Chapter 19
The Sword of Damocles: Whither the Next Pandemic

Robert F. DeFraites

Abstract This chapter discusses the nature and characteristics of infectious diseases, the particular circumstances in which they can produce epidemics, and how outbreaks can be detected and mitigated in a timely manner. Factors favoring epidemics include the innate capability of the infectious agent to infect individuals, the ease with which the agent is transmissible from one individual to another, and the susceptibility of the population for outbreaks to occur. Susceptibility to outbreaks is increased when the immune defense mechanisms of individuals are degraded through malnutrition and stress, and large numbers of people are crowded together in an environment lacking basic public health protections. Such circumstances often accompany disasters and complex emergencies. The public health community worldwide has developed mechanisms for earlier recognition and response to epidemics, and is striving to refine techniques and approaches to better anticipate them.

- To describe the historical impact of epidemics and pandemics
- To understand risk factors and conditions favourable for pandemics, epidemics, including natural disasters
- To describe responsibilities and activities of the World Health Organization and other international bodies in preparing for and responding to pandemics and epidemics
- To describe actions to be taken in responding to these events, including the discrimination of "naturally occurring" outbreaks from synthetic, or man-made ones

Keywords Pandemics • Epidemics • Risk factors • Control • Intervention • Predictions

R.F. DeFraites, MD, MPH
Department of Preventive Medicine and Biometrics,
Uniformed Services University of the Health Sciences,
4301 Jones Bridge Road, Bethesda, MD 20814, USA
e-mail: robert.defraites@usuhs.edu

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Objectives

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Background

Epidemics, Outbreaks, Pandemics Defined

An epidemic is defined in Last's Dictionary of Epidemiology as incidence of a condition or a disease "clearly above" the expected rate for the population and time frame being considered. In popular usage, the term evokes images of widespread pestilence and serious illness; some in public health (including the World Health Organization) refer to these circumstances with terms such as "cluster" or "disease outbreak" reflecting somewhat the dread associated with the term "epidemic". Pandemics are large outbreaks that occur over a broad area and may involve a substantial proportion of the population. Infectious causes of global pandemics include cholera, typhus, plague, influenza, and HIV.

Infectious Diseases and Pandemics/Epidemics in Culture and History

Epidemics and pandemics occur only if there is a sufficiently large population of susceptible persons available for sustained transmission. Early hunter-gatherer societies were generally spared from plagues since small, mobile groups could not support the chain of transmission for very long; infrequent contact between groups prevented easy transmission from one group to another. The development of agriculture and resulting urban centres provided stable and concentrated populations of susceptible individuals allowing introduced infections to spread. Many infections causing outbreaks in these early civilizations were zoonotic agents transmitted from newly domesticated animals, especially swine, cattle, sheep, and poultry.

Flowering of industry and trade resulted in denser urbanization and facilitated the plagues associated with crowding, through person-to-person transmission, sanitation, faecal-oral transmission, and increased contact with rats, lice, and fleas as vectors of disease in cities. There are lists of outbreaks, “plagues”, and pandemics noted through history of every human society. In more recent history, seven pandemics of cholera have been described since the first in the early nineteenth century. The current (seventh) pandemic started in Asia in 1961, spread to Africa by 1971, and the Americas 20 years later. Cholera remains an endemic disease in many countries around the world, including its original home in South Asia. Pandemics of influenza occur every several decades, the most recent caused by a H1N1 strain originating in North America in 2009 and rapidly spreading around the world.

