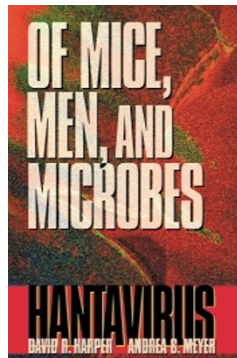


ried by members of a large subfamily of New World rodents. Since the 1993 outbreak, there have been 20–30 confirmed cases of HPS annually in the United States—a relatively minor public health problem compared with the effect of many other infectious diseases. Nevertheless, mortality is high (now about 43%) and the disease is dramatic, as are the life-support measures often required for HPS patients (extra-corporeal membrane oxygenation is not uncommon).

There has been a fascination with hantavirus disease in the media as well as among the American public. The Four Corners outbreak has been the subject of television specials and newspaper and magazine articles, and has been referred to in novels. HPS has become a premier example of an ‘emerging infectious disease’ in the many popular books on the subject. At the CDC, the staff handle numerous daily phone and e-mail queries from the public and the scientific community. In response to this demand for information, the CDC has printed a small mountain of handouts and posters, developed an extensive web page, produced videos in English and Spanish, held national and international audio and video conferences, and conducted monthly telephone conference calls with state and local public health professionals. Apparently virologist David Harper of the University of London was also fascinated by HPS and the story of its emergence. He left London and traveled to the arid, desolate Four Corners area, where he teamed with local journalist Andrea Meyer and devoted a sabbatical to researching and documenting the story of SNV.

The authors use the Four Corners outbreak as a point of departure to relate, in a detailed and comprehensive fashion, the epidemiology and natural history of hantaviruses and hantavirus disease. The intended audience is the layman who is interested in science and medicine. However, because it compiles a great deal of historical and peripheral information about an important event in a way not possible in the scientific literature, the book may appeal to interested public health professionals and ecologists. The 247 pages of text, in easy-to-read large type, are supplemented by



two sections of color plates containing 38 figures and photographs (mostly in color). Three appendices provide CDC guidelines for risk reduction, a list of sources for additional information (mostly popular accounts of ‘emerging diseases’ and internet web pages, but also includes one professional review of hantavirus disease and Harper’s test on molecular virology), and a list of the abbreviations used in the text.

The book opens with a detailed and accurate, if somewhat dramatized, account of the Four Corners outbreak. The outbreak and investigation involved real-life elements of mystery, fear, suspicion, rumors of government plots, ethnic stereotyping, ruined tourism, lots of politics, and some top-notch science. Relying on interviews, newspaper accounts and scientific literature, this clear and culturally sensitive account reads almost like a novel and is the most interesting section of the book. Subsequently, the style and direction change frequently. Several chapters, in review-article style, describe hemorrhagic fever with renal syndrome and the history and the spectrum of hantaviruses in Asia and Europe. Then the authors slip into a loosely structured textbook style. Although these chapters are interesting and clearly written, I tended to forget the subject of the book as I toured through the origin of life, biology and evolution of viruses, biological warfare, genetic engineering, antigenic drift, recombination, and xenotransplantation. The subject returns to hantaviruses in the closing chapters, introducing the spectrum of hantaviruses recognized in the Americas, and the clinical and laboratory aspects of the disease and its diagnosis, as well as prospects for prevention and control. Four paragraphs in the penultimate chapter, clearly directed at clinicians, seem out of place.

The book has many strong points. In clear, generally non-technical language, it provides not only a detailed account of the Four Corners outbreak, but also a worldwide perspective of hantaviruses and hantavirus diseases. The information presented is carefully researched and scientifically sound. I applaud the authors for carefully researching details and debunking some popular myths. One example is the widespread belief

that scientists demonstrated large (10-fold according to the popular press) increases in deer mouse populations in the Four Corners area prior to the outbreak—in fact, deer mouse populations in the outbreak area were not monitored.

On the negative side, I was uncomfortable with the changing style and the wandering format, which jumped from subject to subject both within and among chapters. Often the same subject was treated in several different places, leading to redundancies. The complete lack of references severely limits the book’s utility for scholarly applications. I cringed at the frequent use of “anthropomorphism”—including application of human motives to viruses, genes and the immune system. I think we do the public a disservice by using such devices to explain science.

Nonetheless, for the scientifically inclined layman, especially the emerging disease buff, this book is well worth reading. It provides a scientifically accurate introduction to the world of emerging viruses and ties together many not-so-simple concepts in plain English.

