Emerging Epidemics
Management and Control

Chapter 1
Prologue

Introduction

Epidemiology is considered the basic science of public health or a quantitative basic science built on a working knowledge of probability, statistics, and sound research methods. It is a tool for public health action to promote and protect the health of people based on science, causal reasoning, and a dose of practical common sense. The method of causal reasoning is based on developing and testing hypotheses pertaining to the occurrence and prevention of morbidity and mortality (Figure 1.1). Hence, the essential role of epidemiology is to improve the health of populations by involving both science and public health practice. The term *applied epidemiology* is sometimes used to describe the application or practice of epidemiology to address public health issues.

The word *epidemiology* originated from the Greek words *epi*, meaning "on or upon"; *demos*, meaning "people"; and *logos*, meaning "the study of." For epidemiology, many definitions have been proposed, but the correct definition based on the underlying principles and the public health spirit is "the study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to the control of health problems (Last, 1988). Epidemiology actually arose from Hippocrates's observation more than two thousand years ago that environmental factors influence the occurrence of disease. However, it was not until the 19th century that the distribution of disease in specific human population groups was measured to any large extent. Comparing rates of disease in subgroups of the human population became common practice in the late 19th and early 20th centuries. This approach was initially applied to the control of communicable diseases, but it proved to be a useful way of linking environmental conditions or agents to specific diseases.

In the second half of the 20th century, these methods were applied to chronic noncommunicable diseases such as heart disease and cancer, especially in middle- and high-income countries. Epidemiology in its modern form is a relatively new discipline (Beaglehole and

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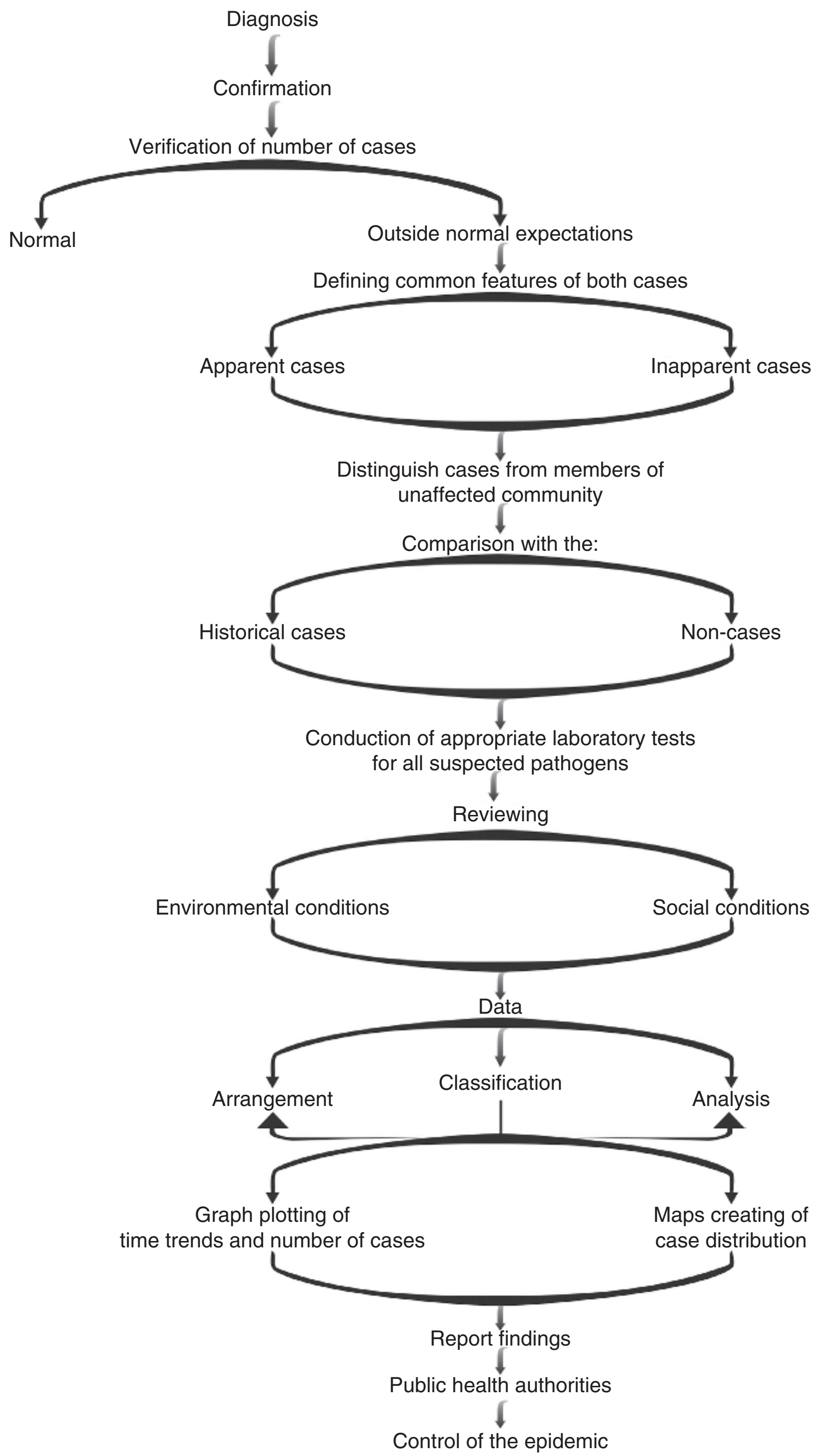

Figure 1.1. Steps to investigate an epidemic.

Bonita, 2004) and uses quantitative methods to study diseases in human populations to inform prevention and control efforts. For example, Richard Doll and Andrew Hill (1954) studied the relationship between tobacco use and lung cancer, beginning in the 1950s; their work was preceded by experimental studies on the carcinogenicity of tobacco tars and by clinical observations linking tobacco use and other possible factors to lung cancer.

Epidemiologists are concerned not only with death, illness, and disability, but also with more positive health status and, most importantly, with the means to improve health. The term *disease* is actually an uncomfortable feeling that encompasses all unfavorable health changes, including injuries and mental health. Epidemiology is concerned with the frequency and pattern of health events in a population. Frequency includes not only the number of such events in a population, but also the rate or risk of disease in the population. The patterns by which epidemics spread through groups of people is determined, not just by the properties of the pathogen carrying it, including its contagiousness, the length of its infectious period, and its severity, but also by network structures within the population it is affecting. The social network within a population recording who knows whom determines a lot about how the disease is likely to spread from one person to another. A focus of an epidemiological study is the population defined in geographical or other terms; for example, a specific group of hospital patients or factory workers could be the unit of study. A common population used in epidemiology is one selected from a specific area or country at a specific time.

Although epidemiologists and physicians in clinical practice are both concerned with disease and control of disease, they differ greatly in how they view the patient. Clinicians are concerned with the health of an individual; epidemiologists are concerned with the collective health of the people in a community or other area. While examining a patient with diarrheal disease, for example, the clinician and the epidemiologist have different responsibilities. Although both are interested in establishing the correct diagnosis, the clinician usually focuses on treating and caring for the individual, whereas the epidemiologist focuses on the exposure (action or source that caused the illness), the number of other persons who may have been similarly exposed, and the potential for further spread in the community, and interventions to prevent additional cases or recurrences.

