Introduction

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The world is witnessing the emergence and reemergence of infectious diseases as a significant threat to public health (2, 3). In contrast to predictions earlier in this century, infectious diseases remain the leading cause of death worldwide and have been increasing as a cause of death in the United States since 1980 (6). Many complex factors contribute to this growing threat and to the broader array of recognized pathogens.

Emerging infections, as defined in a report by the Institute of Medicine in 1992, include diseases whose incidence has increased within the past 20 years or whose incidence threatens to increase in the near future (2). The term includes infections caused by new agents, reemerging pathogens whose incidence had previously declined, and organisms that are developing antimicrobial resistance. Established diseases with a recently discovered infectious origin (e.g., peptic ulcer disease caused by *Helicobacter pylori*) are also included in this definition.

The world's population has been increasing explosively and currently exceeds 5 billion individuals. Population is projected to double by the year 2050, with the most marked rise in population occurring in Asia and Africa.

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Concomitantly, the trend towards urbanization is continuing in both the developed and the developing world, and cities marked by poverty and overcrowding favor the spread of many diseases, including tuberculosis. Lack of adequate sanitation and rodent control fosters the spread of cholera and plague, respectively. Lack of adequate infection control practices aids the spread of Ebola virus and other pathogens in impoverished nations in Africa.

Demographic and social changes have contributed to the emergence of infectious diseases.

Demographic and social changes have contributed to the emergence of infectious diseases. Changes in sexual behavior have promoted the spread of human immunodeficiency virus (HIV) and other sexually transmitted diseases. The use of illicit injection drugs has contributed to the rapid spread of HIV as well as to the spread of hepatitis C and other blood-borne infectious agents.

The dramatic increase in the number of women entering the workplace has resulted in greater numbers of young children in day care. These children are more likely to be exposed to and to acquire respiratory and diarrheal infections; in addition, the high rates of antibiotic use by children attending child care facilities may contribute to the development of antibiotic resistance, particularly in *Streptococcus pneumoniae* and other common community-acquired bacterial pathogens.

Changes in technology also create new niches for microorganisms. The use of newly developed superabsorbent tampons has been associated with toxic shock syndrome, and air conditioning systems have been associated with outbreaks of Legionnaires' disease. Changes in food processing methods (e.g., mass production of hamburger patties or ice cream) have allowed small amounts of food contaminated with pathogens such as *Escherichia coli* O157:H7 and *Salmonella* to contaminate large amounts of a final product.

The widespread use of invasive medical devices has been accompanied by an increased incidence of bloodstream and other infections. Many microorganisms, such as microsporidia and cryptosporidia, are being recognized as significant pathogens of the growing population of patients who are immunosuppressed as a result of chemotherapy, organ transplantation, or HIV infection. As xenotransplantation becomes a more likely therapeutic option, concerns have been raised regarding the risk of transplant recipients acquiring xenozoonoses caused by organisms such as retroviruses that have not previously infected or caused disease in humans.

Changes in land use also affect the incidence and geographic distribution of infectious disease. The emergence of Lyme disease in the eastern United States, for example, coincided with an explosive increase in the deer population, as land previously used for farming was reforested and suburban communities were established. The emergence of other tick-borne diseases, such as human monocytic ehrlichiosis and human granulocytic ehrlichiosis, may also relate to the changing vector-host ecology. Climate changes may affect the emergence or reemergence of disease; drought followed by heavy rains in the Four Corners area in the southwestern United States led to an explosion in the rodent population, which in turn contributed to the outbreak of hantavirus pulmonary syndrome in 1993. The impact of global warming

on infectious diseases, particularly vector-borne diseases, is uncertain and warrants further study.

International travel and commerce are increasing at an astounding pace, and both play a significant role in the spread of disease. In the mid-1990s, more than 500 million international trips on commercial airlines were recorded per year; these flights carried persons with drug-resistant tuberculosis, cholera, malaria, and other diseases from one country to another in a few hours. The importation of reptiles carrying *Salmonella* and the shipment of fresh fruits and vegetables contaminated with enteric pathogens from one geographic region to another are examples of international commerce that have resulted in outbreaks of disease. Ebola virus has spread from the Philippines to the United States via the transport of infected nonhuman primates and from Gabon to South Africa via travel of an infected person. The global mixing of pathogens will continue, and disease will emerge if circumstances in the new environment allow survival and proliferation of the introduced pathogen.

The Centers for Disease Control and Prevention, the World Health Organization, and other agencies and organizations have published documents which outline the steps required to respond effectively to microbial threats (1, 5, 7). Priority areas include enhancing disease surveillance, conducting needed epidemiologic and laboratory research, and implementing effective prevention and control programs. Strengthening the capacity to diagnose infectious pathogens is considered a critical step in addressing each of these areas, and laboratory diagnosis of an infectious disease often depends on contributions from many fields. Development and availability of inexpensive and practical diagnostic tests for field use are particularly emphasized. In addition, understanding the pathogenesis of the disease may help in the prevention of the disease as well as its treatment; a research agenda for emerging infectious diseases developed by the National Institutes of Health includes better understanding of the pathogenesis of and host susceptibility to emerging pathogens as a goal (4).

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This book illustrates the enormous contribution that pathologists can make, in collaboration with colleagues from other areas such as epidemiology, clinical care, veterinary medicine, and microbiology, to the diagnosis of infectious agents, as well as to the elucidation of the pathogenic mechanisms, which is vital to research of emerging pathogens. Frequently, the responsible pathogen is demonstrated in specimens and then isolated through culture techniques. Since some infectious agents, such as many of the fungi, are morphologically distinct, they can be accurately identified by direct microscopic examination. Various histologic stains are helpful for the diagnosis of such infections as plague and Buruli ulcer; a modification of the acid-fast stain has been helpful in the diagnosis of cryptosporidiosis from stool specimens.

New molecular techniques such as polymerase chain reaction and in situ hybridization have emerged as major technologies, and both of these techniques have been applied to the field of infectious disease pathology. Immunohistochemistry has extended the contributions of pathologists beyond

conventional histopathology and has provided new avenues for the detection of specific microbial pathogenic agents, from filoviruses to *Leptospira*. Not only are these techniques helpful in diagnosis, they have also been extremely useful in elucidating the pathogenesis of newly recognized diseases, such as hantavirus pulmonary syndrome and Ebola hemorrhagic fever. Their potential as species-specific diagnostic techniques for diseases such as microsporidiosis is also recognized.

New techniques in pathology may allow for more practical means of surveillance for pathogens

New techniques in pathology such as immunohistochemical examination may allow for more practical means of surveillance for pathogens such as filoviruses. Formalin-fixed biopsy specimens are not infectious, may be transported without special precautions or refrigeration, and may be taken in the most basic field conditions. This technique is being used for surveillance of Ebola hemorrhagic fever in Zaire.

As illustrated in the following chapters, the field of pathology in conjunction with epidemiologic and other expertise is contributing enormously to the prevention and control of both newly recognized and resurgent infectious diseases. Further research and training in infectious disease pathology will be a critical component in the worldwide efforts to address emerging microbial threats.

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