

The Spanish Flu And Its Legacy

Science Cases for Classroom Use

College Entrance Examination Board

New York

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The following members of the Advisory Committee gave generously of their time and expertise to help shape the issues and content of this book.

Larry Arbogast. Biology teacher, Orange County High School, Orange, VA.

Madeline Bennett. Biology teacher, Mountain Brook High School, Mountain Brook, AL.

Ann G. Carmichael. Associate Professor, History and Philosophy of Science, Indiana University, Bloomington, IN.

Marie Charron. Science teacher, Haverhill High School, Haverhill, MA.

Barbara Gabriel. Associate Professor of Biology, James Madison University, Harrisburg, VA.

Peter Garik. Research Associate, Physics Department, Boston University, Boston, MA.

Eric G. Jakobsson. Senior Research Scientist, Beckman Institute, University of Illinois, Urbana, IL.

Susan Mooney. Biology teacher, Haverhill High School, Haverhill, MA.

Eric Neumann. Biologist/Education Researcher, Bolt, Beranek & Newman, Cambridge, MA.

Louise A. Paquin. Professor of Biology, Western Maryland College, Westminster, MD.

Lois A. Peterson. Biology teacher, Albany High School, Berkeley, CA.

Robert Seigman. Biology teacher, McDonough School, Ownings Mills, MD.

Phil Talbot. Biology teacher, Skyline High School, Salt Lake City, UT.

This work has also profited from the past and ongoing counsel of the College Board's Academic Advisory Committee for Science, whose members have encouraged the efforts of those involved in the research and writing of this volume.

Peggy O'Neill Skinner. Chair, College Board Academic Advisory Committee for Science. Head, Science Department, The Bush School, Seattle, WA.

Doris Helms. Professor of Biology, Clemson University, Clemson, SC. Past Chair, College Board Academic Advisory Committee for Science.

Mary Alice Legendre Cain. Chair of Earth Science Department, East Jefferson High School, Metairie, LA.

Henry W. Heikkinen. Professor of Chemistry, University of Northern Colorado, Greeley, CO.

John Layman. Professor of Physics, University of Maryland, College Park, MD.

Jerry D. Mullins. Chair of Science Department, Plano Senior High School, Plano, TX.

Louise A. Paquin. Professor of Biology, Western Maryland College, Westminster, MD.

Nuria C. Rodriguez. Professor of Physics, Santa Monica Junior College, Santa Monica, CA.

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Samuel O'Neill Skinner. Computer artist.

Contributors

Carolyn Buxton Bridges, M.D. Medical Epidemiologist, Influenza Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, CDC.

Alfred W. Crosby. Professor of American Studies, University of Texas, Austin, and author of *America's Forgotten Pandemic: The Influenza of 1918*.

Marvin Druger. Professor of Biology and Science Education and Chair of the Department of Science Teaching, Syracuse University.

Diana B. Dutton. Independent scholar and the author of *Worse Than the Disease: Pitfalls of Medical Progress*.

Mary Evilsizer. Graduate student, Department of Biomedical Engineering, Boston University.

Peter Garik. Research Associate, Physics Department, Boston University.

Abby Hansen. Independent consultant, author of many teaching cases and co-author of *Teaching and the Case Study Method*.

Eric Neumann. Biologist and computer scientist at Bolt, Beranek & Newman, Cambridge, MA.

George Ochoa. Writer, Corey & Ochoa.

Louise A. Paquin. Professor of Biology, Western Maryland College, Westminster, MD.

Peter A. Patriarca, M.D. Deputy Director, Division of Viral Products, Center for Biologics Evaluation and Research, Food and Drug Administration. Also co-chair of the federal working group on influenza pandemic preparedness.

Ann H. Reid, M.S. Molecular biologist, Division of Molecular Pathology, Armed Forces Institute of Pathology, Washington, DC.

Robert Seigman. Biology teacher, McDonough School, Owings Mills, MD.

Peggy O'Neill Skinner. Head, Science Department, The Bush School, Seattle, WA.

Daniel Sullivan, M.D., M.P.H. Instructor, Harvard Medical School.

Jeffery K. Taubenberger, M.D., Ph.D. Pathologist, Armed Forces Institute of Pathology and chief of Division of Molecular Pathology, Washington, DC.

Selma Wasserman. Professor in the Faculty of Education at Simon Fraser University, West Vancouver, Canada. Author of *Introduction to Case Method Teaching: A Guide to the Galaxy*.

Michael Williams. Consultant, formerly a researcher, Center for Biologics Evaluation and Research and author of articles on the history of the development of vaccines.

About This Book

The Spanish Flu and Its Legacy encourages you to adopt an interdisciplinary approach to teaching and learning. The events surrounding the appearance of the Spanish Flu in 1918 have influenced science, sociology, economics, history, and literature. It is impossible to confront these events from only one perspective. The human story modifies the scientist's objective view, while science and a sense of inquiry enable others to validate historical and medical information. We hope that a natural curiosity about events, a scientific turn of mind, or a personal connection to people and their stories create not only the desire to know more about the pandemic of 1918 but also to develop a deeper understanding of what it means to inquire and to investigate. This is all the more important today as every week, and even daily, newspapers and scientific journals around the world are reporting remarkable discoveries about both old and emerging diseases.

WHY CASES?

A case study approach to learning creates a positive atmosphere for inquiry. The approach begins with essential questions or a provocative issue embodied in a case. Each case leaves unanswered questions that direct students and teachers to different “pathways” of study. Each pathway is driven by the need to know more. By its nature, a pathway is flexible and circular, rather than linear.

The case study approach accomplishes several objectives. It engages student interest. It gets students involved in solving real-world problems. It develops thinking skills. It teaches concepts. Few other pedagogical methods can accomplish all these objectives with such economy. Although long used in schools of law and business, in the past decade secondary school teachers have also begun using the case study approach successfully in biology, social studies, and the arts.

The cases in *The Spanish Flu* can be used at many grade levels, from middle school to high school, in the Advanced Placement Program®, and in college. The cases have even been used to teach science to nonscientists at the graduate level.

PLANNING AND PATHWAYS

The Spanish Flu is organized into four major sections:

- I. History and the Cases
- II. Teaching Approaches

III. Activities

IV. Resources

Each section supports a flexible approach to course development. The Planning Matrix on page 49 allows you to plot out activities and resources to support a case selection. In this way, you can develop a general plan into which you can fit “pathways” that achieve your course objectives.

The Spanish Flu comes with a three-ring binder to allow you to put the cases, activities, and resources into the order that works best for your plan. This also enables you to photocopy any materials for handouts or reference reading. (Since most sections of *The Spanish Flu* begin on a new page, you will find that photocopying is easy to organize.) The format is designed to encourage you to add your own resources (for example, pages from Web sites, articles from newspapers or magazines, or student essays).

Select and assign a case. Determine what questions and issues will most likely emerge from reading it. For example, after reading Case 1, students will ask many basic questions, such as

- What is the nature of a virus?
- Why was the viral strain of 1918 so deadly?
- What is the difference between an epidemic and a pandemic?

- What are the chances of the 1918 virus returning?
- How is a virus transmitted from one person to another?

You can use these questions to begin the dialogue that opens the subject to any pathway that you have devised.

I. HISTORY AND THE CASES

After a brief one-page introduction, Section I presents “The Enigma of the 1918 Influenza Pandemic” by the eminent historian Alfred W. Crosby. This offers a comprehensive overview of the historical and scientific context of the epidemic. You can read it for background to the cases. You can also photocopy it for distribution to your class. It sets the stage and introduces the facts.

The Cases

Three cases follow the history. Each case in *The Spanish Flu* relates to the influenza catastrophe of 1918. Case 1, “An Incident in Boston,” is similar to a documentary and refers to real persons. Case 2, “Around the World,” develops from historical facts, and Case 3, “The Coming Pandemic,” is fiction.

Getting Acquainted With the Cases

Following the cases and starting on page 29, we provide a simple self-test for each case. These are useful for students who like quizzes or find them an effective way to retain essential facts. Each quiz is presented on one page and the answers appear at the bottom of the page. You can photocopy a quiz for distribution to a class or to individual students.

II. TEACHING APPROACHES

Section II introduces a broad approach to using the material in *The Spanish Flu* and offers a well-focused, real-life example of how to open a pathway with an imaginative tactic.

Teaching With Cases

In this article, Selma Wasserman reviews and explains the basic pedagogy of working with cases. She discusses topics such as what makes a good case, what types of questions work and how to compose them, working with groups, and the dynamics of debriefing.

Using Cases in the Classroom

In this article, Robert Seigman lays out many of the practical aspects of using cases in a classroom setting. He covers topics such as how to link case work to other course material, getting ready to teach a case, using questions to guide a discussion, pathways, and testing.

Pathways

Pathways are intended to guide you on two levels: the general direction of your course and the specific direction of the class work. This discussion of the role of pathways and how to work with them provides sample pathways that start with assigning a case.

Using Activities, Resources, and the Matrix

Here is a brief overview of the contents and role of the Activities and Resources sections and an introduction to the Planning Matrix that appears on page 49.

Background Readings and Internet Sources

These pages offer a selection of books, articles, and Web sites for further investigations in case teaching, scientific research, and the Spanish flu pandemic.

III. ACTIVITIES

This section begins with an overview of the learning objectives for each activity. The 14 activities in *The Spanish Flu* are intended for class use, but they are also models for designing your own activities (and Activity 14 suggests some specific ideas).

Each activity opens with a list that keys the activity to a case and to resources. It then gives learning objectives for the activity. For example, Activity 1 (p. 57) is keyed to Case 1 and to Resources 1, 7-9. Then three learning objectives follow.

Most activities also provide a suggested pathway for developing the activity with your class. The pathways incorporate some of the practical suggestions outlined and discussed in the teaching approaches presented in Section II. The activities vary in their focus. For example, Activity 1 deals with the scientific method and problem solving. Activities 4 and 5 involve laboratory procedures. Activity 6 is more speculative and asks students to examine the impact of the pandemic on other sectors of society while focusing on progress in disease research. Activity 7 involves evaluation of public health policies during the pandemic. Activity 8 examines insurance reports to demonstrate the social and economic consequences of the pandemic. Activity 9 looks at medical ethics, and Activity 12 explores the literary record.

The activities provide core support for the issues raised in the cases. Working with the activities, the teacher and the student meet in a curriculum context that encourages student initiative and intellectual maturity.

Handouts

Some of the activities include handouts for students. These provide information or directions for working with the activity. For example, in Activity 2, "Reviewing the Evidence," students critically examine hypotheses offered by contemporary scientists for the cause of the 1918 pandemic. Handouts, such as "Pfeiffer's

Bacillus" (p. 60), give students a summary of the pertinent research followed by resources for more information. The directions and comments in the handouts are addressed to the students. The student handouts are indicated by a black box ■ to the left of the activity name.

IV. RESOURCES

This section presents resources that range from scientific to historical, literary, and sociological subjects. The section begins with a short summary of each of the 10 resources. Resource 1 presents a collection of firsthand reports entitled "Notes from the Pandemic." Resource 2 offers a clear and thorough description of the current state of our knowledge about the virus. Resource 4 gives a complete description of the viral mechanism and the immune system.

Section IV also includes an in-depth recounting of the confusing swine flu episode of 1976 as well as revealing interviews with personnel from the Food and Drug Administration and testimony from a 1919 hearing before the House Committee on Appropriations for flu victims. (For a complete review of the contents of the Resource section, see page 115.)

The resources are rich in information, insight, and ideas. You can use them to support class work or to round out your own background on the 1918 pandemic and its implications.

BIBLIOGRAPHY

The Bibliography lists the books and journals referenced in the text as well as the basic research and resource books and articles that were used to prepare the text.

I. HISTORY AND THE CASES

This section begins with a historical overview, “The Enigma of the 1918 Influenza Pandemic.” It provides a background for the cases. (If helpful, you can photocopy this overview for distribution to your students.) The three cases in *The Spanish Flu and Its Legacy* are not simply effective vehicles for teaching biology. They lend themselves to larger issues and important conclusions not only about the nature of scientific knowledge but also about the role of science in history and daily life.

CASE 1. AN INCIDENT IN BOSTON

The first case describes the onset in 1918 of one of the first outbreaks of Spanish influenza. The case is written from the point of view of Lieutenant Junior-Grade J. J. Keegan, a young naval physician and scientist. Keegan really existed, but for dramatic purposes, the case fictionalizes his thoughts and feelings. His colleagues, Milton Rosenau and Ernest Goodpasture, were also real persons, but their conference with Keegan featured in the case has been invented.

CASE 2. AROUND THE WORLD

The second case is entirely factual. It recounts the devastation caused by the Spanish influenza and describes the inability of scientists to halt it. Of all the pandemics that have swept the earth, none has killed so many in so short a time as Spanish influenza in 1918 and 1919: not bubonic plague, not smallpox, not cholera, not typhoid fever. Before the war in Europe ended in November 1918, Spanish influenza proved more lethal than artillery shells to soldiers on both sides of the Front. In India, it was said that the death count in October 1918 was “without parallel in the history of disease.”¹ In Western Samoa, 22 percent of the population died.

CASE 3. THE COMING PANDEMIC

The third case is fiction, but it demonstrates a real and chilling possibility. Set in the present day, the case offers evidence for the appearance of a new and highly virulent strain of influenza. Faced with a possible repeat of the 1918 Spanish influenza pandemic, a team of experts tries to decide what course of action to recommend to the president of the United States. The team debates many issues (scientific, social, political, and ethical), but the case ends with the recommendation still unmade. The implied question for the student is *What would you recommend?* The case also draws on the memory of the 1976 episode known as the “swine flu fiasco.” In that episode, the fear that Spanish influenza was about to return led to an abortive and widely criticized mass vaccination program, even though no pandemic materialized.

While Case 1 and Case 2 are set in a time when little was known about influenza, Case 3 is set in the present. Our knowledge is now extensive, but still incomplete. For that reason, Case 3 incorporates more technical detail about the intricacies of the influenza virus, molecular biology, and vaccine production. This case is an effective tool for introducing or reviewing some of the most current knowledge about the flu virus and other microbes, as well as immunology, genetics (particularly RNA), and, to some extent, the maintenance of dynamic equilibrium. Case 3 also focuses, even more than Cases 1 and 2, on the social and ethical issues involved in public health decision making.

Note

1. Great Britain, Ministry of Health, Reports on Public Health and Medical Subjects, No. 4: *Report on the Pandemic of Influenza, 1918-19* (London: His Majesty’s Stationery Office, 1920), 383, 386.

The Enigma of the 1918 Influenza Pandemic

By Alfred W. Crosby

The disease we call *influenza* or *flu* or *grippe* is not one the general public particularly fears. That is odd because the only event in history that compares with the world wars of this century as a killer in terms of absolute numbers and exceeds them in the swiftness and universality of its deadly effect is the influenza pandemic of 1918 and 1919. It killed millions of people, and it did so in less than a year. The "Spanish flu," as it was nicknamed in 1918, killed a large number of people more rapidly than the deadliest war, not because it was as lethal to the individual sufferer as a bullet or bomb, but because it spread rapidly and affected millions of people. By a conservative estimate, a fifth of the human species suffered the fever and aches of influenza in 1918 and 1919, and serological evidence indicates that the great majority of those who did not suffer the discomforts of flu had subclinical forms of the disease.

WHAT WAS KNOWN AND NOT KNOWN

Why was the Spanish flu pandemic so catastrophic? Explanations abound. Perhaps World War I starved and debilitated so many that they were especially susceptible to infection. That seems plausible if you are referring to Europeans, but why was the flu in well-fed America and in faraway New Zealand as deadly as it was on the continent where the war was being fought?

Maybe the flu mortality was so high because the political attitudes of the time, as well as the state of communication technologies available to governments, hampered efficient mobilization, such as the use of quarantine, the stockpiling of medical supplies, and the conscription of doctors and nurses. That might or might not be true in parts of the world, but the governments and citizens of the belligerents, including the United States, already had mobilized against their human enemies. Unfortunately, there were no magic bullets to shoot at the flu virus.

Perhaps medical science was simply unequal to the challenge of the 1918 flu. There were neither cures nor vaccines, although varieties of both were conjured up during the pandemic. The modern germ theory of infection that Louis Pasteur and Robert Koch had demonstrated again and again was not much more than a half-century old and only widely accepted by the American medical profession for half

that amount of time. Anyway, germ theory was not immediately useful because the most advanced technological aid of the bacteriologist was still the optical microscope. No one would see the incredibly tiny flu virus until the invention of the electron microscope years later.

A greater disadvantage was the fact that the experts thought they already knew what caused influenza. In the pandemic of the disease at the beginning of the 1800s, Richard Friedrich Johann Pfeiffer, a colleague of the great Robert Koch and head of Berlin's Institute for Infectious Diseases, had found a bacillus, known ever since as *Pfeiffer's bacillus*, in the sputum of influenza sufferers. He identified this as the cause of the disease. It was not. It proved to be, so to speak, a germ without a disease, and its misidentification as the cause of influenza hampered research for decades to come.

In 1918, however, scientists began by not knowing that they did not know the identity of the causative organism of influenza. When they lost faith in Pfeiffer's discovery, they began to look for what amounted to a needle in a haystack. They did not know yet that the needle was too small for them to see. No wonder scientists fumbled in 1918.

But perhaps we have too much confidence in the power of knowledge in and of itself. If scientists had known about the flu virus in 1918, had they even been able to photograph it

through electron microscopes, would that actually have empowered them to halt the pandemic?

There was no cure for the disease then, or now. Vaccines? Another generation would pass before even partially effective vaccines against influenza were developed. Even if all the knowledge and technology to produce flu vaccine had been at hand in 1918, would it have been possible to produce it in sufficient quantity and to distribute it across oceans and continents in time to stop the swiftly spreading breath-borne pandemic? Even today, when similar questions are asked each time a new strain of the virus appears, the answer falls short of being a confident "yes."

The influenza of the 1900s is still something of an enigma, but the influenza that was sweeping around the world at the time of the Armistice ending World War I remains profoundly so. It killed tens of millions, usually by opening the way for secondary bacterial infections, such as those of Pfeiffer's bacillus. Today, we presume that such infections can be controlled with antibiotics. But a significant fraction of those who died in the pandemic of 1918-19 did not live long enough after the onset of illness to contract a secondary infection. They turned slate blue in a couple of days and died of viral pneumonia. Even more disturbing was the fact that the Spanish flu was especially dangerous to young adults for reasons that have been plausibly, but never definitely, explained.

Although influenza did not significantly affect mortality in the United States until September 1918, its impact was so tremendous during the fall and early winter of that year that it skewed the distribution of age-specific deaths into unprecedented proportions. Ever since the U.S. Office of Vital Statistics started publishing statistics on the age incidence of influenza deaths, the distribution has been high at the extremes of infancy and old age and very low in between. In 1918, however, age-specific death rates were high for the very young, higher yet for 20-to-40-year-olds, and lower

than normal for the elderly. The common explanation is that this strain of influenza was so new that it startled its victims' immune systems into overreaction, and the more vigorous the victim, the greater and deadlier the overreaction. The defensive swelling of membranes and increased secretion of fluids of the respiratory system went to extremes in young adults, filling their lungs with liquid until they drowned. Overstimulation of the immune system is a plausible theory, but we could subject it to rigorous testing only if something like the 1918 virus returned.

This distinctive influenza epidemic swept over the world in three major waves during 1918 and 1919. We cannot be sure where and when the initial wave in the spring of 1918 started, but the earliest scientific and statistical evidence points to the United States in March 1918. It attracted very little attention because pneumonic complications were rare and deaths even rarer. Initially, the flu seemed no more than just another respiratory disease of the kind that so often circulates at that time of year. Only later did the statisticians notice that an unusually large proportion of the relatively few victims of the spring of 1918 had been young adults.

THE FIRST WAVE

The first wave that spread across North America in March and April temporarily disrupted the operation of some military camps and a few factories and then disappeared. However, as it waned in North America, it rose to greater heights in the Old World than had been experienced at any time since the previous influenza pandemics of 1889 and 1890.

According to the record (by no means as complete in 1918 as today), the disease in Europe first reached epidemic proportions in April in France. It swept across Europe in the spring and summer, attacking troops indiscriminately on both sides and interfering with military operations. (General Erich von Ludendorff blamed the flu, among other factors, for the

halting of Germany's last victory drive in July 1918.) The number of Europeans not at war that were laid low by the flu that summer was impressive: 53,000 in July alone in tiny Switzerland and so many in Spain that the rest of the world began to call the malady "Spanish" flu.

The new flu showed up in North Africa in May 1918, in Bombay and Calcutta in June, and by the end of July half of Chungking was sick with it. By then, it had already reached New Zealand, the Philippines, and Hawaii. Even in the age before air travel, influenza had circled the world in less than five months.

But the pandemic still seemed no more dangerous than similar experiences. Multitudes of people were ill. Offices, factories, armies, navies were often disrupted, but only a few of the stricken were sick for more than a week and very few were dying. Still, the number with flu was so great that even the small percentage who proceeded to develop pneumonia and die was becoming impressive. Some health professionals pointed to the strangely large proportion of young adults among the dead, but, all in all, the pandemic was looked upon only as a hindrance and a distraction, not a disaster.

At the end of summer 1918, the world health picture was encouraging, though a little perplexing. A pandemic due to a new strain of flu had rolled over humanity, but in August it was in decline for lack of fresh populations to infect. The odd feature was that the United States (where the new strain may have originated) was almost without influenza, although the country was in daily contact by steamer with islands and continents where the pandemic was raging more fiercely than it had in America in the spring. Nevertheless, the outlook was rosy.

THE SECOND WAVE

If there was a threat worthy of attention, it was that the war might enhance the propagation and diversification of influenza organisms. Millions of people of the ages most susceptible

to severe influenza infection were jammed together in industrial cities, military camps, and ships, and were shifting about the world in immense numbers. Americans were moving at a rate of 200,000 to 300,000 a month from influenza-free America to a European continent rife with the disease.

In the latter days of August, the influenza virus changed into the most dangerous strain or strains ever recorded. It appeared to do so almost simultaneously (although this would seem impossible) in three major ports of the North Atlantic thousands of miles apart. One was Freetown, Sierra Leone, where local West Africans mixed with British, South African, East African, Australian, and New Zealand soldiers and sailors bound to and from the front in Europe. Another was Brest, France, the chief disembarkation port for Americans and others from all over the world who had come to fight *le Boche*. The third was Boston, Massachusetts, one of America's chief embarkation ports and a crossroads for soldiers, sailors, and citizens of every nation involved directly or indirectly in the allied war effort.

The renewed malady had three appalling characteristics: it often opened the way for dangerous secondary bacterial infections, it was more dangerous for young adults than for any other cohort, and it killed more often than any flu before it.

Beginning at the end of August, the second wave of the newly virulent disease rolled out from these three cities to strike nations, cities, villages, families, and individuals. Three percent of the entire native population of Sierra Leone died in September. The new wave peaked in Boston and Bombay in the first week of October. The mortality in India that month was, according to official reports, "without parallel in the history of disease." In Western Samoa the disease struck an isolated and immunologically almost defenseless people in November and killed 7,500 of a total population of 38,000 in less than two months. Many thousands of soldiers on both sides of the

Western Front were stricken, and the American Expeditionary Force's only full-scale drive of the war, the Meuse-Argonne Offensive, sputtered and stalled as 69,000 medical cases, most of them of flu and its complications, swamped an evacuation and hospital system already overtaxed with 93,000 wounded and gassed.

The German Revolution and the establishment of the German Republic stalled as Prime Minister Prince Max von Baden fought his own case of flu. Seemingly all the important figures of the era had, were having, or were to have a bout with the Spanish flu or at least some sort of respiratory illness. Prince Max, Lloyd George, Clemenceau, Woodrow Wilson and his chief adviser Colonel House were among the sufferers. Wilson came close to dying of influenza in April 1919 at the tag end of the pandemic's third wave, an event that would have twisted the peace conference into an even more appalling snarl than was attained with the American president healthy.

THE STORY OF ONE CITY

Because the full history of the pandemic is too broad to relate here, let us focus on the story of one city, San Francisco. The spring wave of the 1918 flu passed over the city and sickened a few without any unusual interest. The second wave could never have been so benign and retiring, no matter what the circumstances, but it might have been less lethal if forewarned had truly meant forearmed. The startling news of the September morbidity and mortality rates in Boston reached the West Coast several weeks before the full brunt of the pandemic, but the skepticism and confusion of public health officials and political leaders and the ignorance and apathy of the general population stalled preparations to combat the Spanish flu.

As the pandemic rolled westward, San Francisco, typical of nearly all American cities, concentrated on the marches and other public gatherings of the Fourth Liberty Loan Drive. The crowds enhanced the rapid spread of communicable diseases. When the first flu victim

(a traveler from Chicago) appeared in late September, barely a month after the first cases occurred in Boston, Brest, and Freetown, the city of the Golden Gate was just beginning to focus on the threat to its well-being.

Full preparations (dividing the city into districts, each with its own medical personnel, telephones, transportation, and supplies; creating emergency hospitals in schools and churches; recruiting hundreds of drivers and other volunteers) were not completed until November, after the worst days were over. Should San Francisco's leaders be condemned because they moved too slowly? Perhaps, but the situation was unprecedented and a little incomprehensible even to health professionals. Public inertia precluded any preparations involving inconvenience to large numbers of people.

The factors that overruled all others during the pandemic were its velocity and virulence. To illustrate, the San Francisco Hospital, which was rated as the finest in the state, earned the dreadful honor of being the city's isolation ward for pneumonia patients during the pandemic, and it came within a hair of failing. Seventy-eight percent of its nurses fell ill and it is a safe guess, considering their known devotion to duty, that many of the "healthy" nurses should have gone to bed as well.

At the end of October, the San Francisco Hospital had 1,100 cases of pneumonia, not just flu. Patients were packed under its roof, and the superintendent announced that there was not room in the wards or the halls or porches for one more patient. Luckily, the number of new flu and pneumonia patients began to drop precisely at the end of October. During the course of the pandemic, the San Francisco Hospital admitted 3,509 cases of respiratory disease and 26 percent of them died.

In that October the city tried every remedy that had been used on the East Coast to cure the flu or, at least, slow its advance. Literature on how to avoid or survive influenza and its jackal, pneumonia, was widely distributed. All schools and places of public entertainment

were closed. Thousands of citizens were inoculated with totally useless and possibly dangerous anti-flu vaccines imported from the East Coast or whipped up locally.

Like several other cities in the West, San Francisco devoted much of its anti-flu effort to persuading its populace to wear gauze masks. The city Board of Supervisors passed a law making the wearing of masks obligatory in all public places, and on October 22 the Mayor, the Board of Health, the Red Cross, and other organizations announced in the *San Francisco Chronicle*, "WEAR A MASK and Save Your Life! A mask is 99% Proof Against Influenza."

For the next month, the great majority of San Franciscans obeyed, and hundreds who did not paid fines and went to jail. On Armistice Day, a wildly enthusiastic crowd swirled up and down Market Street and spilled over into the rest of the city, the ecstatic celebrants surrealistically swathed in white masks. Happily, the masks seemed to work. So did the vaccines and all the other amulets that San Franciscans were clutching to shield themselves from sickness and death.

In November, for unknown reasons, the flu slackened and the number of cases declined dramatically. On November 21, every siren in the city shrieked the message that the moment for unveiling had come and the masks came off amid general scenes of hilarity and triumph. Not bad—a war won and a deadly disease defeated in the same month. As of that day, the total number of flu cases and deaths in San Francisco was far below what had been predicted on the basis of the experience in eastern cities. Authorities and the public credited the city's success to the mask.

Although not universally true, communities on the East Coast characteristically had one terrific wave of Spanish flu and only ripples thereafter. In contrast, communities in the West often had two major waves.

Barely two weeks after San Franciscans removed their masks from round two, the

number of new flu cases began to ease upward. The chief of the Board of Health expressed the hope that they were mostly misdiagnosed colds, but soon an avalanche of new cases—5,000 in December alone—confirmed the fear that the Spanish flu was back for round three.

THE THIRD WAVE

The third wave, in San Francisco and elsewhere in the world, was less virulent and deadly than the second. Although round three sent hordes more to their sickbeds and a considerable number to their graves before it took its final leave in the spring of 1919, the death rate was about half that of the peak weeks of round two.

The most memorable features of round three in San Francisco were what one normally expects of an anticlimax: apathy and foolish antics. Medical authorities again trotted out their vaccines, but this time the audience showed little interest. The city government again made masks compulsory, but this time against the stiff opposition of Christian Scientists, civil libertarians, and merchants who were worried about what masks were doing to Christmas shopping. People were simply fed up with masks, flu, and everything else. Some disgruntled soul sent the head of the Board of Health a bomb. It didn't go off.

The most effective opponents to the masks were experts from various public health departments. They pointed out that there seemed to be no consistent difference in morbidity and mortality of communities that adopted the mask and those that did not. The San Francisco politicians noted, as one supervisor put it, that 99.5 percent of the city's citizens opposed the compulsory mask law. On February 1, 1919, the masks came off officially. They had come off in fact some days before.

San Francisco, a city of 550,000, had made widespread use of all known preventives and remedies for influenza and pneumonia. It had enforced ordinances for the control of the pan-

demic that were as stringent as any implemented in any of the larger cities of the United States. Still, thousands of her citizens had fallen ill and 3,500 had died. San Francisco's record was not very different from that of the city of Boston, the first city in America to be struck by the fall wave.

In San Francisco, as elsewhere, nearly two-thirds of those who died of flu and pneumonia were between the ages of 20 and 40.

By mid-spring in 1919, the third wave was over everywhere except in the remotest reaches of such places as Alaska and Melanesia. The virus of Spanish flu declined in virulence in the 1920s and ceased to circulate among human beings sometime around the end of the decade. Serological evidence indicates that it may have been holed up ever since in the pigs of the Midwest and other areas of the world with a heavy swine population.

Three-quarters of a century ago, Spanish flu put a fifth or more of humanity to bed and killed 20 to 30 million people, or more. (We know little of its impact in the heavily populated interior of China, but we may be sure the disease killed many there.)

Despite all these appalling statistics accepted as true by medical professionals everywhere, one of the chronic problems that the public health community faces is the general lack of fear or even respect for influenza. A rapidly diminishing minority of humanity actually remembers 1918 and rarely mentions it to younger generations. History books contain little or nothing about the World War I pandemic. Most college-educated people know more about the fourteenth-century's Black Death than the twentieth-century's Spanish flu.

Why? One can only speculate. The World War and the Armistice were more fascinating than the flu, and the pandemic did not have much, if any, effect on who won the war. The virus played no favorites among the belligerents, though we might note that the starving Germans often blamed the naval blockade for

their flu deaths, which helped to poison international relations after the war. The Bolshevik Revolution was making Americans hypersensitive to ideological matters, and influenza had no relation to ideology whatsoever. The flu virus infected all groups and classes, thus damping that stimulus to memory, the sense of injustice encouraged by, for instance, the tuberculosis germ, with its preference for the poorly fed and poorly housed. There are no obvious sequelae to influenza. Encephalitis lethargica may follow upon its heels, but tardily, months (even years) later. Unlike polio, it leaves behind no permanently injured victims, such as Franklin Delano Roosevelt, to remind the healthy of what could have or could yet happen to them. Unlike smallpox, it leaves no one permanently scarred, like George Washington, to remind the lucky of what they had escaped by mere chance and might not escape the next time.

Above all, it is influenza's insidiously low profile as a killer that has enabled it to kill so many and not be adequately feared. If I may quote myself:

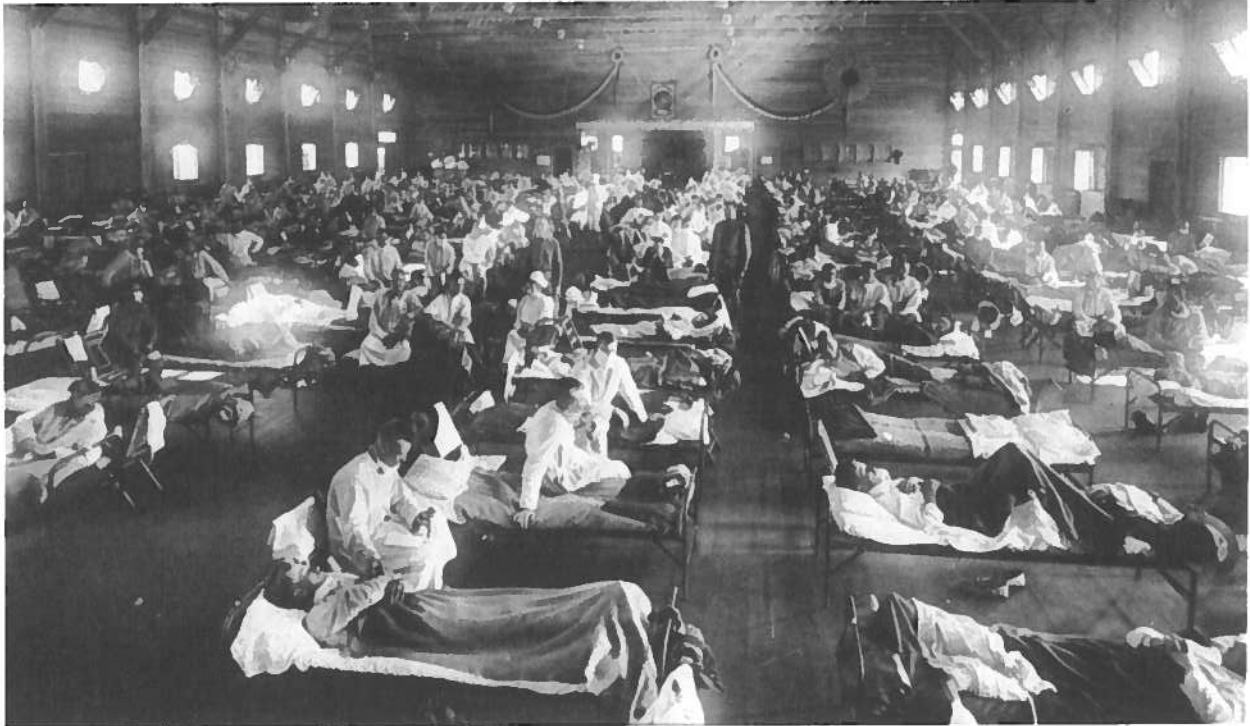
If yellow fever afflicts 10,000 people in New Orleans, 5,000 of whom die, panic sweeps the continent, and people in Labrador stare into mirrors and stick out their tongues, looking for telltale yellow traces. If influenza afflicts ten million people across this land, 50,000 of whom die, few outside the health professions take much notice. On the whole we humans are more frightened of diseases with high mortality rates, which we are not apt to get, than diseases with low but quite real mortality rates, which we are almost certain to get eventually.¹

The American comic poet, Ogden Nash, was a typical American of the twentieth century in his attitude toward influenza. He was 16 years old in 1918 and an inhabitant of Providence, Rhode Island, a city where thousands fell sick in the great pandemic and more than 1,500 died. His published work contains but one piece devoted even indirectly to influenza, a small chuckler of

a poem entitled “Song for a Temperature of a Hundred and One.” It compares flu favorably to

distemper, pip, hookworm, and hoof-and-mouth disease, and ends ecstatically:

**So let man meet his Maker, a smile on his lip,
Singing hey, double hey, for the goodly la grippe.²**



Emergency hospital during the Spanish flu epidemic of 1918-19, Camp Funston, Kansas. Patients' beds are reversed alternately so that the breath of one patient will not be directed toward the face of another.

Notes

1. Alfred W. Crosby, Preface to *America's Forgotten Pandemic: The Influenza of 1918* (New York: Cambridge University Press, 1989), xii.
2. Ogden Nash, “Song for a Temperature of a Hundred and One,” from *Bed Riddance: A Posy for the Indisposed* (Boston: Little, Brown, 1971), 56.



U.S. Army General Hospital, No. 4, Fort Porter, N.Y., November 18, 1918. Army medical personnel with patient.

Case 1. An Incident in Boston

By George Ochoa

Navy physician J. J. Keegan was expecting a slow August. The wounded from the European battlefields of the Great War would not come here, to the tranquil white wards of Chelsea Naval Hospital overlooking the waters of Boston Bay. And the thousands of inductees passing through Massachusetts on their way to fight the Germans were healthy men in the prime of life, unlikely to get anything more serious in this summer heat than sunburns. For Keegan, a budding researcher with an interest in bacterial diseases, the outlook could not have been much worse.

But in the last days of August 1918, the young lieutenant junior-grade began to hear rumors of an unusual epidemic just across the bay at Commonwealth Pier. An illness something like influenza was sweeping through the large, noisy sailors' barracks called the *Receiving Ship*. This alone was unusual—every doctor in New England knew that August was the least likely time of year for flu epidemics. But what was really mysterious was the severity of the symptoms, which were not at all like the flu most physicians knew.

Soon enough, 50 stretchers carrying very sick men crossed into the wards of Chelsea Naval Hospital from the Receiving Ship, where the medical facilities had been overwhelmed by the new illness. Keegan now had a chance to see what all the fuss was about. From the moment he saw the symptoms, he knew he would never forget them. What these men had was not just flu—that nuisance ailment that made you sniffle, ache, run a low fever, and stay in bed a few days. These men had persistent fevers up to 105.7°F. From their blue faces, sometimes marred with purple blisters, Keegan knew that their hoarse, hacking breath was barely supplying enough oxygen to keep them alive. Some vomited all over the bedsheets, stained the sheets with blood running from their noses, or coughed up bloody pus. This

was no flu. It was more like pneumonic plague or something no one had ever seen.

A physician's job, Keegan had been taught, was first of all to diagnose—to use the symptoms to give the patient's torment a name, a name that allowed the physician to predict what could be expected. In this case, however, the disease's name was uncertain and he had no idea what to expect. If this was influenza, one thing could be said: it rarely killed adults in the 20 to 45 age group. Children or the elderly might succumb to it, but not strapping young sailors like these. Why then did he feel that the sick men from Commonwealth Pier were hanging by a thread between life and death and that some of them would end on the wrong side?



