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Bacterial Pneumonia Caused Most Deaths in 1918 Influenza Pandemic

Implications for Future Pandemic Planning

The majority of deaths during the influenza pandemic of 1918-1919 were not caused by the influenza virus acting alone, report researchers from the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health. Instead, most victims succumbed to bacterial pneumonia following influenza virus infection. The pneumonia was caused when bacteria that normally inhabit the nose and throat invaded the lungs along a pathway created when the virus destroyed the cells that line the bronchial tubes and lungs.

A future influenza pandemic may unfold in a similar manner, say the NIAID authors, whose paper in the Oct. 1 issue of *The Journal of Infectious Diseases* is now available online. Therefore, the authors conclude, comprehensive pandemic preparations should include not only efforts to produce new or improved influenza vaccines and antiviral drugs but also provisions to stockpile antibiotics and bacterial vaccines as well.

The work presents complementary lines of evidence from the fields of pathology and history of medicine to support this conclusion. "The weight of evidence we examined from both historical and modern analyses of the 1918 influenza pandemic favors a scenario in which viral damage followed by bacterial pneumonia led to the vast majority of deaths," says co-author NIAID Director Anthony S. Fauci, M.D. "In essence, the virus landed the first blow while bacteria delivered the knockout punch."

NIAID co-author and pathologist Jeffery Taubenberger, M.D., Ph.D., examined lung tissue samples from 58 soldiers who died of influenza at various U. S. military bases in 1918 and 1919. The samples, preserved in paraffin blocks, were re-cut and stained to allow microscopic evaluation. Examination revealed a spectrum of tissue damage "ranging from changes characteristic of the primary viral pneumonia and evidence of tissue repair to evidence of severe, acute, secondary bacterial pneumonia," says Dr. Taubenberger. In most cases, he adds, the predominant disease at the time of death appeared to have been bacterial pneumonia. There also was evidence that the virus destroyed the cells lining the bronchial tubes, including cells with protective hair-like projections, or cilia. This loss made other kinds of cells throughout the entire respiratory tract — including cells deep in the lungs — vulnerable to attack by bacteria that migrated down the newly created pathway from the nose and throat.

In a quest to obtain all scientific publications reporting on the pathology and bacteriology of the 1918-1919 influenza pandemic, Dr. Taubenberger and NIAID co-author David Morens, M.D., searched bibliography sources for papers in any language. They also reviewed scientific and medical journals published in English, French and German, and located all papers reporting on autopsies conducted on influenza victims. From a pool of more than 2,000 publications that appeared between 1919 and 1929, the researchers identified 118 key autopsy series reports. In total, the autopsy series they reviewed represented 8,398 individual autopsies conducted in 15 countries.

The published reports "clearly and consistently implicated secondary bacterial pneumonia caused by common upper respiratory flora in most influenza fatalities," says Dr. Morens. Pathologists of the time, he adds, were nearly unanimous in the conviction that deaths were not caused directly by the then-unidentified influenza virus, but rather resulted from severe secondary pneumonia caused by various bacteria.

Absent the secondary bacterial infections, many patients might have survived, experts at the time believed. Indeed, the availability of antibiotics during the other influenza pandemics of the 20th century, specifically those of 1957 and 1968, was probably a key factor in the lower number of worldwide deaths during those outbreaks, notes Dr. Morens.

The cause and timing of the next influenza pandemic cannot be predicted with certainty, the authors acknowledge, nor can the virulence of the pandemic influenza virus strain. However, it is possible that — as in 1918 — a similar pattern of viral damage followed by bacterial invasion could unfold, say the authors. Preparations for diagnosing, treating and preventing bacterial pneumonia should be among highest priorities in influenza pandemic planning, they write. "We are encouraged by the fact that pandemic planners are already considering and implementing some of these actions," says Dr. Fauci.

Visit <http://www.PandemicFlu.gov> for one-stop access to U.S. Government information on avian and pandemic flu.

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Reference

DM Morens et al. Predominant role of bacterial pneumonia as a cause of death in pandemic influenza: Implications for pandemic influenza preparedness. *The Journal of Infectious Diseases* DOI: 10.1086/591708 (2008).

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