

Study of ancient and modern plagues finds common features

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In 430 B.C., a new and deadly disease—its cause remains a mystery—swept into Athens. The walled Greek city-state was teeming with citizens, soldiers and refugees of the war then raging between Athens and Sparta. As streets filled with corpses, social order broke down. Over the next three years, the illness returned twice and Athens lost a third of its population. It lost the war too. The Plague of Athens marked the beginning of the end of the Golden Age of Greece.

The Plague of Athens is one of 10 historically notable outbreaks described in an article in *The Lancet Infectious Diseases* by authors from the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health. The phenomenon of widespread, socially disruptive disease outbreaks has a long history prior to HIV/AIDS, severe acute respiratory syndrome (SARS), H5N1 avian influenza and other emerging diseases of the modern era, note the authors.

"There appear to be common determinants of disease emergence that transcend time, place and human progress," says NIAID Director Anthony S. Fauci, M.D., one of the study authors. For example, international trade and troop movement during wartime played a role in both the emergence of the Plague of Athens as well as in the spread of influenza during the pandemic of 1918-19. Other factors underlying many instances of emergent diseases are poverty, lack of political will, and changes in climate, ecosystems and land use, the authors contend. "A better understanding of these determinants is essential for our

preparedness for the next emerging or re-emerging disease that will inevitably confront us," says Dr. Fauci.

"The art of predicting disease emergence is not well developed," says David Morens, M.D., another NIAID author. "We know, however, that the mixture of determinants is becoming ever more complex, and out of this increased complexity comes increased opportunity for diseases to reach epidemic proportions quickly."

For example, more people travel more often over greater distances and in less time now than at any time in the past. One consequence of the increased mobility in the modern age can be seen in the 2003 outbreak of the novel illness SARS, which rapidly spread from Hong Kong to Toronto and elsewhere as infected passengers traveled by air.

To better understand and predict disease emergence, Dr. Morens and his coauthors stress the need for research aimed at broadly understanding infectious diseases as well as specifically understanding how disease-causing microorganisms make the jump from animals to humans.

In a narrow sense, epidemics are caused by particular microorganisms, and the study of infectious disease has historically been microbe-focused. For example, the Black Death (bubonic plague), which killed some 34 million Europeans in the middle of the 14th century, was caused by the bacterium *Yersinia pestis*. In a broader sense, however, epidemics are caused by complex and not fully predictable interactions between the disease-causing microbe, the human host and multiple environmental factors, the authors note. The Black Death, for instance, was borne westward along newly established land and sea trade routes from its probable origin, China, into multiple European countries. Similarly, patterns of human movement along trade routes, specifically truck routes throughout Africa, played a role in the spread of HIV throughout that continent. Greater consideration must be given, say the

NIAID authors, to broader, interlinked factors such as climate, urbanization, increased international travel and the rise of drug-resistant microbes, and the ways in which these factors combine to spark new epidemics.

Aside from commerce and travel, the NIAID authors point to several other factors that underlie many notable emerging diseases: poverty, the breakdown of public hygiene practices, and susceptibility of human populations to microbes against which they have no pre-existing immunity. This last factor played a key role in the smallpox epidemic that afflicted the Aztecs of 16th century Mexico. Smallpox had ravaged European communities for centuries, but until the Spanish arrived on the Yucatan coast in 1519, the disease was unknown in the New World. Historians believe that some 3.5 million people in central Mexico died in the first year of the epidemic.

Epidemics also can spur advances in public health, note the authors. They point to the yellow fever epidemics of 1793-98, which began in the then-U.S. capital, Philadelphia. Though the entire federal government and most Philadelphians fled, those who remained formed an emergency government and mobilized such marginalized groups as African-Americans and immigrants to fight the outbreak. In 1798, Congress established the Marine Hospital System—forerunner of the modern U.S. Public Health Service—to provide, at public expense, medical care for sick and injured merchant seamen. Historians generally agree that a prime impetus for creating the Marine Hospital System was the yellow fever epidemics.

Modern epidemiology began in reaction to another epidemic, says Dr. Morens. In the early 1830s, as cholera made its way along waterways from Asia towards Europe, French officials attempted to prepare their country in advance of an outbreak. Teams of scientists were sent to Poland and Russia to observe the outbreaks there. Throughout France,

coastal health agencies and new quarantine stations were established; in Paris, a network of health inspection offices was created to coordinate inspection of wells, cesspools and latrines of both public and private buildings. Despite these efforts, cholera arrived in Paris on March 29, 1832, with explosive effect—within two weeks, there were 1,000 cases, 85 percent of them fatal. Daily newspapers published lists of cases allowing armchair epidemiologists to see trends in illness and deaths. "For the first time in history," write the NIAID authors, "a large-scale emerging epidemic was scientifically investigated in 'real time' using census data in a prospective population-based approach that featured analyses of morbidity and mortality stratified by age-group, sex, occupation, socioeconomic status and location."

Reference: DM Morens, GK Folkers and AS Fauci. Emerging infections: A perpetual challenge. *The Lancet Infectious Diseases* DOI: 10.1016/S1473-3099(08)70256-1 (2008).

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