## Flu

### THE STORY OF THE GREAT INFLUENZA PANDEMIC OF 1918 AND THE SEARCH FOR THE VIRUS THAT CAUSED IT

By Gina Kolata

Farrar, Straus and Giroux, 256 pages, \$25.00  
ISBN 0374157065, 1999

REVIEWED BY NICHOLAS P. RESTIFO

Principle Investigator  
National Cancer Institute, Bldg. 10, Room 2B/42  
National Institutes of Health  
Bethesda, Maryland 20892-1502, USA

There is a cemetery in a small railroad town in northern Ohio where I grew up that tells a sliver of the story of the great ‘Spanish’ influenza pandemic of 1918. One section of the cemetery is full of simple, rough, limestone markers that tilt willy-nilly in the perpetually damp sod of the graveyard. These unembellished memorials mark the graves of unfortunate souls who died one week during the fall of 1918 from the flu. In other towns all over the country there are similar hastily prepared grave sites. At least 10,000 people died in the city of Philadelphia during one three-week pe-

riod during the month of October, overwhelming doctors, hospitals and undertakers.

The pandemic occurred just at the moment in history when the nightmare of World War I was finally ending, and it killed far more than the Great War itself. The death toll from the flu of 1918 was more than a half-million people in the United States, and more than 20 million people worldwide. This modern day plague is the topic of a new book by Gina Kolata, a science writer for the *New York Times*. Although the subject of the 1918 flu pandemic is certainly compelling stuff, there is little in this new book that has not already been said better by others, most notably by Alfred Crosby in a book entitled *America's Forgotten Pandemic*, originally written in the 1970s but since updated. In that book the student of flu can find the primary data underlying many of Kolata's generalizations.

It is unfortunate that much of the book reads like a newspaper article written on a tight deadline. The reader often feels that only the most lurid anecdotes are mentioned, apparently precluding any in-depth description of our burgeoning understanding of the structure and function of the virus itself. The virus is, after all, the 'mass murderer' in this detective story. There are no thoughts here about how viruses propagate or kill or evolve. There is not a word about the molecular virology underlying the phenomena of antigenic drift (a change in surface protein, usually resulting from a base pair mutation) or antigenic shift (which for flu is usually the acquisition

of a whole new segment of RNA). Any scientist or physician interested in the influenza virus itself, and all its fascinating efficiencies and complexities, will be sorely disappointed with this book.

The author does, however, vividly illustrate how the great devastation wrought by the flu pandemic continues to affect more recent history. Two chapters of ten in this new book concern the swine flu fiasco of 1976. A series of unfortunate events was started with the death of a single soldier at Fort Dix, New Jersey. The causative agent in the soldier's case was determined to be an influenza virus of a type that normally infects pigs. Because of work in the decades after the 1918 flu pandemic that suggested a link between flu in humans and flu in pigs, scientists feared that the soldier's case was only the first in a deadly pandemic that could engulf the nation and the world. Using scant evidence, and what seems in retrospect to be numerology, a small group of prominent vaccinologists convinced President Gerald Ford to immunize the entire nation. The swine flu epidemic never occurred, but 43 million Americans were vaccinated, leading to scores of lawsuits of patients who claim to have been injured after being immunized.

The most original part of the book is where the author describes recent efforts Jeffery Taubenberger and his team at the Armed Forces Institute of Pathology to sequence the 1918 influenza virus using polymerase chain reaction (PCR)-based techniques. These careful workers have successfully isolated fragments of RNA from the 1918 influenza virus. The ac-

quisition of the tissues for these experiments, either from paraffin-embedded specimens recovered from a government warehouse or from snippets of tissue obtained from bodies buried in the permafrost, is the stuff of high drama.

Even after the latest round of PCR analysis of the flu genome, it remains a mystery why the flu virus of 1918 was so deadly. The most pressing question remains: Can such a deadly virus ever emerge again? On one hand it seems unlikely, given the rapid advances in our medical knowledge. New drugs, such as zanamivir (Relenza), can inhibit the ability of the flu virus to proliferate by blocking the activity of the neuraminidase enzyme. When the Spanish flu pandemic hit, doctors around much of the globe were still using venesection as a treatment.

On the other hand, drug-resistant variants of the flu virus could emerge. Furthermore, the flu virus of 1918 killed quickly—there are many cases of documented mortality in under 48 hours. A large-scale epidemic could overwhelm our modern, sophisticated medical system. Because our overcrowded cities are massively interconnected by commerce and travel, an emerging virus could be spread today at a rate that is orders of magnitude faster than the rate of spread eight decades ago.

So the questions remain: Can such a pandemic happen again? How will we deal with the deadly viruses that will undoubtedly emerge in the future? Greater knowledge about what happened in the 1918 flu pandemic and a deeper understanding of the virus that caused it would be useful. And although Kolata's book provides a lot of heat, it does not shed much light on the questions that really matter.

