

# The challenge of emerging and re-emerging infectious diseases

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Infectious diseases have for centuries ranked with wars and famine as major challenges to human progress and survival. They remain among the leading causes of death and disability worldwide. Against a constant background of established infections, epidemics of new and old infectious diseases periodically emerge, greatly magnifying the global burden of infections. Studies of these emerging infections reveal the evolutionary properties of pathogenic microorganisms and the dynamic relationships between microorganisms, their hosts and the environment.

**E**merging infections (EIs) can be defined as "infections that have newly appeared in a population or have existed previously but are rapidly increasing in incidence or geographic range"<sup>1</sup>. EIs have shaped the course of human history and have caused incalculable misery and death. In 1981, a new disease — acquired immune deficiency syndrome (AIDS) — was first recognized. As a global killer, AIDS now threatens to surpass the Black Death of the fourteenth century and the 1918–1920 influenza pandemic, each of which killed at least 50 million people<sup>2,3</sup>. Of the 'newly emerging' and 're-emerging/resurging' diseases that have followed the appearance of AIDS (Fig. 1), some have been minor curiosities, such as the 2003 cases of monkeypox imported into the United States<sup>4</sup>, whereas others, such as severe acute respiratory syndrome (SARS), which emerged in the same year<sup>5</sup>, have had a worldwide impact. The 2001 anthrax bioterrorist attack in the United States<sup>6</sup> falls into a third category: 'deliberately emerging' diseases. EIs can be expected to remain a considerable challenge for the foreseeable future. Here we examine the nature and scope of emerging and re-emerging microbial threats, and consider methods for their control. We emphasize that emergence results from dynamic interactions between rapidly evolving infectious agents and changes in the environment and in host behaviour that provide such agents with favourable new ecological niches.

## Global burden of infectious diseases

About 15 million (>25%) of 57 million annual deaths worldwide are estimated to be related directly to infectious diseases; this figure does not include the additional millions of deaths that occur as a consequence of past infections (for example, streptococcal rheumatic heart disease), or because of complications associated with chronic infections, such as liver failure and hepatocellular carcinoma in people infected with hepatitis B or C viruses<sup>7</sup> (Fig. 2).

The burden of morbidity (ill health) and mortality associated with infectious diseases falls most heavily on people in developing countries<sup>8</sup>, and particularly on infants and children (about three million children die each year from malaria and diarrhoeal diseases alone<sup>9</sup>). In developed nations, infectious disease mortality disproportionately affects indigenous and disadvantaged minorities<sup>10</sup>.

## Emerging infections in historical context

EIs have been familiar threats since ancient times. They were once identified by terms such as *λεηλασία* (*leimasia*)<sup>11</sup>,

and later as 'pestilences', 'pestes', 'pests' and 'plagues'. Many examples can be cited in addition to the Black Death and the 1918 influenza pandemic, such as certain biblical pharaonic plagues and the unidentified Plague of Athens, which heralded the end of Greece's Golden Age<sup>12</sup>. The Age of Discovery, starting in the fifteenth century, was a particularly disastrous period with regard to the spread of infectious diseases. Importation of smallpox into Mexico caused 10–15 million deaths in 1520–1521, effectively ending Aztec civilization<sup>13,14</sup>. Other Amerindian and Pacific civilizations were destroyed by imported smallpox and measles<sup>15–17</sup>. Historians have referred to these events as apocalypses<sup>18</sup> and even as genocide<sup>19</sup>.

For centuries, mankind seemed helpless against these sudden epidemics. But the establishment of the germ theory and the identification of specific microbes as the causative agents of a wide variety of infectious diseases<sup>18–20</sup> led to enormous progress, notably the development of vaccines and ultimately of antimicrobials<sup>21</sup>. In fact, the era of the identification of microbes had barely begun<sup>22</sup> when optimists at the end of the nineteenth century predicted the eradication of infectious diseases<sup>23</sup>. By the 1990s, which witnessed the widespread use of penicillin, the development of polio vaccines and the discovery of drugs for tuberculosis, complacency had set in<sup>24</sup>, and in 1967, the US Surgeon General stated that "the war against infectious diseases has been won"<sup>25</sup>.

Some experts remained sceptical, aware of recurrent lessons from history. They were less persuaded by successes than alarmed by failures such as the lack of progress against infections in the developing world and the global spread of antimicrobial resistance. Richard Krause, then the director of the US National Institute of Allergy and Infectious Diseases, warned in 1981 (ref. 24) that microbial diversity and evolutionary vigour were still dynamic forces threatening mankind. As Krause was completing his book *The Restless Tide*<sup>26</sup>, AIDS — one of history's most devastating pandemics — was already insidiously emerging. The emergence of AIDS led to renewed appreciation of the inevitability and consequences of the emergence of infectious diseases<sup>27–29</sup>. In the past 25 years, some of the factors that resulted in AIDS have also led to re-emergences of historically important diseases such as cholera, diphtheria, trench fever and plague. Many re-emergences have been catalysed by wars, loss of social cohesion, and natural disasters such as earthquakes and floods, indicating the importance not only of microbial and viral factors, but also of social and environmental determinants<sup>29–31</sup>.

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