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EMERGING INFECTIOUS DISEASES

Emerging infectious diseases are those that have newly appeared in the human population or are rapidly increasing in incidence (number of cases) or geographic range. As with the periodically reported outbreaks of Ebola (a viral hemorrhagic fever with high mortality) in Africa, emerging infectious diseases may seem mysterious and dramatic, but in fact specific factors responsible for their emergence can be identified (Table 1). The emergence of an infectious disease can be seen as a two step process—introduction and establishment/dissemination—that these factors precipitate or promote in one, or both, phases. HIV/AIDS, Ebola, and hemolytic uremic syndrome (caused by certain strains of the bacterium *Escherichia coli* in food or water) are among the notable infectious diseases that were first identified in the latter decades of the twentieth century. Others, such as influenza, reappear periodically causing major epidemics or even pandemics (epidemics that affect the entire world). With increasing globalization and geographic mobility of populations, each part of the world is now vulnerable to infections that might first arise in any other part.

Introduction of Infectious Disease

In analyzing infections that have emerged, it is apparent that many diseases existed in nature before gaining access to the human population, often as a result of changed ecological or environmental conditions that placed humans in contact with previously inaccessible pathogens or the natural hosts that carry them. The term *viral traffic* (or, more generally, microbial traffic) was coined to represent processes involving the access, introduction, or dissemination of existing pathogens to new host populations. Ecological changes and major demographic changes (such as population migrations) often precipitate emergence. Many of these changes are anthropogenic. Infections transmitted by mosquitoes, which include malaria, dengue, yellow fever, West Nile fever, Rift Valley fever, and many others, are often stimulated by the presence of dams, irrigation projects, or open water storage since mosquitoes breed in water.

In terms of the introduction phase, examples of infections originating as zoonoses (infections transmissible from animals to humans) suggest that the *zoonotic pool*—introductions of pathogens from

TABLE 1

Factors in the Emergence of Infectious Diseases

Factor	Examples of specific factors	Examples of diseases
Ecological changes (including those due to economic development and land use)	Agriculture; dams, changes in water ecosystems; deforestation/reforestation; flood/drought; famine; climate changes	Schistosomiasis (dams); Rift Valley fever (dams, irrigation); Argentine hemorrhagic fever (agriculture); Hantaan (Korean hemorrhagic fever) (agriculture); Hantavirus pulmonary syndrome, southwestern US, 1993 (weather anomalies)
Human demographics, behavior	Societal events: Population growth and migration (movement from rural areas to cities); war or civil conflict; economic impoverishment; urban decay; factors in human behavior such as: sexual behavior (including urban prostitution and "sex-for-drugs"); intravenous drug use; diet; outdoor recreation; use of child care facilities (high-density settings)	Introduction of HIV; spread of dengue; spread of HIV and other sexually transmitted diseases
International travel and commerce	Worldwide movement of goods and people; air travel	Dissemination of HIV; dissemination of mosquito vectors such as Aedes albopictus (Asian tiger mosquito); ratborne hantaviruses, intoduction of cholera into South America, dissemination of O139 (non-O1) cholera organism (ships)
Technology and Industry	Food production: Globalization of food supplies; changes in food processing and packaging; Health care: New medical devices; organ or tissue transplantation; drugs causing immunosuppression; widespread use of antibiotics	Food processing: Hemolytic uremic syndrome (E. coli contamination of hamburger meat), bovine spongiform encephalopathy; Health care: Contaminated injection equipment (Ebola, HIV); Transfusion associated hepatitis (hepatitis B, C); opportunistic infections in immunosuppressed patients; Creutzfeldt-Jakob disease from contaminated batches of human growth hormone (medical technology)
Microbial adaptation and change	Microbial evolution, response to selection in environment	Changes in virulence and toxin production; development of drug resistance (antimicrobial resistant bacteria, chloroquine resistant malaria); "antigenic drift" in influenza virus
Breakdown in public health measures	Curtailment or reduction in prevention programs; lack of, or inadequate, sanitation and vector control measures	Resurgence of tuberculosis in United States; cholera in refugee camps in Africa; resurgence of diphtheria in former Soviet republics

Note: Categories are not mutually exclusive; several factors may contribute to emergence of a disease.

SOURCE: Morse, S.S. (1995).

other species—is an important and potentially rich source of emerging pathogens or their precursors, some of which might become successful under conditions that favor transfer to human hosts. HIV is a possible case of such transfer. Although the original ancestors of HIV-1 are not known with certainty, the best current evidence suggests that HIV-1 originated as a zoonotic introduction, possibly from chimpanzees; this may have occurred several times. There is somewhat better evidence for a probable zoonotic origin as regards HIV-2 (another lentivirus that causes AIDS), with the sooty mangabey monkey the likely source. As an illustrative example, an infected man, identified in rural Liberia, had a strain of HIV-2 that closely resembled viruses taken from the sooty mangabey monkey, the presumed reservoir of a virus with a close ancestral connection to HIV-2. That such individuals can be identified suggests that zoonotic introductions of viruses such as HIV may well occur from time to time in isolated populations, and probably often escape notice. In the case of HIV-1, key factors in its success after introduction were the social and demographic changes in the last half of the twentieth century (such as migration to cities) that gave the virus access to a larger population, and other social changes (e.g., drug-related use of contaminated injection equipment, growth of the commercial sex trade) that allowed more facile transmission of the virus to new individuals despite its relatively low natural transmissibility.