Epidemic sweating sickness recurred several times in medieval Europe, but it has vanished since. The Black Death or plague that struck Europe in 1347 killed between one-third and one-half of the people in many cities and towns, arresting the advance of civilization for several generations. Some epidemic diseases, such as the plague, smallpox, typhus, and influenza, have persisted throughout recorded history. Smallpox was eradicated worldwide by 1980. Cholera appeared along the world's major trade routes in several devastating epidemics beginning in the 18th century, and it still causes massive epidemics, most recently in South America in early 1990s.

In the final quarter, of the 20th century more than 30 new infectious pathogens were identified. Many of these have caused deadly localized epidemics (e.g., *Ebola* virus, *Hantavirus*, and other viral hemorrhagic fevers), and some have spread worldwide; HIV/AIDS being the foremost among these. Since its first recognition in 1981, HIV has affected almost 40 million people and killed more than 10 million, making it the most lethal and dangerous pandemic, second only to the Black Death. Other new and emerging infections that have caused epidemics include Legionnaire's disease, Lyme disease, newly identified hepatitis viruses that spread in epidemic form through contaminated blood and blood products used in transfusion services, and several bacterial and viral diseases affecting the gastrointestinal tract.

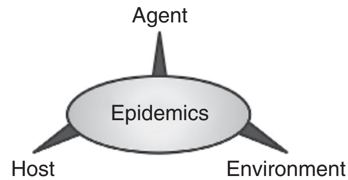

Figure 1.2. An epidemiological triad.

In an epidemiological investigation, three attributes should be considered; the host (the affected individuals), the agent (the cause of the condition), and the environment (Figure 1.2) along with their physical, biological, social, behavioral, and cultural factors. Investigating an epidemic can be as exciting as detective fiction, and such investigations (both real and fictional) have yielded many best-selling books and movies. The Epidemic Intelligence Service (EIS) of the US Centers for Disease Control and Prevention (CDC) has an illustrious record of successfully investigating and controlling epidemics, including some great public health importance.

While studying a disease outbreak, epidemiologists depend on clinical physicians and laboratory scientists for the proper diagnosis of individual patients, and at the same time, epidemiologists contribute to physicians' understanding of the clinical picture and natural history of disease. For example, in late 1989, three patients in New Mexico were diagnosed as having myalgias (severe muscle pains in the chest or abdomen) and unexplained eosinophilia (an increase in the number of eosinophils). Their physician could not identify the cause of their symptoms or put a name to the disorder. Epidemiologists began looking for other cases with similar symptoms, and within weeks had found enough additional cases of the eosinophilia-myalgia syndrome to describe the illness, its complications, and its rate of mortality. Similarly, epidemiologists have documented the course of HIV infection, from the initial exposure to the development of a wide variety of clinical syndromes that include AIDS. They have also documented numerous conditions that are associated with cigarette smoking from pulmonary and heart disease to lung and cervical cancer.

A basic task of a health department is counting cases to measure and describe morbidity. When physicians diagnose a case of a reportable disease they send a report of the case to their local health department. These reports are legally required to contain information on time (when the case occurred), place (where the patient lived), and person (the age, race, and sex of the patient). The health department combines the reports and summarizes the information by time, place, and person. From these summaries, the health department determines the extent and patterns of disease occurrence in the area and identifies clusters or outbreaks of disease. A simple count of cases, however, does not provide all the information required by the health department. To compare the occurrence of a disease at different locations or during different times, a health department converts the case counts into rates, which relate the number of cases to the size of the population where they occurred. Rates are useful in many ways. With rates, the health department can identify groups in the community with an elevated risk of disease. These so-called *high-risk groups* can be further assessed and targeted for special intervention; the groups can be studied to identify risk factors that are related to the occurrence of disease. Individuals can use knowledge of these risk factors to guide their decisions about behaviors that influence health.

Causative Factors

Although analytic epidemiology used to search for causes of disease, this is not a straightforward matter. First, not all associations between exposures and disease are causal relations. In addition, the accepted models of disease causation require the precise interaction of factors and conditions before the occurrence of disease. Finally, the concept itself continues to be debated as a philosophical matter in the scientific literature. Nonetheless, the following models and guidelines provide a framework for considering causation at a practical level. An increase in the factor leads to an increase in disease; similarly reduction in the factor leads to a reduction in disease. If the disease always results from the factor, then it is termed as the causative factor *sufficient*. For example, exposure to *Mycobacterium tuberculosis* is necessary for tuberculosis to develop, but it is not sufficient because not everyone infected develops disease. On the other hand, exposure to a large inoculum of rabies virus is a sufficient cause in a susceptible person because clinical rabies and death will almost inevitably occur. A variety of models of disease causation has been proposed. Models are purposely simplified representations. In this instance, the purpose of the model is to facilitate the understanding of nature, which is complex. Two of these models are discussed herein.

The Epidemiologic Triangle or Triad: Agent, Host, and Environment

It is the traditional model of infectious disease causation. It has three components: an external agent, a susceptible host, and an environment that brings the host and agent together (*see* Figure1.2). In this model, the environment influences the agent, the host, and the route of transmission of the agent from a source to the host.

Agent Factors

Agent refers to an infectious microorganism, such as virus, bacteria, fungi, protozoa, and helminth, etc. Generally, these agents are necessary, but not always sufficient, to cause a disease. As epidemiology has been applied to noninfectious conditions, the concept of agent in this model has been broadened to include chemical and physical causes of disease. These include chemical contaminants, such as the l-tryptophan contaminant responsible for eosinophilia-myalgia syndrome, and physical forces, such as repetitive mechanical forces associated with carpal tunnel syndrome. This model does not work well for some noninfectious diseases because it is not always clear whether a particular factor should be classified as an agent or as an environmental factor.

Host Factors

These are intrinsic factors that influence an individual's exposure and susceptibility toward a causative agent. These include age, race, sex, behaviors (e.g., smoking, drug abuse, lifestyle, sexual practices and contraception, eating habits), nutritional and immunologic status, genetic composition, and socioeconomic status, etc.

Environmental Factors

These are extrinsic factors, which affect the agent and provide the opportunity for exposure. Generally, environmental factors include physical factors such as geology,

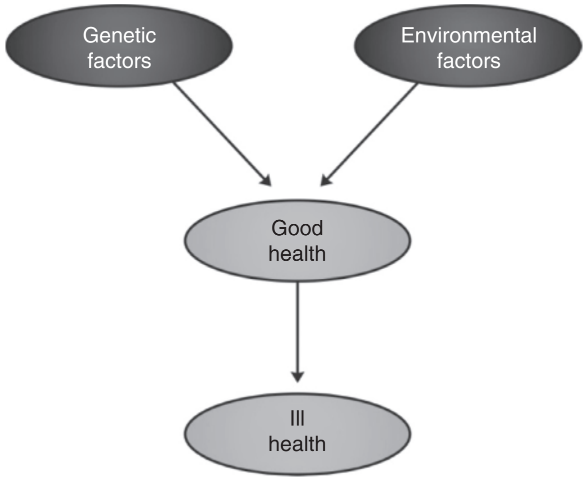

Figure 1.3. Disease causation.

climate, and physical surroundings (e.g., a nursing home, hospital); biologic factors such as insects that transmit the agent; and socioeconomic factors such as crowding, sanitation, and the availability of health services.

