have been identified between 1975 and 2016.

significant benefit is that, due to the One Health approach, the industries (livestock, wildlife, and captive cervid), as well as public health officials, jointly approach the state and federal authorities for increased funding relating to research and control programs in bTB.

References

Alton, G.D., Berke, O., Reid-Smith, R., Ojkic, D., and Prescott, J.F. (2009). Increase in seroprevalence of canine leptospirosis and its risk factors, Ontario 1998–2006. *Can J Vet Res* 73(3), 167–175.

American Lung Association (2017). 10 of the Worst Diseases Smoking Causes. Available at: http://www.lung.org/our-initiatives/tobacco/reports-resources/sotc/by-the-numbers/10-worst-diseases-smoking-causes.html (accessed November 14, 2017).

Anyamba, A., Linthicum, K.J., Small, J., Britch, S.C., and Pak, E. (2010). Prediction, assessment of the Rift Valley fever activity in East and Southern Africa 2006–2008 and possible vector control strategies. *Am J Trop Med Hyg* 83, 43–51.

Atkinson, N. (2014). The Impact of BSE on the UK Economy. Available at: http://www.veterinaria.org/revistas/vetenfinf/bse/14Atkinson.html (accessed November 14, 2017).

Biggerstaff, M., Cauchemez, S., Reed, C., Gambhir, M., and Finelli, L. (2014). Estimates of the reproduction number for seasonal, pandemic, and zoonotic influenza: a systematic review of the literature. BMC Infect Dis 14, 480.

Brunning-Fann, C.S., Robbe-Austerman, S., Kaneene, J.B., et al. (2017). The use of whole genome sequencing and evaluation of the apparent sensitivity and specificity of antemortem tuberculosis tests in the investigation of an unusual outbreak of Mycobacterium bovis in cattle herds in Michigan, USA, 2013. *Am J Vet Res* 251, 206–216.

CDC (Centers for Disease Control and Prevention) (1992). *Principles of Epidemiology*, 2nd edn. Atlanta: U.S. Department of Health and Human Services.

CDC (Centers for Disease Control and Prevention) (2000). *MMWR-Morbid Mortal W November 03*, 49(43), 982–985.

CDC (Centers for Disease Control and Prevention) (2013). Rift Valley Fever. Available at: https://www.cdc.gov/vhf/rvf/symptoms/index.html (accessed November 14, 2017).

CDC (Centers for Disease Control and Prevention) (2015) Lyme Disease Fast Facts. Available at: https://www.cdc.gov/lyme/stats/index.html (accessed November 14, 2017).

CDC (Centers for Disease Control and Prevention) (2016). 2014 Ebola Outbreak in West Africa - Case Counts. Available at: https://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/case-counts.html (accessed November 14, 2017).

CDC (Centers for Disease Control and Prevention) (2017). Variant Creutzfeldt-Jakob Disease (vCJD). Available at: https://www.cdc.gov/prions/vcjd/risk-travelers.html (accessed November 14, 2017).

CDC (Centers for Disease Control and Prevention) and WHO (World Health Organization) (2014). History and Epidemiology of Global Smallpox Eradication, slides 16 and 17. Available at: stacks.cdc.gov/view/cdc/27929/cdc_27929_DS1.pdf (accessed November 14, 2017).

Chadha, M.S., Comer, J.A., Lowe, L., et al. (2006) Nipah virus-associated encephalitis outbreak, Siliguri, India. *Emerg Infect Dis* 12, 235–240.

Costa, F., Hagan, J.E., Calcagno, J., et al. (2015). Global morbidity and mortality of leptospirosis: A systematic review. *PLoS Negl Trop Dis* 9(9), e0003898.

Doucleff, M. (2016). Killing reindeer to stop anthrax could snuff out a nomadic culture. National Public Radio (NPR). Available at: http://www.npr.org/sections/goatsandsoda/2016/10/12/496568291/killing-reindeer-to-stop-anthrax-could-snuff-out-a-nomadic-culture (accessed November 14, 2017).

Dupuis, G., Petite, J., Peter, O., and Vouilloz, M. (1987). An important outbreak of human Q fever in a Swiss Alpine Valley. *Int J Epidemiol* 16(2), 282–287.

Glass, R.J., Glass, L.M., Beyeler, W.E., and Min, H.J. (2006). Targeted social distancing design for pandemic influenza. *Emerg Infect Dis* 12(11). Available at: https://wwwnc.cdc.gov/eid/article/12/11/06-0255_article (accessed November 14, 2017).

Goldsmith, J.R. and Kordysh, E. (1993). Why dose-response relationships are often non-linear and some consequences. *J Expo Anal Environ Epidemiol* 3(3), 259–276.

Gordis, L. (2014). *Epidemiology*, 5th edn. Elsevier.

Gradmann, C. (2014). A spirit of scientific rigour: Koch's postulates in twentieth-century medicine. *Microbes Infect* 16(11), 885–892.

Guan, Y., Zheng, B.J., He, Y.Q., et al. (2003). Isolation and characterization of viruses related to the SARS coronavirus from animals in Southern China. *Science* 302(5643), 276–288.

Guarino, B. (2016). Anthrax sickens 13 in western Siberia, and a thawed-out reindeer corpse may be to blame. *Washington Post*, July 28. Available at: https://www.washingtonpost.com/news/morning-mix/wp/2016/07/28/anthrax-sickens-13-in-western-siberia-and-a-thawed-out-reindeer-corpse-may-be-to-blame/ (accessed November 14, 2017).

Hassan, O.A., Ahlm, C., Sang, R., and Evander, M. (2011). The 2007 Rift Valley fever outbreak in Sudan. *PLoS Negl Trop Dis* 5(9): e1229.