Structure of Pandemics and Epidemics

The pandemic/epidemic potential of an infectious disease is influenced by characteristics of the agent, such as mode of transmission, requirement for a vector (such as a mosquito), and resistance to environmental conditions; the host, by behaviour and immune status; and the environment, by temperature, humidity, and salinity of water. All of these factors are brought to bear in a simple conceptual model for pandemic/epidemic potential: whether, on average, the infection in a single host/person is transmitted to more than one susceptible person. This tendency is summarized in the basic reproductive rate, commonly abbreviated as R_0 (“*R* subzero”)—the need for the disease to propagate itself in the host population to survive and grow. The higher the R_0, the more readily disease propagates through the population. An infection with $R_0 < 1$ will not persist. If $R_0 = 1$, the infection can be sustained in a steady state as long as susceptible persons remain to be infected. A condition with $R_0 > 1$ will spread through the susceptible population in an exponential manner. The R_0 is a function of the ease of transmission (a low vs. high infectious dose, efficient means of transmission through aerosol, direct contact, or food and water), the length of time that an infected person remains contagious, and the likelihood that an infectious person will achieve effective contact with a susceptible person during that time. Some infections, such as measles, varicella, pertussis, and other infections are extremely transmissible, with large amounts of infectious particles being shed over an extended period by the host and result in infecting well over 60 % of susceptible household contacts. On the other hand, ingestion of a very small inoculum (a few dozen to several hundred bacilli) of Shigella is required to cause dysentery. Hepatitis A virus survives in the environment and can remain viable on surfaces for many days. Emerging and re-emerging infectious agents such as viruses newly adapted to humans (or having developed new immune characteristics) may spread quickly and with devastating effect in populations of susceptible hosts.

Pandemics and Epidemics Occurring in Conjunction with Natural Disasters and Emergencies, Including Myths and Misconceptions

Concern about potential outbreaks and rumours of pandemics/epidemics often accompany natural disasters, although this risk is mostly overstated. One of the more common misperceptions is that of the risk of infection posed by numbers of unrecovered human remains. With the rare exceptions of deaths caused by cholera and certain hemorrhagic fever virus infections, dead bodies require no special precautions to preclude customary, respectful, and documented disposition. Several key factors determine the likelihood of infectious disease outbreaks as a consequence of natural disasters. The type of disaster is important. Water-related disasters such as floods may provide ideal conditions for outbreaks of waterborne diseases such as leptospirosis, cholera, and enteric viral hepatitis. Conversely, other disasters such as earthquakes may alter habitats of vector arthropods or increase the risk of exposure to vector bites causing malaria and dengue. The size, nutritional and immune status, and living conditions of populations affected or displaced by the disaster may predispose to outbreaks of infections associated with crowding and person-to-person transmission, such as measles, acute respiratory infections including influenza, meningococcal infections, and noroviruses. Finally, the absence or prolonged interruption of public utilities such as electrical power, fuel, potable drinking water supply, and sanitary waste disposal services will increase the risk of food- and waterborne infections. Therefore, to mitigate the risk of outbreaks following a disaster that involves a large population of displaced persons, focused effort should be directed toward rapid provision of sufficient and sanitary accommodations, vector protection, and safe food and water. Other interventions, such as immunization programmes against specific pathogens, such as measles and tetanus, should also be considered.

Outbreaks and Mass Gatherings

Massive gatherings of people create conditions favourable for outbreaks. Planned mass gatherings include events such as the Olympics, the World Cup, and the annual Hajj in Saudi Arabia. Persons from all over the world converge for these events, burdening local food, water, and sanitation infrastructure. Although participants in these kinds of events are usually fairly healthy, some can be expected to be incubating potentially contagious infections; outbreaks of meningococcal disease have occurred in conjunction with the Hajj. Other mass gatherings occur as unplanned consequences of conflicts or natural disasters; the persons displaced by such events can be expected to include a greater proportion of those with impaired immune systems due to poor nutrition, underlying illnesses (including contagious diseases), and extremes of age.

How Does a Pandemic/Epidemic Start? Can They Be Predicted/ Forecasted?

Most outbreaks cannot currently be predicted with adequate accuracy and timeliness to permit specific countermeasures to be employed in advance. However, a series of observations suggest a framework upon which prediction might be focused. First, the majority of agents comprising newly emerging infections of humans since the middle of the twentieth century are zoonoses, and second, most of these have been transmitted from wildlife. Some have suggested that more vigorous ongoing monitoring of zoonotic activity, especially among equatorial populations with frequent contact with wildlife may provide early warning of potentially devastating epidemics of emerging zoonoses, especially viruses.

To cause large outbreaks in humans, these infections must not only possess the ability to infect a single human, but then to become well enough adapted to the new host so that person-to-person transmission can be sustained free of the need for repeated contact with the original animal host. In the future, systematic and reliable determination of genetic and other intrinsic factors of emerging agents that might predispose them to cause epidemics may be possible.

Once these infections are established in humans, earlier detection of epidemics may be possible by monitoring reports of prodromal symptoms or illness-related behaviour patterns tracked through Internet searches, telephone use, or other proxy means. Finally, regional and global detection and response efforts would benefit from a more unified and better integrated rapid communication and analytic capability.