Agent, host, and environmental factors interrelate in a variety of complex ways to produce disease in humans. Their balance and interactions are different for different diseases. All the three components and their interactions should be analyzed to find practical and effective prevention and control measures of epidemics.

An Interaction of Genetic and Environmental Factors

Although some diseases are caused solely by genetic factors, most of them result from an interaction between genetic and environmental factors (Figure 1.3). Diabetes, for example, has both genetic and environmental components. Any biological, chemical, physical, psychological, economic, or cultural factors can affect health. Personal behaviors affect this interplay, and epidemiology is used to study their influence and the effects of preventive interventions through health promotion. Epidemiology is often used to describe the health status of population groups. Knowledge of the disease burden in populations is essential for health authorities.

Disease rates change over time. Some of these changes occur regularly and can be easily predicted. For example, the seasonal increase of influenza (flu) cases with the onset of cold weather is a pattern that is familiar to everyone. This helps health departments to effectively design their flu shot campaigns. Other disease rates make unpredictable changes. By examining events that precede a disease rate increase or decrease, causes may be identified and appropriate actions taken to control or prevent further occurrence of the disease. Some epidemics are transferred from one host to another (Table 1.1), whereas some are unique to a specific host.

Causation is an essential concept in the practice of epidemiology, but a single cause may not always be sufficient for an epidemic to occur. For example, tobacco smoking is a cause of lung cancer, but it is not a sufficient cause. First, the term *smoking* is too

Table 1.1. Epidemics that are transferred from one host to another.

Host-to-Host Epidemics			
Disease	Causative Agent	Infection Sources	Reservoirs
Diphtheria	*Corynebacterium diphtheriae* (B)	Human cases and carriers; infected food and fomites	Humans
Hantavirus pulmonary syndrome	*Hantavirus* (V)	Inhalation of contaminated fecal material	Rodents
Meningococcal meningitis	*Neisseria meningitidis* (B)	Human cases and carriers	Humans
Pneumococcal pneumonia	*Streptococcus pneumoniae* (B)	Human carriers	Humans
Tuberculosis	*Mycobacterium tuberculosis* (B)	Sputum from human cases; contaminated milk	Humans, cattle
Whooping cough	*Bordetella pertussis* (B)	Human cases	Humans
German measles	*Rubella* virus (V)	Human cases	Humans
Influenza	*Influenza* virus (V)	Human cases	Humans, animals
Measles	Measles virus (V)	Human cases	Humans
HIV disease	HIV (V)	Infected body fluids, blood, semen, etc.	Humans
Chlamydiasis	*Chlamydia trachomatis* (B)	Urethral, vaginal, and anal secretions	Humans
Gonorrhea	*Neisseria gonorrhoeae* (B)	Urethral and vaginal secretions	Humans
Syphilis	*Treponema pallidum* (B)	Infected exudates or blood	Humans
Trichomoniasis	*Trichomonas vaginalis* (P)	Urethral, vaginal, prostate secretions	Humans

B, bacteria; P, protozoa; V, virus.

imprecise to be used in a causal description. One must specify the type of smoke (e.g., cigarette, cigar, pipe), whether it is filtered or unfiltered, the manner and frequency of inhalation, and the onset and duration of smoking. More importantly, smoking, even defined explicitly, will not cause cancer in everyone. Apparently, there are some people who, by virtue of their genetic makeup or previous experience, are susceptible to the effects of smoking and others who are not. These susceptibility factors are other components in the various causal mechanisms through which smoking causes lung cancer.

Infectious disease at a fairly constant level is described as being *endemic*. Endemic disease may rise to a higher level, but if it remains at this new plateau it is not described as an epidemic. Usually, however, rises are followed by a fall. This occurs for a number of reasons: Those most likely to be infected have died, or the survivors have built up a resistance to the disease; among those infected, many have a natural resistance; the densest populations have already been decimated. Some infectious diseases do not provoke strong immune reactions, and hence it is difficult to produce vaccines: examples are cholera and modern bubonic plague. The vocabulary employed is descriptive but not analytical. Nearly all terms come from Greek, through Latin and French into English. Several are built around the Greek word, *demos*, from which *demography* is derived; examples are endemic (among people), epidemic (through or over people), and pandemic (among all people). There are many infectious diseases, which may become epidemic: measles, whooping cough, chicken pox, scarlet fever, influenza, smallpox, cholera, influenza, and poliomyelitis. In the following section, three examples are given that can be called pandemics because they infected many people over broad areas and were associated with high mortality. These are:

1. The plague (in various forms)
2. Spanish influenza
3. HIV/AIDS

The plague pandemics were once thought to be identical, but this is now doubtful (Herlihy 1997; Cohn 1997, 2002, 2003). Oriental bubonic plague emerged from Southern China in 1894 and attacked Hong Kong, then Bombay, and other places including Sydney. It is not yet extinct. In Hong Kong, it was shown to be caused by a bacillus (*Yersinia pestis*), and in Mumbai (Maharashtra, India) it was proved that this was transmitted by a rat flea. Because it was characterized by buboes, or pronounced swellings of the lymph glands in the groin, it has long been assumed that Oriental Bubonic Plague was identical with the Black Death and the Great Plague. So it was believed that by studying this pandemic modern science could unlock the secrets of these previous pandemics.

Spanish influenza (usually just Spanish flu) acquired its name because Spain was the first heavily infected European country, but it almost certainly originated elsewhere, possibly in Asia. Its pathogen could not be identified at the time, but efforts are still being made to secure DNA for identification from its long-dead victims. The epidemic burst on Europe in 1918 and spread to the whole world; a spread partly facilitated by troops returning home from World War I.

The symptoms of AIDS as a new disease began to be noticed in the United States in 1979, and official confirmation of its existence and of deaths arising from it came in 1981 and later in the same year in Europe. It was not until 1983 that the pathogen (a retrovirus) was identified, and it was 1985 before a test for its presence was available. The disease has certain unusual characteristics. It kills by suppressing the immune system, thus permitting death from pneumonia, tuberculosis, and other causes. Its average period from infection to death was 10 years and to major symptoms almost as long, compared with a few days in the cases of Black Death or Spanish Influenza. Treatment with antiretrovirals can now lengthen that period, although perhaps not indefinitely. Until the development of antiretroviral treatment, case mortality was 100 percent, which may still be the level of premature death.

Unlike Spanish influenza, and probably Black Death, HIV is not transmitted from person to person through the breath, but through blood in sexual intercourse, shared use of intravenous drug needles, during birth, or in maternal breastfeeding. Where heterosexual intercourse is an important means of infection, as in sub-Saharan Africa or the Caribbean, more females than males may be infected, but where homosexual transmission predominates as in North America, Western Europe, and Australasia, only 20 to 25 percent of those infected are females. By the year 2000, HIV/AIDS had killed 20 million people (15 million of them in sub-Saharan Africa) and had infected 40 million others, condemning the great majority to premature death. Everywhere commercial sex workers have unusually high levels of infection and are themselves a serious source of infection. Table 1.2 details the various death numbers resulting from the top seven infectious diseases of the world.

Table 1.2. Top seven infectious diseases in the world by death number.