Herriman, R. (2015). Mumbai leptospirosis: High deaths linked to treatment delays. Outbreak News Today. Available at: http://outbreaknewstoday.com/mumbai-leptospirosis-high-deaths-linked-to-treatment-delays-55856/ (accessed November 14, 2017).

Heymann, D.L. (2008). *Control of Communicable Diseases Manual*, 19th edn. Washington, DC: American Public Health Association.

Hill, A.B. (1965). The environment and disease: association or causation? *Proc Roy Soc Med* 58, 295–300.

Islam, M.S., Sazzad, H.M.S., Satter, S.M., et al. (2016). Nipah virus transmission from bats to humans associated with drinking traditional liquor made from date palm sap, Bangladesh, 2011–2014. *Emerg Infect Dis* 22 (4).

Kaneene, J.B., Bruning-Fann, C.S., Granger, L.M., Miller, R., and Porter-Spalding, B.A. (2002). Environmental and farm management factors associated with tuberculosis on cattle farms in northeastern Michigan. *J Am Vet Med Assn* 221, 837–842.

Kaneene, J.B., Kaplan, B., Steele, J.H., and Thoen, C.O. (2014). Preventing and controlling zoonotic tuberculosis: a One Health approach. *Vet Ital* 50, 7–22.

Karesh, W.B. (2006). Animal disease surveillance. Presentation at the Institute of Medicine Forum on Microbial Threats, Washington, DC, December 12–13. Global Infectious Disease Surveillance and Detection: Assessing the Challenges—Finding Solutions, Workshop Summary. Washington, DC: National Academies Press.

Katz, D.J., Wild, D., and Elmore, J.G. (2013). *Jekel's Epidemiology, Biostatistics, Preventive Medicine, and Public Health*, 4th edn. Elsevier.

Kew, O.M., Sutter, R.W., de Gourville, E.M., Dowdle, W.R., and Pallansch, M.A. (2005). Vaccine-derived poliovirus and the endgame strategy for global polio eradication. *Ann Rev Microbiol* 59, 587–635.

Ko, A.I., Goarant, C., and Picardeau, M. (2009). Leptospira: the dawn of the molecular genetics era for an emerging zoonotic pathogen. *Nat Rev Microbiol* 7, 736–747.

Krieger, N. (1994). Epidemiology and the web of causation: has anyone seen the spider? *Soc Sci Med* 39(7), 887–903.

Lau, C.L., Smythe, L.D., Craig, S.B., and Weinstein, P. (2010). Climate change, flooding, urbanization and leptospirosis: fuelling the fire? *Trans R Soc Trop Med Hyg* 104(10), 631–638.

Lopes, P.C., Block, P., and König, B. (2016). Infection-induced behavioural changes

reduce connectivity and the potential for disease spread in wild mice contact networks. *Sci Rep* 6, 31790.

Marshall, B.J. and Warren, J.R. (1984) Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. *Lancet* i, 1311–1315.

May, S. and Bigelow, C. (2005). Modeling nonlinear dose-response relationships in epidemiologic studies: statistical approaches and practical challenges. *Dose-Response* 3, 474–490.

Moore, G.E., Guptill, L.F., Glickman, N.W., Caldanaro, R.J., Aucoin, D., and Glickman, L.T. (2006). Canine leptospirosis, United States, 2002–2004. *Emerg Infect Dis* 12(6), 501–503.

Pappas, G., Papadimitriou, P., Siozopoulou, V., Leonidas Christou, S., and Akritidis, N. (2008). The globalization of leptospirosis: worldwide incidence trends. *Int J Infect Dis* 12, 351–357.

Peck, D.F. (2005). Foot and mouth outbreak: lessons for mental health services. *Adv Psychiatr Treat* 11, 270–276.

Plans-Rubió, P. (2012). The vaccination coverage required to establish herd immunity against influenza viruses. *Prev Med* 55(1), 72–77.

Poundstone, K.E., Strathdee, S.A., and Celentano,.D.D. (2004). The social epidemiology of human immunodeficiency virus/acquired immunodeficiency syndrome. *Epidemiol Rev* 26(1), 22–35.

Rich, K.M. and Wanyoike, F. (2010) An assessment of the regional and national socio-economic impacts of the 2007 Rift Valley fever outbreak in Kenya. *Am J Trop Med Hyg* 83, 52–57.

Rothman, K.J. (1976). Causes. *Am J Epidemiol* 104, 587–592.

Rothman, K.J. (2012). *Epidemiology: An Introduction*, 2nd edn. Oxford University Press.

Sakula, A. (1983). Robert Koch (1843-1910): founder of the science of bacteriology and discoverer of the tubercle bacillus. A study of his life and work. *Can Vet J* 24, 124–127.

Stuart-Harris, C. (1984) Prospects for the eradication of infectious diseases. *Rev Infect Dis* 6(3), 405–411.

Thompson, D., Muriel, P., Russell, D., et al. (2002). Economic costs of the foot and mouth disease outbreak in the United Kingdom in 2001. *Rev Sci Tech Off Int Epiz* 21(3), 675–687.

Thompson, R.C. (2013). Parasite zoonoses and wildlife: One health, spillover and human activity. *Int J Parasitol* 43, 1079–1088.

UNDG (United Nations Development Group)-Western and Central Africa (2015). Socio-economic impact of Ebola virus disease in West African countries: A call for national and regional containment, recovery and prevention. Available at: http://www.africa.undp.org/content/dam/rba/docs/Reports/ebola-west-africa.pdf (accessed November 14, 2017).

Vineis, P. (2003). Causality in epidemiology. *Soz Praventivmed* 48(2), 80–87.

WHO (World Health Organization) (2017). Rabies Fact Sheet. Available at: http://www.who.int/mediacentre/factsheets/fs099/en/ (accessed November 14, 2017).