World Health Organization Pandemic Response Framework and Public Health Security

International Health Regulations (IHR) 2005

With the 2005 update of the International Health Regulations, the WHO members greatly expanded the scope of infectious disease reporting and surveillance activities. Under the legacy regulations adopted in 1969, WHO member nations were legally bound to track and report four diseases of international interest: yellow fever, plague, cholera, and smallpox. The expansion of infectious disease reporting under the 2005 IHR reflected the realization of the significance of emerging and unanticipated infectious diseases and their potential to cause disruptive and destructive epidemics. Under IHR 2005, WHO conducts global surveillance to detect and assess significant public health risks. The WHO has established the Global Outbreak Alert and Reporting Network to support outbreak detection and response preparedness. Members of the network support IHR 2005 by establishing global surveillance and response standards, creating networks of partners for preparedness and rapid response, strengthening laboratory capacity and laboratory networks, providing training in field epidemiology, and assessing and strengthening national surveillance systems. Once detected, outbreaks or clusters must be verified and assessed for potential international public health significance. Based on this assessment, WHO must inform member states about the threats and, upon request, assist members in outbreak investigation and control. A declaration of a Public Health Emergency of International Concern (PHEIC) is to be considered in rare and "extreme" cases. On April 25, 2009, the Secretary General of the WHO announced the H1N1 influenza outbreak as the first PHEIC to be declared under the IHR 2005.

Influenza Pandemic Phases

The WHO developed a pandemic staging system uniquely for influenza, last updated in 2009. In anticipation of a predictable ongoing threat of global outbreaks of influenza, the WHO describes six phases of response to potential influenza pandemics, as a basis for coordinated planning and national, regional, and global response. These pandemic phases reflect the model of influenza manifesting itself as initially an infection of birds, swine, or other animals with varying degrees of threat to humans. Once human infection is documented, the phases reflect the occurrence of person-to-person transmission and regional and global distribution of the infection. Phases 1 through 3 are characterized by zoonotic influenza, with rare human infections and no sustained transmission by humans. Documentation of sustained person-to-person transmission characterizes phase 4, the pandemic alert phase. Transmission in at least two countries in the same WHO region initiates phase 5; the pandemic phase 6 is declared when at least one country in another of the six WHO regions is affected, in addition to the conditions for phase 5. There are two additional phases: the "post-peak" phase, in which surveillance and preparation is focused on a possible "second wave" of cases, and a post-pandemic phase, when influenza rates revert to the level typical of seasonal infection. While the phases generally reflect the temporal pattern of influenza pandemics, they are intended as a guide for nations to increase their public health and national readiness, and not to predict the course of an epidemic. There are no comparably mature systems for preparing for or tracking of other infections with pandemic potential.

Response Activities During Outbreaks/Epidemics

Outbreak Investigation Technique, Goals, Steps

The recognition of an unusual number or distribution of cases of disease or injury should trigger an investigation of the event as a potentially significant outbreak. The extent of this investigation will vary based on circumstances, from a cursory checking of facts to a more formal investigation with extensive data collection and field work, usually supported with laboratory resources. More aggressive and complete investigation is indicated to identify sources or causes and to mitigate or interrupt the outbreak, especially for unusually severe or extensive cases, unusual presentations, or potential for rapid spread. An essential initial step is confirmation of the existence of the outbreak, which entails comparing the number of cases in the cluster compared with the number that would be expected to occur in the population during the time interval under consideration. This step requires a clear statement of the definition of a "case" including consideration of time and geographic area constraints. The initial case definition should be more inclusive and less specific "diarrhoea with fever among children in neighbourhood X between dates Y and Z" may suffice. Accurate comparison with baseline cases rates may be difficult using such non-specific case definitions. During the course of the investigation the definition is usually refined. The introduction of more specific case criteria (including results of laboratory tests identifying one or more likely causative agents) can allow for accounting for "suspected" or "possible" and "confirmed" cases, and allow for more accurate comparison of case rates. Initial descriptive statistics include demographic data (age, sex, race/ethnicity) and a plot of case counts over time to create the "epidemic curve" histogram. The shape of this curve reflects key information about the outbreak: a single "peak" with a long "tail" reflects an outbreak that was caused by one-time exposure from a single "point" source. Cases emanating from a continuous or prolonged exposure will yield a broader curve with no single peak. A curve with multiple peaks classically represents an outbreak sustained by waves of person-to-person transmission. Causal hypotheses of risk factors, dose-response relationships, potential confounders, etc. can be analysed using case-control studies or other methods. Any resulting hypothesis of a causal relationship between risk factor(s) and the condition of interest ("caseness") must account for all or almost all cases. Cases lacking the suspected causal risk factors, i.e. "outliers", deserve additional scrutiny. Occasionally, characteristics unique to these case-persons are critical to identifying the source of the outbreak. Additional studies may be needed to confirm initial findings; all pertinent results must be provided to responsible authorities in a timely manner to direct actions to control the outbreak and communicate with the public. As control measures are implemented, surveillance for additional cases must continue in the population at risk and instituted elsewhere as indicated.