Although it is common to think of infectious diseases as causing acute outbreaks, at the beginning

of the twenty-first century there is increasing recognition that infections can also be the cause of chronic diseases. Hepatitis B is responsible for many cases of liver cancer worldwide. Recent pioneering work by gastroenterologist Barry Marshall implicated the bacterium *Helicobacter pylori* in gastric ulcers and cancer. Molecular biologists Yuan Chang and Patrick S. Moore, of Columbia University, identified a novel herpesvirus (now known as human herpesvirus 8) as the likely cause of Kaposi's sarcoma.

Establishment and Dissemination

Once introduced, the success of the pathogen in a new population depends on its establishing itself and then disseminating within the population. Many zoonotic introductions are highly virulent but not readily transmissible from person to person, thus preventing their establishment. Both chance and the evolutionary potential of the pathogen play a role in determining whether the infection will establish itself.

Human intervention and social change, in addition to providing opportunities for the introduction of pathogens, also provide increasing opportunities for dissemination. Ebola in Africa is usually introduced into humans by contact with its still unknown natural host in the forest, but most of the subsequent cases of the disease occur in hospitals through use of contaminated injection equipment. A number of factors have led to the resurgence in tuberculosis worldwide: HIV infection increases susceptibility to tuberculosis, while high density settings such as day care centers, homeless shelters, and prisons enhance the probability of transmission. Human migration from rural areas to cities, especially in areas with a high degree of biodiversity, can introduce remote pathogens to a larger population. HIV is the best known beneficiary of introduction by migration, but many other diseases may proliferate in this way. After its likely first move from a rural area into a city, HIV-1 spread via highways to other regional cities. Later, by long distance routes including air travel, it progressed to places even further away than the initial site of the infection. The increasing volume of air travel affords pathogens vast opportunities for globalization.

The globalization and industrialization of the food supply and other goods also offer pathways for microbial traffic. The strains of *Escherichia coli* that cause hemolytic uremic syndrome were probably once limited to a few relatively isolated populations of cattle, but have spread as cattle are collected into large central processing facilities. Bovine spongiform encephalopathy (BSE, so-called mad cow disease), which has been identified in Britain since the 1980s, may have been an interspecies transfer of scrapie from sheep to cattle. Widespread use of animal byproducts as feed supplements, in combination with changes in rendering processes that allowed the scrapie agent in sheep byproducts to contaminate the feed, may have been responsible for its introduction and spread in cattle and eventually, in a variant form, to the human population.

Basic public health measures, including clean water and immunization, and improving nutrition have made major contributions to the relative decline of infectious diseases, and remain essential. Reemerging diseases are those that were previously decreasing in the human population but are again on the upswing. Usually the diseases are those that were once controlled but are staging a comeback due to breakdowns in public health or control measures. The resurgence of diphtheria in the former Soviet Union in the 1990s (as immunization programs lapsed due to lack of resources) is an example. Reemerging diseases should be a reminder that complacency can lead to the resurgence of many infectious diseases that were once thought to be vanquished.

Infectious diseases have a long history, and are likely to remain significant causes of illness and death in the foreseeable future. Some emerging diseases, like HIV/AIDS, have become worldwide public health crises (there were an estimated 40 million HIV infected individuals at the end of 2001, and according to the World Health Organization, an annual death toll of about 3 million.) Other diseases, such as Ebola, are dramatic but fortunately have remained localized, with limited public health impact.

Biowarfare and Bioterrorism

At the beginning of the twenty-first century, biowarfare and bioterrorism have emerged as related concerns. While nature has been the main source of emerging infections, humans have also on occasion attempted to introduce or disseminate disease intentionally. Historians have suggested that the Tatars catapulted dead bodies into the Crimean city of Kaffa (present day Feodossiya in Ukraine) during a siege in 1346, possibly starting the Black Death (bu-

bonic plague). Smallpox, a dreaded natural scourge since ancient times, was declared conquered in 1980 after a major, and successful, eradication campaign. As a result, control measures were ended, and most of world population is now vulnerable to reintroduction, raising concerns in the event that terrorists succeed in obtaining samples of the virus. In autumn 2001, anthrax letters—envelopes containing a powder of highly concentrated anthrax spores enclosed in a letter—were sent to media and Senate offices in the United States. By the end of the outbreak in late November, there had been 23 cases of anthrax, with 5 deaths; none of the victims were themselves the actual addressees of the letters. Both emerging infectious diseases and bioterrorist attacks can be viewed as involving unexpected outbreaks of infectious disease (although, in the case of biowarfare or bioterrorism, introduced through direct human intervention rather than by the other, usually incidental, means described for natural outbreaks). Conceptually, many of the steps that need to be taken to avoid both types of introduction are similar, beginning with effective public health surveillance to detect and respond to unexpected infectious disease outbreaks.

Detection and Prevention

Fortunately, since most new natural infections have limited ability to establish themselves or disseminate, public health catastrophes like the AIDS pandemic are rare. But which infection will be the next smallpox or AIDS, or even the next pandemic influenza, and how can one prevent it? Global events such as AIDS will occur from time to time, and the risk may well be increasing as factors favoring emergence increase worldwide. Many, although not all, of the facilitating factors for infectious disease emergence are anthropogenic. And though early warning and detection are prerequisite to an effective response, public health infectious disease surveillance remains fragmented and incomplete. An enhanced global system, with the capability to recognize both common and novel infectious diseases, is both possible and necessary.

See also: *AIDS; Disease and History; Diseases, Infectious; Mortality Reversals; Tuberculosis.*

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EMPLOYMENT

See *Labor Force*