Whatever it was, it spread fast. The medical officers at the Receiving Ship told Keegan that the epidemic had escalated from two or three cases on August 27 to eight new cases the next day and to 58 the day after that. The fourth day, 81, the fifth day, 106! The peak was reached on day seven with 119 new cases. After that the number of new patients per day began to fall. If this was flu, it was an astonishingly contagious one—hitting its epidemic peak within only one week.

Some of the other navy doctors were talking about keeping it contained, but Keegan knew they would not. Within days, two physicians at Chelsea were as sick as their patients. With no magic shield to protect him, Keegan himself might be next.

If, from the beginning, they could have chained up the Receiving Ship's doors and let no one in or out until everyone was well or had died—maybe then they could have contained it. But there was a war, and no one had ordered a quarantine (a period of mandatory isolation) on the Receiving Ship. Unless they were bedridden, those sailors had to keep moving.

They had to crew the huge transports that sailed every day across the stormy Atlantic, ferrying thousands of fresh conscripts to the heavy guns and trenches of Belgium and France. All across America, army camps were crammed with recruits, who rode day and night on the nation's railroads to the steamships that would take them to fight the hated Kaiser overseas. Often they were greeted at train stops by patriotic civilians, who cheered, offered candy, and showed their support in rallies, parades, and drives to buy liberty bonds to finance the war. If one sick man left the Receiving Ship, even a man who did not know that he was sick, he would carry the disease into the great global web of transportation and war and commerce and contact. From there, what could stop it?

On September 3, the day after the worst had passed at Commonwealth Pier, Keegan heard that the first unlucky civilian had been admitted to Boston City Hospital with the new influenza. The day after that, there were a few more cases, then many more. Within two weeks after the first case on Commonwealth Pier, thousands of people in Boston were sick—and thousands more all over the area were in danger—navy men, army men, mothers, fathers, children. It was all horribly predictable.

The thing that had *not* been predictable was also now clear: the fate of the young men in the Chelsea wards. For most, the worst of the symptoms—the tortured breathing, the aching body, the feverish delirium that made them scream and thrash in the night—subsided in a few days. They were left feeble but alive. They seemed likely to recover gradually but fully over the next few weeks. But in their weakened conditions, some patients developed complications that extended their period of danger. In what were called *secondary* infections, the microscopic organisms called *bacteria* invaded their ears or their bronchial tubes, the air passages leading into the lungs. In some cases, bacteria infected the lungs themselves and caused pneumonia. By September 11, pneumonia had already killed 35 patients.

It was astonishing, unbelievable. These were boys barely out of their teens! Just two weeks earlier, they had been at the peak of physical condition in a safe place at the healthiest time of the year. Ordinary influenza could sometimes lead to secondary infections, but not in these proportions, not with this age group. Even more disturbing was the fact that some victims died long before they had time to develop secondary infections. Their throats felt sore, a fever began, and within a day or two they were dead. It seemed as if influenza itself had killed them.

What had happened inside the bodies of this last group of men? This was answered in the Chelsea Naval Hospital morgue by Keegan's colleague, a gentle-faced, 31-year-old southerner named Ernest W. Goodpasture. Keegan was just a little jealous of Goodpasture, who was a lieutenant rather than a lieutenant junior-grade and an up-and-coming instructor at Harvard Medical School. Yet this rising star, normally unflappable when cutting up cadavers, was shaken by what he saw inside the bodies of patients who had been swiftly killed by the influenza. Their lungs showed little of the consolidation—the coarsely solidified tissue—typically left behind by pneumonia. Instead, every passage in the lungs was soaked with a thin, bloody, foamy fluid that oozed out under Goodpasture's scalpel. What the fluid contained, what caused it to drown the lungs, was as yet a mystery.

In the absence of knowledge about what causes a disease, a disease can only be defined by its symptoms—by what it tends to do to a body over time. Keegan could now predict what this disease might do, and in that sense he could define it. By now, he could also name it, though the name meant very little. All over the area, people were calling it *Spanish influenza*.

The name arose because in Spain, in May and June, there had been a flu epidemic that infected about 8 million people. Because Spain was a neutral country without wartime censor-

ship, no one tried to cover up that figure. What was not widely realized was that this Spanish epidemic had been part of a worldwide *pandemic*, an epidemic that strikes in many locations. The pandemic may have started first in the United States, where it had coursed across the country back in March and April. It then traveled to Britain, France, Germany, India, China, Hawaii—everywhere ships went, especially ships carrying troops. As of July, it was not yet over. In early August, the U.S. Navy Bureau of Medicine and Surgery released a bulletin warning its doctors in case this Spanish influenza appeared here—as if it had not already appeared here once in the spring.

Keegan thought that he knew all about this Spanish influenza. He had seen cases of it in March and April. It was, in almost every respect, just your basic flu, unpleasant but not fearful—not something with a high risk of death. How could this new influenza be the same thing as the Spanish one? If it were the same, how had it changed so quickly?

One thing linked the two waves of the disease—a little statistical detail that Keegan did not learn about until much later, when there was time to sift through all the data about morbidity and mortality. The mild flu did not kill many people, but when it did, it had a tendency to kill people between 20 and 45 years of age. In this it was unlike every other variety of flu recorded by history—but exactly like its severe cousin.

By early September, Keegan the physician was feeling the powerlessness of his profession. He had a name—Spanish influenza. He knew what to expect—the patient might recover in these ways or die in those ways. He could order the nurses to look after the patients, and they would do a good job, keeping the patient warm and nourished and making sure the pus and blood were cleaned away. He could prescribe medicines, but he knew most of these were variations on chicken soup: they might

not help, but they probably wouldn't hurt. The sad truth was that there was no proved cure or vaccine for influenza or pneumonia. All he could do as a physician was watch while his patients recovered or died.

In the meantime, leaning close to them as they coughed and sneezed, he knew he stood a good chance of catching the disease himself—and he was in the age group at greatest risk of dying from it. Every day he wondered if the phantom tickle in his throat or the passing ache in his head was at last the signal that his own time had come.

But Keegan the researcher was something else. This Keegan knew neither fear nor despair. He had been born into the age of modern medicine, when scientists at last had a grasp of how disease was caused and transmitted and how it might be prevented or cured. Their knowledge was based on the germ theory of disease, first proposed by French chemist Louis Pasteur about 50 years earlier. Infectious diseases were caused not by bad weather or the stars but by microbes—living creatures, such as bacteria, too small to be seen with the naked eye. Using a microscope and other lab equipment, scientists could theoretically identify the pathogen that caused any infectious disease. That knowledge could teach them how to fight it or how to control the conditions that encouraged its spread or, more glamorously, how to develop a vaccine (a solution with weakened or killed microbes) that would make potential victims immune.

Keegan's predecessors had already done much to combat such ancient disorders as smallpox, cholera, diphtheria, typhoid, rabies, yellow fever, and malaria. Keegan himself had long hoped for the chance to accomplish something equally great. Now, it appeared, he had that chance—although, as he walked past the bodies of his dying patients on his way to the laboratory, he felt strangely guilty for having wished for it at all.

Keegan, Goodpasture, and other researchers at Chelsea Naval Hospital sat down at an imposingly long table headed by the equally imposing director of the laboratory, Milton J. Rosenau. With his severe nose, thick mustache, and sharp eyes behind pince-nez glasses, his face often made Keegan the slightest bit afraid that he was doing something wrong. And Dr. Rosenau was a man whose respect you wanted to earn. One of the nation's top authorities on the science of public health, he had literally written the book on the subject. His *Preventive Medicine and Hygiene* had been required reading for Keegan in medical school. Famed for his work against anaphylaxis, yellow fever, and diphtheria, the 49-year-old Rosenau had founded the world's first school of public health (at Harvard) and was also head of the vaccine and biologic labs of the Massachusetts Board of Health. If anyone could find a way to fight Spanish influenza, Rosenau could.

Now they talked, as scientists will, about what was happening and what was to be done. There were certainly many crazy ideas in the air, for which the scientists had only contempt. One popular rumor was that German spies had deliberately seeded Boston Harbor with the germs that cause Spanish influenza. Even if this were true, it was still germs, not Germans, that had to be fought.

The fight had to start with a guess—some reasonable hypothesis that could be tested in the lab. Keegan's guess was that an especially virulent strain of Pfeiffer's bacillus was behind the epidemic. Most of the men at the table thought so. They had learned in medical school that this bacterium, called in Latin *Bacillus influenzae* or *Haemophilus influenzae*, was most probably the cause of all influenza epidemics. But Dr. Rosenau was skeptical. With the deftness of a seasoned teacher, he pointed out several holes in the original argument made by the German bacteriologist Richard Pfeiffer in the 1890s.

The holes all had to do with how well Pfeiffer had fulfilled Koch's Postulates. These generally accepted rules for identifying a pathogen had been developed in 1884 by Robert Koch, as a result of his own work in cultivating bacteria and studying disease.

Postulate 1: The microbe must be found in every case of the disease and in such a relation to the damaged tissue as to explain the damage.

Postulate 2: The microbe must be isolated and cultivated in pure culture outside an animal's body.

Postulate 3: When this pure culture is transmitted to healthy animals, it must cause a disease with the same characteristics as those that naturally occur.

Postulate 4: It must be possible to recover the microbe from all cases of the disease produced by experiment.

Pfeiffer's bacillus was often found in the respiratory tracts of influenza victims (**Postulate 1**). And although it was technically difficult to culture Pfeiffer's bacillus, Pfeiffer had found a way to do it (**Postulate 2**). The problem was with the last two postulates. Pfeiffer was never able to find a laboratory animal that had definitely caught influenza (**Postulate 3**). The best he could do was work with animals (rabbits and monkeys) that developed respiratory illnesses similar to flu, but without the characteristic lesions, or damage, that the flu typically left in human lungs. And though he found some Pfeiffer's bacilli in the diseased rabbit and monkey lungs, he did not find quite enough to be sure they had caused the disease (**Postulate 4**). The bacilli, which should have overrun the lungs, appeared in only small quantities, sometimes in isolated clumps.

Like a good scientist, Pfeiffer had been honest about these discrepancies and had stated his reservations. But somehow, the discomfort of uncertainty and the pleasure of

knowledge had persuaded many scientists to forget all about the holes in Pfeiffer's case and claim victory. Not Rosenau—and, his tone made clear, not Rosenau's team.

Now Keegan knew less than he had when he walked into the room. Maybe Pfeiffer's bacillus caused influenza; maybe not. If it did not, what did? Goodpasture—ever the go-getter—had an idea: *pneumococcus*. The lungs of the cadavers he had examined were crawling with this species of bacteria. Pfeiffer's bacillus appeared only in smaller quantities, if at all. Yet Rosenau distrusted this finding too. "Just because you don't see it now, young man, doesn't mean it wasn't there once." Pfeiffer had argued that his bacillus might produce a toxin so virulent that it alone could cause influenza. The Pfeiffer's bacilli in these lungs might have died, but their poison would go on poisoning. Meanwhile, in the patient's weakened state, an opportunistic organism such as pneumococcus would multiply wildly, confusing young pathologists.

Keegan was now scratching his head. Maybe Pfeiffer's bacillus, maybe pneumococcus. Other researchers at the table suggested streptococcus, staphylococcus. Why not? In the absence of knowledge, any guess was possible. Yet the most bizarre guess came not from the young initiates but from the middle-aged master himself. Rosenau suggested that influenza might be caused by a filterable virus.

Now this was just on the border of looniness, not far from the image of Germans slipping influenza into Boston Harbor. It was reasonable to say that bacteria existed. You could see them swimming under microscopes. You could feed them nutrients in an agar medium and grow them in a glass plate. You could kill them with boiling water. But no one had ever seen a filterable virus.

By definition, filterable viruses were small enough to pass right through the porcelain filters used to screen out bacteria. They were also small enough to be invisible under the most powerful available microscopes. They could

not be cultured outside the bodies of living creatures. But inside a living body, they reproduced quickly, and they could spread from one living body to another.

First proposed by Dutchman Martinus Beijerinck in the 1890s, the idea of a filterable virus was so outlandish that Keegan was surprised to hear a man of Rosenau's stature mention it. But Rosenau pointed out that much evidence had been collected since Beijerinck to support the existence of filterable viruses. German scientist Walther Kruse, for example, had shown that the nasal drippings of a person with the common cold could be filtered clean of bacteria, inserted into a healthy volunteer's nose, and cause a cold. Drippings collected from that volunteer could then be collected, filtered, and cause a cold in another healthy volunteer. Since cold symptoms were similar to those of flu, Rosenau suggested that flu might also be caused by a filterable virus.

It was the team's turn to look skeptical. One person proposed that the so-called "virus" might be nothing more than a very small bacterium. *Bacterium pneumosintes* was difficult to cultivate outside a body and known to be small enough to pass through present-day filters. Other researchers said, "Oh, no, it may well be a virus," trying to humor the boss, but Rosenau would have none of it. His suggestion, he told them, was a hypothesis—a proposition to be tested, nothing more. The answer would come not by vote but by experiment.

That now became the subject of discussion: what experiments to do? They had powerful laboratory equipment. They had a hospital full of sick patients. Like Pfeiffer, they had no ideal laboratory animal, but perhaps human volunteers could be found. The Spanish influenza pathogen would be isolated: that Keegan believed for sure.

However, as a dean of American public health, Rosenau reminded his team that finding the pathogen would not be the same as stopping the epidemic. Perhaps a safe and effective vaccine could be developed in time; perhaps

not. Perhaps new information would help public health officials control the microorganism's spread; perhaps not. Anything Rosenau and his team learned might be of use—or it might not. Their obligation was to try.

It was exciting, it was exhilarating. Keegan was part of the big push against Spanish influenza. He had a chance to write his name in scientific history. He had feared a slow August, but it had been the furthest thing from slow. He had seen men die under his care, and though it had shaken him, it had also spurred him. If the flu didn't kill him first, he could do something to save the millions of people still at risk.

Out of curiosity, Keegan began to make estimates of how bad the epidemic could get, given the incomplete data he had on hand. His preliminary conclusion shook him all over again. After refining it further, he would soon publish his conclusion in the *Journal of the American Medical Association*: Spanish influenza “promises to spread rapidly across the country, attacking between 30 and 40 percent of the population.”¹

Even by now, in mid-September, the Spanish flu was spreading. It had appeared at naval bases all along the Atlantic seaboard, from Rhode Island to Florida. Even more worrisome, there were reports that epidemics of equal virulence were raging thousands of miles away at Freetown, Sierra Leone, a port in Africa, and at Brest, a port in France. These epidemics appeared to have begun a few days before the Boston epidemic. Whatever this new killer was, it had already become international before it was even noticed at home.

In Boston in the second week of September, 46 people died, their lungs destroyed by influenza or pneumonia. In the third week, 265 deaths were reported. In the fourth week, 775. In one month, in one city, more than a thousand lives had been ended by a disease that threatened to spread everywhere, all over the country, all over the world. His excitement tempered by his dread of the stakes, Keegan prepared to go to work.

Note

1. J. J. Keegan. “The Prevailing Pandemic of Influenza,” *Journal of the American Medical Association* 71 (Sept. 1918): 1052-55.

Case 2. Around the World

By George Ochoa

As the autumn months of 1918 turned colder, scientists across the United States and around the world struggled to discover the cause of Spanish influenza while there was still time to prevent a global disaster. They all failed. By spring 1919, the cause of Spanish influenza was still a mystery, and tens of millions of people were dead.

It is estimated that the pandemic of 1918-19 killed 20 to 30 million people—two to three times as many as were killed among all combatants in World War I. In the United States alone, Spanish influenza infected about 25 million people—a quarter of the country's population. During the pandemic, about 675,000 Americans died of influenza and pneumonia (approximately six-tenths of 1 percent of the U.S. population), more Americans than were killed on both sides of the Civil War, the nation's bloodiest conflict.

War was the best friend of Spanish influenza. As scientists had feared, the influenza pathogen took full advantage of the movements of sailors and soldiers. In the last days of August, American troops were infected with influenza while boarding transports in Britain. By early September, they had carried it to their assigned stations in Archangel, Russia. On September 11, flu was diagnosed in Philadelphia, just four days after arriving there with sailors from Boston.

Traveling through the Panama Canal with another shipload of sailors, the flu became epidemic in Seattle, Washington, on September 25. A train of soldiers brought the flu inland to Kentucky on September 27. On the South Pacific island of Guam, 4.5 percent of the population died after a U.S. Navy transport with a cargo of influenza dropped anchor on October 26.

The flu could also be carried by civilians—railroad workers, traveling salesmen, merchant

seamen. New Orleans, Louisiana, and Tampico, Mexico, received the flu from the sick crew of the steamship *Harold Walker*, lately sailed from Boston.

Once the flu arrived, it spilled through the community like water spewing from a burst pipe. Doctors and nurses exhausted themselves visiting one case after another. Hospitals packed with feverish patients had to shut their doors. Families went hungry because parents were too sick to get up and make meals. In an Eskimo village near Nome, Alaska, children froze to death because no adult was well enough to rekindle the fires in their cabins. Businesses and public services around the world faced absences of up to half their employees. In Germany, much of the potato crop spoiled in the ground because farmers were too ill to harvest it and railroad workers were too ill to transport it.

The population of death grew. In some cities, corpses lay for days in houses and hospitals, held up by shortages of hearses, caskets, and gravediggers.

In Philadelphia, five emergency morgues had to be established. A health bulletin offered this advice to communities not yet hit:

Hunt up your wood-workers and cabinet-makers and set them to making coffins. Then take your street laborers and set them to digging graves. If you do this you will not have your dead accumulating faster than you can dispose of them.¹

With each passing day in a given community, the number of new cases (the case rate) boomed until it reached a peak, or *crest*. After that, each day would tend to bring fewer new cases. The worst cases lingered on their beds a while longer before they were resolved by death or recovery. For that reason, the number of deaths (the mortality rate) usually did not peak until a few days after the case rate.

In the United States as a whole, the deaths escalated twentyfold from one month to the next: from 10,000 in September to 200,000 in the peak month of October. In November and December, the numbers dropped—to about 100,000 new deaths.

Many communities experienced not one but two or three crests. In the week ending October 22, New York City suffered a peak of 5,222 deaths from influenza and pneumonia. The number of new deaths dwindled to 424 in the week ending November 30 before climbing back to 1,212 in the week ending February 1, 1919. That second peak was low compared to the first peak, but it was three times worse than the low reached in November.

Behind the statistics were thousands of individual struggles and tragedies. There were horror stories of how fast Spanish influenza could sicken and kill. A man in Rio de Janeiro, Brazil, asked a bystander for directions to the streetcar, thanked him, then died. A health officer in Manchester, England, observed schoolchildren succumbing to flu: “They simply dropped on their desk like a plant whose roots have been poisoned.”² In San Francisco, California, one night, a secretary went home from a bridge game. When she awoke next morning, “I was too ill to get out of bed, and the friend at whose house we played was dead.”³

There were stories of heroism. In rural Russia, an 8-year-old child, himself feverish, was found caring for the five others in his family, all of them sicker than he. There were stories of misery and kindness. Private Robert James Wallace came down with the flu while aboard the U.S. troopship *Leviathan*, as did 2,000 others. He developed a fever of 103.7°F, but because there was no room in sickbay, he had to lie on the open deck in the middle of a storm. He was at last brought inside, where a nurse washed his feet. “That gentle washing of my feet with her soft, soapy hands,” he recalled, “engraved a mem-

ory in my mind I shall record in Heaven when I get there.”⁴

The flu could change life forever for those who survived. Katherine Anne Porter was a young journalist in Denver, Colorado, when influenza struck her. Days of high fever followed. Doctors all but gave up on her. Funeral arrangements were made. She recovered, but the soldier whom she loved and who had faithfully tended her, died. She later said of the event, which became the basis for her short novel *Pale Horse, Pale Rider*: “It seems to me true that I died then. I died once and I have never feared death since.”⁵

Most cruel of all were the stories of orphans. Orphans proliferated everywhere, the result of Spanish influenza’s preference for adults aged 20 to 45, those most likely to be raising children. One family in Seattle decided to move to Minneapolis at the height of the epidemic. While on the train, both parents and their four children became gravely ill. Within days of arriving in Minneapolis, the parents died. Left to be raised by cold and miserly relatives, one of the children, Mary McCarthy, who grew up to win literary fame, remembered:

We became aware, even as we woke from our fevers, that everything, including ourselves, was different. We had shrunk, as it were, and faded, like the flannel pajamas we wore, which during these few weeks had grown, doubtless from the disinfectant they were washed in, wretchedly thin and shabby...[A] new image of ourselves—the image, if we had guessed it, of the orphan—was already forming in our minds.⁶

What was to be done? It was a plague, a calamity out of the Middle Ages, rushing around the world on steamships and trains. Could anything stop it?

In the midst of the pandemic, people everywhere tried. Scientists like Keegan tried to track down the pathogen, but their results were confusing, and those whose lives were in danger could not afford to wait. Public health offi-

cials, doctors, nurses, and ordinary individuals had to do something now.

Today, Americans would probably expect the federal government to wage a war on Spanish influenza. But in those days public health campaigns were mostly the duty of states and towns. Congress appropriated only \$1 million to fight the pandemic—one cent per person in a population of about 100 million.

If you were in charge of a town's public health, what could you do? You could distribute guidelines about treatment: stay in bed, drink fluids, see a doctor, go to a hospital if necessary. But what if there were not enough doctors, nurses, or hospital beds to go around? What would you tell people to do then?

You could issue information on how to avoid catching the flu. But what could you say? No one was sure how the flu was transmitted, whether by air, on dust, or in sick people's secretions. It was common sense that the healthy should stay away from the sick. But in practice, how could you keep infected people without symptoms away from healthy ones?

You could order a quarantine on infected dwellings. But people still might be contagious even before they showed symptoms. You could order several days' quarantine on all incoming ships, trains, and vehicles, until it was evident that they harbored no flu cases. But how would you make sure no one sneaked through, and what would such a blockade do to a town's economy?

You could order the closing of public gathering places—schools, theaters, churches, shops, restaurants, factories, streetcars, even streets. You could order the disinfection of the public places left open (if it were true that alcohol or carbolic acid could kill the flu germ). You could make it illegal to sneeze or cough without covering the face. Some experts believed that gauze masks could keep out the flu. Why not order every citizen to wear a mask at all times?

Fine, you could order away—if you were Napoleon. But, in reality, your authority might not go far enough. You might need approval

from city councils or mayors, who might not like the idea of their economies grinding to a halt. In democracies, civil rights advocates might have something to say about jailing an entire city without due process. Even in a dictatorship, you would have to reckon with enforcement. Would you have a police officer in every room, waiting for someone to sneeze without covering the mouth?

In practice, governments usually balanced public health with other interests, such as supporting business, obtaining votes, preventing panic, and supporting the war effort. One of the hardest things to do during the fall of 1918 was to order people not to hold "Liberty Bond" rallies to raise money for the boys overseas.

If you were the mayor, you had to remember the problem of public services. Mass absences were straining workforces everywhere. How could you make sure the city had enough garbage collectors, telephone operators, and gravediggers?

If you were a doctor, and you knew of no cure for influenza, what could you do for your patients? Lewis Thomas recalled that during the pandemic, his physician father in New York prescribed "fantastic formulations, containing five or six different vegetable ingredients" to be carefully prepared by a pharmacist. Like many other physicians, his father doubted the effectiveness of the drugs, but prescribed them anyway. "They were expected by his patients; ... if nothing else, they gave the patient something to do while the illness, whatever, was working its way through its appointed course."

Was it ethical to prescribe this sort of drug when you knew it probably wouldn't work? If you didn't prescribe something, patients would find their own remedies. These included laxatives to "purge" germs from the bowels, alcohol-laden "elixirs" hawked in magazine ads, pinches of arsenic and strychnine, and garlic rubbed into the skin.

What if you were an epidemiologist whose job was to make sense of the statistics

of the plague? Your job was hampered from the start. Until well into the pandemic, flu was not even a reportable disease in many places. Like athlete's foot, it was considered too mild to be worth any space in the health records. Even when doctors were required to report cases of flu, diagnoses were not always accurate and records were not always kept faithfully. Mortality data were more reliable (death is easy to spot) but still incomplete. In the United States in 1918, deaths were compiled from a registration area comprising only 78 percent of the population. In undeveloped regions of Africa, Asia, and Latin America, accurate records of any kind were, and are, hard to come by.

Statistics mattered because they were the only way to tell whether a particular strategy was working or not (whether things were getting better or worse) or whether you had learned anything that some other community might find useful. But statistics are only as valuable as the care with which you analyze them. Did the case rate in your city fall because of the heroic efforts of your public health czar or would it have fallen anyway, given the characteristic cycle of the epidemic?

One thing was certain: *morbidity* (the proportion of the population who fell ill) and *mortality* (the proportion of the population who died) varied greatly from place to place. In the last four months of 1918, Atlanta suffered 3 influenza and pneumonia deaths per 1,000 people. San Francisco suffered 5.4. Darien and Milford, two towns in Connecticut, suffered none. In 1918-19, Germany logged 5.9 deaths per 1,000 people. The United States logged 4.2; Western Samoa, 220.0; American Samoa, none. Even within a city, some ethnic groups, some streets, suffered more severely than others. Why the differences?

By June 1919, Spanish influenza no longer appeared to be epidemic anywhere in the world. There was a new influenza pandemic in 1920, but it was not severe enough to be considered part of the earlier one. After striking in

at least three waves—spring 1918, fall 1918, and winter 1919—Spanish flu seemed to be gone. Where had it gone? How long until it came back?

Over the years, influenza has regained its reputation as a relatively mild disease. From time to time, flu pandemics have broken out, but none have come close to the devastation of 1918-19. Even so, many history books fail to mention the 1918-19 pandemic, or mention it only in passing. Why is it so little remembered?

Even during the pandemic, the forgetting was beginning. In the worst months, the spirit of wartime optimism led many people to deny it altogether. Politicians and generals underplayed it. Newspapers underreported it. The pandemic brought many deaths, but so did World War I. Many people remembered the one as just another theater of the other.

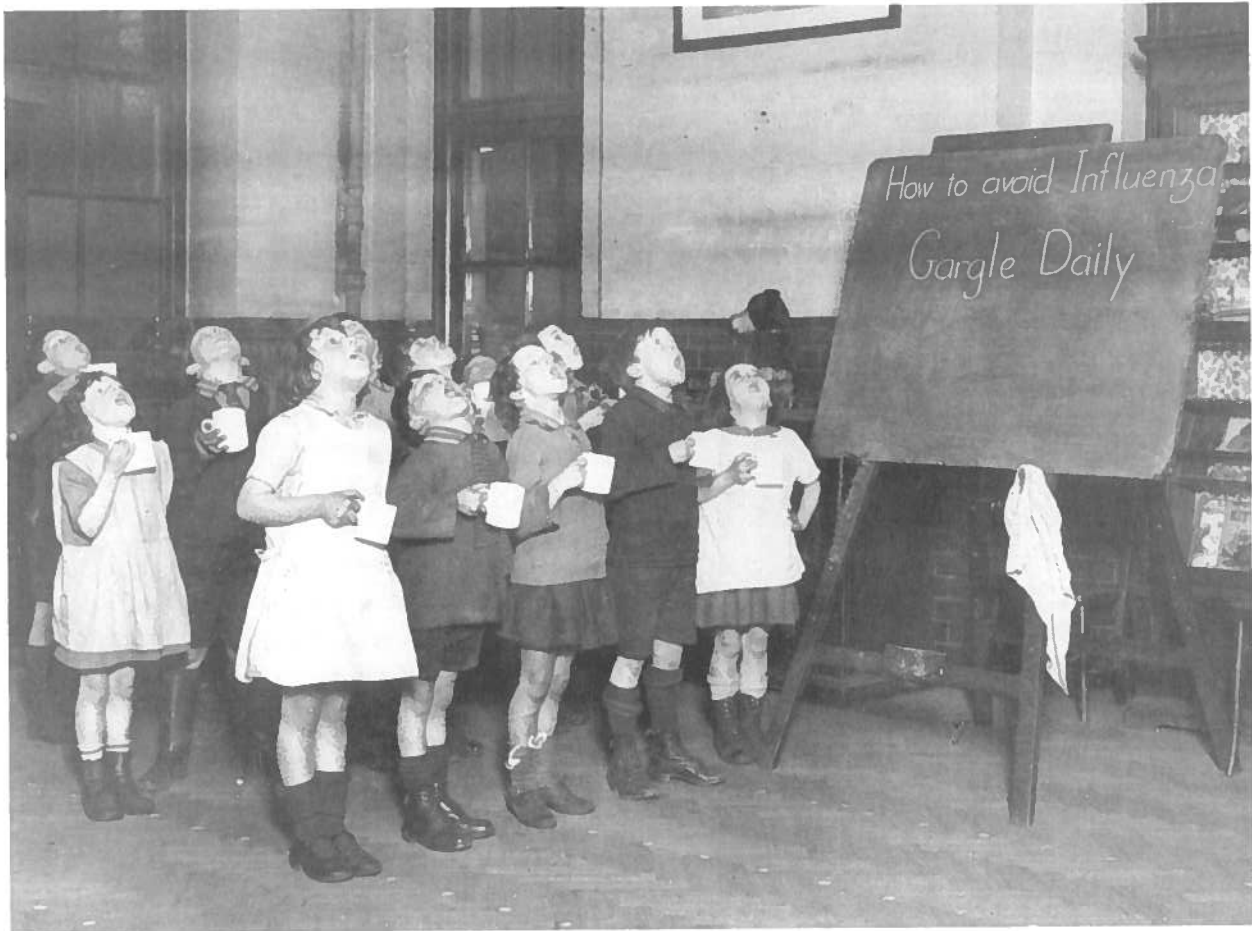
Those who survived the plague mourned family members who had not. For years, they might react with fear when their children caught even mild flu. But they might never realize that their own experience had been repeated in towns and villages across the world. Since few historians or novelists wrote about it, the whole experience seemed to pass from human memory.

Like almost everything else about Spanish influenza, the reason for our amnesia about it remains a mystery. Could it be that we are too embarrassed to admit our bodies are that frail, our knowledge that limited? Maybe we like to think that science marches only from success to success. The *New York Times* obits of Milton J. Rosenau and Ernest W. Goodpasture summarize their many scientific triumphs, but neglect even to mention their frustrating battles with Spanish influenza.

All the more remarkable, then, that scientists kept returning to the place that was not safe. Year by year, the world's memory of Spanish influenza grew fainter, but not for the scientists. Their research went on into the mysteries of death by contagion, filterable

beasts, 105 fevers, the country of microbes. Nearly everyone forgot, but the scientists

remembered. They owed that much to both the living and dead.



School children learning to gargle. Gargling was thought (incorrectly) to be one way to prevent influenza.

Notes

1. Quoted in Jack Fincher, "America's Deadly Rendezvous with the 'Spanish Lady,'" *Smithsonian* 19 (Jan. 1989) 140.
2. Great Britain, Ministry of Health, Reports on Public Health and Medical Subjects, No. 4: *Report on the Pandemic of Influenza, 1918-19* (London: His Majesty's Stationery Office, 1920) 472. As quoted in Fred R. van Hartesveldt, "Manchester." In *The 1918-1919 Pandemic of Influenza: The Urban Impact in the Western World*, ed. Fred R. van Hartesveldt (Lewiston, N.Y.: Edwin Mellen, 1992), 101.
3. *Ibid.*
4. Robert James Wallace, D.D.S., to Alfred W. Crosby, Seattle, Washington, Feb. 10, 1970. As quoted in Alfred W. Crosby, *America's Forgotten Pandemic: The Influenza of 1918* (New York: Cambridge University Press, 1989), 131.
5. Joan Givner, *Katherine Anne Porter: A Life* (New York: Simon and Schuster, 1982), 128.
6. Mary McCarthy, *Memories of a Catholic Girlhood* (New York: Harcourt, Inc., 1948), 36.
7. Lewis Thomas, *The Youngest Science: Notes of a Medicine-Watcher* (New York: Penguin, 1995), 15.

Case 3. The Coming Pandemic

By Daniel Sullivan With Abby Hansen

Characters

Mike Franklin. Secretary, Health and Human Services

David McCord, M.D. Head, Centers for Disease Control and Prevention (CDC)

Claire Howe, M.D., M.P.H. President's chief health policy adviser

Nancy Anderson, Ph.D. International influenza expert

Tom Rose. A leading spokesperson for the U.S. pharmaceutical industry

Early on the morning of February 21, Mike Franklin felt a tension headache begin as his car neared his Washington, D.C. office. A group of high-level health policy experts and scientists awaited him there, ready for an emergency discussion of a problem Mike wished he understood more thoroughly. Two weeks ago, he had been told that a Centers for Disease Control (CDC) field station in China had received an isolate of an influenza virus that had killed a young, healthy farmer in a remote agricultural village. The virus was of a type the CDC had not previously seen, and they were worried. At first Mike had thought, "A new flu, what's the big deal?" But what he had learned about flu and its policy implications over the past two weeks had made him realize this could be a very big deal indeed. Well-known for his ability to analyze problems and make careful decisions, Mike was not used to feeling so full of conflict and, frankly, confusion.

Mike reached his office at 8 a.m. There he met David McCord, head of the CDC; Claire Howe, the president's chief health policy adviser; Nancy Anderson, a leading influenza expert; and Thomas Rose, who spoke for the pharmaceutical companies that manufacture flu vaccines. Seated around the conference table, they all had big folders full of notes in front of them. Mike took his seat at the head of the table, spread out his notes, and looked around at the group. His attempt at a hearty smile of welcome did little to change people's tense expressions.

"Thank you all for coming on this short notice," Mike began. "I appreciate your time, help, and input. As you know, it's now clear that we may be facing a health crisis—in fact a worldwide influenza pandemic. The president wants my recommendations on this situation tomorrow." He nodded at David McCord. "David, could you start us off by summarizing what CDC knows so far?"

McCord nodded briskly. "CDC operates several laboratories in China to conduct surveillance of influenza. We try to get some advance warning of significant, possibly dangerous, changes in the influenza virus by analyzing isolates of viruses the Chinese give us. Three weeks ago one of our labs received a viral specimen taken from a 25-year-old farmer from a remote district in northern China. He had come down with a flu-like illness and died just four days later. Because of the unusual nature of his case, a local doctor sent our lab a nasopharyngeal swab for culture. The lab isolated a type A influenza virus, subtype H7N2.

Mike cut in. "Without getting too technical, can you explain those letters?"

McCord continued, "Certainly. The 'H' is for *hemagglutinin*, the H antigen. The 'N' is for *neuraminidase*, the N antigen. In recent years, we've seen two type A flu viruses—H1N1 and H3N2. Haven't seen H7N2 until now."

Mike asked, "Do I understand correctly that the differences in the antigen mean the current vaccine won't work?"

Everyone around the table nodded. Mike said, "That's what I was afraid of. But could this just be a freak occurrence? Have other people died of this strain of flu?"

David McCord said this was difficult to pinpoint because of the remoteness of this area of China, its lack of hospitals, and the scarcity of doctors. "We hear there have been some other illnesses—and some deaths too—but there's no good central information source. We've sent a team to the village where the index patient died. They'll look for other cases of flu and draw blood samples to test for evidence of infection in other people."

"Where did this new virus come from?" Mike asked.

McCord shook his head. "We have no precise answer. My best guess is that the H7N2 variant came from some animal, probably a pig. We assume the pig was simultaneously infected with an H3N2 strain from a human and an H7 virus from an avian, probably a duck. We've seen H7 viruses before, but only in animals. We didn't think they infected humans."

"Well, we think so now, don't we?" Mike said grimly. "Do I have this right—the viral strains recombined in the pig and formed this new strain, which somehow got transmitted to humans?"

Nancy Anderson raised her hand and joined the conversation. "Actually, transmission of flu viruses from pigs to humans isn't all that rare. And in that part of China, people, pigs, and ducks live in close proximity. So it's not too much of a surprise that this thing happened in that environment."

Mike looked back at her. "I want to know, is it likely to be a big problem for us in the U.S.?"

Nancy's expression was somber. "I really think we may be looking at a major catastrophe. The H7 antigen is completely new. Nobody has any preexisting immunity to it. And it's already killed at least one young, healthy person. If this doesn't have the potential to turn into a devastating worldwide pandemic, like the Spanish influenza of 1918, I don't know what does."

Mike sat back in his seat. "You're saying this virus could race around the world destroying everyone in its path?"

"That's a little overdramatized," Nancy answered. "The danger depends on three things: the susceptibility of the population, the communicability of the virus, and its virulence."

"By virulence, you mean how severely it damages the human body?" Mike asked.

Nancy nodded. "Exactly. Because we've never seen in circulation a strain of flu closely related to this one, we think it likely that the population is very susceptible. As for its communicability, we know flu is easily transmitted from person to person by coughing or sneezing. Its virulence is the hardest thing to tell at this point. We have to remember how deadly influenza can be. The 1918 flu killed a much higher percentage of infected individuals than any flu since. Even scarier, while other flus tend to kill only the very old or sick, the 1918 flu killed a lot of young, healthy adults. That's why we have to take this new strain very seriously."

Mike sighed. "We are. But what about susceptibility? Can't we make people less susceptible—immune even—by making a vaccine against this flu?"

Tom Rose spoke up. "I feel sure the pharmaceutical industry could make a vaccine against this strain the way we do for any other flu. We'd grow large quantities of the virus on embryonated chicken eggs, then purify and inactivate the virus. Since CDC has already isolated this virus, it shouldn't be hard to prepare a vaccine. But the manufacturers have to know about timing and quantity."

Mike said, "What do you need to know?"

Tom answered, "How much vaccine to prepare, and when—and we'd need answers very soon. It's already February, and we choose the flu strains for the next fall's vaccine in January and February. As for quantity, if we vaccinate everyone in the U.S. we'd have to make hundreds of millions of doses."