Name of Infectious Disease	Number of Deaths
Respiratory infections	4,259,000
Diarrheal diseases	2,163,000
HIV/AIDS	2,040,000
Tuberculosis	1,464,000
Malaria	889,000
Childhood infections	847,000
Tropical diseases	152,000

International Federation of Red Cross and Red Crescent Societies. 2009. The epidemic divide. Accessed March 25, 2013, at http://www.ifrc.org/Global/Publications/Health/170800-Epidemic-Report-EN-LR.pdf.

Salient Features

Epidemiology played a crucial role in identifying the cause and in the control of what was one of the first reported epidemics of disease caused by environmental pollution. The first cases were thought to be infectious meningitis. However, it was observed that 121 patients with the disease mostly resided close to Minamata Bay. A survey of affected and unaffected people showed that the victims were almost exclusively members of families whose main occupation was fishing and whose diet consisted mainly of fish. On the other hand, people visiting these families and family members who ate small amounts of fish did not suffer from the disease. It was therefore concluded that something in the fish had caused the poisoning and that the disease was not communicable or genetically determined (McCurry, 2006). All epidemics usually follow some common characteristic features:

1. An unexpected number of cases of a particular disease occur at a particular point of time affecting large segment of the population.
2. Generally confined to a definite population or geographical area and hence geographic patterns provide important sources of clues about the causes of diseases.
3. Usually have a common source of infection. For containment of epidemics, it is important to identify the source of infection so that the appropriate measures can be adopted to eliminate the common source of infection to prevent further spread of epidemic.
4. An epidemic generally tends to follow a pattern and repeat periodically when the conditions are favorable again.
5. The way an epidemic presents it in the community depends on the distribution and characteristics of people living in that area, their social pattern, their cultural behavior, and the various environmental factors.

Emerging Epidemics

Epidemiology has been a major contributor to the success of the disease control efforts of the past century, culminating in such signal triumphs as the global eradication of smallpox and the eradication of polio from the Western Hemisphere. However, in recent years, partly because these very successes led to a pervasive optimism about infectious diseases in the future, there has been a waning interest in infectious disease epidemiology even though infectious diseases remain the leading cause of death worldwide and an important cause of death in the United States (Lederberg et al., 1992; McGinnis and Foege, 1993).

AIDS, like many of the plagues of the past, falls into the category of emerging infections (seemingly new diseases that appear suddenly and unexpectedly). Emerging infections can be defined as those that either have newly appeared in a population or that are rapidly increasing their incidence or expanding their geographic range (Morse, 1991). Other recent examples include hanta virus pulmonary syndrome, Lyme disease, hemorrhagic colitis, and hemolytic uremic syndrome (resulting from a food-borne infection caused by certain strains of *Escherichia coli*), and Ebola hemorrhagic fever in Africa (Satcher, 1995). Past scourges can also recur and are referred to as *re-emerging diseases*, which are often conventionally understood and well-recognized public health threats that have increased or reappeared because previously active public health measures have lapsed or sanitary infrastructure has deteriorated. Figure 1.4 illustrates various emerging and re-emerging epidemic diseases that struck the world in the past 30 years. The researchers stressed the need for at-risk countries to act quickly for the expansion of surveillance to these epidemics and access to testing, prevention, and treatment services for persons at risk.

So many factors participate in the emergence of epidemics, and modern life conditions and human behavioral changes make these factors more prevalent, giving reason to expect increased occurrence of emerging diseases. Sources of epidemics vary depending on the causative agent (Table 1.3) and the environmental conditions of a particular geographical area. Historically, "new" diseases had appeared and spread as by-products of exploration, trade, or warfare, when the movement of people, animals, or goods brought geographically isolated infections to new grounds (McNeill, 1976). In the 19th century, steamships carried cholera to Europe and Africa. Today, trucks, freighters, and airplanes have largely replaced caravans and steamships, allowing even richer opportunities for infections to emerge and spread efficiently. Speed of travel and global reach of infections are borne out by studies modeling the spread of influenza epidemics (Longini et al., 1986) and of HIV (Flahault and Valleron, 1992), as well as by the actual progress of known epidemics.

Other factors are also allowing emerging infections to appear at increasing rates and could facilitate wider and more rapid spread. In many parts of the world, economic conditions are encouraging the mass movement of workers from rural areas to cities. It has been estimated that, largely as a result of this migration, by the year 2025, 65 percent of the world population, including 61 percent of the population in developing regions, will live in cities. The phenomenon of rural to urban migration can allow infections arising in isolated rural areas, which may once have remained unrecognized and localized, to reach larger populations, with the city serving an amplifying function. An infection can become further disseminated when other migrants return home with an infection acquired in the city, a pattern now being observed with HIV in Asia.

Epidemics such as AIDS demonstrate the interplay of complex ecological, social, and behavioral factors. As of 2009, an estimated 33.3 million people worldwide had HIV, according to the latest United Nations data, and 22.5 million of those live in sub-Saharan Africa. There is little published data on the Middle East and North African regions, and Ghina Mumtaz, who led the study with colleague Laith Abu-Raddad, said this had been