Table 19.1 Outbreak control: breaking the chain of transmission

The importance and priority of these varies with the infectious agent and circumstances:
Treat and isolate cases
Quarantine and prophylax potentially infected contacts
Sanitize or eliminate contaminated sources of food and water
Protect against arthropod vectors with barriers, repellents, and vector control interventions
Enhance personal hygiene (hand-washing, cough hygiene)
Dispose of waste
Immunize susceptible persons (measles, meningococcal, influenza)

Natural vs. "Unnatural" Outbreaks

In the course of investigating a disease outbreak, one is sometimes confronted with the question of whether the epidemic could have been generated by specific human activity, as opposed to "natural" forces. There are few specific indicators of such activity, aside perhaps from communication of a specific threat. Many infections and outbreaks emerge as unintentional consequences of human activity; these events usually follow well-established epidemiological patterns. The presence of several characteristics not encountered in most outbreaks should raise suspicion. The discovery of a truly novel agent will certainly warrant additional scrutiny. Similarly suspicious is a well-documented infectious agent that manifests markedly atypical clinical manifestations, for example, pneumonia as opposed to gastrointestinal symptoms, increased severity, or transmissibility. Extremely large point-source outbreaks, multiple simultaneous outbreaks, and those which reflect downwind spread of airborne infectious agent suggest a possible man-made source. Unnatural features of zoonotic disease outbreaks include the concurrence of large numbers of ill or dead animals, or evidence for reverse transmission (human to usual animal host) of well-known zoonoses.

Outbreak Intervention *(Table 19.1)*

Actions needed to mitigate or control an outbreak are typically related to factors which caused the outbreak in the first place. For example, the response to an outbreak caused by introduction of a vaccine-preventable disease (such as measles) into a susceptible population must include immunization (or re-immunization) programmes among other measures. The route of exposure will also suggest mitigation and control measures—food- and waterborne outbreaks respond to interruption of transmission through sanitary countermeasures directed against the offending medium.

For example, cholera transmission can be halted by providing safe drinking water and sanitary disposal of waste, and taking enteric precautions when caring for case patients and handling remains of fatal cases. Although antibiotics may have a role in treating case patients, mass antibiotic prophylaxis is contraindicated. Cholera immunization has likewise been considered to have limited use as a disease control measure; however, with the introduction of oral cholera vaccines, immunization may be a useful adjunct in some situations, such as reducing the incidence of disease in endemic areas or protecting a well-defined population against an imminent epidemic.

For an agent with antigenic variability like influenza A, outbreaks are often caused by subtypes and strains of the virus for which there is no effective vaccine. In other cases, outbreaks occur in population with poor vaccine coverage. Even with immunization with an effective vaccine, protection may be delayed for several weeks, allowing outbreaks of illness to occur after immunization. Although antiviral prophylaxis and treatments are effective for preventing illness or blunting the clinical course of influenza, widespread use in large communities is unfeasible. Other mitigation strategies include social distancing (including hand and cough hygiene) and quarantining of potentially infected persons. Respiratory and droplet isolation of cases can stop transmission as well. However, in practice, use of social distancing to interrupt transmission of influenza is complicated by several characteristics of the virus and the illness. Influenza has an incubation period of only several days to a week; rapid laboratory diagnosis of cases (if available) early in the illness is hampered by relatively low test sensitivity, so infected persons may not be identified before transmitting the infection. Once infected, an ill person can shed infectious viruses for over a week; effective isolation for the duration of viral shedding may be difficult to maintain.

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