Mike asked, "Where is the industry right now with vaccines?"

Tom replied, "Well, we obviously haven't started a vaccine against the H7N2 strain, since it's just been discovered. At the moment, manufacturers are starting production of the regular vaccine, which combines three strains. We'd need time to switch."

Nancy Anderson looked over at him. "Tom, I know it's more complicated than just switching to a new vaccine."

Tom nodded. "You bet. We need to plan the size of the egg-hatching flock at least six months in advance in order to have enough mature birds to produce the eggs when we need to grow the virus. This year we've planned to produce about 70 million doses for the U.S. market. It would be difficult to make more than 70 million. We don't have enough eggs."

Mike whistled softly. "Isn't there a higher-tech way to make vaccine?"

Tom said, "Sadly, no. We still make the vaccine the way we have for decades. It's effective and safe, and we can do it for a reasonable cost. There is research on recombinant DNA technologies and growing virus in tissue culture instead of eggs, but it's still in the early stages."

Claire leaned toward Tom. "Isn't there any way to stretch the supply of vaccine, Tom?"

"There might be," he answered. "Perhaps we could use a monovalent, rather than a trivalent, vaccine. All other things being equal, this could give us something over 200 million doses by the fall—assuming the virus grows pretty well and one dose of vaccine is enough to prevent this flu."

Mike's headache really throbbed now. "One dose isn't always enough?"

David McCord jumped in. "No. In 1976, the swine flu year, children had to have two doses, given a month apart."

Mike winced. "I'm glad you reminded us of swine flu. It's a good example of how not to prepare for a pandemic that never comes. Even so, what's the bottom line? Can we make enough vaccine for all 260 million Americans or not?"

Tom Rose said, "Possibly. In the best-case scenario."

Claire Howe interjected, "But we have to consider the worst-case scenario too."

Tom said, "I believe David and Nancy will back me up on this. Flu vaccines are a pretty well-known quantity. We ought to be able to handle this one."

David McCord said, "I just don't believe in rose-colored glasses. Even after field tests, some vaccines turn out to have unexpected long-term consequences."

Tom said, "I'm not forgetting that. I just think we can do this, under the right circumstances. There are a lot of complicated issues from the pharmaceutical industry's point of view. For a huge production run like this, we'll have to be certain we can sell all the vaccine we make. It's not reasonable for the government to ask us to produce 260 million doses of vaccine without guaranteeing it will be purchased. For all we know, there may be large surpluses of unused vaccine. At a minimum, if the government won't purchase the whole vaccine supply, we'll need an agreement for compensation for unsold doses above what we would produce in a normal year."

Claire gave him an ironic smile. "Some people might object to that, Tom. They think you guys are rich enough already. But you do raise another issue: liability. During the swine flu episode, insurers thought a new vaccine to be given to every American was too risky to cover. They refused full indemnity to the drug companies. Congress stepped in and passed a special act to make the government liable for damage claims."

Mike said, "And there were damage claims—big ones, I understand."

Claire nodded grimly. "And how. Even after the largest field trials ever, a few months into the program it was discovered that the vaccine increased the likelihood of getting GBS."

"What's GBS?" Mike asked.

"Oh, sorry—it's Guillain-Barré Syndrome," Claire explained. "It's a rare but serious neurological disease that can lead to death. It occurred 5 to 10 times more frequently in

people who received the swine flu vaccine. Overall there were several hundred cases of GBS and a dozen or so deaths. The government had to halt the vaccination campaign.”

“Could this happen again?” Mike asked.

McCord said, “It’s unlikely, but since we don’t know why it happened that time, we can’t be absolutely sure it won’t happen again. Any vaccine can trigger unexpected side effects. For that matter, so can any medical treatment. And if you’re giving the vaccine to tens of millions of people, of course there’s going to be some risk. We just don’t know what.”

Mike responded, “Will the act Congress passed to cover the swine flu campaign in 1976 also cover the liability issue for any campaign we might recommend?”

Claire answered, “No, that was a one-shot deal, and may I point out, Congress was not at all pleased. It felt coerced by the pharmaceutical industry into accepting liability and thought it could be a very dangerous precedent to encourage drug companies to back off from what should be their responsibility.”

Tom Rose interrupted, “Hold on, Claire. Why should our industry take the hit? If the government won’t do the right thing, pretty soon the drug companies will have to stop manufacturing vaccine. We can’t run that kind of business risk over and over. That would be irresponsible. The real problem is the insurance companies. They won’t cover us. Why don’t you talk to them? If the government doesn’t back us up, it’s going to find itself in the flu vaccine manufacturing business. Then there won’t be any question about whose liability it is.”

Claire smiled calmly. “I appreciate your position, Tom. I’m just saying how Congress felt in 1976 and how it will probably feel this time. How many members of Congress are going to vote in favor of making the government liable for damage caused by a product of the pharmaceutical industry, which the public regards as very wealthy? Put yourself in their shoes.”

Mike waved his hand. “You’ve both made your points. Liability is going to be an issue in

any widespread vaccination campaign. Now, David, could we redirect this discussion a bit? How are people actually getting flu vaccine now?”

McCord said, “We practice selective vaccination. We target people who are at greatest risk of death from the current flu—older people and those with chronic medical problems. There are about 60 million of them, and maybe another 25 million in other groups for which we recommend vaccination. These people get their shots largely from the private sector. I mean, they go to their doctors for the vaccine. This has become pretty much routine over the past decade, because Medicare now reimburses doctors for flu vaccinations. Right now about 60 percent of the high-risk group gets yearly flu vaccinations.”

Mike surveyed the faces around the table. “What do other people think about that? Does the new strain mean we should plan a larger campaign—a universal campaign—and try to vaccinate everyone in the U.S.? By this I mean not only can we, but should we?”

McCord responded, “I’m glad you asked both questions. We’ve raised the issues of making enough vaccine in time, liability for unexpected harm it might do, and the logistics of vaccinating 260 million people. None of these pose insurmountable problems. But we haven’t talked enough about whether this is the right thing to do. We really don’t yet know if there will be an influenza pandemic. In the swine flu fiasco, if I may use that term, of 1976, I think there was a rush to mount a campaign, an assumption without enough convincing evidence that there truly would be a pandemic. And it came to nothing, except some unanticipated cases of a neurological disease.”

Claire said, “Of course, nobody wants that to happen again.”

Mike smiled grimly. “Least of all the secretary of Health and Human Services. Okay, look—I don’t want to cry wolf, but I certainly don’t want to ignore a real, worldwide health

crisis. Does anybody know how many people were killed in the 1918 pandemic?"

Nancy answered, "More than 500,000 Americans died, plus at least 20 million people worldwide."

Mike said, "Well, if there's a chance this new flu strain is anything like that, we have a responsibility to try to prevent those deaths. Don't we?"

Nancy said, "I think we do. If the 1918 pandemic teaches us anything, it's how great the risk of proceeding too cautiously can be. That year the flu appeared in the late spring, then sort of hid out over the summer, and exploded in the fall. Think of it, in October alone nearly 200,000 Americans died from influenza. What assurance do we have that this new flu won't do something similar? The 1918 pandemic swept the globe in months—and that was before jet travel. Today, with people flying from continent to continent every day, a deadly pandemic could cover the globe in a couple of weeks. And remember, it takes the vaccine about two weeks to produce an immune response in people. We just can't afford a wait-and-see approach. A lot of people could die."

David leaned forward, "Nancy, we do have one important technical difference now. In the other flu years, there was a shift in both the H antigen and the N antigen, but this time just the H has changed. The population may already have some immunity."

Nancy countered, "Most virologists consider the H antigen the more important factor in epidemics."

Mike interrupted, "You're talking over my head. What are people's objections to a large-scale vaccination program?"

Claire said, "Well, there's cost. If the government purchases around 260 million doses of vaccine—assuming the drug companies can manufacture that much—and each dose costs one dollar, we're talking about a quarter of a billion dollars right there. And there's the cost of putting together a program of distribution and then administration to get the vaccine to as

many people as possible. And what delivery system will we set up to reach the uninsured and people who don't regularly go to doctors? Congress has only so much money to allocate for health. Won't this fact divert resources from programs people really need?"

Nancy added, "The liability issue has a price tag too. The swine flu episode cost the government nearly 100 million dollars in damages. And I think we agree, society is even more litigious now."

Mike said, "Sure, but if a killer pandemic really did hit, wouldn't all these costs look like a bargain?"

Claire sighed, "Of course. But what if it didn't hit? A mass immunization program like this would require congressional authorization, and it would probably cost in the billions. Congress would think it was like asking them to sign a blank check. And the American people are skeptical of large government programs. No, I wouldn't expect enthusiastic support from Congress. And I also wouldn't expect the president to be able to help very much."

Mike looked at her. "Could you clarify that, please?"

Tom spoke up, "Even I can see the political risk in aligning oneself too closely with any mass immunization program. There's so much to lose. If there is no pandemic, you'll look as if you alarmed the public unnecessarily and spent taxpayer money on something the taxpayer didn't need. If the pandemic does come and people die, you'll probably be accused of doing too little, no matter how big a vaccination campaign you supported. It's a no-win political situation. Am I right, Claire?"

Claire nodded. "Could be. But we have to make a decision. Everything is a risk-benefit calculation, and most of the time we also cross our fingers for good luck. I think the president will support any carefully thought-out plan."

Mike looked around the table. "Well, are there other concerns?"

David McCord raised a hand. "We haven't considered any international scenarios. Only

the U.S., Australia, and some of the western European countries make much flu vaccine. If there's a devastating worldwide pandemic, third world countries would call on us for assistance. What would we do, given our limited supply of vaccine?"

Mike rested his chin on his knuckles. "OK, another issue to think about. Let's review a bit. We have a lot of questions. Do we have our priorities straight? Should we recommend a mass vaccination for this new flu? Is this the right allocation of resources? Are we calculating the risks well enough? Are we making a mistake keeping this decision-making process among ourselves? Maybe we, as a group, are

missing something. And what about the press? Would they sensationalize this? And if they did, what effect would that have? We'll need some kind of plan to inform the public. And then there's the liability issue, and the logistics of getting vaccine out to all Americans who need it—not to mention sharing it with other countries. Since the president wants my written recommendation tomorrow, I'd appreciate further input from you during the day. We'll meet here tomorrow for lunch to critique my draft recommendation. I need to know what specific actions you people favor and why. And, of course, let me know if there's something we haven't thought of."

Getting Acquainted With Case 1

You can use the following self-test to help you remember the characters and facts of the narrative in Case 1, "An Incident in Boston." The answers are given below the questions.

1. **J. J. Keegan was a navy physician working in**
 - a. Boston Board of Health
 - b. Chelsea Naval Hospital
 - c. The Receiving Ship
2. **The first signs of a medical event were rumors in August 1918 of an unusual infection appearing in the Receiving Ship.**
True / False
3. **It was immediately apparent to J. J. Keegan that the symptoms of the sailors in the Receiving Ship were symptoms of flu.**
True / False
4. **The epidemic spread quickly, from two or three cases on August 27 to 106 on the fifth day after.**
True / False
5. **Within two weeks after the first case, how many persons had become sick?**
 - a. None
 - b. Thousands
 - c. An unknown number
6. **Even when recovering, infected persons were afflicted with debilitating secondary infections from opportunistic bacteria.**
True / False
7. **In the absence of knowledge about what causes a disease, a disease can only be defined by its symptoms.**
True / False
8. **The second wave of the Spanish flu had hit the Boston area in**
 - a. December
 - b. November
 - c. September
9. **Keegan's colleague, Milton J. Rosenau, founded the world's first school of public health.**
True / False
10. **Keegan at first guessed that the cause of the Spanish flu was**
 - a. Pfeiffer's bacillus
 - b. Pneumococcus
 - c. A small bacterium

Answers 1. b 2. True 3. False 4. True 5. b 6. True 7. True 8. c 9. True 10. a

Getting Acquainted With Case 2

You can use the following self-test to help you remember the facts of the narrative in Case 2, "Around the World." The answers are given below the questions.

1. **By spring of 1919, the cause of Spanish flu was**
 - a. Clear to scientists
 - b. Still a mystery
 - c. Recognized as a bacteria
2. **The pandemic killed two to three times as many persons as were killed among all the combatants in World War I.**
True / False
3. **Normally, the mortality rate peaked after the case rate peaked because some patients lingered until recovery or death.**
True / False
4. **During the Spanish flu pandemic, Congress appropriated**
 - a. Extensive funds for medical needs
 - b. Insufficient funds for medical needs
 - c. Funds sufficient for covering medical needs
5. **Although scientists did not know the cause of the Spanish flu, they knew how it was transmitted.**
True / False
6. **Closing public places such as theaters and schools was a common practice for blocking the transmission of the Spanish flu.**
True / False
7. **Because doctors were required to report cases of Spanish flu, records of the numbers afflicted became very reliable.**
True / False
8. **Compared to the rate of infection, the rate of mortality was more accurately compiled.**
True / False
9. **Morbidity and mortality varied greatly from place to place.**
True / False
10. **By June 1919, the Spanish flu was**
 - a. No longer epidemic anywhere in the world
 - b. Epidemic only in Spain
 - c. Waning in all countries except the United States

Answers 1. b 2. True 3. True 4. b 5. False 6. True 7. False 8. True 9. True 10. a

Getting Acquainted With Case 3

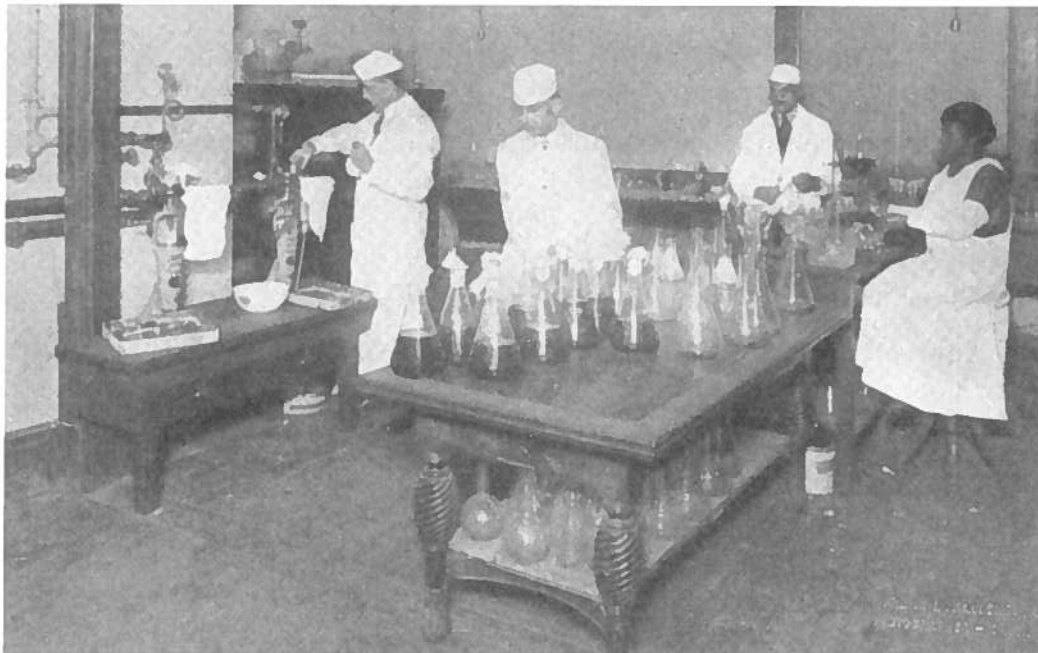
You can use the following self-test to help you remember the characters and facts of the narrative in Case 3, “The Coming Pandemic.” The answers are given below the questions.

1. **Mike Franklin was the**
 - a. Head of the Centers for Disease Control
 - b. Secretary of Health and Human Services
 - c. Spokesperson for the pharmaceutical industry
2. **The reason for the meeting on February 21 was that the CDC field station in China had received a sample of a fatal virus.**
True / False
3. **The virus from China probably came in part from an avian and in part from a human, recombining in the pig to make a new virus.**
True / False
4. **According to Nancy Anderson, transmission of viruses from pigs to humans is rare.**
True / False
5. **The extent of danger that a new virus represents depends on the**
 - a. Susceptibility of the population
 - b. Virulence of the virus
 - c. Both of the above
6. **In order to manufacture a vaccine, the pharmaceutical industry needs access to a convenient supply of chicken eggs.**
True / False
7. **The swine flu epidemic occurred in 1976.**
True / False
8. **Tom Rose pointed out that in case of a pandemic, the government might require the pharmaceutical industry to produce**
 - a. 150 million doses of vaccine
 - b. 200 million doses of vaccine
 - c. 260 million doses of vaccine
9. **Claire Howe felt that Congress would not rush to cover the liability that the pharmaceutical companies might encounter in creating massive doses of vaccine.**
True / False
10. **Flu vaccine is made mostly in industrialized nations such as the United States and Australia.**
True / False

Answers 1. b 2. True 3. True 4. False 5. c 6. True 7. True 8. c 9. True 10. True

<p>HEALTH ORDER DOOMS LODGE HALL COBWEBS</p>	<p>POLICE RAID SALOONS IN WAR ON INFLUENZA; KEEP CHURCH WINDOWS OPEN</p>	<p>'NONESSENTIAL' CROWDS BARRED IN EPIDEMIC WAR</p>
<p>Grip Ban on All Meetings Until Places Are Renovated; 21 Theaters Reopen.</p>	<p>Stringent New Orders Are Issued for Preventing Spread of Epidemic; Police Ambulances Are Drafted; 100,000 Doses of Vaccine on Way,</p>	<p>Churches and Saloons Exempt; Conventions, Athletics, Parties Hit.</p>
<p>GRIP VIGILANCE STILL NEEDED</p>	<p>1,613 NEW CASES SHOW DECREASE IN CITY; DOWNSTATE HIT WORST</p>	<p>FREE DOCTOR Influenza victims unable to pay for a doctor can obtain one by calling Main 447, Local 108, day or night.</p>
<p>Dr. Robertson Warns Against Relaxing Precaution, Despite Wane of Epidemic</p>	<p>FLU CURFEW TO SOUND FOR CITY SATURDAY NIGHT</p>	<p>CHURCH WINDOWS MUST STAY OPEN, SAYS ROBERTSON</p>
<p>'OPEN-FACE' SNEEZERS TO BE ARRESTED</p>	<p>Persons Not on Business Expected to Quit the Streets at 9 o'Clock.</p>	<p>Health Department Gives Out New Rules in Fight on Influenza.</p>
<p>Orders to arrest any person indulging in the "open face" sneeze or cough in</p>	<p>The curfew will ring or, rather, blow in Chicago tomorrow night. Promptly at 9 o'clock the whistles of</p>	<p></p>
<p>CHICAGO DEPT. OF HEALTH - CUT 400</p>		

Headlines from Chicago newspapers in 1918.



Laboratory workers in 1918 used high-speed centrifuges to separate organisms from broth cultures.

II. TEACHING APPROACHES

If your students need background about the Spanish flu, you can photocopy and distribute “The Enigma of the 1918 Influenza Pandemic” (pp. 3-10) for a historical context and Resource 2, “What We Now Know About the Influenza Virus” (pp. 127-133), for a virological and clinical perspective. (Of course, you will want to review all the Resources because you may also find that some of these are suitable handouts for general information or as support for an activity.) In general,

1. List the concepts you want to teach.
2. Select the case that you want to work with first.
3. Incorporate any activities.
4. Outline the direction (“pathway”) you want to take.
5. Plan your time.

You can cover a case and a related activity in a short time. But if you string together several activities, with time for lectures and discussion, you should plan your pathways and time carefully. If you intend to follow Cases 1 and 2 with Case 3, try to define how you will link the cases. (For example, you could link them in terms of past, present, and future.)

Peggy O’Neill Skinner, a biology teacher in Seattle, began one of her classes on the Spanish flu not with one of the cases but with an image: a photo from the 1918-19 pandemic that shows a man in a gauze mask holding what looks like an insecticide sprayer. (See cover photograph.) She showed this picture to students and asked: *What’s going on? When is this taking place? What is this man doing?*

The students inferred from the man’s clothing that he lived in the early twentieth century, but beyond that they were stumped. His mask looked medical, but the sprayer suggested that he was trying to kill insects. Insecticide is used for garden plants or crops, but this man was on a busy street. *Why is the street deserted? Where are the people?* The students all felt that the picture insinuated something “sinister and odd.”

At this point, with student interest already aroused, Skinner distributed the first case, “An Incident in Boston.” Students read it as homework and then, in class, Skinner walked them through it page by page.

We mention Skinner’s tactic of starting with the photo not because it is the best tactic, but because it worked for her. It demonstrates one of the great advantages of teaching with cases: *flexibility*. This flexibility allows you to adapt the material to the needs and interests of your students. The Spanish flu pandemic really happened and so historical material like the photograph Skinner used provokes a contemporary perspective and brings the Spanish flu and the issues it raises home to students.

Whatever teaching plan you make, be prepared to change it. The whole point of working with cases is to let your students’ curiosity and intellectual inclinations drive the instruction, within a plan that ensures that they absorb the core ideas.

Teaching With Cases

By Selma Wasserman

In the following brief academic scenario, you will find all the key components of case-method teaching.

FIFTH PERIOD, BIOLOGY 11

The afternoon is sunny and much too warm for October, but the students' attention remains riveted on the class discussion.

As homework for yesterday's class, Laurie Bick, the instructor, had assigned "Old Age Ain't for Sissies," a case by Selma Wasserman. It deals with the biological issues of aging. Key topics examined in this case included the normal aging process that occurs in all living things (such as changes in skin, hair, and muscles as well as loss of teeth, failing eyesight and hearing, chronic disease) and the variability of the process among individuals.

Laurie divided the class into small groups and gave each group the same list of discussion questions. These questions were open-ended, designed to promote an examination of issues rather than to lead students to single, correct answers. The first question asked students how the aging process affects living things. Students immediately became engaged. Differences in perspectives activated the discussions and were informed by students' experiences and background reading. Forty-five minutes of small-group discussion melted away like a popsicle on a summer afternoon.

Now, in today's session, Laurie calls for the groups to come together for a class discussion (or *debriefing*). During the small-group work, Laurie's role was that of a nonparticipant observer, but debriefing requires Laurie to play an active role in leading the discussion.

During debriefing, Laurie works with each student's ideas, helping each one to examine assumptions and to reason from data. She notes inconsistencies in thinking and differences in perspectives, bringing these under thoughtful examination. All of Laurie's questions and responses are respectful, without

judgment in word or tone, making the climate safe for any student to present his or her ideas. One goal of debriefing is to teach a student how to reason from data and how to assume responsibility for ideas. In this way, a student learns to think more intelligently about concepts, and so understanding grows.

The students spend this class time working with questions about chronic diseases associated with the elderly (such as arthritis and diabetes) and the vulnerability of the elderly to these diseases. The class entertains the question of why individuals age differently and discusses strategies used to retard aging and their effectiveness. Society's preoccupation with youth and the feelings of younger people about aging spark intense debate.

As Laurie continues the debriefing, more students volunteer their ideas and allow them to come under the scrutiny of Laurie's clarifying responses. The discussion is rarely less than intense. Student participation is extensive and the class remains highly engaged. When the bell sounds the end of Laurie's biology 11 class, no student makes a move for the door. There is still much more that the students want to say.

"We'll pick this up on Monday, everybody," says Laurie, collecting her notes from the desk. "Don't forget to do the Resource reading that I've assigned for this case. I think you'll find it very helpful background information."

Now let's look at some of the key components of case-method teaching:

- A case with a compelling narrative containing core curriculum concepts put under examination.
- Students engaged in discussions in which they examine issues and their own ideas.

- A teacher using questioning and responding skills to debrief the class, encouraging students to learn how to present their ideas cogently and how to reason from data.
- Follow-up work involving additional reading as well as gathering and examining additional data.
- More discussion.

Like peeling the layers of an onion, each stage of study brings a deeper and more intelligent examination of the core issues. Students come to a greater understanding of concepts by working through a case that demands active cognitive involvement in which they must construct their own meanings. In a case-method class, there is little likelihood of a disengaged student.

WHY CASE-METHOD TEACHING?

There are many ways to teach, and the extent and variety of curriculum material available for you to use in any subject area is staggering. Apart from textbooks, you might, for example, use stories from newspapers or magazines to enrich students' understanding of issues. Films, both documentary and commercial, are a rich source of content. Even novels find their way into courses other than English. Lectures, textbooks, and other sources provide depth and breadth of information about specific topics. Each method of teaching carries with it certain expectations about how to satisfy the goals of a curriculum.

In the past decade, a unique pedagogy has emerged from professional schools and found its way into secondary classrooms. Case-method teaching, used for over 60 years at Harvard Business School, is now applied in a variety of classes and schools. It has had considerable success in many subject areas, such as biology, social studies, economics, government, fine art, law, and journalism. Some secondary teachers have embraced case-method teaching as their primary mode of instruction. Others use it as a supplementary pedagogy. Whether primary or

supplementary, reports are consistent: Students enjoy learning with cases. Interest is high. Subject matter learning is enhanced. Case-method teaching helps students to

- Learn how to reason from data.
- Examine complicated issues more critically.
- Develop improved habits of thinking.
- Grow more interested in a subject and enjoy classes more.
- Extend their knowledge base.
- Develop motivation to read subject-related material outside of class.
- Respect each other's ideas.
- Improve their ability to make thoughtful and wise decisions.

As an instructional design, case-method teaching shifts emphasis from single, correct answers to open-ended problem solving, from offering solutions to raising dilemmas, from extensive teacher talk to student discussions and independent investigations, and from center-stage teaching to student initiatives that determine what questions the student should examine and why. In case-method teaching, the students construct their own meanings, based on their deepening and broadening experiences and guided by the teacher's skillful use of questions.

WHAT MAKES A GOOD CASE?

A case is to case-method teaching what yeast is to dough. It produces rising and fermenting. It creates a nourishing curriculum. While a case is a narrative, it is not just a story. It is a complex instrument constructed around issues that appear in the form of a narrative. The content can include information and data as well as psychological, scientific, and anthropological observations. It may also include technical material. While a case is linked to a

specific subject area, such as history, economics, government, biology, humanities, or art, it is interdisciplinary by its very nature. A good case illuminates “big ideas” (concepts that warrant serious study).

Good cases are written around “real-life” problems. Their narratives are compelling and immediately engage student interest. Good cases lead to good questions, such as these (from students):

What is it about viruses that make them so hard to cure?

Did Spanish flu kill people in their twenties because they were in the war?

How did people finally find out what was causing the flu?

Why did the pandemic go away without a cure?

Why can't doctors do some of the same things for AIDS or for cancer?

Not every case is a good case and in determining what is suitable for a particular class, you may find a few criteria helpful.

It's Relevant

A good case is relevant to the content of the course. It provides opportunities for students to study important issues in the curriculum. So before selecting a particular case, be sure that the issues raised in it are consistent with what is being studied.

It's Well Written

A good case is both interesting and well written. The writing should be engaging and provocative. If the case does not stimulate interest and motivate students to want to know more, it will have failed in its primary function.

It's Readable

A good case is readable. It should be appropriate to a student's level of understanding. Students who can decode, but whose experience with language limits their ability to com-

prehend the ideas, will not be able to discuss these ideas intelligently no matter how well the narrative is written. Conversely, if the content is too simplistic, students might not take the ideas seriously.

It's Exciting

A good case elevates feelings. It has the power to raise students' passions and to stir “emotional juices” about issues. This power sustains the desire to know more.

It Leaves Unresolved Issues

A good case ends with unresolved issues. A successful narrative presents a dilemma and leaves it unresolved. There is no “happy ending,” no closure, no simple solution. Cases that end with a resolution require no further thinking: students can put the issues at rest once the class is over. “Been there. Done that. Got the T-shirt for it.”

A narrative with unresolved issues is unsettling but essential to maintaining student interest and ongoing discussions. None of us can remain for long in a sea of uncertainty. We must wrestle with the issues until we have constructed our own meanings. This is a critical factor in helping a student to develop the habit of thinking, and it keeps the issues of a case alive long after the class is over.

It Realizes Objectives

A good case is a vehicle for realizing curriculum objectives. It enhances learning by providing important information about a subject while building critical thinking skills.

COMPOSING QUESTIONS

Like textbook material, cases are usually developed through study questions. However, instead of asking for recall of factual information, case questions require students to examine the important ideas, concepts, and issues relevant to the case. The way you frame questions should demand intelligent thinking about the issues. Don't be concerned with detail.

Good questions do not require students to come up with single “correct” answers.

Don’t be alarmed if you don’t know the answer to a student question. In case-method teaching, you are not expected to be the font of all knowledge. Case study encourages students to do their own research and investigation. A question such as *Why was the Spanish flu so much more deadly than ordinary flu?* still has no definite answer, even to top scientists in the field. But trying to answer it can increase your students’ ability to think.

Use questions that help students to see the complexity of issues and to understand that complex issues defy simplistic answers. The goal is to promote intelligent understanding of issues by encouraging students to use reliable data in constructing meanings. For example, a question such as *How do you explain how the flu spread so quickly?* is more effective than a question that asks *Can you give me three reasons that explain why the flu spread so quickly?* The first question asks students to generate hypotheses that must come from processing the data from their reading of the case. The second question is not well written because it explicitly instructs students to give reasons (that is, to come up with those reasons that the teacher might think of as “correct”).

WORKING WITH SMALL GROUPS

Teachers sometimes ask why small-group work precedes class debriefing. Why not proceed directly from reading a case to class engagement? What are the benefits of small groups?

Teachers who have been using cases for several years value small groups. In them, students have a chance to express their ideas in a safer context than in the more formidable class forum. The small group is an initial testing ground. It provides an opportunity for students to learn how to express themselves clearly, to accept responsibility for their statements, and to participate as a cooperative member of a discussion. Students who are less likely to volunteer

ideas in a full class are more easily able to talk in a group of three, four, or five. After all, learning to express thoughts develops the ability to express thoughts clearly and responsibly.

Critics of small groups suggest that these offer opportunities for students to “exchange ignorances,” and any observer of a case-study class will note that students may, in their first forays in a case, make outrageous or irresponsible statements and present these as facts. Yet, over time, and especially as a consequence of the teacher’s role in debriefing, students who have worked in small groups improve because they are held by their peers to give examples, to reason from the data, and to examine assumptions.

Small groups are as productive as the members of the group choose to make them. You can provide the following guidelines for your students. Ask them to

- Listen carefully to each other’s ideas and to treat all ideas respectfully.
- Work hard at trying to understand what is being said.
- Participate and offer ideas.
- Focus the discussion on the issues.
- Examine ideas instead of searching for correct answers.

Of course, communication skills do not improve overnight, but improvement is better assured with evaluation guidelines.

EXPLAIN EVALUATION

Students want to know how you are going to evaluate them, and it is helpful to make the criteria explicit before you begin small-group work. For example, tell students you are going to assess them on

- The quality of their contributions to discussions.
- Their ability to reason from data.

- The extent of their preparation.
- The nature of their participation.

In their follow-up work, tell students that they will be evaluated on the quality of their research. Since evaluation is invariably the “tail that wags the dog,” by making your criteria explicit, you will tilt both expectations and classroom climate in the direction of more productive student engagement.

During small-group work, you should observe the groups. To what extent are questions and issues intelligent? How does an individual student function within the group? Which student takes the initiative most of the time? Which student feels inhibited about speaking, even in a small group? Which student tends to dominate the discussion? Which student seems too eager to go along with what others have said or is reluctant to voice his or her own views? Note also which group seems to race through the questions, touching each only briefly, and with minimum analysis. Which group tends to go off topic, meandering through personal or anecdotal recollections? Data from observing groups at work will yield high returns when you want to know more about how your students think and how they function interpersonally. You can use this data in the evaluative process and to provide individual help.

DEBRIEFING DYNAMICS

If a case narrative is as yeast to dough, then the teacher’s ability to lead a case discussion is as the baker to the bread. Without the baker, there is no bread. Without debriefing, there is no case-method teaching.

In case-method teaching, the quality, texture, and content of discussion is significantly different from a teacher-dominated discourse. Instead of giving information, your role is to put important issues under intelligent scrutiny. Effectively done, debriefing promotes thoughtful reflections on the issues and builds good thinking habits. There are other important benefits. Because cases present dilemmas and

unresolved issues and because students have different perspectives, debriefing encourages students to learn more and motivates them to continue the cycle of investigation, reflection, and discussion.

For example, you can prepare debriefing questions in advance. Try to focus on the examination of the big ideas. Questions can follow a hierarchy: for example, move from the level of shared understanding of the data to more sophisticated questions that call for analysis of the data. Then move to evaluation based on criteria, to value issues that call for examination of personal beliefs and attitudes, and finally, to suggestions for action. In this way, students implicitly practice data gathering and analysis as a basis for determining values and action.

Try to limit your responses in discussions to the following categories: basic responses (that encourage reexamination of an idea), responses that call for analysis of an idea, and responses that challenge.

Basic Responses

These include paraphrasing an idea, interpreting an idea, or asking for more information. Basic responses are the core of interactions. You can use them as a way to help students articulate their ideas clearly, deepen their level of understanding, and take responsibility for their statements. Even as simple a response as “Tell me more” or “Help me to understand what you are saying” can elicit clarity from a student having difficulty in expressing his or her thoughts. Keep in mind that the basic response grounds the inquiry and allows for slow and studied examination of issues.

Responses That Call for Analysis

These responses ask for alternatives or for supporting data. They require students to function on higher cognitive levels. Therefore, use them less frequently than basic responses. Use them when you are satisfied that a student is ready to

“shift gears” from clarity of understanding to providing a rationale for that understanding.

Responses that call for analysis raise the ante in the interactive process and should never be aggressive to avoid making a student feel pressured to hold a certain point of view. These responses are not used to put a student on the spot. Use them to establish the realization that statements about issues require the examination of assumptions, the consideration of alternatives, and support with data. Even so, it is more helpful, for example, to respond with “I’d be more interested to hear about any assumptions you have made, Andrew” than with “What assumptions are you making, Andrew?”

Responses That Challenge

These call for the generation of new ideas. You can ask students to extend their thinking beyond firsthand statements into uncharted territory. These responses put students at the highest cognitive risk, and so use them sparingly during debriefing and intersperse them appropriately within the basic response pattern. Challenging responses include asking students to generate hypotheses, to interpret data, to identify criteria in making judgments, to apply principles to new situations, to make predictions about what is theoretically possible, to explain how a theory might be tested, and to create new and imaginative schemes.

Challenging responses are least used in debriefing. They provoke student anxiety. They shift the discourse into new territory and thus leave behind the preceding issues. Too many challenging responses can result in a dialogue in which no one issue gets adequate examination because the discussion shifts from issue to issue in a fragmented trail of ideas. Used inappropriately, challenging responses may stump students (especially those who are new to thinking about complex issues) and may frustrate them rather than inviting them to examine their ideas.

Debriefing is an artful combination of all three ways of responding. Remember, the im-

portant purpose is not to interrogate or lead students to particular answers or ways of thinking but to encourage serious discussions of the issues from increasingly informed perspectives.

Handling Unwanted Ideas

What happens when a student expresses an idea that is inappropriate or even repugnant? How can you respond in a way that makes it safe for students to continue to express their ideas without rejecting the inappropriate idea or sanctioning it?

Even in a classroom where ideas are welcome and open discussion is the rule, you may get one (or more) students who express opinions that are disturbing, incorrect, mean-spirited, or otherwise inappropriate. How should you respond? For example, how is it possible to maintain a climate of openness while not sanctioning the ideas of a racist? The answer is “not easily.” Try to remain neutral and, instead of arguing, request supporting evidence or examples or ask the student to tell the class how he or she came to that conclusion. Thus, the validity of the idea is put under public scrutiny. And that is the nature of the exercise. To do this without malice or manipulation is the skill.

Successful Debriefing

The secret of successful debriefing is this: always treat students and their ideas respectfully. That makes it safe for students to express their ideas. Your questions and responses give students something more to work with, taking them to new levels of understanding and keeping their attention riveted on the issues. When you are clear about the big ideas and when you are clear about how you are sequencing and phrasing your questions, you will be better able to help students construct meanings and come to a richer appreciation of the complexities and ambiguities of the case.

IS THERE LIFE AFTER DEBRIEFING?

What happens after debriefing? The answer depends on the students’ desire to know more.

Because the case does not provide “answers,” ambiguities are elevated and tension increased. So students want to know more.

Some cases, such as those in *The Spanish Flu*, come with a healthy list of activities and resources. These may include articles from newspapers and magazines, tables and charts with primary data, photographs, research reports, editorials, textbook references, and other written information. As previously noted, novels can provide rich and varied perspectives. Films, both commercial and documentary, are vital sources of information.

You can follow up a case in a variety of ways. You can incorporate activities into subsequent classroom sessions or assign them as out-of-class work. You can assign them to individuals or to small groups. Whatever follow-up activities you choose, their value is further enhanced by additional debriefing in order to create new perspectives for extended examination.

SUMMARY: THE CASE METHOD

The case method is an instructional design that incorporates the following components:

1. Small groups. These encourage students’ active engagement in the learning task. In small groups, students work cooperatively to carry out “minds-on” investigations of study questions that require a higher order of thinking. Students have greater control over their own learning, and this control increases their sense of personal power.

2. Debriefing. During debriefing, a teacher can use instructional strategies (teacher-student interactions) that increase students’ understanding of issues and teach them to reason from the data. Debriefing promotes thoughtful reflection on the issues and allows students to construct meanings.

3. Follow up: Activities and Resources. Increased motivation and interest in issues

drives further study. Students reexamine issues and expand background knowledge from a variety of activities and resources including supplementary texts, novels, films, journal articles, newspaper reports, and other related materials.

Peeling the Onion

Case-method teaching is also a cyclical instructional design. It evolves in complex spirals of inquiry in which ideas and issues undergo intensive, repeated scrutiny from different and new perspectives. From these, students construct meanings from data. It constantly challenges student thinking.