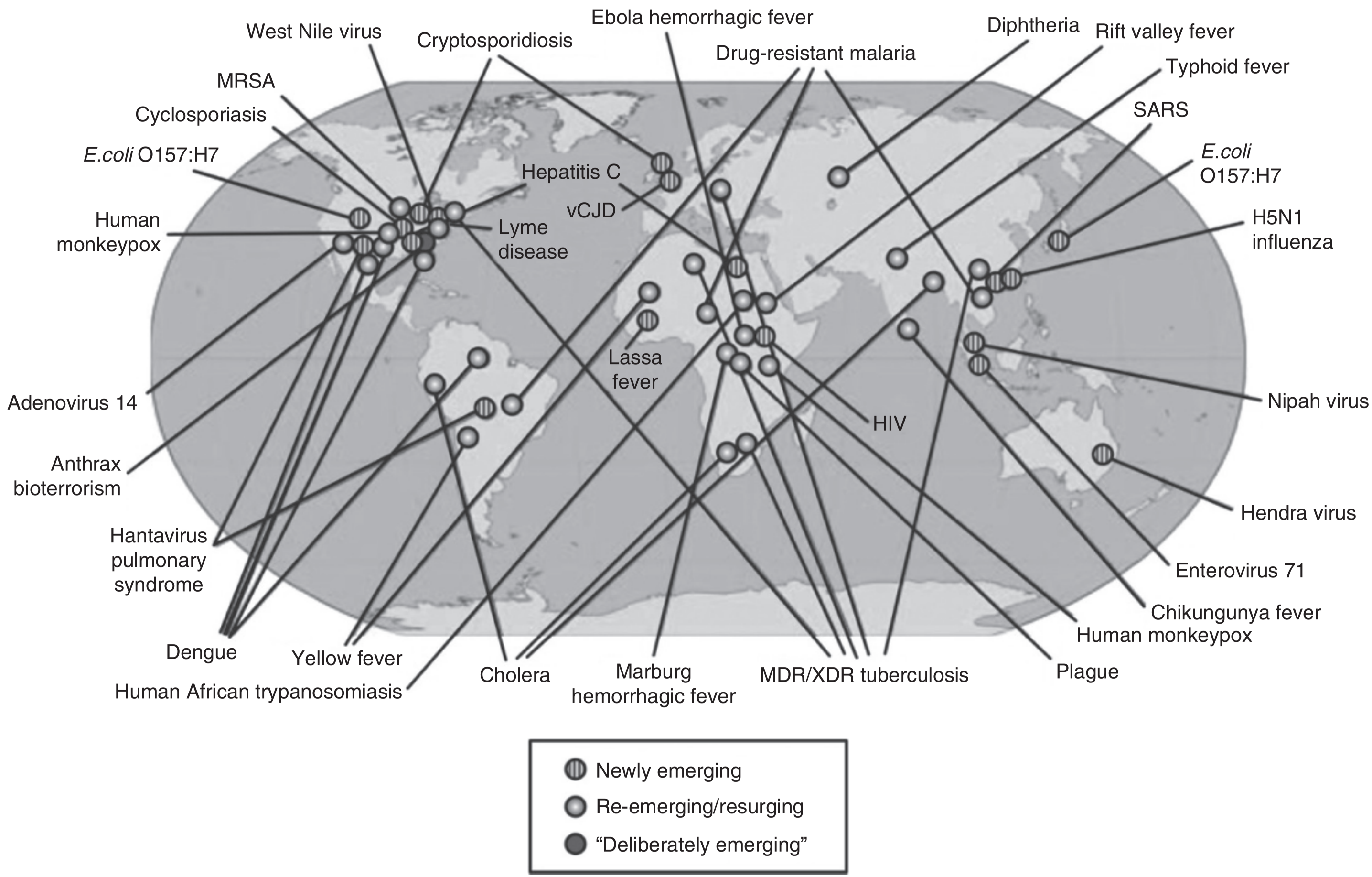

Figure 1.4. Newly emerging, re-emerging/resurging, and “deliberately emerging” diseases. Selected emerging diseases of public-health importance in the past 30 years (1977–2007).

Table 1.3. Sources of some common epidemic diseases.

Disease	Causative Agent	Source of Infection	Reservoirs
Anthrax	*Bacillus anthracis* (B)	Milk or meat from infected animals	Cattle, swine, goats, sheep, horses
Bacillary dysentery	*Shigella dysenteriae* (B)	Fecal contamination of food and water	Humans
Botulism	*Clostridium botulinum* (B)	Soil-contaminated food	Soil
Brucellosis	*Brucella melitensis* (B)	Milk or meat from infected animals	Cattle, swine, goats, sheep, horses
Cholera	*Vibrio cholerae* (B)	Fecal contamination of food and water	Humans
Giardiasis	*Giardia* spp. (P)	Fecal contamination of water	Wild mammals
Hepatitis	Hepatitis A, B, C, D, E (V)	Infected humans	Humans
Paratyphoid	*Salmonella paratyphi* (B)	Fecal contamination of food and water	Humans
Typhoid fever	*Salmonella typhi* (B)	Fecal contamination of food and water	Humans

B, bacteria; P, protozoa; V, virus.

driving misconceptions that there is no reliable information at all (Kelland, 2011). Controlling the infections of tomorrow will increasingly require understanding and assessing the roles of each of these factors in disease and designing appropriate strategies that take them into account. Epidemiology must integrate approaches to studying the ecological, social, and behavioral context of disease into its own core subject matter. There have been epidemiologic traditions that have incorporated strong ecological underpinnings (Pavlovskii, 1996), and there are opportunities now to develop an integrated epidemiology that will further develop these approaches (Koopman, 1995; Susser, 1995). Human behavior, which is often a key factor in appearance and spread of infections, must also, be included in the equation. Many of the difficulties in dealing with the AIDS pandemic have stemmed precisely from the inability to deal effectively with these social factors that have allowed the virus to spread.

Being prepared for emerging infections will require strengthened surveillance and response capacity (Henderson, 1993). Numerous expert analyses have called for the development of an effective global early warning and response system (Berkelman et al., 1994) while noting the perilous and fragmented state of present systems. In all of this, epidemiology must play a central role. However, epidemiologists trained in infectious disease surveillance and control remain in short supply, with limited attention to the subject in both medical and public health curricula. There is an equally critical need to integrate epidemiologic and laboratory surveillance functions. The availability of powerful new tools makes this an opportune time. Biotechnology continues to expand the power of laboratory-based surveillance and increases the feasibility of field applications worldwide. New analytic tools, including geographic modeling and electronic data collection and analysis, have similarly expanded capabilities that can be harnessed on the epidemiologic side, making it possible for the epidemiologist and laboratorian to share information.

The next essential step is to integrate these elements at the front line, by fostering settings for infectious disease surveillance in which the specialties work closely together and learn to share data and vocabularies. At the same time, it is critically important to improve communication and collaboration between clinicians and clinical microbiologists, who are often the first to recognize emerging and re-emerging infections, and public health professionals with expertise in epidemiology and microbiology.

Molecular epidemiology is one promising product of the interaction between epidemiology and the laboratory (Moore, 1992). As indicated by recent progress in applying molecular approaches to ecology (Berry et al., 1992), this interaction can even mutually reinforce the priority of integrating ecological, social, and behavioral sciences into epidemiology. Even with the appropriate structures in place, however, there are serious problems that must be overcome. In addition to trained personnel, now in short supply, a career path, requiring stable funding for these efforts, must also be assured. The recent responses to outbreaks of plague in India and Ebola hemorrhagic fever in Zaire demonstrated how thin the resources are, both in terms of trained personnel and laboratory capacity. The international community was able to mount an adequate ad hoc response only by stretching available capabilities to the limit. In the case of plague, for example, the CDC had the only functioning World Health Organization Collaborating Center for plague, and this center was staffed by only one full-time scientist. Assembling a team to assist with the international investigation in India required the involvement of epidemiologists, microbiologists, and experts in rodent and vector control from different parts of the organization. Effective surveillance will also require capturing the clinical data and recognizing the unusual. Ironically, although insurance companies have devised systems for collecting and sharing medical information for claims processing, there is no consistent way to access medical records electronically for medical or public health purposes (Dick and Steen, 1991). Therefore, clinicians and clinical microbiologists play a critically important role in recognizing and reporting such unusual diseases and syndromes.

The 20th-century revolution in health and the consequent demographic transition lead inexorably to major changes in the pattern of disease. This epidemiological transition results in a major shift, in causes of death and disability from infectious diseases to noncommunicable diseases. Health policy makers in the early decades of the 21st century will thus need to address a double burden of disease: first, the emerging epidemics of noncommunicable diseases and injuries, which are becoming more prevalent in industrialized and developing countries alike, and second, some major infectious diseases which survived the 20th century part of the unfinished health agenda.

Whether an emerging microorganism develops into a public health threat, depends on factors related to the microorganism and its environment, or the infected human and his or her environment. Such factors include ease of transmission between animals and people and among people, potential for spread beyond the immediate outbreak site, severity of illness, availability of effective tools to prevent and control the outbreak, and ability to treat the disease. Some of the new agents detected in the past 25 years are now genuine public health problems on a local, regional, or global scale.

The populations of developing countries, and particularly the disadvantaged groups within these countries, remain in the early stages of the epidemiological transition, where infectious diseases are still the major cause of death. Immunization programs have yielded the most significant changes in child health in the last few decades. Although some vaccines represent the most cost-effective public health intervention of all, the world does not use them enough. At least 2 million children still die each year from diseases for which vaccines are available at low cost. Similarly, for diarrheal disease, there exists a simple, inexpensive, and effective intervention: the oral rehydration therapy. Diarrheal diseases and pneumonia together account for a high proportion of deaths of children in developing countries. In several developing countries, therefore, diarrheal disease control programs have been merged with a simplified approach, promoted by the World Health Organization (WHO), to detect acute respiratory infections (primarily pneumonia).