What Students Say

Comments, while they don’t tell the whole story, clearly indicate student enthusiasm for case-method teaching. Students claim that they are more actively involved in courses that use cases. Students say that they feel more responsible working together without teacher supervision. (There is little need to manage student behavior.) Students say that they are more interested in the issues and more willing to express opinions and to get involved in discussion and outside reading. Consequently, they are generally better prepared. Students say that they enjoy class more and suggest that this enjoyment improves grades. As some students put it:

I feel I can communicate more. When I first came into class, I was very shy and did not want to say anything because I was afraid of what the others would think of me. But now, if I have something to say, I say it.

Case study gives me an atmosphere and surroundings where I feel comfortable. This has increased my ability to communicate and understand other points of view.

I think that if all my classes were taught in the case method, I would have a very high GPA.

Using Cases in the Classroom

By Robert Seigman

The three cases in *The Spanish Flu and Its Legacy* are most appropriately used in a standard biology course associated with one of the following three areas.

1. An introduction to classic studies of diversity. This course begins with an examination of viruses and bacteria. The difficulties that physicians and scientists faced in determining the cause of the Spanish flu should stimulate students to examine the differences between viruses and bacteria. In addition, students will also be able to review the scientific process and Koch's Postulates.

2. The connection between genetics and evolution. The yearly changes in the strains of flu illustrate the practical problems caused by genetic evolution. In addition, this evolution is a good model of speciation and of the importance of mutations.

3. The functions of the immune system and how vaccines are constructed. Clearly, this area is a natural fit for explaining both the virulence of the Spanish flu and how we now try to prevent a recurrence of such a disaster.

Multiplicity of application is one of the strengths of using cases. Since you can use the same case to teach different topics, you do not have to use it in the same way each year. In fact, you should alter your presentation of a case in order to accommodate differences in classes and to prevent the case from becoming a rote exercise. Do not hesitate to modify questions or your presentation. After all, one of the advantages of the case method is its flexibility.

The cases in *The Spanish Flu and Its Legacy* are well-documented. This allows you to use a variety of approaches with a single tool. With some adaptations, you can work with relatively young students who have better than average reading skills. A higher reading level may be required for students to work with material in the Resources. However, even students with average reading skills should have no difficulty reading the cases, and with

some help, they should be able to work with the Resources. The projects that you can generate from the cases are very suitable for introductory science courses in advanced high school classes, community college classes, or even standard programs at the college level. The only limits are reading levels and the imagination of the instructor.

LINKING TO OTHER DISCIPLINES

The Spanish Flu cases also provide avenues for teachers to coordinate with their colleagues in other disciplines. For example, there are obvious connections to American and European history. For instance, *Why is this flu called the Spanish flu if it did not originate in Spain? How did World War I contribute to the spread of the flu and the number of deaths?* Other, less obvious, connections emerge from the political and economic aspects of the decisions associated with vaccine production.

The connections to other subject areas are numerous, and the material in the Resources has been collected with this in mind. Experience has shown that students develop better retention and a greater understanding of ideas when materials are connected over a range of academic areas. The connections tend to break down some of the natural compartmentalization that seems to prevent students from seeing the "real-world" relevance of what they are learning in school.

EXPANDING A CASE: THE IMMUNE SYSTEM

This example of case development illustrates how to expand a case study to cover topics that are not necessarily obvious from a cursory look. For example, after reading Case 3, "The Coming Pandemic," you can present students

with questions that lead into the topic of immunology. *How does the disease seem to function and what are its causes?* Most students will have made the connection between the Spanish flu and our current yearly exposure to a new flu. So at this point, you could ask questions about vaccines (what they are and how they work) to move the class into immunology. You could also assign readings about the immune system. Use the Resources.

Through an open discussion of the readings, all students can explore different aspects of the problems related to vaccine use and development as they apply to Asian flu strains. Or they can use information from the Centers for Disease Control (CDC) or the World Health Organization (WHO) to chart the prevalence of different flu strains in the past or present. Depending on the level of the class, students may discover the meaning of the code letters used to identify various strains of the flu virus. This can lead to an exploration of the connection between genes and proteins and, in turn, to the fact that the immune system responds to antigens, which are basically proteins.

Students usually want to know how another outbreak like the 1918 pandemic can be prevented, and so they will work to find some of the answers. By regulating the level of detail, you can use Case 3 in almost any situation, whether you are working with ninth graders or college students.

PREPARING TO TEACH A CASE

One key to using a case effectively is carefully judging the amount of time you have available to become familiar with the topic and the related activities and resources. After you have done that, you need to remember that the case is just a tool for presenting a problem in a way that will encourage students to want to know more about the issues. The real work begins after they have read a case and discussed it in a preliminary way, either in small groups or in a class session. From the discussions, students should be able to develop the issues they want to pursue.

Using Questions to Guide a Discussion

You can guide a discussion into issues that are of immediate interest to most students. For example, point out that the cases in *The Spanish Flu* illustrate why those who are young, old, or who have impaired immune systems make an annual pilgrimage to a physician or a local clinic to receive a shot of flu vaccine.

You can use questions to guide a discussion, but students, of course, will also provide questions of their own. You can respond to these in ways that continue to expand the discussion.

Ask students to track down answers to questions such as *What is a vaccine? How is a vaccine made and how does it work?* This kind of question helps students to become conversant with the differences between bacteria and viruses. They can even look into the biochemistry of viruses in order to learn how the different strains are identified. They can explore the economic issues associated with the production of vaccines. For example, *How do the pharmaceutical companies protect themselves from lawsuits when producing vaccines?*

Students can explore the relationship between genetics and evolution when answering the question, *Why is there a new vaccine each year?* Answers can lead to such practical questions as, *How does the CDC determine which strains to use to make a vaccine in a given year? Is it possible to produce enough vaccine in a relatively short time to protect all those who need to be protected?*

Questions also offer potential for a productive discussion of disease, vectors, and ecology. For example, *Why is a flu named after Asia? Did the historical period in which the Spanish flu developed contribute to its spread and high death rate? How many people actually died?*

The list of questions is long, although these are among the most common questions that students develop from reading the cases.

SHAPING A DISCUSSION

You need to be prepared to direct discussions because students will raise more questions

than can be reasonably answered within any introductory course in either high school or college. However, take care not to discourage the questioning process. It is the key to the success of using cases. Most of the questions raised by students also should be answered by students. If you force the questioning process, students will not explore answers as effectively as they might have otherwise, and their responses may become too directed.

Basic or complex questions can emerge at unexpected levels. You do not need to deal with basic factual questions at the beginning of a discussion. In fact, sometimes these are best reserved until after the students have identified more controversial issues. Then, these questions are helpful in order to verify student understanding of the underlying facts and ideas on which a case is based. More conceptual questions can play different roles. Use them to provoke discussion or to expose issues that have not been previously considered. Suggest them as debate topics for groups or as assessment questions for the end of the unit.

Good answers should be accurate, but they also should exhibit a recognition of tangential issues that impinge on the science. If a discussion inhibits students' natural curiosity, they will tend to focus only on the science and ignore other material. Instructors who have success with cases encourage students to make an investment in an answer. They give students the freedom to roam in finding that answer.

Try to alternate periods of independent work with class discussions. Two reasons for this are:

1. It is a good model for how the scientific process actually works.
2. It stimulates students to cooperate with each other.

Students will retain the information better if they discuss it, and they will develop self-confidence by learning how to find solutions for difficult problems by teaching one another.

PLANNING SUGGESTIONS

You need to make a few basic decisions.

First, where does this particular case work best for me, based on the material I need to cover this year? Most cases will generally fit into a couple of different concept areas in a typical introductory science course. The reason is obvious but worth making note of here. Cases present “real-world” science problems, and a science problem is rarely limited to one specific area. Although the cases fit best into a general biology program, you can use *The Spanish Flu* cases to teach aspects of virology, histology, and biochemistry. You can also relate the cases to issues in history, social studies, or mathematics.

Second, how much time can I invest in this topic? Most instructors feel pressed to cover either the prescribed or self-imposed curriculum, and using a case may seem like a major time investment. It depends on how much time you devote to the “coring” process (peeling away the layers of the topic to get at the core). It works this way: we begin with what we know. Then, in a spiral-like way, we “peel” away a layer and gain knowledge more focused on the answer to the original question. Eventually we arrive at an answer that seems to agree with the information that we have assembled. You can pace this process by the amount of information you provide versus the amount that students have to gather for themselves.

Time and Connections

Although extensive investigations, such as those in a few of the activities, are effective for student learning, they take time. So how extensive you let them become depends on the time available. Also, the nature of the questions you propose to the class determines the depth of student research and the time needed for it. On the other hand, all the research does not have to be done in class, and where connections can be made to other study areas, the time commitment can be shared. For example, what are history classes

doing that might relate to Case 2 when you are ready to present it? What other classes are students taking that could be tied into Case 3? Furthermore, it is not necessary for all of your students to be taking the same classes. Cases can generate connections to other classes and each student in those related classes becomes a unique focus for developing the material.

Defining Pathways

When planning, you need to develop an appropriate pathway. A pathway outlines the direction you want students to take in solving problems or answering questions. Compare time to material. On the pathway, determine the points at which it is most effective to provide information to students rather than having them search for it. The pathway will help you to define the best use of time. (For a more specific discussion of pathways, see page 47.)

Testing and Evaluation

The final step in planning is an assessment design that enables you to determine how well a student has understood the material. It forms the basis for a grade. Your design depends on how you used the case. Students also need to know what is expected of them in terms of evaluation.

Testing is always the most straightforward (but not always the best) way to measure achievement. However, students must know the basic concepts and testing is the simplest method to determine that. How well students can explain and apply concepts is easily measured by asking them to explain these concepts to each other verbally or to you in a written form.

If students have worked in small groups, the best assessment mechanisms are short oral reports with written papers that are slightly

more extensive. In their oral presentations, encourage students to be clever and dramatic as well as accurate. For example, you can assemble the papers from the presentations into a “class book.” Another possibility is to have the students put out a “newspaper,” with headlines and stories about emerging viruses. Teams could become experts on some aspect of a story while other students take the role of reporters who interview and write the story.

SUMMARY

The Spanish Flu cases provide a unique mechanism for encouraging students to search for knowledge. They can be fun, and they can be exciting, especially if information gathering has some competitive components with defined rewards for students (“Nobel prizes,” for example).

The cases also work effectively with classes that do not respond well to competition but perform better with cooperative goals. The range of students who will find these cases enjoyable is broad based. The only factor that really seems to limit participation is reading level, and you can compensate for this if you are the primary resource center.

Using cases for the first time is not easy because you must prepare. However, cases have inherent flexibility. Once you have mastered the information and conducted the class once or twice, you will have a broadly functional tool for learning.

Cases cannot supplant instructors, and they do not turn all students into investigators. However, cases give teachers a tool that is more exciting than standard classroom presentations. Their value lies in the challenges that they pose to students.

Pathways

What is a pathway? It is the general direction of your teaching plan. First list the concepts that you want your students to work with. These are the core ideas of your curriculum. Then select a case. Now you can outline a pathway to guide the development of the course work. Here are a few sample pathways keyed to *The Spanish Flu* cases.

Be sure to note that for all cases, the Activities (pp. 55-114) provide course enrichment and the Resources (pp. 115-188) provide background material that you can use to fill in information for yourself or for your class. Be sure to look through the Resources and note for reading assignments any selection that fits into your pathway and is suitable for the course level. You can also use the Planning Matrix (p. 49) as an organizing tool.

SAMPLE PATHWAY 1

Start with Case 1, “An Incident in Boston,” and then follow it with Case 2, “Around the World.”

1. Assign Case 1.
2. Devise one broad question that is suitable for small-group work. For example, for a beginning class, you might ask *What was the cause of Spanish flu?* For a more advanced class, you might ask *How would you find out the cause of Spanish flu?*
3. Select an activity that supports the question or expands the answers that you can anticipate from the class. For the question *How would you find out the cause of Spanish flu?* you might want the class to work with Activity 1, “Designing an Experiment.” If the question is *What could authorities have done to stop the spread of Spanish flu?* you could work with Activity 7, “Saving Communities.”
4. Separate the class into small groups and assign the question.
5. Assemble the groups for debriefing. Remember the importance of appropriate responses. (See pages 39-40.) Guide the discussion.
6. Assign Case 2.

SAMPLE PATHWAY 2

Start with Case 1, “An Incident in Boston,” and then follow it with Case 2, “Around the World.”

1. Assign Case 1.
2. Separate the class into small groups and assign Activity 1, “Designing an Experiment.”
3. Assemble the groups for debriefing.
4. Separate the class into small groups. Assign Activity 2, “Reviewing the Evidence.”
5. Assign Case 2.
6. Assemble the groups for debriefing and a discussion of Cases 1 and 2.
7. Work with the whole group in an exploration of Activity 8, “Unexpected Losses.”

SAMPLE PATHWAY 3

Start with any case or cases.

1. Assign the case(s).
2. Separate the class into small groups.
3. Assign each group a different activity. For example, assign one group the lab activities in Activity 4, “Investigating Microbes,” while the other groups work with Activity 1, “Designing an Experiment.” (The lab work informs students how to carry out the theoretical work.) Or you

might alternatively assign each group a different but related activity. For example, you could assign Activity 10, “Digging Into the Past,” to one group and Activity 7, “Saving Communities,” to another.

4. Ask each group to report to the class.

SAMPLE PATHWAY 4

If you prefer not to work with small groups or with the activities, assign a case and use it as

a basis for class discussion and individual projects.

If you have a large class but still want to concentrate on discussion rather than activities, focus primarily on questions. Ask students to provide questions and open the best of them to the class for discussion.

Keep a list of the good questions as a guide for discussions and potential assignments for small groups.

Using Activities, Resources, Matrix

The Activities and Resources sections support the cases. The activities are extensions from the cases and can broaden and intensify student efforts to understand the issues raised in the cases.

ACTIVITIES

The Spanish Flu and Its Legacy includes activities that range from designing an experiment to writing a case study. Each activity lists the case(s) and resource(s) most immediately related to it. However, you can relate the activities to cases in any way that fits into your course objectives.

Each activity also lists the learning objectives associated with that activity. (To review the activities from the point of view of these objectives, see pages 55-56 where they are listed for easy reference.) Following the list of objectives, most activities provide a suggested pathway for directing the activity. However, you should regard the pathways only as suggestions.

Some of the activities feature handouts for students. These provide the information that they will need for the activity. You can copy handouts before the class begins its work. (For an example of a handout, See Activity 4, “Investigating Microbes,” page 69.)

RESOURCES

The Spanish Flu and Its Legacy includes 10 important resources. For a brief summary of

the contents of each resource, see page 115. Skim through the summaries to get a sense of the extent of the information that the resources can provide.

You can also copy a resource and use it as a handout if you feel that a student will not have the time or ability to pursue his or her own research.

You may want to include “The Enigma of the 1918 Influenza Pandemic” (p. 3) as a resource. It provides an excellent background for students who are less familiar with the pandemic than you would like. It is superbly written, short, and yet complete.

PLANNING MATRIX

The matrix is a quick view of some of the broad relationships between the cases, activities, and resources.

You may find the matrix useful as a planning tool. For example, under the heading for the case you want to assign, check off the Activity (or activities) and Resource (or resources) that you select to support the case.

PLANNING MATRIX

Class _____

Activities	Case 1	Case 2	Case 3
1. Designing an Experiment			
2. Reviewing the Evidence			
3. Comparing Experiments			
4. Investigating Microbes			
5. What Causes Yogurtiness?			
6. What Was to Be Done?			
7. Saving Communities			
8. Unexpected Losses			
9. A Question of Ethics			
10. Digging Into the Past			
11. Putting It Into Numbers			
12. Literary Witnesses			
13. Writing Your Own Case			
14. More Ideas for Activities			
Resources			
1. Notes From the Pandemic			
2. What We Now Know About the Influenza Virus			
3. Immunology and the Influenza Virus			
4. Recovering a Killer			
5. Preparing for the Worst			
6. Lessons From the Swine Flu Episode			
7. Hearing Before House Committee on Appropriations			
8. Medical Reports From A.E.F in France and England			
9. Report of the Spanish Flu in India			
10. Using the Case in Postsecondary Education			

Background Readings and Internet Sources

BOOKS

Christensen, C. Roland. *Teaching and the Case Method.* Boston: Harvard Business School, 1987. Although developed and published by a member of the business school faculty, this book is directed to teachers in a wide range of disciplines. As well as containing actual teaching cases, its contributors address issues such as leading class discussions, questioning, and day-by-day management.

Crosby, Alfred W. *America's Forgotten Pandemic: The Influenza of 1918.* New York: Cambridge University Press, 1989. The definitive book on Spanish influenza for the general reader. It covers the social, political, and scientific progress of the 1918-19 influenza pandemic in a comprehensive and highly interesting fashion.

Garrett, Laurie. *The Coming Plague: Newly Emerging Diseases in a World Out of Balance.* New York: Farrar, Straus and Giroux, 1994. A mine of information on humanity's contemporary struggle against infectious diseases. Includes a discussion of the swine flu episode.

Hagen, Joel, Douglas Allchin, Fred Singer. *Doing Biology.* New York: HarperCollins, 1996. A set of case histories about the individuals responsible for many of the concepts that underlie our thinking in biology. Each case is accompanied by a set of questions that extends the concept or examines its implications for scientific thinking. Although these histories are not "case studies" as the term is used in this book, they contribute to the understanding of science as a human endeavor by placing scientific discoveries in a social context.

Henig, Robin M. *A Dancing Matrix.* New York: Vintage Books, 1993. Brings us up-to-date on scientific thought regarding the emergence of new viruses (and the reemergence of old ones). Very thorough and well written.

Karlen, Arno. *Man and Microbes: Disease and Plagues in History and Modern Times.* New York: Simon and Schuster, 1995. This book charts the age of epidemics. It summarizes the characteristics of new diseases and describes the conditions that may give rise to them. It contains excellent summaries of classic diseases such as polio and influenza, but it also gives a chilling projection of future diseases.

Levine, Arnold J. *Viruses.* New York: Scientific American Library, 1992. One of the most readable and authoritative introductions to virology, with a thorough discussion of the history, structure, and function of influenza A. Very good graphics and clearly written. A good reference.

Morse, Stephen S., ed. *Emerging Viruses.* New York: Oxford University Press, 1993. A collection of papers that had their origin in a conference, "Emerging Viruses: The Evolution of Viruses and Viral Diseases," that was held in 1989. The contributors are varied, with wide-ranging interests. They "try to elucidate some of the salient characteristics and underlying mechanisms for emerging diseases, and how these might inform strategies for their control." Both scientists and nonscientists are represented.

Nesse, Randolph M. and George C. Williams. *Why We Get Sick.* New York: Random House, 1996. This book gives a unique perspective on diseases. Using evolutionary explanations, it explores diseases such as allergies, cancer, Huntington's disease, and depression.

Oldstone, Michael B. A. *Viruses, Plagues, and History.* New York, Oxford: Oxford University Press, 1998. Virologist Michael Oldstone describes several viral challenges in historical context. The success stories of smallpox, yellow fever, measles, and polio are combined with more current diseases like lassa fever, AIDS, and ebola.

Radetsky, Peter. *The Invisible Invaders: Viruses and the Scientists Who Pursue Them.* Boston: Back Bay Books/Little, Brown and Co., 1994. Good popular account of the history of virus research. Accessible to students. Includes a chapter on Martinus Beijerinck's discovery of tobacco mosaic virus and a chapter on the influenza virus.

Silverstein, Arthur. *Pure Politics and Impure Science.* Baltimore: Johns Hopkins University Press, 1981. In 1976, the author, a biologist at Johns Hopkins, spent a sabbatical year advising the Senate Health Subcommittee. One of the results of his work is an informed and highly readable account of "what really happened during the swine flu affair of 1976."

van Hartesveldt, Fred R., ed. *The 1918-1919 Pandemic of Influenza.* Lewiston, N.Y.: Edwin Mellen, 1992. A set of case histories describing the impact of the pandemic in nine cities throughout the world. Good for detail.

Wasserman, Selma. *Introduction to Case Method Teaching.* New York: Teachers College Press, 1994. A practical guide to developing and using cases in classroom teaching.

The author includes many explicit suggestions for writing and choosing cases, teaching them, and evaluating students' progress. The book also includes a set of examples of cases and follow-up activities. It is an invaluable sourcebook for those who wish to widen their use of cases.

Zinsser, Hans. *Rats, Lice and History.* Boston: Little, Brown, 1934. This book is at times zany while it chronicles the disease of typhus. The author is witty and engaging. Experiencing a resurgence in readers, this book is a classic.

ARTICLES

Ewald, Paul. "On Darwin, Snow, and Deadly Disease," *Natural History Magazine* 103, no. 6 (June 1994): 42-45. Microbiology and evolu-

tion. A clear and interesting introduction to the theory of evolutionary microbiology.

Fincher, Jack. "America's Deadly Rendezvous with the 'Spanish Lady,'" *Smithsonian* 19 (Jan. 1989): 130-45. Readable, well-illustrated article on the Spanish influenza pandemic.

Gladwell, Malcolm. "The Dead Zone," *New Yorker* (Sept. 29, 1997): 52-65. Fascinating article on present-day attempts to recover genetic material from the 1918 flu virus.

Kolata, Gina. "Lethal Virus Comes Out of Hiding," *New York Times* (Feb. 24, 1998): F1, F5. Concise account of recovery of genetic material from the 1918 flu virus.

Scientific American. "Life, Death, and the Immune System" (Special Issue, Sept. 1993). A collection of articles by immunologists. The articles discuss general aspects of the immune system as well as how it functions in relation to specific diseases.

INTERNET Surveillance

The ability to control against influenza pandemics rests with an elaborate, worldwide monitoring system that tracks the disease and uses this information to determine yearly vaccinations. While its global hub is the World Health Organization (WHO) in Geneva, Switzerland, the Centers for Disease Control and Prevention (CDC) is its center in the United States.

WHO's *Statistical Information System* supplies reports on influenza activity worldwide. WHO's *Weekly Epidemiological Record* can be downloaded onto a hard disk. In addition, you can have the table of contents sent electronically on a weekly basis. You can also access country-by-country summary reports of individual strains of influenza. Students can organize these data and analyze their significance. They can use the data to track the global

spread of different types of virus throughout the year.

The Web address is

www.who.int/wer/

CDC's *Morbidity and Mortality Weekly Report* and the *Journal of Emerging Infectious Diseases* are available electronically. You can subscribe through the CDC Web site and the material will come to your e-mail address. The Web addresses are

www2.cdc.gov/mmwr/mmwr_wk.html
www.cdc.gov/ncidod/EID/index.htm

You can also obtain earlier reports that give information on the occurrences and morbidity of different strains from previous years.

Outbreak is a news service that gives up-to-date information on outbreaks of infectious diseases. It also contains a listserv that may be subscribed to for latest developments. The Web address is

www.outbreak.org/cgi-unregdynaserve.exe/index.html

General Background

Jack Brown's Site. Good, simple explanations of scientific microbiology terms.

falcon.cc.ukans.edu/~jbrown/

All the Virology on the WWW. There are excellent pictures of viruses here, as well as good sources for information about infectious diseases and vaccines.

www.tulane.edu/~dmsander/garryfavweb.html

EIINet (Emerging Infections Information Network) at Yale University is a global Web site for scientific research. It has transcribed a set of seminar lectures on disease along with the slides that were used in the presentations. In addition it has a highly selective but very useful set of related Web links.

info.med.yale.edu/EIINet/

ProMED is a project of the Federation of American Scientists to promote global monitoring of emerging diseases. Correspondents are continually reporting from throughout the world on incidents of infectious disease. Although not directly concerned with influenza, this site will give students a good understanding of the variety of diseases that humans must deal with on a worldwide basis. Included in this section is a paper that describes the rationale behind ProMED and discusses the importance of using the Internet to promote public awareness and control of disease.

www.fas.org/promed/#whatis

III. ACTIVITIES

The activities in *The Spanish Flu and Its Legacy* are ready for class use, but they also provide models for developing other activities built around objectives that can serve your core curriculum. Where necessary, you can use the activity handouts to make copies of information that students will need in working with an activity. You can also use the Planning Matrix (p. 49) to plot a pathway for teaching a case. The following list provides an overview of the learning objectives for the activities. (The objectives are also listed with each activity.)

Activity 1. Designing an Experiment

- To acquire problem-solving skills
- To increase understanding of the elements of the scientific method
- To reason and form conclusions from data

Activity 2. Reviewing the Evidence

- To critically analyze scientific evidence
- To define some of the difficulties involved in biological research

Activity 3. Comparing Experiments

- To compare student designs with known experiments
- To explore the reasons why the identity of the Spanish flu pathogen eluded scientists

Activity 4. Investigating Microbes

- To employ laboratory procedures
- To interpret data obtained from a biology experiment
- To use Koch's Postulates to determine the cause of a plant disease
- To reach a scientific conclusion from data and to defend that conclusion
- To distinguish between a bacterial and viral infection

Activity 5. What Causes Yogurtiness?

- To use Koch's Postulates to find a causative agent for disease
- To practice microbial techniques
- To design a controlled experiment
- To reach a scientific conclusion from data and to defend that conclusion

Activity 6. What Was to Be Done?

- To examine the impact of disease on other sectors of society
- To link case studies to other disciplines
- To demonstrate the global effect of a pandemic
- To highlight the progress in disease research

Activity 7. Saving Communities

- To examine the impact of disease on public health policy
- To demonstrate the global effect of a pandemic
- To highlight progress in disease control

Activity 8. Unexpected Losses

- To evaluate medical information derived from insurance data
- To demonstrate the social and economic consequences of the pandemic
- To highlight the role of interdisciplinary links in research

Activity 9. A Question of Ethics

- To explore ethical issues associated with experiments on human subjects
- To define some of the difficulties in recruiting subjects for experimentation
- To stress the role of medical ethics in a public health context

Activity 10. Digging Into the Past

- To conduct historical research from a medical perspective
- To explore the links between medical events and current events
- To stress the human consequences of medical events

Activity 11. Putting It Into Numbers

- To explore the value of medical statistics
- To acquire research skills in the area of epidemiology
- To demonstrate the advances in medical documentation

Activity 12. Literary Witnesses

- To explore the human and emotional impact of disease
- To highlight interdisciplinary links in research: literature, history, and science

Activity 13. Writing Your Own Case

- To construct a narrative that conforms to the standards of a good case
- To work from a given situation into a case situation

Activity 14. Ideas for More Activities

- To establish the framework for additional activities

Activity 1. Designing an Experiment

Case 1

Resources 1, 7-9

Objectives

- To acquire problem-solving skills
- To increase understanding of the elements of the scientific method, including hypothesis, observation, and control
- To reason and form conclusions from data

Historical Background

In 1918, scientists could culture bacteria, but they could not culture viruses outside of an infected living body. They had no reliable animal model for influenza. There was no animal known to “come down with flu” in the same way people did. They had the same difficulties then as we have now in experimenting with people—the ethics involved in obtaining consent and the inability to control where people had been and so whether or not they had already exposed themselves to the disease in question.

Scientists could sterilize laboratory equipment through heat and chemicals, but they had no antibiotics to control bacterial contamination once an experiment was underway. They could use porcelain bacteriological filters to filter out bacteria and isolate viruses, but they had no means to see the viruses. Microscopes of the day were too weak. (Electron microscopes, which are powerful enough, had not yet been invented.) The structure and functioning of viruses was a mystery, although some scientists had made guesses in the right direction.

Describe these restrictions to your students. Or if there is time, have them find these restrictions out for themselves. Send them to the library and the Internet to discover what was known about influenza in 1918.

Suggested Pathway

1. Assign Case 1, “An Incident in Boston.” After the class has read and discussed the

case, ask the students to imagine that each of them is a scientist in 1918 with no greater knowledge or technology than that available to J. J. Keegan. Ask, *How would you design an experiment to find out what causes Spanish flu?*

2. Break the class into small groups. Ask each group to write a report answering the question. If you want to phrase the assignment more formally, try this: “Form and describe a hypothesis about the causative agent of the Spanish influenza. Design a controlled experiment to test the hypothesis, using only the equipment and information available in 1918. State what you predict the outcome would be and explain how that outcome would support your hypothesis. Write a report on your experimental design and predicted outcome and present it orally to the class.”
3. Ask each group to present its report to the class. In debriefing, encourage students to query the reports and point out omissions or false assumptions in experimental designs.

Some students may disagree with each other about the hypotheses themselves. This gives you a chance to help them appreciate the uncomfortable fact that only data can settle empirical questions. By the end of this activity, students will have learned much about how scientists solve problems, but they will not

have examined actual data about what causes influenza. They will do this in Activity 2, “Reviewing the Evidence.”

Variation: Write a Funding Report

Ask each group to imagine that it is writing a research proposal for funding an experiment. Explain that the class will review the proposals and then vote on the merits of each one.

This activity gives you an opportunity to discuss what qualities go into good proposals as well as good experimental design. (Note that well-designed proposals get funding; poorly designed proposals don't.) You can even have the group establish a budget for its experiment. The group can entertain issues such as

Should we try to fund three small-scale laboratory experiments testing three different hypotheses or one expensive, large-scale experiment pursuing only the hypothesis that seems most promising?

During debriefing, considering this issue will give the class a chance to discuss the economic and social factors that affect how science gets done.

Also during debriefing, you could have the class play the role of a grant-making body deciding which proposals are worthy of funding. As individual assignments, you could ask each student to write a paper explaining which proposal was most worthy of funding.

Activity 2. Reviewing the Evidence

Case 1

Resources 1, 7-9

Objectives

- To critically analyze scientific evidence
- To define some of the difficulties involved in biological research

4 Handouts

- Pfeiffer's Bacillus (pp. 60-61)
- Filterable Virus (pp. 62-63)
- Pneumococcus, Streptococcus, and Staphylococcus (p. 64)
- Bacterium pneumosintes (p. 65)

Suggested Pathway

1. Assign Case 1, "An Incident in Boston."
2. In class discussion, review carefully the hypotheses suggested at the conference headed by Milton J. Rosenau at the Chelsea Naval Hospital (p. 14). The hypotheses proposed that the cause of the Spanish flu was Pfeiffer's bacillus, a filterable virus, pneumococcus (or streptococcus or staphylococcus) or a bacterium. Let the class discuss these briefly in order to clear away any simple confusion. Tell the class that scientists, including Rosenau, Keegan, and Goodpasture, tested these hypotheses during the pandemic. Then tell the class that you want them to review some of their findings.
3. Break the class into small groups. Ask each group to become an expert on one of the hypotheses proposed at the conference. The studies they will use for their research are included in the handouts for this activity. Each handout is named for a hypothesis. (Assign each group as few or as many hypotheses as seems appropriate for the time you want them to spend on this activity.)
4. Ask each group to write a report and to

prepare an oral presentation that answers the questions *What does the evidence show? Does the evidence adequately support the hypothesis? Do you have any questions or criticisms about the researcher's assumptions, methods, execution, or conclusions?*

5. During debriefing, encourage the class to ask questions and to give opinions. You could ask them to imagine that they are attendees at a scientific convention reviewing results and trying to decide which kinds of further research would be most productive.

If the students have previously worked with Activity 1, "Designing an Experiment," let the fit or nonfit between their predicted outcomes and the scientists' actual results become part of the discussion.

Note that the studies referred to in the handouts are a summary of evidence on the cause of Spanish influenza as collected by scientists during the Spanish flu pandemic. The descriptions are based on accounts in Alfred W. Crosby, *America's Forgotten Pandemic: The Influenza of 1918* (New York: Cambridge University Press, 1989). You can find a more concise summary of a few selected studies in Resource 1, "Notes From the Pandemic" (p. 117).

■ Pfeiffer's Bacillus

The following studies from 1918 to 1920 were relevant to the hypothesis that Pfeiffer's bacillus caused Spanish influenza. Note that Pfeiffer's bacillus is difficult to grow in the laboratory. Great care must be taken in preparing the medium. Cultures can easily become contaminated and overwhelmed by other microbes, such as streptococcus and pneumococcus. These are often found in the same respiratory systems with Pfeiffer's bacillus and can inhibit its growth. The studies are listed in alphabetical order by principal investigator. Full references follow each summary.

1. Russell L. Cecil, Francis G. Blake

Cecil and Blake noted that some experimenters had difficulty transmitting influenza through inoculation with Pfeiffer's bacillus cultured in pure form. Cecil and Blake hypothesized that Pfeiffer's bacillus best kept its virulence within a living body. As described in their article published in 1920, they obtained a sample of Pfeiffer's bacillus from a flu patient and inoculated a mouse with it. After recovering a sample of bacillus from the mouse, they passed it serially through 10 more mice. The first 10 mice survived, but the eleventh died. They passed a sample from the dead mouse through a series of 13 monkeys. The monkeys became ill. On autopsy, they showed lung lesions similar to those seen in human influenza.

Cecil, Russell L., and Francis G. Blake. 1920. "Pathology of Experimental Influenza and a Bacillus Influenza Pneumonia in Monkeys." *Journal of Experimental Medicine* 32: 719-44.

2. J. J. Keegan, Ernest W. Goodpasture, et al.

Researchers in many places in 1918 searched for Pfeiffer's bacillus in Spanish influenza victims—in the secretions of living ones and in the cadavers of dead ones. Their results varied. According to J. J. Keegan, 80 percent of the autopsies of the first cases at Chelsea Naval Hospital near Boston revealed the presence of Pfeiffer's bacillus. The same microbe was found in cultures taken from flu sufferers in many other pandemic locations, including Camp Devens, Massachusetts. But in studies of 32 cadavers at Chelsea Naval Hospital from September 1918 to January 1919, Keegan's colleague Ernest W. Goodpasture found that

either pneumococcus or streptococcus was dominant in the lungs, and that in many cases Pfeiffer's bacillus was entirely absent. Similar reports came from other locations, such as Cook County Hospital, Chicago, where researchers in September and October discovered Pfeiffer's bacillus in only 8.7 percent of cultures taken from patients.

Keegan, J. J. 1918. "The Prevailing Pandemic of Influenza." *Journal of the American Medical Association* 71 (Sept. 28): 1053; Goodpasture, Ernest W. 1919. "Broncho-pneumonia Due to Hemolytic Streptococci Following Influenza." *Journal of the American Medical Association* 72 (March 8): 724-25; Jordan, Edwin O. 1927. *Epidemic Influenza: A Survey*. Chicago: American Medical Association: 391; "Influenza Discussions." 1919. *American Journal of Public Health*: 9 (Feb.): 134.

3. H. B. Maitland, Mary L. Cowan, H. K. Detweiler

After 1918, researchers continued to obtain contradictory results as to the presence of Pfeiffer's bacillus in the bodies of flu sufferers. In England during 1919, Pfeiffer's bacillus was discovered in almost every case of Spanish influenza from which a culture was taken. But in Toronto, Canada, in 1920, it was found in only 24 percent of cases.

Maitland, H. B., Mary L. Cowan, and H. K. Detweiler. 1920. "The Etiology of Epidemic Influenza: Experiments in Search of a Filter-Passing Virus." *British Journal of Experimental Pathology* 1 (6): 262.

4. Eugene L. Opie, Francis G. Blake, James C. Small, Thomas M. Rivers

At Camp Pike, Arkansas, in fall 1918, Opie, Blake, Small, and Rivers searched for Pfeiffer's bacillus in cultures taken from the

throat and nose secretions and sputum of 23 Spanish flu sufferers. The bacillus was found in all 23 cases (although in some cases, not until more than one culture had been taken). When monkeys were inoculated with the bacillus, they developed an illness similar to flu in humans.

Opie, Eugene L., Francis G. Blake, James C. Small, and Thomas M. Rivers. 1921. *Epidemic Respiratory Disease*. St. Louis: C. V. Mosby Co.: 25-26, 30, 43, 49.

5. W. H. Park, A. W. Williams,

Alexander Fleming, Francis J. Clemenger

In 1918-19, two teams of researchers investigated whether the same or different strains of Pfeiffer's bacillus were present in populations of flu sufferers in Britain and the United States. If Spanish influenza were caused by Pfeiffer's bacillus, they predicted that most of the samples collected would belong to one strain or lineage of descent (since it was likely that only one distinctive strain, not many, was responsible for the unique characteristics of Spanish influenza).

After testing specimens of Pfeiffer's bacillus from numerous cases on both sides of the Atlantic, the researchers found that the strains were much more likely to be different than to be the same. In one experiment by Park, nine samples of the bacillus from nine different autopsies proved to represent nine different strains.

Park, W. H., and A. W. Williams. 1919. "Studies on the Etiology of the Pandemic of 1918." *American Journal of Public Health* 9 (Jan.): 49; Park, 1919. "Bacteriology of the Recent Pandemic of Influenza and Complicating Infection." *Journal of the American Medical Association* 73 (Aug. 2): 321; Fleming, Alexander, and Francis J. Clemenger. 1919. "Specificity of the Agglutins Produced by Pfeiffer's Bacillus." *Lancet* 197 (Nov. 15): 871.

6. Julia T. Parker

As she reported in 1919, Parker cultured five strains of Pfeiffer's bacillus from the sputum of patients suffering from influenza pneumonia. After passing each pure strain through a bacteriological filter, she inoculated rabbits with the bacteria-free fluid. The rabbits died. Parker

concluded that Pfeiffer's bacillus produced a filterable toxin, or poison, that killed the animals.

Parker, Julia T. 1919. "A Filterable Poison Produced by B. Influenza (Pfeiffer)." *Journal of the American Medical Association* 72 (Feb. 15): 476-77.

7. Milton J. Rosenau

Rosenau investigated the way Spanish influenza was transmitted, along with the hypothesis that Pfeiffer's bacillus caused the disease. In November-December 1918, he recruited 68 sailors from the Deer Island Training Station near Boston. Spanish influenza had been epidemic at Deer Island in September and October, but 39 of the 68 men had no recorded history of having suffered the illness. Many were prisoners who had been promised pardons for cooperating.

To minimize contact with the outside world, Rosenau housed the volunteers in the Quarantine Station on Gallups Island in Boston Harbor. He inoculated them with material from Spanish flu patients, including respiratory tract secretions and blood. To test the theory that the pathogen was Pfeiffer's bacillus, Rosenau inoculated some men with strains of the bacillus, some of which had been collected from the lungs of patients recently killed by flu. During the several days of observation that followed, not one volunteer inoculated with any material developed signs of flu.

Rosenau reasoned that Spanish influenza might be more easily transmitted under conditions that resembled normal human contact between the sick and the well. He brought 10 of the men to the influenza wards at Chelsea Naval Hospital. The volunteers got as close to the sick as they would under normal street conditions: sitting close, breathing their exhalations and coughs, shaking their hands. One man got a mild respiratory ailment that was probably not influenza. The nine others developed no disease symptoms at all.

Rosenau, Milton J. 1919. "Experiments to Determine Mode of Spread of Influenza." *Journal of the American Medical Association* 73 (Aug. 2): 312-13.

■ Filterable Virus

The following studies from 1918 to 1920 were relevant to the hypothesis that a filterable virus caused Spanish influenza. The studies are listed in alphabetical order by principal investigator. Full references follow each summary.

1. John R. Bradford, E. F. Bashford, J. A. Wilson

Working in France from June 1918 to February 1919, the British team filtered sputum from influenza patients and cultivated what they considered a pure culture of the filterable virus. They inoculated the filtrate into some animals and the pure culture into others. Their 20 animals included guinea pigs, rabbits, and monkeys. Nineteen of the 20 animals developed lesions in the lungs, liver, kidneys, and heart similar to influenza, regardless of whether they were inoculated with the filtrate or the pure culture. The filterable virus was recovered from the lesions.

After their findings were published in April 1919, J. A. Arkwright, a researcher, attempted to reproduce Wilson's methods of "cultivating" filtrate. He reported in August that the supposedly "pure" virus culture he obtained was contaminated with the bacteria staphylococci. Arkwright also discovered staphylococci in tubes of "pure" virus culture submitted to him by Wilson.

Bradford, John R., E. F. Bashford, and J. A. Wilson. 1919. "The Filter-Passing Virus of Influenza." *Quarterly Journal of Medicine* 12 (April): 259-60, 267, 273, 277, 298; Arkwright, J. A. 1919. "A Criticism of Certain Recent Claims to Have Discovered and Cultivated the Filter-Passing Virus of Trench Fever and of Influenza." *British Medical Journal* 2 (Aug. 23): 233-37.

2. H. Grame Gibson, F. B. Bowman, J. I. Connor

A team of British, Canadian, and Australian researchers, working in France during the pandemic, passed human influenza sputum through a bacteriological filter. They introduced filtered sputum into the noses of various kinds of animals (guinea pigs, monkeys, rabbits, and baboons). As a control, they

introduced unfiltered sputum into the noses of other animals. Animals in both groups showed mild symptoms of illness (such as prostration and bristling of fur), although none developed fevers. Whether the material introduced was filtered or unfiltered, the animals, upon autopsy, were found to have developed lung lesions similar to those caused by flu.

Gibson, H. Grame, F. B. Bowman, and J. I. Connor. 1918. "The Etiology of Influenza: A Filterable Virus as the Cause." *Medical Research Committee Special Report No. 36. Studies of Influenza in Hospitals of the British Armies in France, 1918*: 19-36; 1918. "A Filterable Virus as the Cause of the Early Stage of the Present Epidemic of Influenza." *British Medical Journal* 2 (Dec. 14): 645-46.

3. J. J. Keegan

Working with Milton J. Rosenau in September 1918, J. J. Keegan tested the hypothesis that Spanish influenza was caused by a filterable virus. Nine sailors from the Deer Island Training Station near Boston (men who as yet had no record of catching the Spanish flu) volunteered to take part.

Keegan collected secretions from the throats and noses of two flu patients. He passed the secretions through a bacteriological filter and dripped the resulting filtrate into the noses of the healthy volunteers. During a 10-day period of observation, the men developed no symptoms of flu.

Keegan, J. J. 1918. *Journal of the American Medical Association* 71 (Sept. 28): 1055.

4. H. B. Maitland, Mary L. Cowan, H. K. Detweiler

The British team inoculated some animals with filtrates of human flu secretions; other animals were not inoculated. The researchers

did not find conclusive evidence that the filtrates caused influenza in the animals.

Maitland, H. B., Mary L. Cowan, and H. K. Detweiler. 1920. "The Etiology of Epidemic Influenza: Experiments in Search of a Filter-Passing Virus." *British Journal of Experimental Pathology* 1 (No. 6): 262.

5. Charles Nicolle, Charles Le Bailly, D. Thomson, R. Thomson

In 1918-19, the two French researchers injected monkeys with filtrate of human flu secretions. Flu-like symptoms resulted. They also inoculated the eyes and noses of monkeys with filtrate. Again, flu-like symptoms resulted.

The researchers tried injecting flu filtrate under the skin (subcutaneously) of one human volunteer and into the vein (intravenously) of another. The subject who received the subcutaneous injection developed mild symptoms of influenza. The subject who received the intravenous injection developed no symptoms.

Nicolle, Charles, and Charles Le Bailly. 1919. "Recherches Experimentales sur la Grippe." *Annales de l'Institut Pasteur* 33: 395-402; Thomson, D., and R. Thomson. 1933 and 1934. "Influenza." Monograph No. 16. *Annals of Picket-Thomson Research Laboratory*. London: Bailliere, Tindall, and Cox 9: 603-5.

6. Julia T. Parker

As she reported in 1919, Parker cultured five strains of Pfeiffer's bacillus from the sputum of patients suffering from influenza pneumonia. After passing each pure strain through a bacteriological filter, she inoculated rabbits with the bacteria-free fluid. The rabbits died. Parker concluded that Pfeiffer's bacillus produced a deadly filterable toxin, or poison.

Parker, Julia T. 1919. "A Filterable Poison Produced by B. Influenza (Pfeiffer)." *Journal of the American Medical Association* 72 (Feb. 15): 476-77.

7. Dugarric de la Rivière, R.

In 1918, the French scientist inoculated human subjects subcutaneously with filtered flu secretions. Flu-like symptoms developed.

Dugarric de la Rivière, R. 1918. "La Grippe Est-Elle un Maladie à Virus Filtrant?" *Académie des Sciences* 167: 606.

8. D. Thomson, R. Thomson

During the pandemic, a German researcher (Selter) sprayed his own throat and those of his assistants with a filtrate of human flu secretion. Symptoms resembling influenza developed.

Thomson D., and R. Thomson, *Annals of Picket-Thomson Research Laboratory* 9: 603-5; 1918. *Journal of the American Medical Association* 71 (Nov. 9): 1577.

9. T. Yamanouchi, K. Skakami, S. Iwashima

From December 1918 to March 1919, Japanese researchers tried several different experiments. They introduced filtrate of flu sputum into the noses and throats of 12 healthy people. They introduced filtrate of blood from flu sufferers into the noses and throats of six more healthy people. They injected filtrate of flu sputum subcutaneously into four healthy people. To provide a control, the investigators introduced pure cultures of Pfeiffer's bacillus and mixed cultures of various microbes, including Pfeiffer's bacillus, pneumococcus, staphylococcus, and streptococcus, into the noses and throats of 14 healthy people.

Of the subjects who had not already had a recorded case of flu, 100 percent of those who received filtrates of any flu material developed influenza. Of the people in the control group, zero percent developed any kind of sickness.

Yamanouchi, T., K. Skakami, and S. Iwashima. 1919. "The Infecting Agent in Influenza." *Lancet* 196 (June 7): 971.

■ Pneumococcus, Streptococcus, Staphylococcus

The following studies from 1918 to 1920 were relevant to the hypothesis that pneumococcus, streptococcus, or staphylococcus caused Spanish influenza. The studies are listed in alphabetical order by principal investigator. Full references follow each summary.

1. Ernest W. Goodpasture, et al.

Numerous investigators in many locations in 1918-19 discovered that pneumococcus, streptococcus, and/or staphylococcus were often, although not always, present in the respiratory tracts of Spanish influenza patients. Sometimes one of these varieties of bacteria dominated a particular location; sometimes another. Sometimes none of them.

In a study of 16 cadavers of flu victims at Chelsea Naval Hospital near Boston from September to November 1918, Ernest W. Goodpasture found pneumococcus dominant in the lungs of all the victims. In some cases he collected pneumococcus in pure culture. In a similar study in December 1918 and January 1919, he found streptococcus dominant in the lungs of all 16 cadavers, sometimes in pure culture.

In a 1918 study at Camp Meade, Maryland, streptococcus was found in 87 percent of cultures taken from 110 influenza patients. However, in other locations, in other populations of flu patients, streptococci were not found at all.

In 1918, researchers in Chicago often found streptococci in the respiratory tracts of flu patients. But in 1920, during another influenza outbreak in the same city, the same researchers were unable to find streptococci.

Goodpasture, Ernest W. 1919. "Broncho-pneumonia Due to Hemolytic Streptococci Following Influenza." *Journal of the American Medical Association* 72 (March 8): 724-25; Jordan, Edwin O. 1927. *Epidemic Influenza: A Survey*. Chicago: American Medical Association, 419, 423.

2. Edward C. Rosenow, B. F. Sturdivant, et al.

The American researcher Rosenow collected samples of streptococcus from flu patients from 1918 to 1920. By injecting the streptococci into guinea pigs, he produced symptoms and lesions he described as similar to those found in human flu patients.

Other researchers tried but were unable to duplicate Rosenow's results definitively. Similar attempts to cause influenza by injecting human volunteers or animal subjects with either pneumococcus or staphylococcus were also unsuccessful.

Rosenow, Edward C., and B. F. Sturdivant. 1919. "Studies in Influenza and Pneumonia, IV." *Journal of the American Medical Association* 73 (Aug. 9): 396-401; Rosenow, E. C. 1920. "Studies in Influenza and Pneumonia, V." *Journal of Infectious Disease* 26 (June): 478, 485-86; Jordan, Edwin O. *Epidemic Influenza*, 423; Thomson, D., and R. Thomson. 1933 and 1934. "Influenza." Monograph No. 16. *Annals of Picket-Thomson Research Laboratory*. London: Bailliere, Tindall, and Cox 9: 531, 575.

■ Bacterium Pneumosintes

The following studies from 1918-20 were relevant to the hypothesis that *Bacterium pneumosintes* caused Spanish influenza. The studies are listed in alphabetical order by principal investigator. Full references follow each summary.

Bacterium pneumosintes (now known as *Dialister pneumosintes*) is small enough to pass through filters that screen out most other bacteria. It was found in some flu patients, though it was notoriously difficult to culture in the lab.

1. Peter K. Olitsky, Frederick L. Gates

Having developed methods of culturing *Bacterium pneumosintes*, Olitsky and Gates carried out studies of the microbe from 1918 to 1923. They injected samples of the bacteria into the tracheae of rabbits and guinea pigs. The animals became ill, and autopsies showed lesions in the lungs similar to those of human influenza. Olitsky and Gates were able to collect *Bacterium pneumosintes* from the dead animals' lungs.

In 1920, British researchers H. B. Maitland, Mary L. Cowan, and H. K. Detweiler reported results that bore on the claims of Olitsky and Gates. Maitland and collaborators inoculated one group of animals with filtrates of human flu secretions; another group was not inoculated. The researchers found that if they killed an animal by the Olitsky-Gates method of striking it on the back of the head, the animal's heart would keep beating for several minutes, producing lesions in the lungs like those that Olitsky and Gates had observed. The animals developed these lesions regardless of whether or not they were inoculated with flu filtrate. If they killed the

animals by cutting into the hearts, no lung lesions were visible, regardless of whether the animals had been inoculated.

Olitsky, Peter K., and Frederick L. Gates. 1921. "Experimental Studies of the Nasopharyngeal Secretions from Influenza Patients." *Journal of Experimental Medicine* 33 (June 1): 713-28; Maitland, H. B., Mary L. Cowan, and H. K. Detweiler. 1920. "The Etiology of Epidemic Influenza: Experiments in Search of a Filter-Passing Virus." *British Journal of Experimental Pathology* 1 (6): 263-68; 1921. "Spontaneous and Artificial Pulmonary Lesions in Guinea Pigs, Rabbits and Mice." *British Journal of Experimental Pathology* 2 (Feb.): 8-15.

2. Assorted Studies

A study in England failed to produce conclusive cases of influenza when *Bacterium pneumosintes* was introduced to human subjects. In Germany, a researcher sprayed his own throat with a sample of *Bacterium pneumosintes*, but did not develop influenza.

Thomson, D., and R. Thomson. 1933 and 1934. "Influenza." Monograph No. 16. *Annals of Picket-Thomson Research Laboratory*. London: Bailliere, Tindall, and Cox 9: 583-84.

Activity 3. Comparing Experiments

Cases 1-2

Resources 1-2, 8

Objectives

- To compare student designs with known experiments
- To explore the reasons why the identity of the Spanish flu pathogen eluded scientists

Suggested Pathway

This activity is a follow-up to Activities 1 and 2. Students should have completed both of those activities before attempting Activity 3.

1. Have your students assemble in the same groups as in Activity 1, “Designing an Experiment” (p. 57). Each group will now focus on the hypothesis that it worked with in Activity 1.
2. Ask each group to compare the experiment that it designed against the actual research conducted by scientists.
3. Have each group prepare a written report and an oral presentation that address the following questions.

What does the evidence show?

What are the similarities or differences between your proposed experiment and the experiments described by the scientists?

Do the scientists’ findings match or contradict the results you would have predicted?

Do you have any questions or criticisms concerning the researchers’ assumptions, methods, execution, or conclusions?

Most likely, students will be perplexed by the contradictory evidence gathered by scientists during the pandemic. Allow students to express their confusion. Let them know that scientists at the time experienced the same confusion. Discuss the reasons why the Spanish flu pathogen was so hard to pin down.

For example,

- Lung lesions and symptoms caused by influenza are similar to those caused by other respiratory illnesses. (In one instance, lung lesions similar to influenza could have been caused by the way the scientist killed the test animal for the autopsy.)
- In the days before antibiotics, cultures considered pure were easily contaminated by other microbes.
- Scientists at the time knew of no animals besides humans that could definitively be said to contract influenza.
- Humans are unreliable “lab animals.” Their whereabouts and contacts prior to an experiment cannot be known with certainty. So it is always possible they have already had a mild or asymptomatic case of the disease being studied, thereby acquiring immunity. This risk is especially high during a pandemic, when nearly everyone is exposed.

Summary

By the end of Activities 1 to 3, students will have learned firsthand how scientists go about solving problems. They will have learned a great deal about how to analyze scientific evidence. They will also have learned that conclusions do not always follow easily from evidence.

Science does not always find an answer. Knowledge accumulates slowly, with many false steps, and sometimes the race to save lives is lost.

Activity 4. Investigating Microbes

By Peter Garik with Eric Neumann and Mary Evilsizer

Cases 1-2

Resource 1

Objectives

- To employ laboratory procedures
- To interpret data obtained from a biology experiment with multiple infected individuals each displaying symptoms in varying degrees
- To use Koch's Postulates to determine the cause of a plant disease
- To reach a scientific conclusion from data and to defend that conclusion
- To distinguish between a bacterial and a viral infection

3 Handouts

- Protocol: *Agrobacterium tumefaciens* (p. 72)
- Protocol: Tobacco Mosaic Virus (p. 73)
- Flowchart: Bacterial and Viral Experiments (p. 74)

Then and Now

The primary question that scientists must answer when confronted by diseased tissues is *What is the causative agent?* Today, scientists recognize at least three major categories of infection: bacterial, viral, and fungal. Now that paradigms for these infections are wholly accepted, the difficulty early researchers had in identifying agents may at first puzzle students.

The laboratory experiments in "Investigating Microbes" provide students with activities analogous to those engaged in by research scientists in their studies on the Spanish flu pandemic.

Why Experimental Activities?

The experiments use infected and uninfected plants. Specifically, for a bacterial infection, we use the gall (cancer) producing *Agrobacterium tumefaciens*, and for a viral infection, we use the tobacco mosaic virus (TMV). Both experiments in Activity 4 are variations on standard experiments, and the materials are also available as kits from laboratory supply houses (but

you may need a permit to use in your state). However, to make the experiments more convenient, you will provide the students with infected and uninfected (control) plants.

The best way for students to learn to appreciate science is to engage in investigative experiments. When an experiment is performed from a kit or a manual, the experiment is, in effect, a positive control to test a student's technique. The anxieties involved in such work arise from trying to do the experiment "right," as opposed to investigating nature. Laboratory technique, of course, must be taught and modeled by the teacher. Nevertheless, for students to appreciate the special anxieties and pitfalls of research, they must engage in activities that capture the difficulties and personal involvement of an investigation of the unknown.

To start from diseased specimens and discover the bacterial nature of the *A. tumefaciens* infection or the viral nature of the TMV infection is nearly as challenging for student inves-

tigators as it would have been for the original scientists who researched these diseases.

Modern students accept the existence of bacteria and viruses. Also, they do not have to struggle with the notion of invisible sources of infection. Nevertheless, because biological systems respond with greater variability than mechanical or simple chemical systems, the emphasis in Activity 4 is on process, not final answers. The reinfections necessary to verify the bacterial nature of the galls or the viral nature of the TMV disease can produce arguable results on a given plant. This is particularly true over the short time available for student investigations.

Students will learn about standard laboratory procedures. These include

- Defining controls and double-blind studies.
- Sterilizing.
- Filtration.
- Culturing.

Suggested Pathway

The experiments are designed to parallel the cases. So it makes good sense for the class to begin the experiments at the same time that it begins reading. (The connections between the two may elicit some “ah-hahs” when the conundrums faced by Spanish flu researchers appear in the students’ own investigations.) Depending on facilities and the size of the class, you can have some students work on the bacterial infection and others on the viral infection. (The protocols are similar.) Protocols and a flowchart for both of the plant experiments are included in the handouts (pp. 72-74). First set up the plants for the class. Then

1. Break the class into teams.
2. Assign a protocol to each team and ask each team to review its protocol.
3. Give each team a chance to present any questions about the protocol to the class.

4. Give each team four infected and 16 uninfected plants.
5. Each team follows its protocol and reports on the results of its investigations.
6. The class critiques the results. (New experiments are performed as needed.)
7. Assign final reports and ask each team to defend its conclusions.

Either the bacterial or the viral experiment will need about a month to complete through regular laboratory activities. In both experiments, the object for each team is to determine whether the disease symptoms of the leaves are due to a bacterial or viral infection or are simply the result of how a plant has been treated during growth. Either of these experiments could be completed separately to demonstrate the steps of Koch’s Postulates. The experiments demonstrate these diseases:

- A plant cancer in the form of a gall grown on a sunflower seedling and caused by bacteria.
- A viral infection of pinto bean seedlings caused by the tobacco mosaic virus.

Set Up the Plants:

Agrobacterium tumefaciens

You can use materials available in kits from biological supply companies. A kit comes with sunflower seeds, pots, soil, and *Agrobacterium tumefaciens* in a slant. You can also purchase these items separately. (In some states, you may need a permit to use this organism.)

To set up the infected plants, you plant the sunflower seeds and allow the seedlings to grow until their primary leaves appear. Then inoculate with *A. tumefaciens* at the internode (the point at which the stem bifurcates into two primaries). Here is the procedure.

1. Germinate enough sunflower seeds to provide each team with four infected plants and 16 uninfected plants. Place the

seeds between two damp paper towels in a sealed container (for example, a petri dish) for two days or until the seeds germinate. (Wet the paper towels as necessary to keep them damp.)

2. Transfer the seeds to soil in a pot (or paper cup) and expose them to plenty of light until primary leaves appear (roughly five days).
3. Using sterile transfer techniques, insert an inoculating needle into the *A. tumefaciens* culture and then puncture the internode of the plant. Expect to penetrate fairly deeply, about a centimeter, along the stem. Do this three or four times.
4. Allow the plants to grow for a week to 10 days. After this time, galls will appear.

Set Up the Plants:

Tobacco Mosaic Virus

TMV is a large virus (about 0.3 microns in length) that can infect tobacco, tomato, sunflower, bean, and a variety of other plants. Its infection can either be systemic, resulting in the wilting and wrinkling of whole leaves, or localized, producing brown lesions.

You can find descriptions of the TMV experiment in many laboratory manuals on microbiology and in other curricula. This experiment is based on a kit from a supply company.¹ (Some states may require a permit.) The kit comes with specially selected pinto bean seeds, soil, planters, diatomaceous soil, applicators, and ground leaves infected with TMV. (Of these items, only the TMV cannot be immediately replaced by local purchases.) This experiment is faster than that for *A. tumefaciens*

because TMV infections are visible after two or three days. Here is the setup procedure.

1. Germinate the pinto beans. This takes two to three days.
2. Transfer the germinated seeds to soil. Plant the seeds with the hilum (or *eye*) downward. Leave the top surface of the seeds exposed. Allow the plants to develop until the primary leaves appear. This takes roughly one week.
3. Prepare a slurry of the TMV infected material by adding a small amount of water. If available, prepare your solution with a pH7 to 7.4 buffer.
4. Pat the leaves with diatomaceous soil. Rub the leaf surfaces with a fine emery board or use an equivalent mechanical action to lightly abrade the leaves. Wash the leaves off afterwards with distilled water and then gently dry with a paper towel.
5. With a cotton or foam applicator, apply solution from the slurry to a leaf. You can do this by patting the leaf with the damp applicator.
6. You should see the effects of the TMV virus after two or three days. You will see either puckering and mottling or localized brown spots.

The instructions that come with the kit will indicate that pinto beans should develop a localized infection. We have observed what appears to be a nearly systemic infection of the leaf. Apparently, the response can vary with application method, species, or even variety of plant.

Note

1. Carolina Biological Supply Company.

■ Protocol: *Agrobacterium Tumefaciens*

This protocol has three steps. Your instructor has set up the plants and will provide you with infected and uninfected plants.

- 1. Extract and purify.** Take four infected plants and excise galls. Mash galls with mortar and pestle and mix with about 10 mLs distilled water to create a slurry. Divide slurry into halves. Control: take four *uninfected plants* and process identically.
- 2. Using Luria Bertani (LB) broth, investigate for infectious agent.**
 - a. Pour one-half of the slurry from the infected plants into a test tube of sterile LB broth. Place the tube into an incubator at 37°C for 24 to 48 hours. For the control, repeat this step with the uninfected plants.

Optional: to test for presence of specific bacteria

 - i. Prepare LB culture plate. Streak the LB plate with an inoculating loop dipped into the LB broth from the infected plants. (See Streaking Pattern illustration, page 78.) Repeat this step with control plants.
 - ii. Place culture plates into incubator at 37°C for 24 hours or until colonies are apparent.
 - iii. Examine the colonies. Select and mark a colony by indicating it on the cover of the petri dish with a felt pen. With an inoculating loop, take a portion of this colony and culture in an LB broth at 37°C. If some colonies appear to be from different types of bacteria, perform multiple cultures. Make sure to code the colonies on the plate. If the control plate also shows colonies, follow the same steps to culture them.
 - b. Make one person the code keeper. Your control for this experiment is the LB broth from uninfected plants. The code keeper labels the control broth tube and the potentially infectious broth tube with codes. (From this point on, other members of the team should refer to the broths by their codes; they will not know the nature of the infection.)
 - c. After incubating all culture tubes for 24 hours or until the broths turn cloudy, infect six new uninfected sunflower plants. Take an inoculating needle, insert the tip into a broth, and puncture the sunflower plant multiple times at the internode. Label each plant, noting the code from the broth used for the inoculation.
 - d. After about 8 days, and continuing over the next 14 days, inspect plants for the development of galls. This inspection should not be done by a code keeper. When you are confident that the plants have either developed or not developed galls, compare results with the code for the plant.
- 3. Using filtrates, investigate for infectious agent.**
 - a. Filter the other half of the slurry from the infected plants (Step 1) through a 0.45 micron filter. Use either a Buchner funnel or filter syringe.
 - b. Create a control tube. Your control is the LB broth from the uninfected plants.
 - c. The code keeper labels the two tubes with a code. From this point on, all members of the team refer to the tubes solely by code.
 - d. Using the two tubes of fluids, inoculate six new sunflower plants. Take an inoculating needle, insert the tip into the fluid, and puncture each plant multiple times at the internode. Label each plant, noting the code from the fluid used for the inoculation.
 - e. Proceed according to Step 2d above.
 - f. **Optional.** Follow instructions in Step 2a for making a streak plate to grow cultures using filtrate instead of broth.

■ Protocol: Tobacco Mosaic Virus

This protocol has three steps. Your instructor has set up the plants and will provide you with infected and uninfected plants.

1. Extract and purify. Take leaves from four infected plants. Mash leaves with mortar and pestle and mix with about 10 mLs distilled water to create a slurry. Divide slurry into halves. Control: take four *uninfected plants* and process identically.

2. Using Luria Bertani (LB) broth, investigate for infectious agent.

a. Pour one-half of the slurry from the infected plants into a test tube of sterile LB broth. Place the tube into an incubator at 37°C for 24 to 48 hours. For the control, repeat this step with the uninfected plants.

Optional: test to exclude presence of bacteria

i. Prepare LB culture plate. Streak the LB plate with an inoculating loop dipped into the LB broth from the infected plants. (See Streaking Patterns illustration, page 78.) Repeat this step with control plants.

ii. Place culture plates into incubator at 37°C for 24 hours or until colonies are apparent.

iii. Examine the colonies. Select and mark a colony by indicating it on the cover of the petri dish with a felt pen. With an inoculating loop, take a portion of this colony and culture in an LB broth at 37°C. If some colonies appear to be from different types of bacteria, perform multiple cultures. Make sure to code the colonies on the plate. If the control plate also shows colonies, follow the same steps to culture them.

b. Make one person the code keeper. Your control for this experiment is the LB broth from uninfected plants. The code keeper labels the control broth tube and the potentially infectious broth tube with codes. (From this point on, other members of the team should refer to the broths by their codes; they will not know the nature of the infection.)

c. Pat the leaves with diatomaceous soil. Rub

the surfaces with a fine emery board or use an equivalent mechanical action to lightly abrade the leaves. Wash the leaves off afterwards with distilled water and then gently dry with a paper towel.

d. With a cotton or foam applicator, apply solution from the slurry to the leaf. You can do this by patting the leaf with the damp applicator.

e. After 2 to 3 days, inspect the plants for development of the TMV virus. If present, you will see either puckering and mottling or localized brown spots. This inspection should not be done by a code keeper. When you are confident that the plants have either developed or not developed virus, compare results with the code for the plant.

3. Using filtrates, investigate for infectious agent.

a. Filter the other half of the slurry from the infected plants (Step 1) through a 0.45 micron filter. Use either a Buchner funnel or filter syringe.

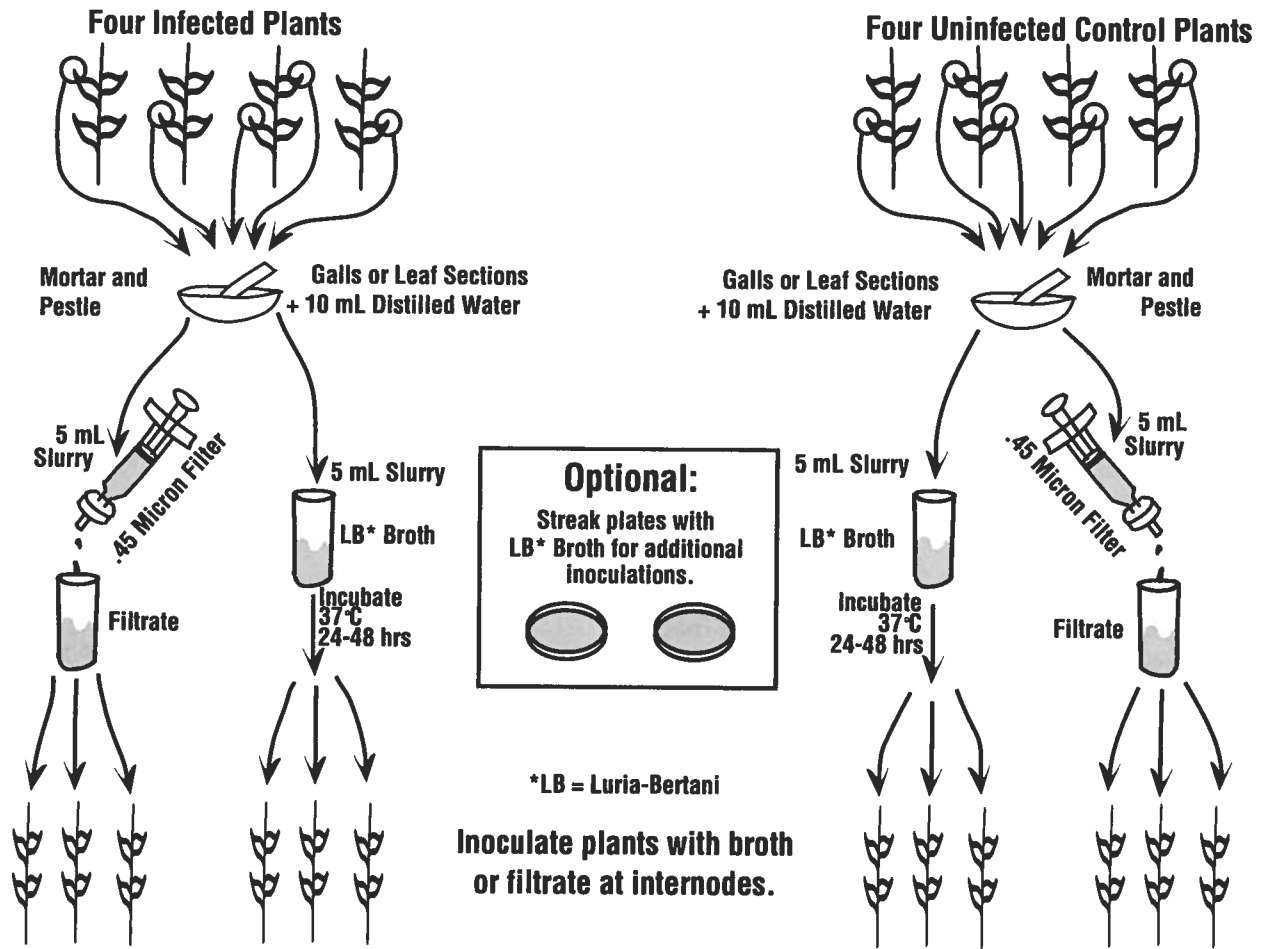
b. Create a control tube. Your control is the LB broth from uninfected plants.

c. The code keeper labels the two tubes with a code. From this point on, all members of the team refer to the tubes solely by code.

d. Using the two tubes of fluids, proceed according to Steps 2c through 2e above, using the filtrates.

e. Optional. Follow instructions in Step 2a for making a streak plate to grow cultures using filtrate instead of broth.

■ Bacterial and Viral Experiments



Activity 5. What Causes Yogurttness?

By Peggy O'Neill Skinner

Case 1

Resource 1

Objectives

- To use Koch's Postulates to find a causative agent for disease
- To practice microbial techniques
- To design a controlled experiment
- To reach a scientific conclusion from data and to defend that conclusion

1 Handout

- Streaking Patterns for Single Colonies

Background

This activity uses very simple techniques and common substances to demonstrate Koch's Postulates. The activity is appropriate for grades 9 to 12. (It is not as complex as Activity 4, which may be more appropriate for advanced students). Koch developed four postulates to identify the causative agent for a particular disease. The postulates follow the logic order of

1. Identifying a possible pathogen in a diseased individual.
2. Isolating and culturing the suspected pathogen.
3. Inoculating a healthy individual with the suspected pathogen to determine if the disease develops.
4. Isolating the same pathogen from the newly infected individual.

Scientists now usually also look for a fifth postulate: common genetic sequences that tie the causative agent to several diseased individuals. In this activity, students conduct an experiment with milk (the healthy individual), yogurt (the diseased individual), and *Lactose acidophilus* or other microbes found in live-culture yogurt. The materials you need for this experiment include:

- pH indicator or pH test papers
- Nonfat yogurt (with live culture)
- Nonfat milk
- Sterile loops (or sterile Q-tips and sterile toothpicks)
- Sterile microcentrifuge tubes or other small sterile test tubes with caps
- Microscope, slides, and coverslips
- Petri dishes with nutrient agar
- Incubator at 37°C (optional)

Suggested Pathway

1. Day 1, Postulate 1:

Identifying a possible pathogen

- Provide students (in groups of 3 to 4) with samples of nonfat milk and nonfat yogurt. Describe the yogurt as "sick milk."
- Provide students with pH paper, microscopes, and slides. Ask them to observe the characteristics of the milk and the yogurt. Since the bacteria are difficult to see at 400x, suggest that they make slides with samples of yogurt and milk on opposite

sides of each slide with two coverslips. (It is easier to note a difference.) Ask students to observe and record the pH and appearance of the milk and yogurt.

- Remind students that determining the disease-causing agent is not easy. Suggest that they think about the laboratory conditions in 1918.

2. Day 1, Postulate 2: Isolating a possible pathogen

- Have the students streak a nutrient agar Petri plate with yogurt. A sterile loop is best to use, but good results have also been obtained with Q-tips from a recently opened box. Give the students copies of the Streaking Patterns handout (p. 78).

- Incubate the plates upside down at 37°C for 1-2 days or at room temperature for 3-4 days.

3. Day 2, Postulate 2: Isolating a possible pathogen

- After the plates have incubated long enough to see colonies, students should observe that there may be more than one type of bacteria on the plate. Since this medium does not provide the best environment for acidophilus bacteria but allows for the growth of other types, you may not have large numbers of colonies. Point out that when isolating causative agents, you should use a general medium to screen for the organism.

4. Day 2, Postulate 3: Infecting a healthy individual

- Have students place the same quantity of healthy milk into at least three microcentrifuge tubes. The experiment can easily be duplicated with the running of at least six tubes (two for each of the conditions mentioned). The number of tubes students use will depend on the number of different kinds of colonies visible on their Petri plates.

- One tube of milk will remain untouched. Designate it the *negative* control.

- Inoculate one tube of milk with a sterile loop of yogurt. This is the experiment's *positive* control. You could also use a sterile toothpick to transfer the yogurt. Agitate the loop or toothpick a bit to transfer all of the yogurt to the tube. Inoculate the third or additional tubes with a bacterial colony from the Petri plate. Be sure to agitate the loop or toothpick to transfer the bacteria.

- The tubes can then be incubated overnight at 37°C or at room temperature for 3-4 days.

5. Day 3, Postulate 4: Identifying and isolating pathogen again

- Students should make observations about the conditions of their three tubes and record their data.

- They should look for pH and microbe characteristics that are similar to yogurt. Remind them that the negative control may change over the time period, but that those changes indicate aging, not disease.

- Students can then streak plates with the newly diseased milk.

- Students may also wish to streak a plate with a more selective medium that encourages the growth of these microbes.

Media for Experiments

Most of these ingredients you can obtain from readily available commercial sources. Most media (unless otherwise noted) are based on 1.0 L volumes. Standard conditions for sterilization are by autoclaving or pressure cooking for 15 minutes at 15 psi pressure (121°C unless otherwise noted).

Nutrient Agar With Glucose

15 g agar

5 g pancreatic digest of gelatin

3 g beef extract

10 g glucose

Add components to distilled water and bring volume to 1.0 L. Mix thoroughly. Gently heat and bring to boiling. Distribute to tubes or flasks and sterilize.

MacConkey Agar

17.0 g pancreatic digest of gelatin
13.5 g agar
10.0 g lactose
5.0 g NaCl
1.5 g bile salts
1.5 g pancreatic digest of casein
1.5 g peptic digest of animal tissue
.03 g neutral red
1.0 g crystal violet

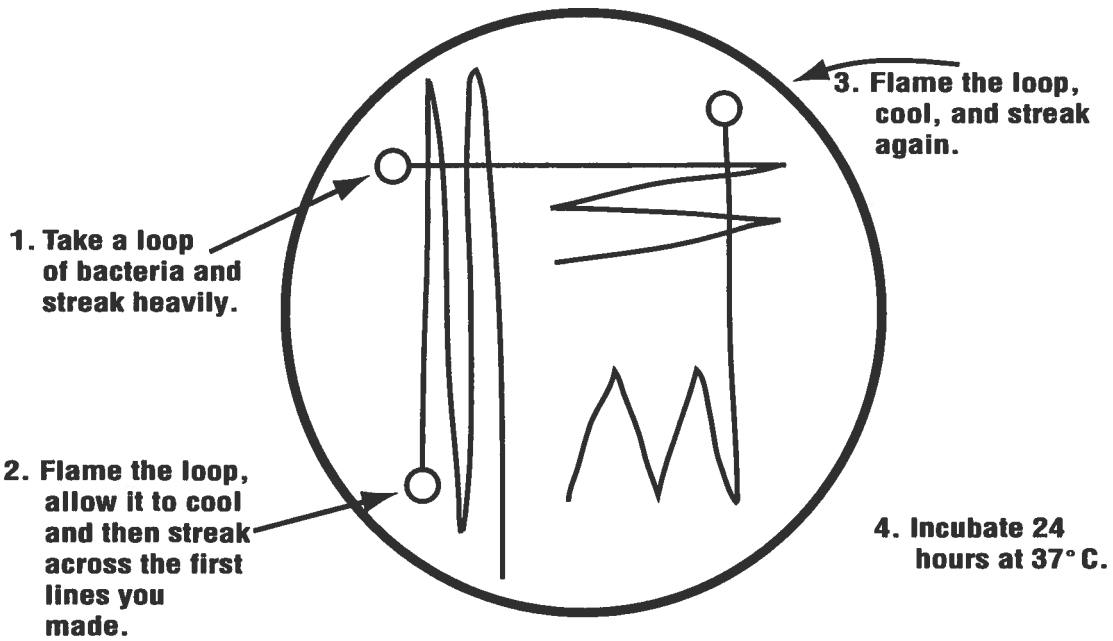
Add components to distilled water and bring volume to 1.0 L. Mix thoroughly. Gently heat while stirring until boiling. Sterilize and then pour into sterile Petri dishes.