Despite the extraordinary advances of the 20th century, a significant component of the burden of illness globally still remains attributable to infectious diseases, undernutrition and complications of childbirth. These conditions are primarily concentrated in the poorest countries, and within those countries they disproportionately afflict populations that are living in poverty. Those living in absolute poverty, compared with those who are not poor, are estimated to have five times higher probability of death between birth and the age of 5 years, and a 2.5 times higher probability of death between the ages of 15 and 59 years.

Emerging infectious diseases result from newly identified and previously unknown infections, which cause public health problems, either locally or internationally. A recent example of an emerging disease is the new variant of Creutzfeldt-Jakob disease, which was first described in the United Kingdom, in 1996. The agent is considered to be the same as that causing bovine spongiform encephalitis, a disease which emerged in the 1980s and affected thousands of cattle in the United Kingdom and some other European countries. Following are examples of some agents causing emerging diseases.

Bacterial Agents

- *Legionella pneumophilia*: The detection of the bacterium in 1977 explained an outbreak of severe pneumonia in a convention center in the United States in 1976, and it has since been associated with outbreaks linked to poorly maintained air-conditioning systems.
- *Escherichia coli* O157:H7: Detected in 1982, this bacterium is typically transmitted through contaminated food and has caused outbreaks of hemolytic uremic syndrome in North America, Europe, and Japan. A widespread outbreak in Japan in 1996 caused more than six thousand cases among school children. During a single outbreak in Scotland in 1996, 496 people fell ill, of those 16 died.
- *Borrelia burgdorferi*: Detected in the United States in 1982 and identified as the cause of Lyme disease, this bacterium is now known to be endemic in North America and Europe and is transmitted to humans by ticks.
- *Vibrio cholerae* O139: First detected in 1992 in India, this bacterium has since been reported in seven countries in Asia. The emergence of a new serotype permits the organism to continue to spread and cause disease even in populations protected by antibodies generated in response to previous exposure to other serotypes of the same organism.

Viral Agents

- Ebola virus: The first outbreaks occurred in 1976, and the virion was discovered in 1977. Indigenous cases have been confirmed in four countries in Africa (Côte d'Ivoire, Democratic Republic of Congo, Gabon, and Sudan). Through June 1997, 1054 cases had been reported to WHO, 754 of which proved fatal. Monkeys infected with an

Asian strain of Ebola (Ebola-Reston) were the cause, but it does not appear to cause illness in humans.

- HIV: It was first isolated in 1983. By the beginning of June 1998, the number of HIV-positive cases reported to WHO by national authorities since the beginning of the epidemic was close to 1.9 million. However, it is estimated that since the start of the epidemic, 30.6 million people worldwide have become HIV infected and nearly 12 million have died from AIDS or AIDS-related diseases.
- Hepatitis C: Identified in 1989, this virus is now known to be the most common cause of post-transfusion hepatitis worldwide, with approximately 90 percent of cases in Japan, the United States, and Western Europe. Up to 3 percent of the world population is estimated to be infected, among which 170 million are chronic carriers at risk of developing liver cirrhosis or liver cancer.
- *Sin nombre* (i.e., an unnamed) virus was isolated from cases of a local outbreak of a highly fatal respiratory disease in the southern United States in 1993. It has subsequently been diagnosed in sporadic cases across the country and in Canada and several South American countries.
- Influenza A (H5N1) virus: Influenza virus is a well-known pathogen in birds and has been isolated from human subjects for the first time in 1997. The emergence of human influenza A (H5N1) initially followed a possible scenario of the expected next influenza pandemic, but in the event, the virus transmitted poorly, and the spread of the virus appeared to have been contained in 1997.

Re-Emerging Epidemics

As stated previously, the re-emerging infectious diseases are the result of the reappearance of, and an increase in, the number of infections from a disease that is known, but that had formerly caused so few infections that it had no longer been considered a public health risk.

Bacterial Diseases

- Cholera: Cholera has been reintroduced into countries and continents where it had previously disappeared and where it can spread because water and sanitation systems have deteriorated and food safety measures are not adequate. In 1991, the seventh cholera pandemic reached the Americas, a place where cholera had not been registered for a century. In that year, more than 390,000 cases were notified in more than 10 South American countries, which altogether accounted for two-thirds of the number of cases in the world. In 1997, cholera outbreaks chiefly affected Eastern Africa, and although the overall numbers have declined since 1991, there were still more than 147,000 cases reported globally in 1997. In 1998, the epidemic spread over eastern and southern Africa and new outbreaks occurred in South America.
- Diphtheria: Diphtheria re-emerged in the Russian federation and some other republics of the former Soviet Union in 1994 and culminated in 1995 with more than fifty thousand cases reported. The re-emergence was linked to a dramatic decline in the immunization programs following the disruption of health services during the unsettled times immediately after the break-up of the Soviet Union.

- Meningococcal meningitis: Meningococcal meningitis occurs worldwide but devastating, large-scale epidemics have mainly been in the dry sub-Saharan regions of Africa, designated the "African meningitis belt." Since the mid-1990s, epidemics in this area have been on an unprecedented scale, and epidemic meningitis has also emerged in countries south of the meningitis belt.

Viral Diseases

- Dengue fever: Dengue fever has spread in many parts of Southeast Asia since the 1950s and re-emerged in the Americas in the 1990s following deterioration in active mosquito control and spread of the vector into urban areas. An infection with dengue virus, dengue hemorrhagic fever (DHF), is common in Asia, but it has also been reported in 24 countries including central and Southern America.
- Rift Valley fever (RVF): It is a zoonotic disease typically affecting sheep and cattle in Africa transmitted by mosquitoes among animals and to humans. The disease in humans is typified by fever and myalgia, but in some cases, progresses to retinitis, encephalitis, or hemorrhage. Following abnormally heavy rainfall in Kenya and Somalia in late 1997 and early 1998, RVF occurred over vast areas, producing disease in livestock and causing hemorrhagic fever and death among the human population.
- Yellow fever (YF): YF is an example of a disease for which an effective vaccine exists, but because it is not widely used in many areas, at-risk epidemics continue to occur. The threat of YF is present in 33 countries, including Africa and eight in South America. YF is typically a disease of the tropical forest areas where the virus survives in monkeys. Humans bring it back to their villages, and if a suitable mosquito vector is present, the disease will spread quickly and kill a large proportion of the susceptible population.

Antimicrobial Resistance

Another emerging public health issue is the rapidly growing number of pathogens becoming resistant to an increasing range of antibiotics. In many regions, the low-cost, first-choice antibiotics have lost their power to clear infections of *E. coli*, *Neisseria gonorrhoeae*, *Pneumococcus*, *Shigella*, *Staphylococcus aureus*, which increases the cost and length of treatment of many common diseases including epidemic diarrheal diseases, gonorrhea, pneumonia, and otitis. Further problems stem from the use of antimicrobial substances in food animal production. This view of antimicrobial resistance predicts that it could be reduced by delaying the emergence of resistance genes or by retarding their dissemination after they emerge.