Lactose fermenting organisms appear as red to pink colonies. Lactose nonfermenting organisms appear as colorless or transparent colonies.

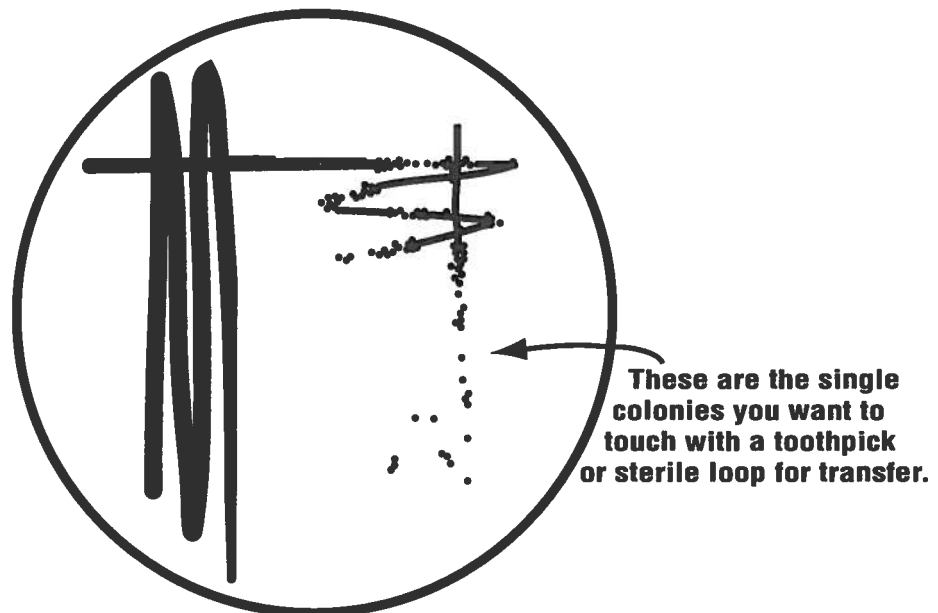
Conclusion

Students should be able to determine that the acidic, solidified nature of yogurt is caused by bacteria acting upon milk.

■ Streaking Patterns



After incubation, results should look like this:



Activity 6. What Was to Be Done?

Case 2

Resources 1, 5-10

Objectives

- To examine the impact of disease on other sectors of society
- To link case studies to other disciplines
- To demonstrate the global effect of a pandemic
- To highlight the progress in disease research

Suggested Pathway

In Case 2, “Around the World,” the narrator contemplates the extent of the medical disaster and asks, “What was to be done? It was a plague, a calamity out of the Middle Ages, rushing around the world on steamships and trains. Could anything stop it?” (p. 18).

1. Assign Case 2 and call attention to the narrator’s remarks. Point out that you expect the class to examine the impact that the Spanish flu pandemic had on persons other than researchers.
2. Break the class into small groups.
3. Let each group select several different points of view. Each group explores the question, *Faced with the implications of a pandemic, what would you do?*

4. Ask each group to present its findings to the class.

Case 2 poses the question *What was to be done?* from the point of view of public officials, physicians, and epidemiologists.

Students can imagine other points of view: military officials, pharmaceutical manufacturers, nurses, ordinary citizens, the president of the United States. (President Woodrow Wilson was stricken with influenza in April 1919, near the end of the pandemic.)

Extend the class discussion to focus on the present. *Given the changes in science, technology, and society, would these persons be able to act differently now than they could have in 1918?* If you want to focus solely on the public health side, try Activity 7, “Saving Communities.”



The conductor on a Seattle streetcar will not permit the man without a mask to board.

Activity 7. Saving Communities

By George Ochoa

Case 2

Resources 8-10

Objectives

- To examine the impact of disease on public health policy
- To demonstrate the global effect of a pandemic
- To highlight progress in disease control

6 Handouts

- Atlanta (pp. 83-84)
- Frankfurt (p. 85)
- Lyon (p. 86)
- Marseille (pp. 87-88)
- San Francisco (pp. 89-90)
- The Samoas (p. 91)

Suggested Pathway

Activity 7 is similar to Activity 6. However, Activity 7 emphasizes the problems encountered in the area of the public health policies and measures used to help fight the Spanish flu pandemic. If the class has not already worked with Activity 6, first lead it in a discussion of the narrator's question in Case 2: *What was to be done?* (See page 79.)

1. Assign Case 2 and call attention to the narrator's remarks.
2. Break the class into small groups.
3. Put each group in charge of saving a community (Atlanta, Frankfurt, Lyon, Marseille, San Francisco, or Western Samoa and American Samoa). Be sure that each group knows the location and general topography and background of each place. Let the students research their communities.
4. Provide a handout for each group. Explain that you expect the group to brainstorm basic questions such as *What did this community do to protect itself from the Spanish flu pandemic? Did this community's actions match what you would have recommended? Did the actions work? Why or why not? Is there anything we could do today that they could not do then?*
5. Ask each group to prepare both a written and an oral report.
6. Have each group present its oral report and lead a class discussion of group recommendations.

Be sure that the class tries to draw conclusions about why some strategies worked and some did not (or whether all strategies seemed equally hopeless). *Would the situation be different now?*

If the class does not specifically mention them, be sure that it notices the obvious problems with the public health measures of 1918:

- The weave of gauze masks may not have been fine enough to keep out viruses.
- Disinfectants may not have been strong enough to kill all pathogens.
- Vaccines were useless unless they inoculated against the right pathogen, and this had not been identified at the time.
- Infected people can be contagious even before they start showing symptoms.

■ Saving Communities: Atlanta

Located in north-central Georgia, Atlanta had a population of nearly 90,000 in 1900 and was still growing in 1918, prospering from its textile and automotive industries. Seeing itself as the leading business center of the Southeast, it prided itself on its healthfulness and on what was known as the “Atlanta Spirit,” a positive, optimistic outlook.

The first wave of influenza in spring 1918 hardly seemed to strike Atlanta, receiving no notice in the press. The severe second wave first struck the week of October 2, 1918, at the army camp of Fort Gordon southwest of the city. By the second week of October, the number of cases at the camp had risen to 2,941.

Atlanta’s health department, which had a record of strong intervention against public health problems, worked fast to try to prevent the flu from spreading. Soldiers were required to wear gauze masks and forbidden to come within Atlanta city limits. Roads in the camp were oiled with antiseptic, on the theory that dust might carry germs. Soldiers were required to sleep outdoors rather than in barracks, on the theory that germs would spread less easily in the open air than in the close confines of indoor housing. Even so, deaths happened every day, with coffins said to be “stacked like cordwood.”

Within the city, throughout October, official sources gave contradictory accounts of the seriousness of the epidemic. Health Officer J. P. Kennedy claimed one day that the city was all but free of influenza. Four days later he said that each doctor in Atlanta was treating 15 to 20 flu patients a week. One newspaper called influenza a “great and terrifying menace to the public health.”² Another claimed everything was under control. Though the government presented an upbeat image, one citizen remembered: “They were dying just like leaves off of them trees.”³

Because gathering in confined spaces was considered dangerous, streetcars and buses were required to travel with their windows

open. Schools, churches, theaters, dance halls, and pool rooms were closed by public ordinance. The courts closed for a month. Yet, under the influence of the Chamber of Commerce, most businesses were allowed to stay open.

The annual Southeastern Fair, which attracted visitors and dollars from all over the Southeast to its exhibition buildings and amusement tents, was staged on schedule in October. Run by the Chamber of Commerce, the fair attracted the largest crowds in its history. The Health Board considered canceling the event, but finally decided only to require attendees to wear face masks. Representatives of the closed theaters and churches complained that they were being treated unfairly. Why was the fair safer than a church?

Factory and shop workers and downtown shoppers were required to wear face masks (an ordinance that was not as strict as that found in cities such as San Francisco, but stricter than cities such as Boston). Police enforcement of antisputting ordinances was stepped up. Garbage removal and street sweeping were forbidden during busy hours in downtown (for fear that flu germs hidden within disturbed filth would infect the crowds of shoppers and workers).

Physicians were required to report all cases of flu. City welfare nurses had to visit all flu patients to assess the cases and give advice. Grady Memorial Hospital closed its doors to flu patients after several nurses fell ill from flu.

Numerous flu preventives were advertised and purchased: throat sprays, nose douches, eucalyptic salve, Listerine-Dioxagen for gargling. One doctor suggested placing sulfur in the bottom of each shoe. Another suggested that a positive attitude would help to ward off the disease.

On October 25, the City Council considered whether to lift the closing ordinances. Some Health Board staff argued that the epidemic was still serious. But Health Officer Kennedy argued that the epidemic had stabi-

lized. The mayor and theater managers also wanted to reopen closed businesses. The council decided to lift the closing ordinances.

There is no exact record of how many Atlantans caught influenza or died from it. The City Health Department records have been lost. The city never filed a 1918 report with the State Health Department. From the beginning, Kennedy claimed that death rates were low and the situation was getting better. His estimate of only 3,000 influenza cases by the time

the epidemic waned near the end of October seems suspiciously low. A relatively mild third wave struck Atlanta in January.

African Americans, who composed 33.45 percent of the population, suffered 34.57 percent of Atlanta's influenza deaths. Overall, the city experienced three deaths per 1,000 population in the last four months of 1918. Most other American cities suffered far worse in the same period. Boston's figure, for example, was 6.7, and San Francisco's 5.4.

Notes

1. Quoted in Francine King, "Atlanta." In *The 1918-1919 Pandemic of Influenza: The Urban Impact in the Western World*, edited by Fred R. van Hartesveldt (Lewiston, N.Y.: Edwin Mellen, 1992), 110.
2. The Atlanta Semi-Weekly Journal, October 15, 1918. As quoted in Francine King, "Atlanta." In *The 1918-1919 Pandemic of Influenza: The Urban Impact in the Western World*, edited by Fred R. van Hartesveldt (Lewiston, N.Y.: Edwin Mellen, 1992), 111.
3. Clifford M. Kuhn, Harlan E. Joye, and E. Bernard West, *Living Atlanta: An Oral History of the City, 1914-1948* (Athens, Ga. and London, 1990), 28. As quoted in Francine King, "Atlanta." In *The 1918-1919 Pandemic of Influenza: The Urban Impact in the Western World*, edited by Fred R. van Hartesveldt (Lewiston, N.Y.: Edwin Mellen, 1992), 108.

■ Saving Communities: Frankfurt

Located in western Germany on the Main River, Frankfurt in 1918 was an important manufacturing and transportation center, a channel for troops and materiel. Like many Germans, the citizens of Frankfurt were malnourished and exhausted, suffering from war and related shortages of food, labor, fuel, and medical help.

In June and July 1918, the first wave of Spanish influenza became epidemic. The flu caused many absences at work, slowing down production and delivery of goods, making supplies even scarcer. The city and national government did not acknowledge that the flu was serious and claimed that the number of cases had been exaggerated. The authorities distributed information on how to prevent and treat the disease, but made little effort to close public places or quarantine sick troops and civilians. Newspapers were censored to avoid spreading negative news that might lower morale or aid the enemy.

The government also refused to grant supplemental food rations or extra medical supplies. This caused people, who believed that the flu was in part caused by hunger and scarce medical care, to panic. A medical conference did not help matters by concluding that almost nothing could be done to fight the flu.

The first wave of influenza waned in late July. In August and September, Frankfurt took steps to reform its food distribution system, allowing the food ration to rise. Then, in late September and October, the second wave of influenza struck. Much more virulent than the first, it sickened an estimated 10 percent of Frankfurt's adult population by October 12 (still the early stage of the second wave).

Again, trains and factories began to slow down as a result of employee absences.

This time, the city authorities responded actively. They raised the food ration twice within two weeks. They closed schools, banned public meetings and performances, and made more quarantine space available for hospitals. They offered advice on how to avoid the flu: stay away from crowded places and streetcars, disinfect, and gargle often. As hospitals became overcrowded, they urged families to care for the sick at home and called for more volunteer nurses. They also required local registrars to issue daily reports on flu cases.

Gauze masks, common in the United States, were not widely used by the general public in Germany. The mortality rate was devastating. Of flu patients brought to city hospitals, 27.3 percent died (compared with 14 percent during the first wave). By the end of October, the second wave was waning. In November, schools reopened and the ban on public gatherings was lifted. But chaos began to descend as the German government collapsed and World War I came to an end. The flu epidemic flared again in late November and early December, just when political disorder throughout the country was disrupting the flow of supplies, making food and fuel shortages even worse. Funerals of flu victims were often accompanied by demonstrations and the looting of food shops. Still, the city government managed to stay in power.

Exact figures for Frankfurt are not available, but the death toll from flu in Germany in 1918-19 is estimated at 5.9 per 1,000 population—considerably higher than the estimate of 4.2 for the United States in the same period.

■ Saving Communities: Lyon

In 1918, Lyon was the third largest city in France. Located on the Rhône River about 170 miles inland from the Mediterranean coast, it had a history of vigorous public health activism that had helped make it a healthier place to live than Marseille. Its mayor, Edouard Herriot, was known for his commitment to health care and sanitation, even at a time of war-induced shortages in physicians, medicine, and hospital space.

Like Marseille, Lyon was struck by a relatively mild wave of influenza in the spring and early summer. Then, in mid-September, the Lyon area was struck by Spanish influenza at its most severe. Deaths from influenza climbed from 22 in August to 85 in September to 956 in the peak month of October. Struck by the death toll among young adults, one physician stated: "I have lost in these five weeks more young mothers than I saw die in the previous ten years."¹

On September 26, the mayor's office in Lyon announced that influenza was epidemic. On the advice of the City Hygiene Bureau and the National Public Health Committee, Mayor Herriot issued orders prohibiting the beating of rugs and requiring that floors be dampened before being swept. This was in accord with the theory that dust and filth might harbor flu germs. The mayor's office also issued advice on preventing flu: gargle with and inhale disinfectants, wash face and hands often, do not spit in public, do not drink much alcohol, avoid crowded or poorly ventilated places. Following the recommendation of the National Education Ministry, the opening of school was delayed.

On October 14, as the death count rose, the mayor took firmer action. A corps of visiting

nurses was organized, with money allocated to hire nurses. All theaters were closed. All public amusements banned. Funeral processions were forbidden; dead bodies had to be buried within 24 hours (with the city expanding its burial aid program for the poor). All public conveyances and public places, including stores and restaurants, were to be disinfected daily. The sickrooms of the dead and of those who had suffered secondary infections were to be disinfected by the city. Herriot tried to get the national government to help assemble an emergency cleanup of city streets, but had no success.

Some critics argued that not all of Herriot's measures were necessary. Herriot responded that medical experts did not know exactly how influenza was caused and transmitted; therefore he was willing to try anything plausible.

As in Marseille, physicians and the general public tried many different methods to combat the disease—antifever remedies, laxatives, herbs, disinfectants. Gauze masks were not widely used by the general public. The city made sure that emergency supplies of quinine, a fever-reducing drug, were delivered to pharmacies for purchase by patients. As in Marseille, the epidemic in Lyon began to wane in November, and was over by spring 1919. On November 5, the ban on theaters and funeral processions was lifted.

Herriot was proud of Lyon's vigorous action against the epidemic. But the City Council was surprised to note that morbidity and mortality in nearby villages, where there were no crowds to control or theaters to ban, had been as bad or worse than in Lyon. From June 1918 to May 1919, Lyon suffered 2,090 deaths, compared with 2,831 in Marseille.

Note

1. Dr. Camescasse, "L'Epidemie de Grippe de 1918," *Revue d'Hygiene et de Police Sanitaire* 41 (1919): 89-90. As quoted in Martha L. Hildreth, "Lyon and Marseille." In *The 1918-1919 Pandemic of Influenza: The Urban Impact in the Western World*, edited by Fred R. van Hartesveldt (Lewiston, N.Y.: Edwin Mellen, 1992), 45.

■ Saving Communities: Marseille

In 1918, France was a nation wearied by four years of war. Physicians, medicine, and hospital beds were all in short supply. They were especially scarce in Marseille, which, historically, had invested little in public health measures, other than maritime quarantine, to protect it from diseases entering from the sea. Located on the Mediterranean coast, Marseille was France's second largest city and the main entry point for soldiers and workers coming from Portugal, the United States, and French colonies in North Africa.

Marseille was struck by a relatively mild wave of influenza in the spring and early summer. Then, in August, physicians were startled by a new kind of infection. In one case, five members of a family fell sick at once; three of them died. At first attributed to typhus or cholera, the deaths from this period were only later identified as due to Spanish influenza. Not until September 12 did the head of the municipal public health council warn Mayor Eugène Pierre that the city might be experiencing an epidemic of Spanish flu, which was then known to be spreading in France. Pierre and the City Council took no action because the weekly death statistics were not above average; national law required no action until they were.

Despite the lack of official action, the public knew from its own experience and from rumor that something deadly was in the air. By September 30, public fear forced the prefect of the department (the region including the city) to act. Information was disseminated, including advice on personal hygiene and on avoiding crowded places. Nothing was specifically prohibited, though the opening of school was delayed following the advice of the National Education Ministry.

On October 10, the mayor's office acknowledged that Marseille was suffering an epidemic. Spitting in public was forbidden, along with beating of rugs (based on the idea

that flu germs might reside in dust and filth). For the same reason, the prefect later authorized daily disinfectant cleaning of cafes and public buildings and vehicles, though the city failed to enforce these measures, claiming that disinfectants were in short supply.

Public terror grew as influenza deaths in Marseille climbed from 126 in August to 537 in September to 799 in the peak month of October. Despite requests from the City Hygiene Bureau and many other concerned people, the city and the department declined to advocate the stricter health measures that Lyon, another French city, had instituted. Many people believed that influenza was spreading because of the open sewage and piles of garbage in the city streets. One person advocated spraying disinfectant directly into the air.

City officials doubted the effectiveness of disinfectants or restrictions on crowds and claimed that the situation in Marseille was not that bad. The mortality rate for influenza, argued Pierre, always went up in the fall. He also thought the rate was inflated by immigrants who were sick before they reached Marseille. Privately, city officials argued that vigorous public health measures would put the citizenry into a panic.

Hospital beds and physicians, already in short supply because of the war, became even scarcer. The city made few attempts to increase the number of beds, though it did set up an emergency medical service that made doctors more accessible, without paying them anything for their additional service.

To combat the disease, physicians and the general public tried many different methods, including anti-fever remedies (quinine, aspirin), purgatives or laxatives, natural herbs, garlic, and disinfectants (mentholated Vaseline for the nose and hydrogen peroxide for the mouth). Gauze masks were not widely used by the general public. Many physicians in France

practiced bloodletting, an old, all-purpose remedy that had become controversial. Medicines of any kind were scarce, and the Marseille government was criticized for not trying to increase the supply.

The epidemic in Marseille began to wane in November and was over by spring 1919. From June 1918 to May 1919, Marseille suffered 2,831 deaths from influenza, compared with 2,090 in Lyon.

■ Saving Communities: San Francisco

In 1918, the West Coast city of San Francisco, an important military center, had a population of 550,000. The city scarcely noticed its first wave of mild influenza in the spring. The first case in San Francisco of the severe second wave was reported in the newspapers on September 24, by which time the city's leaders had heard of the pandemic raging on the East Coast. On September 27, the California State Board of Health made influenza a reportable disease and allowed health officers to isolate cases. City officials did not cancel the next night's Liberty Loan Drive parade, despite the medical profession's belief that crowded conditions encouraged the spread of the disease. Over the next two weeks, many other rallies and marches were held to raise money for the war effort.

Chief Health Officer William Hassler prepared for the worst by designing health districts to make maximum use of personnel, sending nurses to schools to talk about how personal hygiene could prevent flu, and setting aside San Francisco Hospital as an isolation center for flu patients. New cases of flu climbed steadily, although many San Franciscans failed to be alarmed. As late as October 15, the *San Francisco Chronicle* claimed "there is less danger in the Spanish Influenza than in German peace propaganda."¹

On October 18, the Board of Health closed schools and places of amusement and public gathering. On October 20, churches were closed. An atmosphere of panic began to set in. Doctors and nurses were overworked. Hospitals were filled to capacity. Emergency hospitals were set up in churches and auditoriums. Hundreds of telephone operators, policemen, garbage collectors, and others were absent from work, threatening the survival of San Francisco's vital services.

Hassler's health districting system was revised several times, but there were not enough nurses and supplies at the district centers to answer calls for help. By the end of October,

the Red Cross ran ads begging women to volunteer as nurses.

Gauze masks, already widely in use in the eastern United States, became commonplace in San Francisco too. In late October, many people voluntarily donned them, as the Board of Health announced that a mask was "ninety-nine percent Proof against Influenza."² As of November 1, masks were legally required in all public places and wherever two or more people congregated. Exceptions were made only for homes in which only two family members were present and for people eating meals.

The strict mask ordinance was coupled with distribution, after October 22, of a vaccine developed by Massachusetts researcher Timothy Leary, who claimed it would abort flu, prevent pneumonia, and "do away with the death rate almost totally."³

The fall wave of the epidemic peaked on October 25, the day when the greatest number of new cases (2,319) was reported. After that, the number of new cases began to fall. The week ending November 2 produced 7,164 new cases and in the last week of November, there were only 57. The epidemic appeared to be over. Gauze masks and Leary's vaccine seemed to have proved effective in fighting the flu.

On November 21, the mask ordinance was officially revoked. By the first week of December, the number of new cases of flu began to rise again. Chief Health Officer Hassler, who had led the campaign to wear masks, was convinced that lack of masks was the problem. Most San Franciscans refused official calls to resume their masks voluntarily. They were tired of wearing the uncomfortable things, and this new wave of flu did not seem as serious as the last. Still, Hassler pushed on, and on January 17 a new mask ordinance went into effect. From that day forward, the number of new flu cases began to fall. The peak of the December-January wave was reached in the week ending January 18, when the number of new cases was 3,500.

Hassler and many of his public health colleagues were convinced that the masks had been responsible not once but twice for saving San Francisco from a more terrible bout with Spanish influenza. Others, however, disagreed. State Board of Health Officer W. H. Kellogg cited statistics showing that strict mask wearing in Stockton, California, had not prevented a death rate as high as that found in Boston, where masks had hardly been worn at all. One letter writer to the *San Francisco Chronicle* reported that he had come down with flu and

pneumonia despite inoculating himself and his family with Leary's vaccine and despite wearing a mask diligently. He signed himself, "What's the Use?"⁴

Deaths from influenza and pneumonia in San Francisco in the last four months of 1918 numbered 5.4 per 1,000 population. This was a lower figure than some American cities (such as Boston, 6.7), but higher than others (Atlanta, 3.0). San Francisco had the worst epidemic of any city on the West Coast.



During the 1918-19 flu epidemic, citizens in many cities were required to wear masks at all times.

Notes

1. *San Francisco Chronicle*, October 15, 1918. As quoted in Alfred W. Crosby, *America's Forgotten Pandemic: The Influenza of 1918* (New York: Cambridge University Press, 1989), 94.
2. *San Francisco Chronicle*. October 22, 1918. As quoted in Alfred W. Crosby, *op.cit.*, 102.
3. *San Francisco Chronicle*, As quoted in Alfred W. Crosby, *op.cit.*, 100.
4. *San Francisco Chronicle*, December 20, 1918. As quoted in Alfred W. Crosby, *op.cit.*, 108.

■ Saving Communities: The Samoas

Located in the South Pacific, the Samoan Islands were almost completely isolated from the rest of humanity (and its diseases) until the first European contact in 1722. By 1918, the island group was divided into two parts: Western Samoa, administered by New Zealand, and American Samoa, administered by the United States. Previous influenza epidemics had shown that the indigenous people of Samoa were much more susceptible to death by influenza than people of European descent.

On November 7, 1918, the steamer *Talune* arrived in Apia on the island of Upolu, Western Samoa. The *Talune* had sailed from New Zealand, where Spanish influenza was rampant, but no one in New Zealand had radioed a warning to the medical officer at Apia. He did see that the *Talune* was carrying sick passengers and crew, but he took no action to quarantine them. Lieutenant Colonel Logan, administrator of Western Samoa, took no extraordinary measures to prevent or mitigate an epidemic on the islands. He refused a radio offer of medical help from American Samoa, supposedly because he misunderstood the message, but he did permit the arrival of four doctors and 20 orderlies from Australia in early December.

Western Samoa suffered what was perhaps the most lethal epidemic of the entire Spanish influenza pandemic. By early 1919, an estimated 8,500 people (22 percent of the population of 38,302) had died. Many of the deaths were related to malnutrition or starvation because the normal routines of obtaining and distributing food had been interrupted.

Forty miles away, U.S. Navy Commander John M. Poyer, the governor of American Sa-

moa, learned of the pandemic in other parts of the world by reading the daily *Press Wireless*. On November 3, 1918, the S.S. *Sonoma* from San Francisco arrived in Pago Pago on the island of Tutuila, American Samoa, but its two sick people were placed in quarantine, as were three passengers who intended to stay on the island.

On November 23, Poyer ordered a rigorous quarantine on all vessels coming from disease-racked Upolu in Western Samoa, along with a ban on travel to the island. Visitors were not allowed ashore until several days had passed in which their temperature and overall health were carefully monitored and pronounced acceptable. Even mail from Western Samoa was quarantined. A Western Samoan craft ordered to pick up and deposit mail at a mail steamer in American Samoa was not allowed to do so until a quarantine of five days had passed, by which time the mail steamer was gone.

Poyer expected that Western Samoans fleeing the epidemic would try to sneak into American Samoa in small boats under cover of night. He therefore requested the help of Samoan leaders in Tutuila to prevent any unauthorized landings on the island. Eager to avert an epidemic, the Samoan people launched a round-the-clock patrol of their own shores.

Other measures besides quarantine were taken. Mail was fumigated. Dockworkers were required to wear masks. A vaccine was administered. Not until 1920 were the quarantine ordinances rescinded.

No cases of, and no deaths from, Spanish influenza were reported in American Samoa.

Activity 8. Unexpected Losses

Cases 1-3

Resources 5, 7

Objectives

- To evaluate medical information derived from insurance data
- To demonstrate the social and economic consequences of the pandemic
- To highlight the role of interdisciplinary links in research

4 Handouts

- Losses to the Industry (p. 95)
- Patterns of Death (pp. 96-97)
- The Weight Factor (pp. 98-99)
- Losses to the Company (pp. 100-101)

Suggested Pathway

The financial loss as a result of illness and death from the Spanish flu was enormous, although no one knows precisely how much it totaled. An exception to this general lack of precise information was the life insurance industry, whose prosperity depended on collecting information about matters of life and death. (Its well-calculated actuarial tables were rendered useless, not only due to the virulence of the flu but because of the age of most of the victims.) For example, the Metropolitan Life Insurance Company paid out more than \$18 million in initial demands from the beneficiaries of 85,000 policies.

Except for the Questions for Discussion, the text in the four handouts for Activity 8 is taken from a contemporary document titled “A Statistical Report on the Influenza Epidemic As It Affected the Policyholders of the Mutual Life Insurance Company of New York in the Year 1918 Only” by Brandreth Symonds, M.D., Chief Medical Officer of the Mutual Life Insurance Company of New York.

The first handout, “Losses to the Industry,” is a overview of the financial costs of the influ-

enza epidemic. The next three handouts include tables and company commentary on the significance of the data followed by the Questions for Discussion.

By focusing on various data patterns, Symonds’ Report presents not only a picture of the company’s financial losses but also a thorough profile of those who died among the company’s policyholders.

1. Provide the class with copies of the handout “Losses to the Industry” and assign it for reading.
2. Ask for comments and questions on “Losses to the Industry.”
3. Break the class into small groups and assign each group a handout from the remaining three handouts. Explain that the handouts include tables and that the class will work together with the tables.
4. Ask each group to work with the questions following the tables and to prepare an oral report for the class.
5. Debrief the groups with a class discussion. Work with the tables.

Be sure that the class examines the specific factors that correlate with influenza mortality and that they confront the general question:

If you were the company director and assumed that these data represented a permanent change in patterns of influenza mortality, how would you adjust payouts to be both profitable to the company and attractive to policyholders?

Other general questions you want the group to address are:

How do life insurance companies determine their rates so that they do not lose money?

If you had used the data based on previous epidemics as the basis of your prediction of the future, what would be your expectation of the number of deaths in each age group in 1918? How much money would you have lost?

Given what you know now, can you adjust the rates to make sure that you do not lose money?

■ Losses to the Industry

The losses from this epidemic of influenza have been appalling among the life insurance companies in the United States. In 1918 alone, the death-claims paid on this account have been calculated to exceed \$100,000,000, a very conservative estimate, and they are continuing right along into 1919. It seems absurd to think that no methods of prophylaxis have been devised to resist this pestilence except those of ordinary sanitation, hygiene, and isolation.

The most striking feature among the causes of death is the great increase due to influenza. Ever since the epidemic which started in 1890 the company has had a few deaths annually from this disease. The number has varied from 30 to 70 usually, though in 1916 they amounted to 108 deaths. In the whole registration area of the United States the deaths from influenza numbered 18,886 in that year. Early in 1918 reports were received from Europe that influenza had assumed epidemic proportions in the Eastern and Central countries. The accounts were vague owing to difficulties in communication but it finally reached the German army on the Western Front and was recognized as very serious. Soon afterward it appeared in neutral and allied countries, and was given the name of "Spanish Influenza" because it was supposed to have spread from Spain, which it had reached through the medium of German submarines. From the allied countries in Europe it spread to the United States, arriving at the New England ports in the early part of September. Thence it diffused with great swiftness over the entire United States, as it is highly communicable, especially in the early stages of the disease. It proceeded along the lines of transportation, invading the cities first but rapidly spreading out into the rural districts. It took only a few weeks to reach the Pacific Coast.

The number of deaths in the United States from influenza directly and indirectly has probably amounted to 700,000 so far and the epidemic has not yet stopped. It reached maximum toward the end of October and then subsided distinctly, but the fatalities again rose toward the middle of December. They have passed their second maximum, however, which was considerably lower than the first and are again subsiding decidedly at the date of this writing (Jan. 15, 1919).

Among the company's policyholders there were 37 deaths prior to September due to epidemic influenza. Since that time in the last four months of the year 1918, there have been 1431 deaths among the policyholders in the United States and Canada due to epidemic influenza which amounted to \$4,016,000, so far presented to the company. As the death-claims in the United States and Canada are usually presented promptly, it is probable that nearly all of those incurred in 1918 have already been filed, but the epidemic is continuing and deaths on account of influenza are being reported throughout January, 1919, though with less frequency.

Since Jan. 1, 1919, the influenza claims have not appreciably diminished in number below those of December, 1918. Although the peak of the mortality was apparently reached in the end of October, the epidemic is continuing and has not finished its course.

The maximum amount of claims in any one week was \$732,831, which was incurred in the week ending October 26th, coincident with the maximum number of deaths. Prior to this the amount had gone up rather faster than the deaths, owing to some large policies which were caught early in the epidemic.

■ Patterns of Death

The following table shows the distribution of the deaths from epidemic influenza by ages and policy years during the last four months of 1918. For comparison, the last column shows the age distribution of all the deaths that occurred in the company's business in the three years 1915, 1916, and 1917.

Table 1: Distribution of Deaths by Age and Policy Year

Ages at Death	Total		Policy Year 1		Policy Year 2		Policy Years 3-5		Policy Years 6-10		Policy Years 11-20		Policy Years 21+		Deaths 1915-17		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
<20	26	1.7	15	8.0	5	2.7	6	1.63
20-24	118	8.2	29	15.4	25	13.4	47	12.5	17	4.8	1.7
25-29	310	21.7	50	26.6	60	32.5	105	28.1	88	25.5	7	2.5	2.5
30-34	366	25.6	53	28.2	50	27.1	92	24.7	115	33.4	56	19.7	3.7
35-39	264	18.5	28	14.9	26	14.1	73	19.5	58	16.8	78	27.5	1	1.8	5.1
40-44	138	9.6	10	5.3	11	6.0	31	8.3	28	8.1	53	18.7	5	9.1	7.3
45-49	81	5.7	2	1.1	5	2.7	14	3.7	21	6.1	30	10.6	9	16.4	9.0
50-54	56	3.9	1	.5	5	1.3	12	3.5	30	10.6	8	14.6	10.4
55-59	24	1.7	1	.5	1	.5	1	.3	3	.9	11	3.9	7	12.7	12.1
60-64	17	1.2	1	.5	1	.3	10	3.5	5	9.0	11.0
65-69	16	1.1	1	.3	4	1.3	11	20.0	10.9
70-74	7	.5	1	.3	5	1.7	1	1.8	10.0
75-79	4	.3	4	7.3	7.7
80+	4	.3	4	7.3	8.3
Total	1431		188		185		374		345		284		55				

Observations by the Company

It will be noted that about 76 percent of the total influenza deaths occurred below 40 years of age. In the first policy year about 93 percent of the deaths occurred below 40, although the average age at the issue is 28.7 years. In the 2d policy year about 90 percent occurred below 40. In the 3rd to 5th policy years the percentage of deaths below 40 is about 86 percent. On comparison it will be seen that the epidemic of influenza is preeminently a disease of the younger ages, about one-third of our deaths occurring below 30, and three-quarters of them below 40, only 128 deaths occurring above 50, a percentage of about 9 percent.

Out of the 1431 deaths from epidemic influenza, 74 occurred among our women policyholders, occasioning losses that amounted to \$118,800. The average amount is low and, furthermore, the influenza deaths are few compared with men, for these influenza deaths among women number only 5 percent of all the influenza deaths while women are present

among our policy holders to the extent of 7.5 percent. The average age of the influenza deaths among women was lower, being 34.7 years, and the average duration as policyholder was longer, being 7.5 years.

Questions for Discussion

- Among persons who held policies for only one year, what was the age distribution?
- How did the 1915 to 1917 pattern of deaths among policyholders differ from that in previous epidemics?
- Did that pattern change among different groups? For example, did it change for those who had held policies for two years? For three? For five?
- Do you think that the company statistics accurately reflect gender differences within the total population? What is the evidence for your conclusion?

- What general conclusions can you make about the patterns of deaths from influenza among policyholders of Mutual Life?
- What were the implications of these data for Mutual Life's business?

Comparison With Previous Epidemics

In the previous epidemic of influenza, which began toward the end of 1889 and recurred in 1890, 1891, and 1892 and also in subsequent years when it was endemic, influenza affected the older ages. The following table shows the age of the policyholders who died.

Table 2: Influenza Deaths in 1889-92 Among Policyholders

Age of Death	Number of Deaths	Percentage of Total Deaths
20-30 years	13	3.3
30-40 years	38	9.7
40-50 years	69	17.6
50-60 years	71	18.2
60-70 years	89	22.8
70-80 years	81	20.7
80-90 years	27	6.9
90 and over	3	0.8
Total	391	100.0

Observations by the Company

It will be noted that more than half, 51.2 percent, of the deaths occurred over 60 years of age in previous epidemics, while in the present epidemic only 3.4 percent occurred above 60, and more than half, 57.2 percent, occurred below 35. This contrast is greater when we realize that the proportion of living policyholders above 60 years of age was much smaller 30 years ago than now.

Question for Discussion

- How might other factors, such as the popularity of life insurance and longevity, affect the interpretation of these data?

■ The Weight Factor

The influence of weight on the mortality from influenza is set forth in the following table, which is divided into three sections: light weights, medium weights, and heavy weights. At height 5 ft. 8 inches, for example, those who weighed 132 pounds or less were counted as light weights and those who weighed 181 pounds or more were counted as heavy weights. Column 1 shows the percentage of the policyholders who have been insured since 1907 in that age-period in each section. Column 2 shows the percentage of deaths among the policyholders insured since 1907 in each section. Column 3 shows the percentage of deaths from influenza among policyholders insured since 1907. Column 4 shows the number of deaths since 1907.

Table 3: Influence of Policyholders' Weight on Death from Influenza

Ages at Issue	Entrants Since 1907	Regular Deaths of Entrants Since 1907	Influenza Deaths of Entrants Since 1907	
Light Weights				
	(1) %	(2) %	(3) %	(4) No.
15-29	17.6	19.2	14.2	109
30-39	9.3	10.5	7.7	28
40 and over	6.2	6.4	2.4	2
Medium Weights				
	(1) %	(2) %	(3) %	(4) No.
15-29	79.4	78.2	78.9	605
30-39	80.1	77.6	71.2	258
40 and over	76.0	73.2	67.1	57
Heavy Weights				
	(1) %	(2) %	(3) %	(4) No.
15-29	3.0	2.6	6.9	53
30-39	10.6	11.9	21.1	76
40 and over	17.8	20.4	30.5	26

Observations by the Company

It will be noted that in both the light weight and the heavy weight sections the percentages are higher in (2) than in (1), indicating in a crude way that the mortality is larger than normal in these sections, with the exception of the youngest age-period among the heavy weights. Among the light weights this excess is due in the main to tuberculosis, but among the heavy

weights the acute infectious diseases are quite important in determining the excess in the early policy years. That light weight has been a distinct protection against a fatal termination is shown by the low percentage in column (3).

The heavy weights on the other hand show the bad effects of a severe acute infectious disease like influenza by the higher percentages in column (3).

The influenza deaths in the light weight section numbered 139, in the medium weight section 920, and in the heavy weight section 155.

Questions for Discussion

- Would you say that weight was a factor in death from influenza? If so, which group (or groups) was affected?
- How can you account for this pattern? Is age a compounding factor?
- If you were giving advice to an insurance company on selecting policyholders, what recommendation would you make concerning the weight of applicants?