The global spread of microbial resistance is a predominant reason why infectious diseases have not been conquered. It is commonly expressed that physician misuse of antibiotics is the cause of antibiotic resistance in microbes and that, if physicians could be convinced to use antibiotics responsibly, the war against microbes could be won. Unfortunately, this belief is a fallacy that reflects an alarming lack of respect for the incredible power of microbes.

It is obvious that microbes do not need human help in creating antibiotic resistance. On the other hand, what human beings can do is affect the rate of spread of bacterial resistance by applying selective pressure via exposure to thousands of metric tons of antibiotics we have used in patients and livestock over the past half century (Palumbi, 2001). Methods to control unnecessary use of antibiotics include appropriate regulations on use of antibiotics in agriculture (including elimination of use of antibiotics to promote growth of food animals), restriction of antibiotic use to pathogen-specific agents, and limits on the common practice of using antibacterial agents for viral infections Clearly, it is desirable to use antibiotics only when appropriate, to try to limit selective pressure that increases the frequency of resistance. Nevertheless, the distinction between causality of microbial resistance and the rate of spread of resistance must be recognized if a true solution to the problem of antibiotic resistance is to be created. If the misuse of antibiotics causes drug resistance, the solution would be to strictly use antibiotics only when truly indicated and forever defeat microbial resistance.

Antimicrobial effectiveness is a precious, limited resource. Therefore, preserving antibiotic effectiveness can be viewed similar to society's responses to overconsumption and depletion of other precious, limited resources, such as oil and other energy sources, clean water and air, and forests (Laxminarayan et al., 2007). Society has tried to protect this resource against depletion through antimicrobial stewardship, including the placement of appropriate restrictions on antibiotic use and through infection control. Unfortunately, society has not acted to promote antibiotic restoration (i.e., the development of new antibiotics), and antibiotic restrictions have the unintended, negative consequence of further destabilizing an already fragile market situation for antibiotic research and development.

Another problem is that many of the antimicrobial agents no longer kill many strains of bacteria. Those resistant strains make proteins that nullify the effects of the agents in various ways. Each such protein is expressed by a gene that the strain's susceptible ancestors lacked. The rise of the prevalence of such resistance genes in the bacterial populations that always cover and sometimes infect is the problem. It can be seen as two processes: emergence and dissemination. The diversity of resistance genes, the intricacy of the networks of bacterial populations that disseminate them, and the specificity with which the use of antimicrobial agents build those networks and drive that dissemination make the control of resistance a complex and unending task.

The importance of host-to-host transmission of resistant strains makes infection control skills central to the management of resistance. These skills may be strengthened by establishing, targeting, and providing quality assurance for infection control procedures. In addition, skilled clinical use of antimicrobials is essential in retarding the spread of resistance and in treating patients infected with resistant bacteria. Proper usage of antimicrobials may be imparted to other clinicians, for example, by consultation and by collaborating with those clinicians to work out guidelines for usage of antimicrobials. The skills needed to monitor and manage resistance completely are unlikely to be found in one person and are probably not fully available or integrated in many places now. Thus, implementation may often require organization or reorganization of a team, acquisition of new skills, and new management of information. Existing infection control teams may have many of the skills, but assuming accountability for managing antimicrobial resistance might be the occasion for their augmentation.

Several factors contribute to the emergence and re-emergence of infectious diseases, but most can be linked with the increasing number of people living and moving in the world; rapid and intense international travel; overcrowding in cities with poor sanitation; substantially increased international trade in food, mass distribution of food and unhygienic food preparation practices; increased exposure of humans to disease vectors and reservoirs in nature; and alteration of the environment and climatic changes, which have a direct impact on the composition and size of the population of insect vectors and animal reservoirs. Other factors include a deteriorating public health infrastructure that is unable to cope with the needs of the population. Travel has always been a vehicle to spread disease across the world, which needs monitoring and management at the country level because countries may differ greatly in their practices, policies, and problems, and at the global level because resistance genes and strains travel between countries. The most important monitoring and management, however, appear to be that done at the local level at each medical center. The movement of resistance genes and strains through the bacterial populations of a community, a hospital, an intensive care unit, or even a single patient may be more complex than the movement of a strain of influenza virus through humans worldwide. National or regional reference laboratories may test selected pathogens referred from medical centers, but local laboratories supporting the centers generate most of the information. Results of antimicrobial susceptibility tests need to be scrutinized, interpreted, and screened locally for accuracy before they can be used to project national or global trends.

Public Health Implications

Epidemiology is a tool that is essential for carrying out four fundamental functions: public health surveillance, disease investigation, analytical studies, and program evaluation. Although an active epidemiology unit will do other things as well, these are the key areas through which epidemiology contributes to the promotion of the public's health. A health department systematically collects, analyzes, interprets, and disseminates health data on an ongoing basis (Thacker and Berkelman, 1988). Public health surveillance, which has been called "information for action" (Orenstein and Bernier, 1990), is how a health department takes the pulse of its community. By knowing the ongoing pattern of disease occurrence and disease potential, a health department can effectively and efficiently investigate, prevent, and control disease in the community.

At the local level, the most common source of surveillance data is reports of disease cases received from health-care providers, who are required to report patients with certain "reportable" diseases, such as cholera, measles, or syphilis. In addition, surveillance data may come from laboratory reports, surveys, disease registries, death certificates, and public health program data such as immunization coverage. It may also come from investigations by the health department of cases or clusters of cases reported to it. Most health departments use simple surveillance systems. They monitor individual morbidity and mortality case reports, record a limited amount of information on each case, and look for patterns by time, place, and person. Unfortunately, with some reportable diseases, a health department may receive reports of only 10 to 25 percent of the cases that actually occur (Marier, 1977). Nevertheless, health departments have found that even a simple surveillance system can be invaluable in detecting problems and guiding public health action. The principal epidemiologist of a large county health department has said "surveillance is the practicing epidemiologist's primary occupation; it pervades and keynotes all his activities" (Peterson, 1970).

For some diseases, the most appropriate intervention may be directed at controlling or eliminating the agent at its source. In the hospital setting, patients may be treated or isolated, with appropriate enteric, respiratory, and universal precautions and the like for different exit pathways. In the community, soil may be decontaminated or covered to prevent escape of the agent.

Recent epidemiological and modeling studies have attempted to provide explanatory theories for the mechanisms of multiple outbreaks of an infectious pathogen capable of establishing an epidemic (Alexander et al., 2009). Spontaneous behavioral changes (e.g., a change in the number of contacts as a result of modified behavior of susceptible individuals) have been shown to affect the course of infection events and produce subsequent outbreaks in an epidemic episode (Poletti et al., 2009). This has been further investigated through modeling "concerned awareness" of individuals that may result in contagion dynamics of fear and disease (Epstein et al., 2008), and the implementation of public health control measures (e.g., social distancing) that may interfere with the individuals' contact patterns during the epidemic (Caley et al., 2008). Coinfection has also been suggested as a possible explanation for multiple infection outbreaks as a result of increased transmissibility in co-infected individuals and non-synchronicity in the time course of the two co-circulating infections. Other possible mechanisms include transient postinfection immunity and evolutionary changes that may occur in the characteristics of the infectious pathogens.

According to the CDC (2009), control measures available to individuals are simple and include the following: avoiding hand contact with nose and mouth after contact with diverse individuals, regular hand-washing, covering the mouth when coughing and sneezing, staying away from public places when infected to protect others from infection, avoiding overcrowded places, seeking prompt medical attention when suspect symptoms appear, avoiding nonessential travel to areas hit by the epidemic and heeding health agencies' cautions and warnings on the infection, where available. In the home, household surfaces can also be disinfected with a disinfectant or household bleach.

Control measures for adoption by government agencies and corporate bodies include: declaring the real infection rates within the country because countries are known to hide infection figures (Chew, 2007); provision of modern and effective equipment for diagnosis; ensuring effective screening of immigrants and emigrants at borders and where necessary, quarantining to contain infection spread; establishing of surveillance center to monitor and report infections; providing widely available and affordable antiflu medications such as Tamiflu® and Relenza®; and provision of vaccinations.

Effective public health measures regarding containment and management of emergencies, including information dissemination, are at best slow acting and limited largely to the urban center. This leaves the larger proportion of the rural population at ignorant risk of infections to which they lack basic information on preventive measures. Compounding this is apathy to warnings and cautions, when given, from health authorities by the largely illiterate populace.

Since 1992, alarm over emerging and re-emerging diseases has resulted in a number of national and international initiatives to restore and improve surveillance and control of communicable diseases. In 1995, a resolution of the World Health Assembly (WHA) urged all member states to strengthen surveillance for infectious diseases to promptly detect re-emerging diseases and identify new infectious diseases. This resolution led to WHO's establishment of the Division of Emerging and other Communicable Diseases Surveillance and Control (EMC), whose mission is to strengthen national and international capacity in the surveillance and control of communicable diseases, including those that representing new, emerging, and re-emerging public health problems.

References

Alexander ME, Dietrich SM, Hua Y, Moghadas SM. 2009. A comparative evaluation of modelling strategies for the effect of treatment and host interactions on the spread of drug resistance. *J Theor Biol* 259:253–263.

Beaglehole R, Bonita R. 2004. *Public Health at the Crossroads: Achievements and Prospects*, 2nd ed. Cambridge: Cambridge University Press.

Berkelman RL, Bryan RT, Osterholm MT, LeDuc JW, Hughes JM, et al. 1194. Infectious disease surveillance: A crumbling foundation. *Science* 264(5157):368–370.

Berry RJ, Crawford TJ, Hewitt GM. 1992. *Genes in Ecology*. Oxford: Blackwell Scientific.

Caley P, Philip DJ, McCracken K. 2008. Quantifying social distancing arising from pandemic influenza. *J R Soc Interface* 5:631–639.

Centers for Disease Control and Prevention (CDC). 2009. What to do if you get sick: 2009 H1N1 and seasonal flu. Accessed March 25, 2013, at http://www.cdc.gov/h1n1flu/sick.htm.

Chew SK. 2007. SARS: How a global epidemic was stopped. *Bull World Health Org* 85:324–324.

Cohn SK. 1997. Introduction. In: Herlihy D, ed. *The Black Death and the Transformation of the West*, pp. 1–15. Cambridge, Mass: Harvard University Press.

Cohn SK. 2002. *The Black Death Transformed: Disease Culture in Early Renaissance Europe*. London: Edward Arnold.

Cohn SK. 2003. Black Death. In: Demeny P, McNicoll G, eds. *Encyclopedia of Population*, pp. 98–101. New York: Macmillan.

Dick RS, Steen EB. 1991. *The Computer-Based Patient Record: An Essential Technology for Health Care*. Washington, DC: National Academy Press.

Doll R, Hill AB. 1954. The mortality of doctors in relation to their smoking habits; A preliminary report. *Br Med J* 1(4877):1451–1455.

Epstein JM, Parker J, Cummings D, Hammond RA. 2008. Coupled contagion dynamics of fear and disease: Mathematical and computational explorations. *PLoS ONE* 3:e3955.

Flahault A, Valleron AJ. 1992. A method for assessing the global spread of HIV-1 infection based on air travel. *Math Popul Stud* 3:161–171.

Henderson DA. 1993. Surveillance systems and intergovernmental cooperation. In: Morse SS, ed. *Emerging Viruses*, pp. 283–289. New York: Oxford University Press.

Herlihy D. 1997. *The Black Death and the Transformation of the West*. Cambridge, Mass: Harvard University Press.

International Federation of Red Cross and Red Crescent Societies. 2009. The epidemic divide. Accessed March 25, 2013, at http://www.ifrc.org/Global/Publications/Health/170800-Epidemic-Report-EN-LR.pdf.

Kelland K. 2011. HIV epidemics emerging in Middle East, North Africa: Study. Accessed February 11, 2013, at http://www.reuters.com/article/2011/08/02/us-aids-mideast-idUSTRE77165O20110802.

Koopman J. 1995. Brazilian congress highlights new directions for epidemiologic methodology. *Epidemiol Monitor* 16:3–8.

Last JM. 1988. *Dictionary of Epidemiology*, 2nd ed. New York: Oxford University Press.

Laxminarayan R, Malani A, Howard D, Smith DL. 2007. Extending the cure: Policy responses to the growing threat of antibiotic resistance. Washington DC: RFF. Accessed February 11, 2013, at http://www.rff.org/rff/Documents/ETC_fullreport.pdf.

Lederberg J, Shope RE, Oaks SC Jr., eds. 1992. *Emerging Infections: Microbial Threats to Health in the United States*. Washington, DC: National Academy Press.

Longini IM Jr, Fine PE, Thacker SB. 1986. Predicting the global spread of new infectious agents. *Am J Epidemiol* 123:383–391.

Marier R. 1977. The reporting of communicable diseases. *Am J Epidemiol* 105:587–590.

McCurry J. 2006. Japan remembers Minamata. *Lancet* 367:99–100.

McGinnis JM, Foege WH. 1993. Actual causes of death in the United States. *JAMA* 270: 2207–2212.

McNeill WH. 1976. *Plagues and peoples*. Garden City, NY: Anchor Press.

Moore PS. 1992. Meningococcal meningitis in sub-Saharan Africa: A model for the epidemic process. *Clin Infect Dis* 14: 515–525.

Morse SS. 1991. Emerging viruses: Defining the rules for viral traffic. *Perspect Biol Med* 34:387–409.

Orenstein WA, Bernier RH. 1990. Surveillance: Information for action. *Pediatr Clin North Am* 37:709–734.

Palumbi SR. 2001. Humans as the world's greatest evolutionary force. *Science* 293:1786–1790.

Pavlovskii EN. 1996. *Natural Nidality of Transmissible Diseases, with Special Reference to the Landscape Epidemiology of Zooanthroponoses*. Urbana: University of Illinois Press.

Peterson DR. 1970. The practice of epidemiology. In: Fox JP, Hall CE, Elveback LR, eds. *Epidemiology: Man and Disease*, pp. 315–332. New York: Macmillan.

Poletti P, Caprile B, Ajelli M, Pugliese A, Merler S. 2009. Spontaneous behavioural changes in response to epidemics. *J Theor Biol* 260:31–40.

Satcher D. 1995. Emerging infections: Getting ahead of the curve. *Emerg Infect Dis* l:l–6.

Susser discusses "ecologism" as new paradigm. 1995. *Epidemiol Monitor* 16:1,7,13.

Thacker SB, Berkelman RL. 1988. Public health surveillance in the United States. *Epidemiol Rev* 10:164–190.