■ Losses to the Company

The following tables show the deaths and losses from epidemic influenza according to the duration of the insurance. For purposes of comparison with normal conditions, the percentage of deaths and losses that the company has incurred in the business issued from 1885 to 1915 is given in the last column.

Table 4: Influenza Deaths According to Number of Years Policyholders Have Held Policy

Policy Years	Influenza Deaths Reckoned by Applications		Deaths of the Issues of 1885 to 1915
	(1) No.	(2) %	(3) %
1	190	11.6	7.1
2	195	11.8	7.0
3-5	416	25.4	19.1
6-10	418	25.4	26.2
11-20	351	21.4	33.3
21 and over	73	4.4	7.3
Total	1643	100.0	100.0

Table 5: Influenza Losses According to Number of Years Policyholders Have Held Policy

Policy Years	Influenza Losses		Losses of the Issues of 1885 to 1915
	(1) No.	(2) %	(3) %
1	\$630,400	15.7	6.4
2	\$612,900	15.3	6.9
3-5	\$948,100	23.6	17.9
6-10	\$992,000	24.7	24.9
11-20	\$603,200	15.0	35.5
21 and over	\$229,400	5.7	8.4
Total	\$4,016,000	100.0	100.0

Observations by the Company

It will be noted that in the 1st policy year, the deaths from influenza were 1.5 times the normal, and the losses were 2.5 times the normal. In the 2d policy year the deaths from influenza were more than 1.5 times the normal and the losses from influenza nearly 2.5 times the normal. On account of this short duration and the

comparatively young ages at issue, the accumulated reserve on these policies has been small and the net loss to the Company has been large.

Questions for Discussion

- How did the pattern of deaths affect the financial losses incurred during 1918?

- How do companies gain or lose money?
- What do you think would have been a fair price for life insurance in previous years?

- If you had charged that fair price, approximately how much money would you have lost or gained in 1919?

Activity 9. A Question of Ethics

Cases 1-2

Resources 1, 5-7

Objectives

- To explore ethical issues associated with experiments on human subjects
- To define some of the difficulties in recruiting subjects for experimentation
- To stress the role of medical ethics in a public health context

1 Handout

- Highlights of Spanish Flu Experiments (p. 104)

Suggested Pathway

Both Milton J. Rosenau and J. J. Keegan experimented with human subjects in trying to understand the cause of Spanish flu. An account of their experiments is provided in the handout. (The account is taken from the material in Activity 2, “Reviewing the Evidence.”)

1. Assign the handout “Highlights of Spanish Flu Experiments.”
2. Break the class into small groups and tell them that you will provide a list of pertinent questions to initiate group work. (Alternatively, simply lead a class discussion without groups.)
3. Provide critical questions such as these:

Can prisoners who were promised pardons for their participation in the experiments be said to have given “informed consent”?

Should members of the armed forces be asked to “volunteer” for dangerous medical experiments?

Under what conditions, if any, would human participation in such experiments be warranted?

Does human experimentation (perhaps under the more innocuous name “clinical trials”) go on today?

4. Debrief the class.

Variation: Wrongful Death?

None of those who participated in Rosenau’s or Keegan’s experiments died, but suppose that one had. The possibility might put the issue of ethics into a sharper focus for the class. Ask the class to stage a court case in which the family of a sailor who died from an injection of Spanish flu sues the navy and doctors Rosenau and Keegan for wrongful death. *How would you frame the arguments of the plaintiffs (the sailor’s family) and the defendants (Rosenau and Keegan)?*

■ Highlights of Spanish Flu Experiments

1

Working with Milton J. Rosenau in September 1918, J. J. Keegan tested the hypothesis that Spanish flu was caused by a filterable virus. Nine sailors from the Deer Island Training Station near Boston volunteered to take part. (None of these men had a record of previous infection.)

Keegan collected secretions from the throats and noses of two flu patients. He passed the secretions through a bacteriological filter and dripped the resulting filtrate into the noses of the healthy volunteers. During a 10-day period of observation, the men developed no symptoms of flu.

2

In another experiment, Rosenau investigated transmission of Spanish flu and the hypothesis that Pfeiffer's bacillus caused the disease. In November-December 1918, he recruited 68 sailors from the Deer Island Training Station near Boston. Spanish influenza had been epidemic at Deer Island in September and October, but 39 of the 68 men had no recorded history of having suffered the illness. Many of the men were prisoners who were promised pardons for their cooperation.

To minimize contact with the outside world, Rosenau housed the volunteers in the Quarantine Station on Gallups Island in Boston Harbor. There he inoculated them with material from Spanish flu patients, including respiratory tract secretions and blood. To test the theory that the pathogen was Pfeiffer's bacillus, Rosenau inoculated some men with strains of the bacillus, some of which had been collected from the lungs of patients recently killed by flu. During the several days of observation that followed, not one volunteer inoculated with any material developed signs of flu.

Rosenau reasoned that Spanish flu might be more easily transmitted under conditions that resembled normal human contact between the sick and the well. He brought 10 of the men to the influenza wards at Chelsea Naval Hospital. The volunteers got as close to the sick as they would under normal street conditions: sitting close, breathing their exhalations and coughs, shaking their hands. One man got a mild respiratory ailment that was probably not influenza. The nine others developed no disease symptoms at all.

Activity 10. Digging Into the Past

Cases 1-2

Resources 1-3

Objectives

- To conduct historical research from a medical perspective
- To explore the links between medical events and current events
- To stress the human consequences of medical events

Suggested Pathway

Have your students conduct historical research into the human impact of the Spanish flu during 1918-19. Working either as individuals or in small groups, ask them to focus particularly on primary source materials. Using the library and the Internet, have them look for newspaper and magazine stories, medical journal articles, photographs, morbidity and mortality statistics, literary accounts, and diaries. There are many possibilities for good research. For example,

- Go to a local cemetery and if possible collect data (names, ages) about people who died of influenza at the time.
- Get the same kind of data from the local bureau of records.
- Interview elderly people (such as grandparents, who may not remember the pandemic personally but may have heard stories about it from their parents).
- Check newspaper notices from the period, including obituaries.
- Look at biographies of famous people who lived through that time. (A glance at James Cagney's obituary, for example, reveals that his bartender father died of Spanish flu.)

Encourage students to include material only loosely related to the pandemic: for example, popular songs and movies of the time, what people were wearing, advertisements of what was being sold. This kind of material provides

a sense of how day-to-day life was affected by the pandemic.

You can also encourage students to re-search the ways in which the pandemic was interrelated with other major historical events (most notably World War I and the Paris Peace Conference). Interestingly, despite the devastation it caused, the pandemic has been ignored by most historians. *Why?*

Ask students to present their research findings to the class. (If appropriate, perhaps the class can collaborate on a Spanish flu resource book that could be used by future classes.)

Variation: Researching the Science

Instead of focusing on the human side of Spanish flu, have the class conduct research into the scientific side. Initiate a brainstorming session in which students try to articulate some of the most pressing questions about influenza. *How does influenza make people sick? Why do we get a fever? Why was Spanish flu so much worse than regular flu?*

Let each student select the question he or she wants to research. Ask students to research library and Internet sources to get the best available answers to these questions. Students can prepare a written report or oral presentation.

One angle that might arouse special interest is the work of Ann H. Reid and Jeffery K. Taubenberger in retrieving genetic material of the 1918 Spanish flu virus from the bodies of victims. (See the interview with them in Resource 4, "Recovering a Killer," page 141). Their research was widely covered in the

media in 1997 and 1998, including articles in the *New York Times* (Feb. 24, 1998) and the *New Yorker* (Sept. 29, 1997). Students could report on some of these questions: *Is it wise or ethical to unearth bodies that might still contain live Spanish flu virus? Is it possible or wise to reconstruct a genetic blueprint that could potentially be used to reassemble the virus? How great are the risks? Do the benefits outweigh the risks?*

Another area of rewarding research is the history of influenza discovery. This research will encourage a historical perspective on how scientific knowledge accumulates. You can as-

sign one group to find out how the flu virus was isolated, another to find out about the first flu vaccine, another to find out how the three types of flu viruses were discovered, and yet another to find out how the molecular structure of flu viruses was first understood. Another interesting area of research is the flu pandemics of 1957 and 1968 and the swine flu scare of 1976. (For more on that, see Resource 6, "Lessons From the Swine Flu Episode," page 151.) Ask students to record any interesting flu milestones they come across. Perhaps the class as a whole can use the assembled reports to create a time line of flu discoveries.

Activity 11. Putting It Into Numbers

Case 2

Resources 1, 6-9

Objectives

- To explore the value of medical statistics
- To acquire research skills in the area of epidemiology
- To demonstrate the advances in medical documentation

Suggested Pathway

Before beginning this class, you might want to review “The Enigma of the 1918 Influenza Pandemic” (p. 3). It describes the first and second waves of the pandemic.

1. Begin with a class discussion intended to lead students into expressing opinions about the value of medical statistics. *Why is it worthwhile to know how many people are infected by a disease or sick from it? Why is it useful to know where they live and who they are?*
2. From Case 2, “Around the World,” read to students the following passage:

What if you were an epidemiologist whose job was to make sense of the statistics of the plague? Your job was hampered from the start. Until well into the pandemic, flu was not even a reportable disease in many places. Like athlete’s foot, it was considered too mild to be worth any space in the health records. Even when doctors were required to report cases of flu, diagnoses were not always accurate and records were not always kept faithfully. Mortality data were more reliable (death is easy to spot) but still incomplete. In the United States in 1918, deaths were compiled from a registration area comprising only 78 percent of the population. In undeveloped regions of Africa, Asia, and Latin America, accurate records of any kind were, and are, hard to come by.

Statistics mattered because they were the only way to tell whether a particular strategy was working or not (or whether things were getting better or worse) or whether you had learned anything that some other community might find useful. But statistics are only as valuable as the care with which you analyze them.

3. Break the class into groups. Ask them to compile local statistics for deaths from influenza (or pneumonia) before, during, and after the Spanish flu pandemic of 1918-19. If feasible, assign or let each group select the time period for its research: before, during, or after. Ask for oral reports. Be sure that the groups try to address the questions: *Who was most affected and why? Why is it important to know the patterns of infection and death?*
4. Debrief the groups. Be sure that students comment on how current statistics for influenza compare with those from the 1918 pandemic.
5. If desirable, assign written reports.

Current influenza statistics are easier to obtain than those from 80 years ago. For current information, a student can contact the local board of health or the Centers for Disease Control (CDC) in Washington, D.C., for influenza statistics for the last few years.

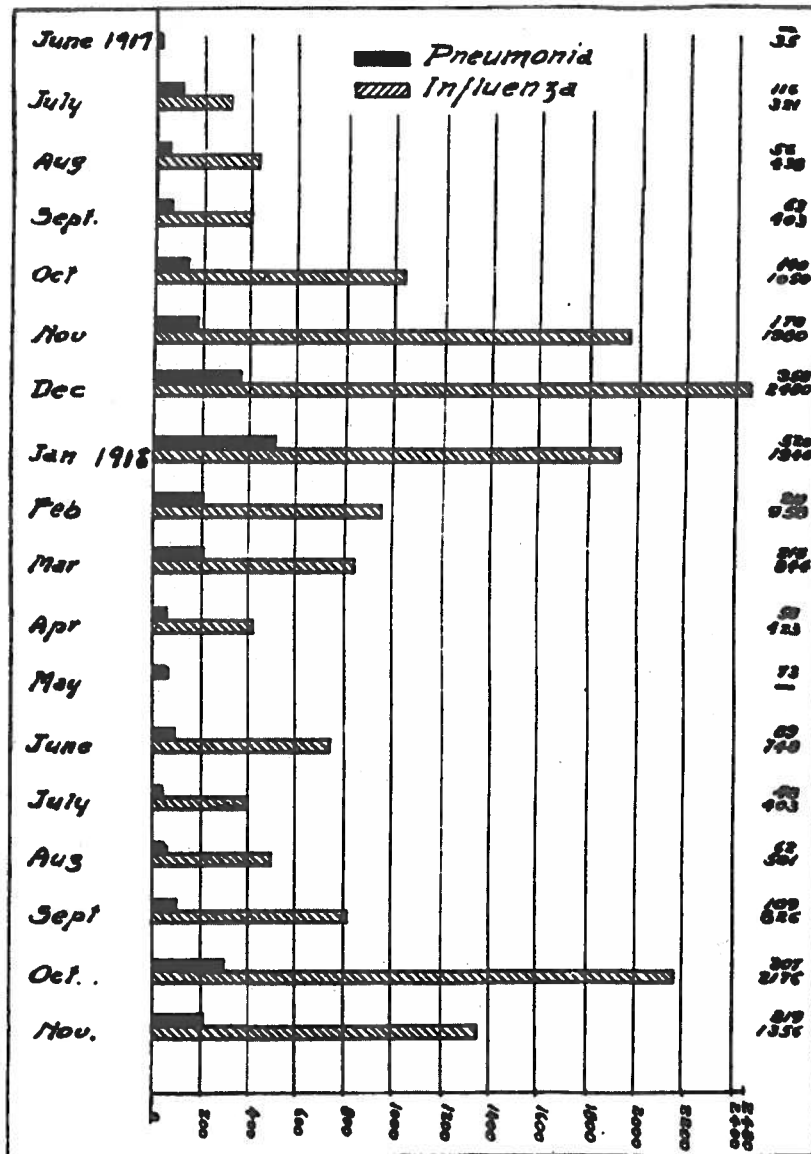


CHART 3.—Morbidity rate per 100,000 troops for influenza and pneumonia. Note that these diseases were relatively more prevalent in December, 1917, than at any time up to November, 1918.

Typical medical report chart from 1919. It compares rates of troop morbidity from both pneumonia and influenza.

Activity 12. Literary Witnesses

Cases 1-3

Resource 1

Objectives

- To explore the human and emotional impact of disease
- To highlight interdisciplinary links in research: literature, history, and science

1 Handout

- Four Poems About the Pandemic (p. 110)

Suggested Pathway

For the most part, writers who lived through the pandemic made little mention of it in their works. Faulkner, Hemingway, and Fitzgerald were mostly silent about it. But a few writers did face the memory head-on. These include

Willa Cather in *One of Ours*

William Maxwell in *They Came Like Swallows*

Mary McCarthy in *Memories of a Catholic Girlhood*

Katherine Anne Porter in *Pale Horse, Pale Rider*

Wallace Stegner in *On a Darkling Plain*

Thomas Wolfe in *Look Homeward, Angel*

1. Review the remarks about Porter (who was a flu patient) and McCarthy (who was orphaned by the flu) in Case 2, "Around the World" (p. 17).
2. Provide the class with copies of the handout "Four Poems About the Pandemic." Lead a discussion of the poems, focusing on the subtle details of infection and death and on the emotional coloring of the events.
3. Break the class into small groups. Let each group select one literary work. (Encourage

students to find their own selections as well.) Ask each group to find out from biographical resources how the Spanish flu affected the writer's life.

4. Ask for oral reports that address questions such as

What impact does Spanish flu have on the characters in this work?

What does the work tell you about the human side of Spanish flu?

In what way has the writer's art allowed the writer to transcend the experience of disease?

5. If desirable, assign written reports.

Variation: A Sharper Focus

Focus on only one or two works, such as the Porter novel and the McCarthy biography. Assign half the class to Porter and half to McCarthy. Ask each group to focus on only one or two of the questions above.

■ Four Poems About the Pandemic

The following four selections are taken from *Kyrie*, by Ellen Bryant Voigt (New York: Norton, 1995).

1

Nothing would do but that he dig her grave,
under the willow oak, on high ground
beside the little graves, and in the rain—
a hard rain, and wind
enough to tear a limb from the limber tree.
His talk was wild, his eyes were polished stone,
all of him bent laboring to breathe—
even iron bends—
his face ash by the time he came inside.
Within the hour the awful cough began,
gurgling between coughs, and the fever spiked,
as his wife's had done.
Before a new day rinsed the windowpane,
he had swooned. Was blue.

2

All day, one room: me, and the cherubim
with their wet kisses. Without quarantines,
who knew what was happening at home—
was someone put to bed, had someone died?
The paper said how dangerous, they coughed
and snuffed in their double desks, facing me—
they sneezed and spit on books we passed
around
and on the boots I tied, retied, barely
out of school myself, Price at the front—
they smeared their lunch, they had no
handkerchiefs,
no fresh water to wash my hands—when the
youngest
started to cry, flushed and scared,
I just couldn't touch her, I let her cry.
Their teacher, and I let them cry.

3

Thought at first that grief had brought him
down.
His wife dead, his own hand dug the grave
under a willow oak, in family ground—
he got home sick, was dead when morning
came.
By week's end, his cousin who worked in town
was seized at once by fever and by chill,
left his office, walked back home at noon,
death ripening in him like a boil.
Soon it was a farmer in the field—
someone's brother, someone's father—
left the mule in its traces and went home.
Then the mason, the miller at his wheel,
from deep in the forest the hunter, the logger,
and the sun still up everywhere in the kingdom.

4

Circuit rider, magic leather credential at my feet
with its little vials of morphine and digitalis,
I made my rounds four days at a stretch
out from the village, in and out of their houses
and in between, in sunlight, moonlight,
nodding on the hard plank seat of the buggy—
it didn't matter which turn the old horse took:
illness flourished everywhere in the county.
At Foxes' the farmhouse doors were barred
by snow;
they prised a board from a window to let me in.
At the next, one adult already dead,
the other too sick to haul the body out—

Activity 13. Writing Your Own Case

Cases 1-3

Resources 1, 7-9

Objectives

- To construct a narrative that conforms to the standards of a good case
- To work from a given situation into a case situation

Suggested Pathway

This activity tries to encourage imaginative writing based on an understanding of scientific information. Remind students that good cases are designed to illuminate “big ideas” (significant concepts that warrant serious study). Good cases are relevant, interesting,

readable, exciting, and focus on unresolved issues. (For a review, see pages 117-125, 171-183.) Assign this activity to groups or for individual work.

Tell students that they can write the case from one of the following two points of view.

1

Focus on a person who lived through the Spanish flu pandemic. The person can be a historical figure or someone you invent. Center the story on a problem or dilemma that this person (patient, family member, doctor, scientist, public health official) faced as a result of the pandemic. Tell the person’s story from his or her point of view. Use historical research (as in Activity 10, “Digging Into the Past”) to back up the details in the story. Be sure that the scientific aspects are accurate (for example, when referring to the clinical symptoms of the disease). Review the section of Case 2, “Around the World,” that begins “Behind the statistics were thousands of individual struggles and tragedies” (p. 18).

2

Focus on a person facing a disease other than the Spanish flu. For example, focus on someone living today and facing AIDS, a genetic disorder, or cancer. (Use a patient, family member, doctor, friend, or a fictitious character.) Be sure the scientific aspects are accurate. Focus on the problem or dilemma that this person faces as a result of the disease.

Students can present the case study as a first-person or third-person narrative or as a play. Tell them to feel free to invent dialogue and fictional details. The case can be open-ended, leaving the problem unresolved, or it can show how the problem is resolved, while making it clear that other resolutions can be imagined. The point of the activity is for students to broaden their understanding of the human issues involved in disease by making those issues concrete and particular.

Activity 14. Ideas for More Activities

The following ideas are sketches for developing more activities. They are intended to serve as prompts for your own thoughts on how to develop the contents of Cases 1, 2, and 3.

Recommend a Plan

Follow up directly on the last paragraph of Case 3 by asking the class *What would you recommend to the president and why?* Break down the last paragraph into questions for small groups. For example, one group can examine issues relating to the allocation of resources. Another can devise a plan to inform the public. In addition, ask all the groups to confront the most pressing issue: *Should we recommend a mass vaccination campaign?* When the class reconvenes, have the small groups report on their deliberations. Let the class debate the most pressing issue and try to reach a consensus of opinion.

Anatomy of a Fiasco

Ask the students if they know anything about the swine flu episode of 1976. Ask them why they think it is called a “fiasco.” Divide the class into small research groups. They can use the library, the Internet, and newspaper archives, and they may want to ask parents what their impressions were of the episode. You can share with students all or parts of the background paper in Resource 6, “Lessons from the Swine Flu Episode” (pp. 151-170). The comments and conclusions at the end of Resource 6 vividly highlight the flaws, problems, and issues inherent in the immunization program designed by the government. Be sure that students become aware of these observations. You might have each group research different aspects: politics, science, media treatment, and so forth. When the class reconvenes, students should discuss *What happened? What went wrong? What can be learned from it?*

Tracking the Flu

Ask the class to obtain current and recent data from the CDC and WHO on the yearly emer-

gence and spread of the influenza virus. Have small groups of students analyze the data to determine which flu strains were active in which years. *What were their types? What characteristics were significant? What problems did they pose for vaccine development?*

A History of Flu

Have the class research historical data, with the goal of discerning patterns among the various flu types and subtypes. *What do pandemic years (notably 1918, 1957, and 1968) have in common? What distinguishes them from each other?*

Other Diseases

Influenza is not the only disease with public policy implications. Assign a small group of students to focus on other diseases (AIDS, tuberculosis, cancer). *What are the key scientific issues in investigating and controlling the disease? What are the public policy issues? How have federal, state, and local governments dealt with the disease in recent years?*

What Are the Odds?

What are the chances that another lethal influenza pandemic on the scale of 1918 will occur sometime in the near future? Discuss how such a probability would be calculated and what variables are involved. Ask small groups to come up with answers. Then have the class debate the answers and try to reach a consensus on the odds.

The China Expedition

In Case 3, “The Coming Pandemic,” David McCord says that a team of CDC investigators has been sent to the Chinese village where the “index patient” died. *Who would be part of such a team? How much does it cost to field the team? What equipment and supplies do the*

team members need? How do they get to rural China? What is it like there? How long are they gone? What will the team do in China? How can the team's findings provide needed evidence? Have small groups of students research these different questions. You can ask students to imagine that they are fielding the China expedition—and that there is no time to waste.

Projecting a Pandemic

Have the class discuss this question: *How would a new flu strain as lethal as the one in 1918 spread if it started in rural India or China and no vaccine was developed to stop it?* Discuss how jet travel, shipping routes, and highways could transport it. *How long would it take to reach the United States? Which parts*

of the country would be likely to suffer the most? How many people would be infected? How many would die? Small groups can work on different aspects of a question. When the class reconvenes to discuss the results, point them to a new question: *What if a vaccine were developed, but, as seems likely, quantities were limited? Who would get protected? How would patterns of morbidity and mortality differ from the vaccineless scenario?* Break the class into small groups again to consider possible scenarios. For example, *What if 50 to 100 percent of the population of a few developed countries were protected, but the rest of the world was entirely unprotected? What patterns of infection and death might emerge?*

IV. RESOURCES

The resources in *The Spanish Flu and Its Legacy* range from general descriptions and reports to specific and detailed accounts of the nature of the virus and its impact on health and society. The following summaries provide a quick look at the contents of each resource.

Resource 1. Notes From the Pandemic

Contemporary field notes from a physician with the American Expeditionary Forces in France and England describe in detail the symptoms of the flu and its effect on the patients' bodies (Case 5002 and Case 2920). Also includes a telegram from a schoolteacher in Alaska to the Commissioner of Education describing the impact of the flu on Alaskan natives; brief summaries of contemporary experiments made in an attempt to find the cause of the flu; and comments and literature from other sources about the cause of the flu, its spread, virulence, and victims.

Resource 2. What We Now Know About the Influenza Virus

A clear and thorough description of the level of current knowledge about the virus. Includes a history and background, clinical manifestations, types of virus, antigenic drift, antigenic shift, the origin of pandemics, and a look at the future. Endnotes provide extensive and useful sources for research.

Resource 3. Immunology and the Influenza Virus

A complete description of viral mechanisms and how the immune system copes with a viral infection. Includes discussions of nonspecific defense mechanisms (phagocytosis, complement system, inflammatory response), the immune response and the components of the immune system (T cells, B cells), antibodies and how they work, and the flu virus itself, as well as an excellent step-by-step overview of infection and defense.

Resource 4. Recovering a Killer

Comments by the team that discovered the Spanish flu virus by examining stored samples of blood from its victims. Describes how they did it by using an enzyme called *reverse transcriptase* to make a complementary DNA copy of viral RNA and then using polymerase chain reaction (PCR) to create copies for more research.

Resource 5. Preparing for the Worst

An interview with medical representatives from the Food and Drug Administration. Includes discussion topics such as what factors define an epidemic, who makes that decision, how a pandemic virus originates. Also discusses the procedures and timetables for producing vaccines and ensuring quality control and addresses political and ethical issues.

Resource 6. Lessons from the Swine Flu Episode

The story of the 1976 swine flu vaccination program. It was a direct result of the nation's experience with the 1918-19 Spanish flu pandemic. The memory of that devastation certainly fueled the urgency that scientific and political leaders felt in dealing with a swine flu outbreak at Fort Dix Army Training Center. The ensuing results, however, were personally catastrophic for many involved and the memory of the events has influenced policymakers ever since.

Resource 7. Hearing Before House Committee on Appropriations

Includes testimony from a meeting on January 13, 1919. Provides some of the testimony from Thomas Riggs, Jr., governor of Alaska. Describes the government's attempts to cope with the Spanish flu pandemic. The human drama is compelling and the testimony is rich in provocative issues about ethics. For example, what are the responsibilities of the government to people who "came with the purchase"?

Resource 8. Medical Report From the A.E.F. in France and England

Selection excerpted from a report that appeared in the *Archives of Internal Medicine* in June 1919. Provides a thorough summary and analysis of the effects of influenza on troops in France and England. Also provides medical observations and describes attempts to identify the nature of the infection. Its medical detail is particularly interesting and demonstrates how scientists examine clinical and statistical data to make inferences about events. Discusses clinical manifestations, pathological anatomy, bacteriology, etiology, and epidemiology.

Resource 9. Report of the Spanish Flu in India

The Spanish flu traveled around the world, but nowhere was the toll greater than in India. This account portrays the spread and devastation of the pandemic and paints a vivid impression of Indian society under the British. Discusses the effects of age and class, with emphasis on the influence of class and nutrition on mortality.

Resource 10. Using the Case in Postsecondary Education

A geneticist and biology professor at Western Maryland College recounts her use of the prototypes of the Spanish Flu cases in her classes. Louise A. Paquin describes in detail student responses to the material and explains how both freshman and adult students benefit from case studies.

Resource 1. Notes From the Pandemic

Observations, Hypotheses, Reflections

OBSERVATIONS

Field Notes: Case 5002

Patient had a slight cold on Saturday, October 5, but took dinner with friends on that date. He was admitted to American Red Cross Military Hospital I from the Hotel Neurice at 6 p.m. on October 7 in a dying condition; died October 8 at 8:30 a.m. Duration of illness was therefore about 60 hours. Pleural cavities contain a few cubic centimeters of cloudy fluid. There are no adhesions. Lungs are both of the size of full inspiration. There is practically no exudate on either pleural surface. The right lung shows the upper two thirds of the upper lobe, the apex of the middle lobe and scattered patches throughout the lower lobe containing solid bluish-red areas, which have ill-defined margins. On section these areas are dark red in color and comparatively airless, the surfaces being bathed with a very large amount of bloody fluid. The remaining portions of the lungs are heavy with congestion and edema, except for a few of the anterior portions, which are dilated and feathery. The outer middle portion of the upper lobe and the outer half of the lower lobe of the left lung are in a similar condition; otherwise it resembles the right. The bronchi of both lungs are deep red in color, bathed with abundant bloodstained frothy mucus and covered with a thin, closely adherent, grayish-yellow, fibrinous pseudomembrane. The peribronchial lymph nodes are not markedly swollen. The sinuses at the base of the skull show some thickening of the mucosa and a small amount of mucoid fluid in the left sphenoid and left frontal. Smears and cultures from the lungs show streptococci and gram-negative bacilli (*B.influenzae?*). Smears from frontal sinus show staphylococci, gram-negative bacilli (*B.influenzae?*) and a short gram-positive bacillus; cultures from the same place show staphylococci. *Prosector: Major H. E. Robertson.*

Field Notes: Case 2920

Patient entered Base Hospital 17 Sept. 2, 1918, having been in France one week. He had been sick since landing, and had been riding in a baggage car for several days. He died September 12 at 11:50 p.m. The necropsy was performed at 3:25 p.m., September 13. The mediastinum is well covered with fat, the right visceral pleura hemorrhagic and injected and covered with fibrinous deposits. The pericardial cavity contains about 70 c.c. of a straw-colored fluid. The left lung weighs 1 pound 13.5 ounces and shows irregular consolidated areas. The right lung weighs 2 pounds 12.5 ounces. The left lung floats in water; on section it shows irregular consolidated areas from which frothy mucus exudes. The lobular type is more evident to the sense of touch than of sight. The entire right lung floats in water as do portions from the most nearly consolidated portions. Bronchi are red and inflamed. Cultures from the brain and from the heart blood are negative; cultures from the right lung show *B. influenzae* and *Streptococcus viridians*. *Prosector: Capt. Henry W. Cattell.*

MacNeal, Ward, M.D. "The Influenza Epidemic of 1918 in the American Expeditionary Forces in France and England," *Archives of Internal Medicine* 23 (1919): 6.

A Telegram

Sent to the U.S. Commissioner of Education from Evans, a schoolteacher in Nome, Alaska.

Nome, Alaska.

January 2, 1919

Hon. P. P. Claxton

Commissioner of Education, Washington, D.C.

Ten villages this district affected. Three wiped out entirely, others average 85 percent deaths. Majority of children of affected villages saved by relief parties sent by the Bureau of Education. Teachers in stricken villages all sick, two dead, rest recovering. Total number of deaths reported 750, probably 25 percent this number frozen to death before help arrived. Over 300 children to be cared for, majority of whom are orphans. Am feeding and caring for surviving population of five large villages. Seven relief hospitals operated in affected villages: no trained nurses or physicians available, but splendid work done by white people in charge. Cost to date estimated \$70,000 for native relief alone; will need about \$15,000 this month. May be necessary to send relief to several quarantined villages owing to regulations preventing natives from trapping, and can not purchase necessities. Impossible at this time to lift quarantine zones in outlying affected villages. Appalling and beyond description. Am giving 90 orphans to mission at Nome to care for at \$10 per month, but hope department will plan for large industrial training school this district next summer. Splendid opportunity for educational advancement for the Eskimos. *Evans*

Influenza in Alaska and Porto Rico. Hearings Before the House Committee on Appropriations. January, 1919.

Experimental Evidence

1

Cecil and Blake obtained a sample of **Pfeiffer's bacillus** from a flu patient and inoculated a mouse with it. After recovering a sample of bacillus from the mouse, they passed it serially through 10 more mice. The first 10 mice survived, but the eleventh died. They passed a sample from the dead mouse through a series of 13 monkeys. The monkeys became ill; on autopsy, they showed lung lesions similar to those seen in human influenza.

Cecil, Russell L., and Francis G. Blake, "Pathology of Experimental Influenza and a Bacillus Influenza Pneumonia in Monkeys," *Journal of Experimental Medicine* 32 (1920): 719-44.

2

At Chelsea Naval Hospital near Boston, 80 percent of the autopsies revealed the presence of **Pfeiffer's bacillus**. The same microbe was found in cultures taken from flu sufferers in many other pandemic locations, including Camp Devens, Massachusetts. But in studies of 32 cadavers at Chelsea Naval Hospital from September 1918 to January 1919, Keegan's colleague Ernest W. Goodpasture found that either pneumococcus or streptococcus was dominant in the lungs and that in many cases Pfeiffer's bacillus was entirely absent.

Keegan, J. J., *Journal of the American Medical Association* 71 (Sept. 28, 1918): 1053.

3

In 1918-19, the two teams of researchers investigated whether the same or different strains of **Pfeiffer's bacillus** were present in populations of flu sufferers in Britain and the United States. After testing specimens of Pfeiffer's bacillus from numerous cases on both sides of the Atlantic, the researchers found that the strains were much more likely to be different than the same. In one

experiment by Park, nine samples of the bacillus from nine different autopsies proved to represent nine different strains.

Park, W. H., and A. W. Williams, "Studies on the Etiology of the Pandemic of 1918," *American Journal of Public Health* 9 (Jan. 1919): 49.

4

Parker cultured five strains of **Pfeiffer's bacillus** from the sputum of patients suffering from influenzal pneumonia. After passing each pure strain through a bacteriological filter, she inoculated rabbits with the bacteria-free fluid. The rabbits died. Parker concluded that Pfeiffer's bacillus produced a filterable toxin, or poison, that killed the animals.

Parker, Julia T., "A Filterable Poison Produced by B. Influenza (Pfeiffer)," *Journal of the American Medical Association* 72 (Feb. 15, 1919): 476-77.

5

In 1918-19, two French researchers injected monkeys with **filtrate** of human flu secretions. Flu-like symptoms resulted. The researchers tried injecting flu filtrate under the skin (subcutaneously) of one human volunteer and into the vein (intravenously) of another. The subject who received subcutaneous injection developed mild symptoms of influenza. The subject who received intravenous injection developed no symptoms.

Nicolle, Charles, and Charles Le Bailly, "Recherches Experimentales sur la Grippe," *Annales de l'Institut Pasteur* 33 (1919): 395-402.

6

From December 1918 to March 1919, Japanese researchers tried several different experiments. They introduced **filtrate** of flu sputum into the noses and throats of 12 healthy people. They introduced filtrate of blood from flu sufferers into the noses and throats of six more healthy people. They injected filtrate of flu sputum subcutaneously into four healthy people. To provide a control, the investigators introduced pure cultures of Pfeiffer's bacillus and mixed cultures of various microbes, including Pfeiffer's bacillus, **pneumococcus**, **staphylococcus**, and **streptococcus**, into the noses and throats of 14 healthy people.

Almost all of the subjects who received filtrates of any of the materials collected from flu patients (blood or sputum) developed influenza. The only ones who did not were those who had previously suffered a recorded case of influenza. None of the people in the control group—the people receiving pure Pfeiffer's bacillus and mixed cultures of bacteria—developed any kind of sickness.

Yamanouchi, T., K. Skakami, and S. Iwashima, "The Infecting Agent in Influenza," *Lancet* 196 (June 7, 1919): 971.

7

In a 1918 study at Camp Meade, Maryland, **streptococcus** was found in 87 percent of cultures taken from 110 influenza patients. However, in other locations, in other populations of flu patients, streptococci were not found at all.

Rosenow, E. C., and B. F. Sturdivant, "Studies in Influenza and Pneumonia, IV," *Journal of the American Medical Association* 73 (Aug. 9, 1919): 396-401.

8

Having developed methods of culturing **Bacterium pneumosintes**, Olitsky and Gates carried out studies of the microbe from 1918 to 1923. They injected samples of the bacteria into the trachea of rabbits and guinea pigs. The animals became ill, and autopsies showed lesions in the lungs sim-

ilar to those of human influenza. Olitsky and Gates were able to collect *Bacterium pneumosintes* from the dead animals' lungs.

Olitsky, Peter K., and Frederick L. Gates, "Experimental Studies of the Nasopharyngeal Secretions from Influenza Patients," *Journal of Experimental Medicine* 33 (June 1, 1921): 713-28.

9

In 1920, British researchers H. B. Maitland, Mary L. Cowan, and H. K. Detweiler reported results that bore on the claims of Olitsky and Gates. Maitland and his collaborators inoculated one group of animals with filtrates of human flu secretions; another group was not inoculated. The researchers found that if they killed an animal by the Olitsky-Gates method of striking it on the back of the head, the animal's heart would keep beating for several minutes, producing lesions in the lungs like those that Olitsky and Gates had observed. The animals developed these lesions regardless of whether they were inoculated with flu filtrate. If they killed the animals another way—by cutting into their hearts—no lung lesions were visible, regardless of whether the animals had been inoculated.

HYPOTHESES

About the Cause of the Pandemic

1

The bacteriological findings have been variable and have usually shown a mixture of various species of microbes. Influenza bacilli, pneumococci of various types, hemolytic and non-hemolytic streptococci have occurred most frequently in the infiltrated lungs... These findings suggest that the disease has been essentially due to an invasion of the respiratory tract by influenza bacilli, followed by and associated with other pharyngeal organisms, and that the fatal outcome, in most instances, has been brought about particularly by these secondary invaders, in some instances streptococci, in others pneumococci.

MacNeal, Ward, M.D. "The Influenza Epidemic of 1918 in the American Expeditionary Forces in France and England," *Archives of Internal Medicine* 23 (1919).

2

Either we deal with one organism which presents itself in two phases, a minute filterable form which becomes haemal and a bacillary form mainly developed in the air passages, or we deal with a symbiosis, and are to regard the filterable form as gaining entrance through the air passages and by its presence favoring the coincident growth of Pfeiffer's bacillus. In such a way the two viruses are conveyed together from individual to individual.

It is along these lines, it would seem, that the problem is to be solved. Will the "filter-passer" remain invisible, or, when grown under suitable conditions, will it develop into a visible streptococcal or a bacillary form? If it will not, then the symbiotic theory will have to be accepted or the closely allied view, which has gained much support from French workers, of composite and successive infection. Here, one organism, the filter-passer, preparing the ground for another, the influenza bacillus, which for a time flourishes and has the upper hand and in its turn prepares the way for, and is replaced by a member of the streptococcus group, or by the pneumococcus, just as in the maturation of a dung-heap we find a succession of forms replacing each other until the cellulose of the straw and the proteids of the excreta are broken down stage by stage into their elementary constituents. Of these two views the symbiosis hypothesis, with coincident conveyance from throat to throat of two or more species of micro-organism, appeals to us, we confess, as meeting more closely the observed facts of the epidemic.

Editorial, *Lancet* (January 4, 1919): 25.

3

It should be realized that bacteriology is at present as much in its infancy as the practice of medicine was in the time of Hippocrates...that investigators often find that many of the supposedly well established and reliable principles are not infallible, and that iron-clad qualities assigned to an organism often fail to prove stable. This being the case, it is easily understood that many of the descriptions given of the form and qualities of particular bacteria fail to define absolutely and differentiate the organisms, so that in attempting to identify any organism difficulties are frequently encountered. It is for this reason that I have written above that "the bacillus of Pfeiffer (or a similar organism)" was the cause of the epidemic, although some of the cultural limitations, etc., described in the textbooks do not hold. This only indicates that the discoverer, and others responsible for the orthodox descriptions of the influenza bacillus, did not learn everything about the organism.

Greeley, Horace, M.D. Letter to the *Medical Times*, December 1918, p. 306.

About Its Spread and Virulence

1

The arrival of American troops in France has been a factor of possible importance in relation to this disease...This increase of more than 50 percent required in many places, the crowding of three or even four men into the quarters previously occupied by two, increased enormously the opportunity for the rapid transmission of respiratory infection. Furthermore, it furnished a large group of newly arrived susceptible individuals and brought them into close association with the influenza endemic among the American soldiers who had preceded them.

MacNeal, Ward, M.D. "The Influenza Epidemic of 1918 in the American Expeditionary Forces in France and England," *Archives of Internal Medicine* 23 (1919).

2

Knowing that influenza bacilli have been constantly with us, one wonders why it is that the disease should suddenly become epidemic. There are only two possible reasons: one that the population became less resistant, and the other, that the organism became more active (*virulent*). There being no apparent reason for the first (in New York City), we turn to the second for the explanation, which may be made as follows: It is known that a given bacterium often becomes totally incapable of pathogenic action after extended cultivation as a saprophyte, but that, when taken directly from an animal sick of the disease, it is most active in reproducing it in others. Conditions in animals, including man, resulting from either chilling, exhaustion, or insufficient feeding, are known to render them susceptible to infections to which they would otherwise be immune...The conditions described have been quite prevalent in European countries during the past two or three years, and armies in the field can hardly escape one or more of the injurious influences mentioned...Thus, the influenza bacillus, after increasing in virulence by successfully producing disease in persons so predisposed to infection, became capable of attacking many persons under ordinary conditions of life, and the present epidemic was the consequence.

Greeley, Horace, M.D. Letter to the *Medical Times*, December 1918, p. 306.

3

Paul Ewald in *The Evolution of Infectious Disease* discusses why the Spanish flu was so deadly. He dismisses the contention that its virulence stemmed from the fact that it was a swine flu:

There is no evolutionary basis for supposing that transmission from swine to humans should be associated with particularly high virulence in humans. To the contrary, transmission into new hosts should often be associated with low virulence in the new hosts because the ability of our immune systems to block novel pathogens should tend to be greater than the ability of novel pathogens to invade new hosts species.

Ewald continues on to cite the explanation offered by the U.S. Office of the Surgeon General that virulence was enhanced by “rapid passage.” This explanation was based on observations that the rapid passage of pathogens among laboratory animals often increases their virulence. That is, the relative immobility of the laboratory animals eliminates the requirement that the host of a disease has to be mobile in order to transmit the pathogen. Since natural selection favors those organisms that are most competitive, immobility favors those pathogen variants that reproduce rapidly at the onset of the disease. Ewald concludes that the virulence of the 1918 pandemic was, consequently, the result of an evolved response to wartime conditions (such as crowding in trenches and hospitals) rather than simply an inflexible characteristic of the type of influenza.

Ewald, P., *The Evolution of Infectious Disease* (New York: Oxford University Press, 1994), 114.

About Its Victims

No definitive explanation has been found to account for why the virus was particularly lethal to the young and healthy, but different factors could have contributed to it, including:

- Older people could have been naturally immunized by previous exposure to a similar strain of the virus that stopped circulating afterwards.
- There were massive movements of troops (young men and women) and shifting of civilian populations during the war, which provided the opportunity for interchange of airborne germs.
- The inflammatory response of young adults has been more reactive and powerful than that of infants and the elderly. It responded to the virus by flooding the infected lung tissues with quantities of fluid, thereby overwhelming the lungs.

For a fuller discussion of these possibilities, see “Age Effect” in Resource 9, “Report of the Spanish Flu in India” (p. 181).

About Its Return

Even if the same strain of the virus continued to reproduce in animal hosts, it has certainly suffered important modifications to adapt to the new environment. Therefore, it is unlikely that the original virus that caused the 1918 pandemic would pose a threat. More likely, the next pandemic will be originated in another recombinant virus using pigs as the mixing vessel.

Crosby, Alfred W., *America's Forgotten Pandemic* (New York: Cambridge University Press, 1989), 217-18.

REFLECTIONS

1

Some scientists have claimed that the problem is not the nature of Spanish influenza, but our approach to the subject. It should be considered, they suggest, not as a pandemic of influenza but as one of pneumonia. After all, the real killer was not the flu but pneumonic complications following the flu...Even if we accept [this theory], it leads to a rephrasing of the original question: now we ask, why was there a pandemic of pneumonia? The answer indicates that by rephrasing

the question we haven't moved one step closer but one step further away. How could it be that several different kinds of pathogens capable of causing pneumonia, such as strep and staph, not to mention the multitudes of strains of each, all mutated simultaneously in 1918 into more virulent strains than had existed in 1917?

Crosby, Alfred W., *America's Forgotten Pandemic* (New York: Cambridge University Press, 1989), 217-18.

2

In order to settle in a convincing fashion the relation of the bacillus of Pfeiffer to the disease it would be necessary to carry out a series of very carefully controlled experiments on a group of thoroughly segregated men, preferably those confined in a prison that has entirely escaped the epidemic. It will not be sufficient to produce by the inoculation of pure cultures the clinical manifestations of influenza merely in the individual inoculated, but a critical demonstration should include the reproduction of the disease with its characteristic epidemic feature.

MacNeal, Ward, M.D. "The Influenza Epidemic of 1918 in the American Expeditionary Forces in France and England," *Archives of Internal Medicine* 23 (1919).

3

As a result of the clinical, bacteriological, and pathological work we did at Camp Pike [during 1918-19], Opie, Blake, Small, and I published a volume in 1922 called *Epidemic Respiratory Diseases*. I think it is one of the best books describing what happened during that pandemic that has ever been written.... There is, however, one chapter in the book that I wish had never been written. Blake and I and the others were brought up to believe that influenza was caused by the influenza bacillus or, as it was known, *Pfeiffer's bacillus*, and naturally, when the epidemic broke out at Camp Pike, Blake and I made every effort to see if we could isolate influenza bacillus from our patients. Well, we managed to get influenza bacilli out of every person that had an attack of influenza. It is true that we had to take more than one culture, and we cultured material from the sputum as well as swabs from the throat and nose. But we found it and quickly jumped to the conclusion that the influenza bacillus was the cause of the pandemic. Well, we were just 100 percent wrong, and it's a chapter I wish had never been written.

Rivers, Thomas. *Tom Rivers: Reflections on a Life in Medicine and Science: An Oral History Memoir*, prepared by Saul Benison. (Cambridge, Mass.: MIT Press, 1967), 59.

4

May I ask why, as my husband was a victim on the long list of doctors who succumbed to the terrible epidemic last month, no mention is made in any periodical or public newspaper of these noble fellows who gave their lives in fighting this disease? Are they not to be mentioned in any way as heroes?

Letter from Mrs. Longino, Fort Stockton, Texas, to the Editor of the *Journal of the American Medical Association*, December 7, 1918.

5

I had a little bird
And its name was Enza
I opened the window
And in-flew-Enza.

Song sung by children during the pandemic

6

Nothing would do but that he dig her grave,
under the willow oak, on high ground
beside the little graves, and in the rain—
a hard rain, and wind

enough to tear a limb from the limber tree.
His talk was wild, his eyes were polished stone,
all of him bent laboring to breathe—
even iron bends—

his face ash by the time he came inside.
Within the hour the awful cough began,
gurgling between coughs, and the fever spiked,
as his wife's had done.

Before a new day rinsed the windowpane,
he had swooned. Was blue.

Ellen Bryant Voigt, *Kyrie*. (New York: Norton, 1995).

7

All day, one room: me, and the cherubim
with their wet kisses. Without quarantines,
who knew what was happening at home—
was someone put to bed, had someone died?
The paper said how dangerous, they coughed
and snuffed in their double desks, facing me—
they sneezed and spit on books we passed around
and on the boots I tied, retied, barely
out of school myself, Price at the front—
they smeared their lunch, they had no handkerchiefs,
no fresh water to wash my hands—when the youngest
started to cry, flushed and scared,
I just couldn't touch her, I let her cry.
Their teacher, and I let them cry.

Ellen Bryant Voigt, *Kyrie*. (New York: Norton, 1995).

8

Thought at first that grief had brought him down.
His wife dead, his own hand dug the grave
under a willow oak, in family ground—
he got home sick, was dead when morning came.

By week's end, his cousin who worked in town
was seized at once by fever and by chill,
left his office, walked back home at noon,
death ripening in him like a boil.

Soon it was a farmer in the field—
someone's brother, someone's father—
left the mule in its traces and went home.
Then the mason, the miller at his wheel,
from deep in the forest the hunter, the logger,
and the sun still up everywhere in the kingdom.

Ellen Bryant Voigt, *Kyrie*. (New York: Norton, 1995).

9

Circuit rider, magic leather credential at my feet
with its little vials of morphine and digitalis,
I made my rounds four days at a stretch
out from the village, in and out of their houses
and in between, in sunlight, moonlight,
nodding on the hard plank seat of the buggy—
it didn't matter which turn the old horse took:
illness flourished everywhere in the county.
At Foxes' the farmhouse doors were barred by snow;
they prised a board from a window to let me in.
At the next, one adult already dead,
the other too sick to haul the body out—

Ellen Bryant Voigt, *Kyrie*. (New York: Norton, 1995).

Resource 2. What We Now Know About the Influenza Virus

By Carolyn Buxton Bridges, M.D.

This century's most deadly influenza pandemic took place in 1918 and 1919 and was known as the *Spanish flu pandemic*. It is estimated that over 20 million people worldwide and 500,000 in the United States alone died from influenza and its complications.^{1,2,3} This staggering number of deaths is in sharp contrast to the 20,000 U.S. deaths attributed to influenza during an average influenza epidemic.⁴ Nearly as many U.S. soldiers died from influenza-related illnesses as died from combat during World War I, and some scholars credit the pandemic with hastening the war's end.⁵ Although most deaths from influenza occur in the elderly and frail or the very young, this particular pandemic's victims were primarily young and healthy adults. The shift in mortality toward young adults during this pandemic has never been fully explained.⁶

BACKGROUND

Historical accounts of influenza epidemics probably date back to the time of Hippocrates in 412 B.C.³ However, according to medical historians, the first clearly described epidemic of influenza occurred in the twelfth century.⁶ The name *influenza* originated in Italy in the fifth century after an epidemic of respiratory infection was attributed to the "influence" of the stars. Heavenly bodies, earthquakes, volcanic eruptions, weather, and a mystery gas have also been blamed for causing influenza.²

At the time of the 1918-19 pandemic, Pfeiffer's bacillus (a bacteria now known as *Haemophilus influenza*) was believed to be the most likely cause since it had been isolated from many victims of influenza. However, scientists were unable to show that introduction of the bacteria into a healthy subject led to symptoms consistent with influenza. In 1918, a veterinarian in Iowa had noted that an outbreak of respiratory illness in pigs occurred coincident with an outbreak in humans in the same region. Expanding on this observation, Richard Shope found in 1928 that he could induce influenza among healthy swine by inoculating their nasal membranes with the mucous from an ill pig, even after filtering the mucous to exclude bacteria. His findings were published in 1931 and provided convincing evidence that the causative agent was a "filterable virus" and not

a bacteria. In 1933, 15 years after the Spanish Flu pandemic, influenza A virus was finally isolated from humans.^{2,3,7,8}

Since the technology to isolate influenza viruses was nonexistent in 1918-19, no viruses were ever isolated from persons ill with the Spanish flu. Besides actually isolating a virus from an ill person, anti-virus antibody detected in a person's serum can serve as evidence of a past infection. By testing for antibody from persons alive during the pandemic, researchers showed that the virus that caused the pandemic was an influenza A virus. The influenza strain isolated from pigs in 1928, named the swine flu virus, is believed to be similar to viruses that caused illness in humans in 1918, and both viruses are believed to have originated from the same source.^{1,6,9} In 1997, Dr. Jeffery K. Taubenberger and colleagues identified fragments of the 1918 virus in the lung tissue from a soldier who died of the Spanish flu.^{9a} Dr. Taubenberger's work confirmed that the Spanish flu virus was influenza.

CLINICAL MANIFESTATIONS

Influenza is a respiratory disease caused by the influenza virus. Epidemics generally strike during the fall and winter months in temperate climates. The virus spreads from person to person when aerosolized droplets of respiratory secretions produced by the coughing and

sneezing of an ill person are inhaled by a susceptible person. Influenza is highly contagious and capable of spreading rapidly through homes, schools, communities, and continents, though as many as 50 percent of people who become infected with the virus may not develop symptoms. Symptoms usually begin abruptly 18 to 72 hours after a person has been infected and may include temperatures as high as 105.7°F, body aches, headache, cough, runny nose, sore throat, and fatigue. Gastrointestinal symptoms can also occur but are less common, affecting children more often than adults. The fever and body aches can last for three to five days, although coughing may persist for two or more weeks.^{1,6} On average, between 10 and 20 percent of the United States population each year develops respiratory symptoms attributable to influenza.^{10,11}

Risk Groups

Some groups of people are at increased risk for developing complications after influenza infection. Complications can include secondary bacterial pneumonia and worsening of underlying chronic heart and lung disease. Most deaths related to influenza occur in people age 65 years and older, the very young, and those with chronic heart or lung disease.^{1,7} The number of deaths each year from influenza can vary widely depending on the particular strain of virus in circulation, the degree of immunity against the virus in the population, and the number and ages of persons who become infected.^{1,6}

Types of Virus

The influenza virus belongs to the Orthomyxoviridae family of viruses and contains single-stranded RNA. There are three types of influenza viruses: types A, B, and C. Specific strains of influenza virus are formally designated by the influenza virus type, the species in which the virus was isolated, the geographic origin of the isolated virus, the strain number, and the year of isolation (e.g., Influenza A/Swine/Iowa/15/30). By convention, names of

isolates from humans do not include the species name (e.g., Influenza B/Beijing/184/93). Influenza A viruses have been isolated from many different animals, but types B and C are limited to human hosts.^{3,6,12} Type C viruses cause only mild cold symptoms and are of less clinical and epidemiologic significance. Therefore, the remainder of the discussion will focus only on types A and B.^{3,12,13}

Types A and B

The influenza A and B virus genomes consists of eight separate RNA segments, each of which codes for one or two proteins. Two of these proteins, hemagglutinin (HA) and neuraminidase (NA), are glycosylated and arranged in spikes over the outer shell of the virus. Hemagglutinin helps the virus attach to host cell walls and initiate infection, while NA helps the replicated viruses exit the infected host cell among other less well understood functions. The other viral genes are necessary for the virus to replicate its RNA genome and to produce essential viral structural and nonstructural proteins. In response to infection, the host makes antibodies to several of the viruses' components. However, antibodies directed against the HA (anti-HA) and NA (anti-NA) provide the primary protection against repeat infection from similar strains of influenza virus. Of the two, anti-HA antibodies are the most important in preventing infection. Anti-NA antibodies help to reduce the severity of infection and probably limit the spread of the virus to other cells within the host.^{3,12,14}

Influenza A viruses are divided further into subtypes based on different combinations of HA and NA glycoproteins. These subtypes are abbreviated H(#N(#). Fifteen HA and nine NA subtypes have been identified. All have been isolated in aquatic birds, which are thought to be the primary animal reservoir of influenza A virus. Subtypes of influenza A virus have been isolated from ducks and other migratory birds, domestic fowl, swine, horses,

and seals, among other animals.^{9,15} The three influenza A virus subtypes that have caused widespread outbreaks among humans are H1N1, H2N2, and H3N2. Two of the three human subtypes (H1N1 and H3N2) have also been isolated in swine.⁷

A CHANGING VIRUS

Influenza virus is unique among respiratory viruses in its ability to undergo continual antigenic change. Genetic changes can lead to antigenic alterations of the virus and, in effect, the creation of new viruses to which the host's immune system has not been previously exposed and against which the host has no protective antibodies. Antigenic change, therefore, enables influenza viruses to cause illness in the same host again and again. The greater the antigenic alteration of the virus from prior years, the less likely it is that individuals and populations will have protective antibodies. The influenza virus's ability to undergo continual genetic and antigenic change helps to ensure that a certain percentage of the population will be susceptible to influenza each year.^{6,7}

Antigenic Drift

Influenza viruses undergo antigenic variation by two major mechanisms: antigenic *drift* and antigenic *shift*. Antigenic drift is a result of random copying errors that occur during gene transcription (the process by which copies of the viruses' RNA genome are made). These copying errors result in point mutations in the genome and may result in changes in the structure and shape of the NA and HA glycoproteins and alter the viruses' antigenic properties. Existing antibody made against prior influenza viruses may not be effective against the changed virus, allowing it to replicate and cause infection in the host. Changes due to antigenic drift are relatively minor, but they are sufficient to lead to yearly epidemics, either localized or global, by generating new variants of a circulating influenza subtype.^{2,16,18} Because influenza is constantly changing, both types A

and B viruses are collected from around the world and tested to monitor changes. If the circulating viruses are substantially different from the vaccine strains, then the vaccine strains are updated. Nearly every year, one or more of the vaccine virus strains are changed. Vaccine containing viruses to combat the previous year's circulating influenza viruses are often not protective against the current year's viruses.^{4,12,14}

Antigenic Shift

Antigenic shift is a completely different mechanism by which the viral genome changes. Shift causes a much more radical change in the viral genome (and antigenic properties) and involves the acquisition of new HA- and/or NA-coding RNA segments. Since anti-HA antibody is protective against infection, the replacement of an old HA or the replacement of both an HA and NA is the first step toward the emergence of a new pandemic viral strain. For a virus with a new HA to have the potential to cause a pandemic, it must also be easily transmitted from person to person and none or most of the world's population has protective antibody against it. Only influenza type A viruses undergo antigenic shift and all influenza pandemics are believed to have been caused by influenza A.¹² Of the three pandemics that occurred during the twentieth century, the Spanish flu in 1918-19 was caused by influenza A viruses of the H1N1 subtype, the Asian flu in 1957 by viruses of the H2N2 subtype, and the Hong Kong flu in 1968 by viruses of the H3N2 subtype.^{1,6,18,19}

ORIGIN OF PANDEMICS

Pandemics may arise when a new HA-coding RNA segment appears in human influenza A viruses. The source of the new genetic material is thought to be the avian population, especially migratory birds, which are considered the primary reservoir of influenza viruses. All known influenza virus subtypes have been isolated from birds, and the influenza viruses iso-

lated from avian sources show little antigenic change over time. Whereas influenza causes respiratory disease in most animals, most birds do not appear to become ill when infected with influenza A virus. These two observations suggest a high degree of evolutionary adaptation between the viruses and birds and a long-standing, stable host-parasite relationship.^{3,19}

In migratory birds, influenza viruses preferentially replicate in the digestive tract, rather than in the respiratory tract as in other animals, and are excreted in the feces. This adaptation facilitates wide dissemination of the virus via bird droppings, which can then contaminate the food and water supplies of other animal species, including domestic birds and swine. Influenza viruses have been isolated from lake water, supporting the idea that untreated water may serve as a vehicle for the transmission of influenza from migratory birds to other species.¹⁹

Gene Reassortment

The major theory of the emergence of new pandemic strains is that new influenza virus subtypes arise after human and avian influenza viruses simultaneously infect an intermediate host, and the genomes from the two viruses mix to form a new virus.^{2,7,12} In essence, the influenza virus RNA segments from two different sources combine to form a new combination of the eight segments necessary to make a complete viral particle. This process is referred to as *gene reassortment*. For the new virus to potentially spawn a pandemic, it needs to contain an HA segment and possibly a NA segment new to most, if not all, of the human population. The virus also must be transmitted to humans from the intermediate host, must be able to be spread from person to person, and must be pathogenic in human hosts. Genetic studies have shown that the 1957 and 1968 pandemic strains were likely composed of RNA segments from human and avian sources. In 1957, the new A(H2N2) strain contained HA and NA genes and a polymerase gene of avian origin, while the rest of the genes were from

the preceding human A(H1N1) strain. In 1968, the new human A(H3N2) strain contained avian genes for HA and a polymerase enzyme, and the remainder of the genes were from the human A(H2N2) virus.¹⁷ This reassortment likely occurs in an intermediate host such as swine, because avian influenza viruses only rarely have been shown to be directly transmitted to humans.^{19a} However, swine are susceptible to infection by viruses from both humans and birds and can pass influenza virus infections to humans.^{19,22}

Gene reassortment and the influenza viruses' ability to be transmitted between different species have been demonstrated in the laboratory and in nature. Laboratory investigations using as intermediate hosts both swine and turkeys as well as cell culture have demonstrated that concurrent infection with two different influenza viruses does lead to reassortment of gene segments and the creation of "new" viruses as intermediate hosts.^{8,23} The interspecies transmission of reassorted influenza viruses in nature has been reported.^{20,24-27}

Other evidence for the theory of gene reassortment in the emergence of pandemics lies in the geographical origin of most pandemics. Both of the pandemic subtypes isolated since the 1957 Asian flu pandemic have originated in China. This may be a result of living conditions in rural China, where people often live in close contact with swine and domestic fowl. Such close contact may facilitate the transfer of influenza virus between species and increase the chance of genetic reassortment and the creation of a new pandemic influenza virus.¹⁹

Direct Transfer

Another theory on the origin of pandemics suggests that new influenza subtypes arise by direct transfer of viruses from other species. This theory has less support as a cause of human pandemics. However, avian viruses were reported to cause disease in horses in 1989 and to infect pigs by direct viral transmission.^{19,21} In addition, human influenza

viruses have been isolated from swine, and swine viruses have been isolated from humans.^{26,28} In 1997, 18 people in Hong Kong became ill after infection with an avian influenza A(H5N1) virus; six people died. This was the first time that an avian virus had caused an outbreak among humans. The outbreak in humans occurred coincident with an outbreak among poultry and no further human cases were detected after the poultry outbreak was controlled.

The appearance of a new influenza virus in the human population does not guarantee a pandemic. For example, in January and February of 1976, over 230 personnel at Fort Dix, New Jersey, became ill with influenza and one person died.^{3,29} Because the virus was the same as an influenza virus concurrently infecting swine in North America and because the virus that caused the 1918-19 pandemic was also a swine virus, there was a great deal of concern.^{2,30} A massive vaccination campaign was initiated in the fall of 1976, but infections did not spread beyond the camp and no widespread epidemic occurred.²⁹ The vaccine campaign was halted in December 1976 because of a lack of swine flu cases and because an association between the swine flu vaccine and Guillain-Barré syndrome, a neurologic disorder, became recognized. Guillain-Barré syndrome has not been clearly associated with any other influenza vaccines since the swine flu vaccine.^{1,4,28}

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THE FUTURE

A new pandemic influenza strain will likely appear in the future, but the timing of such an event is unpredictable. Will the emergence of the next pandemic strain be as devastating as the 1918 pandemic? Since 1918, the ability to treat critically ill patients has improved dramatically, and better communications and surveillance systems may help public health officials detect new viruses in time to provide advanced warning. However, with modern air travel, the amount of time required for a new virus to disseminate throughout the world is potentially very short. Pandemic preparedness planning in the United States and elsewhere will, it is hoped, provide a framework for early initiation of preventive measures in the event of a new pandemic.

Influenza epidemics and pandemics will continue to occur because of influenza viruses' ability to undergo antigenic change through point mutations and gene reassortment. The viruses' changing antigenicity and the presence of animal reservoirs make the eradication of influenza unlikely. Therefore, vigilant surveillance for new emerging influenza virus subtypes and strategic planning for a new pandemic offer the best hope for limiting the impact of future influenza pandemics and epidemics.

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Resource 3. Immunology and the Influenza Virus

By Marvin Druger

The human body has an amazing capacity to defend itself against invasion by microbes and other disease-causing agents. Some of the body's defense mechanisms are nonspecific and serve as protection against any potential invader. Other mechanisms, known collectively as the *immune response*, are highly specific. Both kinds are involved in defending the body against the influenza virus. We will first discuss some nonspecific defenses and then the specialized defenses, or immune response.

NONSPECIFIC DEFENSE MECHANISMS

Of the nonspecific defenses, the most obvious is the skin. It provides a physical barrier against the penetration of viruses and bacteria into the bloodstream, while secretions from its oil and sweat glands have an acid pH that adversely affects pathogens. Perspiration, tears, saliva, and urine contain lysozyme, an enzyme that attacks cell walls of certain bacteria. Cells in the mucous membranes (which line the nose and throat, among other portals to the outside) secrete mucus that traps microorganisms. Nasal hairs filter debris, and cilia in the upper respiratory tract sweep particles toward the throat, where they may be expelled or swallowed. Microbes that have been swallowed are destroyed by the gastric juice of the stomach, which has an acid pH. Microbes that reach the lungs are engulfed and destroyed by phagocytic cells. Finally, the skin, intestinal tract, and vagina normally harbor a variety of microorganisms that usually compete successfully with pathogens and maintain the normal status.

Phagocytosis

When microorganisms enter the body, they are relentlessly attacked and destroyed by certain white blood cells that engulf and digest particulate material (a process known as *phagocytosis*). There are several different types of white blood cells, including lymphocytes, neutrophils, macrophages, eosinophils, and basophils. Neutrophils (the most abundant white blood cells, making up about 60 to 70

percent), lymphocytes, macrophages, and eosinophils, to a limited extent, carry out phagocytosis. Eosinophils discharge enzymes that can destroy larger parasites (such as tapeworms). Basophils secrete chemicals involved in defensive responses.

The most important phagocytic cells are the neutrophils and the macrophages ("big eaters"). These are large cells that begin their existence as smaller monocytes. When penetration by a microorganism occurs, neutrophils are chemically attracted to the site of penetration. Constantly formed in the bone marrow, spleen, and other tissues, neutrophils live only a few days. They destroy invaders, but they suffer self-destruction in the process. Indeed, pus is composed largely of dead neutrophils and cellular debris. Macrophages, which may reside in various tissues or wander throughout the body, can live several weeks, ingesting and destroying bacteria and other particulate matter.

Other white blood cell types include natural killer cells (NK cells), which are important in fighting cancer, and lymphocytes, which contribute to the body's immune response.

Complement System

The complement system is also activated when invaders penetrate the body. This system consists of about 20 different proteins circulating in the bloodstream. When activated, these proteins perform functions such as lysing (or *disintegration*) of bacterial cell walls, increasing capillary permeability, and attracting and signaling neutrophils and macrophages to attack.

Inflammatory Response

An invasion by pathogens also initiates the inflammatory response. Basophils and mast cells (noncirculating white blood cells in connective tissue) release histamine and other chemicals that cause blood vessels to dilate and become more permeable. Blood flows more freely to the site of invasion, enhancing the migration of phagocytic cells and causing the area to become warm and red. Fluid flows into the tissues, causing the area to become swollen. The swelling, along with chemicals released from damaged cells, results in pain. If the inflammatory response is systemic, rather than local, there is a general increase in the number of white blood cells. Macrophages and some other cells secrete pyrogens that set the thermostat of the body at a higher level, causing fever. Unpleasant though it is, moderate fever inhibits the growth of microorganisms and promotes their destruction by white blood cells.

THE IMMUNE RESPONSE

Considering all of these mechanisms for fighting off pathogens, it seems amazing that a specific defense mechanism, called the *immune response*, also operates. Three features are at the core of the immune response: specificity, memory, and the capacity to recognize non-self. This means that specific antibodies can be produced to match specific antigen (any substance introduced into the body that stimulates antibody production).

The term *antigen* comes from “antibody generator.” The system can then retain “memory” of this antigen, which is usually part of a microbe’s surface structure, and resist later invasion by the same microbe. The system normally does not produce antibodies against its own tissues.

COMPONENTS OF THE IMMUNE SYSTEM

What are the major players in the immune response? They include macrophages and lymphocytes, types of white blood cell already

mentioned in passing. Lymphocytes are also divided into *T cells* and *B cells*.

T Cells

Lymphocytes that originate in the bone marrow and mature in the thymus gland are called *T cells*. Once mature, these T cells are distributed to the lymph nodes, spleen, tonsils, and other lymphoid tissues. There are three classes of T cells: cytotoxic (or *killer T cells*), helper T cells, and suppressor T cells. These can be distinguished by the type of glycoprotein receptor molecule they have on their cell surface. Cytotoxic T cells and suppressor T cells have a form of glycoprotein molecule known as CD8; hence, they are called CD8 lymphocytes or T8 cells. Helper T cells have a surface marker known as CD4 and are known as CD4 lymphocytes or T4 cells.

Cytotoxic T cells earn the name “killer” by destroying infected cells. They do so either by secreting a protein called *perforin*, which makes holes in the cell membrane, or by causing cells to destroy themselves through a kind of programmed death. Since cytotoxic T cells directly bind to infected body cells and not to free antigens in the blood, T cells, in collaboration with macrophages, are said to be responsible for cell-mediated immunity. They are especially important in defeating viruses, bacteria, and other parasites that live within cells. Other functions of cytotoxic T cells include releasing lymphokines, which attract macrophages and enhance phagocytosis. Cytotoxic T cells also secrete interferons, enabling healthy cells to resist viral infection by interfering with viral replication.

Helper T cells guide the immune response by activating T and B cells in response to an invader. Suppressor T cells help to regulate the immune response by turning off the B and helper T cells after the pathogen has been controlled.

B Cells

Lymphocytes that mature in the bone marrow are known as B lymphocytes (B cells). During

maturation, each B cell acquires antibody receptors that enable it to recognize only one specific antigen. Mature B cells circulate in the blood and reside in the lymph nodes and lymphoid tissues. When activated, these B cells enlarge and become transformed into plasma cells that secrete large amounts of specific antibodies. Each plasma cell produces only a single type of antibody, which is targeted against a specific antigen. However, the enormous diversity of B cells that will become plasma cells enables recognition of virtually any antigen they meet. The antibodies circulate in the blood plasma and lymph, bind with the surface receptors of the invader, and label it for destruction by phagocytic cells.

These are the steps in activating B cells:

1. Binding of the B cell antibody to the antigen.
2. Recognition and binding of a helper T cell to the sensitized B cell.
3. Secretion of chemical signals (interleukins) by the helper T cell.

The activated B cells then enlarge and become transformed into plasma cells that secrete the particular antibody that provides humoral immunity to an individual.

Other progeny of the activated B cell remain in the lymphoid tissues as memory B cells. These cells remain for many years and provide for a rapid response and large-scale production of antibodies against that same invader, thus preventing the illness from occurring again.

WHAT IS AN ANTIBODY?

An antibody is a protein that can specifically bind to the antigen that stimulated its production. The proteins that make up antibodies are called *immunoglobulins* (Igs). There are five classes of immunoglobulins, based upon their structure and designated by the letters G, A, M, D, and E. These are usually written as IgG, IgA, and so forth. IgG and IgM are most important for specific immunity against infectious pathogens.

Though IgM constitutes only about 10 percent of the total immunoglobulins in the blood, it is the first to appear in response to antigens. It disappears rapidly. So its presence indicates a current infection by the antigen. IgG makes up about 70 percent to 75 percent of the total immunoglobulins in the blood. It persists in the blood even after foreign invaders have been destroyed. Since IgG is able to cross the placenta and enter into the bloodstream of the fetus, it provides immunity for the newborn child, who cannot make its own antibodies until weeks after birth. IgA is involved in immune responses relating to the linings of the digestive, respiratory, and urogenital tracts. IgA combines with pathogens and prevents them from attaching to epithelial surfaces.

Basically, all immunoglobulins are shaped somewhat like a Y and are composed of four polypeptides, or chains of amino acids. The amino acid sequence at the base of the Y is the same for all the Igs, and so it is known as the *constant* (C) region. This region is attached to the membrane of the B cell, while the arms of the Y protrude outward. The arms vary considerably in their sequence of amino acids and are known as the *variable* and *hypervariable* (V) regions. Because variable regions are genetically programmed to have different sequences of amino acids, each can bind with a different, specific antigen. These V regions are what make an antibody specific.

The antibody usually does not combine with the entire antigen, which is generally quite large. Instead, it recognizes a portion of the antigen known as an *antigenic determinant*, or *epitope*. A bacterium may have several epitopes, each of which incites production of a different antibody. The shapes of the antibody's binding sites complement the shapes of the epitopes. They fit together like a lock and key.

HOW DOES AN ANTIBODY WORK?

There are several mechanisms by which an antibody works. Antibodies may neutralize a virus

by binding to the sites the virus uses to attach to a host cell. Antibodies may coat bacterial toxins and neutralize them. Antibodies may clump together bacterial cells or precipitate soluble bacterial antigen molecules, making it easier for phagocytic cells to destroy them. Another mechanism involves activation of the complement system of infection-fighting proteins.

T cells also have antigen receptors, which function similarly, but not identically, to those of antibodies. One key difference is that antibodies recognize antigens in their original form, while T cells recognize them only in association with MHC (major histocompatibility complex) markers on the infected cell surface.

MHC markers are proteins that are imprinted on the surface of all your cells. Each individual has unique MHC proteins (except for identical twins, who share the same ones). These unique molecules identify self. They are the key to the body's self-recognition.

MHC markers come in two varieties: Class I, possessed by most of the body's cells, and Class II, possessed by T cells, B cells, and macrophages. T cells do not respond to cells that contain only Class I self-markers. When a foreign antigen binds with a MHC Class I marker, the cytotoxic T cells (CD8s) recognize it as foreign and bind to the infected cell and kill it.

Helper T cells (CD4 cells) are activated by a foreign antigen that has become associated with Class II self-markers. This occurs when a macrophage (Class II self-marker) engulfs an invading pathogen. Although the pathogen is destroyed, fragments of partially digested antigens remain. They become bound to Class II markers and are displayed on the surface of the macrophage as antigen-MHC Class II complexes. The macrophage is now known as an *antigen-presenting cell* (APC). A helper T cell then combines with the specific antigen-MHC Class II complex displayed on the surface of the macrophage. This activates the helper T cell and stimulates the macrophage to secrete interleukin that, in turn, stimulates the helper T cell to secrete its own interleukins. This starts a chain

of reactions whereby B cells are activated and T and B cells proliferate. (For a complete description, see the summary at the end of this article.)

CHEMICAL MESSENGERS

Chemical messengers (or cytokines) are small proteins secreted by macrophages or lymphocytes that serve as chemical messengers among cells of the immune system. The various kinds of cytokines include interferons, monokines, lymphokines, and interleukins. Interferons are released by virus-infected cells and they influence noninfected cells to produce proteins that inhibit virus reproduction. Monokines are secreted by macrophages to promote development of T cells. Lymphokines are proteins secreted by lymphocytes that influence many aspects of the immune response, including regulation of B and T cell functions and activation of complement proteins.

There are various kinds of interleukins. Interleukin-1 is secreted by antigen-presenting macrophages and activates T helper cells. Activated T helper cells secrete interleukin-2, which stimulates rapid reproduction of the activated helper T cells and promotes differentiation and proliferation of cytotoxic T cells and suppressor T cells. Helper T cells also secrete other interleukins that activate B cells, causing them to divide rapidly and to differentiate into plasma cells.

VIRUSES AND THE IMMUNE RESPONSE

Many human diseases are caused by viruses. These include influenza, poliomyelitis, hepatitis B, herpes, mumps, smallpox, chicken pox, the common cold, rabies, and AIDS. Viral diseases afflict many different plants and animals. Even bacteria can be attacked by viruses called *bacteriophages*. Certain animal cancers, such as mouse leukemia, are caused by viruses, and human cancers are caused by human T-cell leukemia viruses.

In some ways, a virus is alive: it has genes, it can mutate, it can replicate (although only

within a living cell). It invades a cell and causes its machinery to make more viruses. However, viruses lack other properties of living organisms, such as metabolism, which includes adenosine triphosphate (ATP) synthesis.

Basically, a virus consists of a core of nucleic acid (either DNA or RNA) surrounded by a protein coat called a *capsid*. (Some viruses have an envelope surrounding the capsid.) When a virus infects a cell, it introduces its DNA or RNA into the cell and directs the infected cell to synthesize more viruses.

Influenza A, the most troublesome of the influenza viruses known, consists of an RNA core, a capsid, and a viral envelope. Many glycoprotein spikes, each consisting of a hemagglutinin antigen (HA) and neuraminidase (NA), an enzyme, are distributed all over its outer membrane surface.

INFLUENZA VIRUS

The influenza virus infects a cell in an interesting manner.

1. The HA protein binds to a receptor molecule called *sialic* (neuraminic) acid on the surface of red blood cells and certain cells of the lung.
2. Once bound, the neuraminidase cleaves off the sialic molecule, which forms the link between the surface wall of the virus and the cell, allowing the virus to enter the cell (a process called *endocytosis*).
3. The cell's outer membrane pinches inward, forming a vesicle with the virus inside.
4. The enclosed virus is thus protected from antibodies or T cells circulating in the body. Increased acidity within the vesicle causes a dramatic change in the shape of the HA protein. In this process, a peptide shifts in position, causing the vesicle membrane to fuse with the membrane of the virus. This enables the RNA genes of the virus to penetrate to the interior of the host cell.
5. The virus takes over the genetic machinery of the cell and new viruses are produced.
6. The new viruses bud from the infected cell's surface, and the host cell's membrane is wrapped around the virus as it leaves the cell.

Thus, the viral envelope is composed of molecules derived from the host cell's membrane as well as molecules specified by genes of the virus. Cytotoxic cells recognize the viral antigens that appear on the surface of the infected cells and respond to them by boring holes into the cell's membrane, inducing lysis. Meanwhile, when antibodies meet the new viruses free in the bloodstream, they can neutralize them by preventing the HA molecules from attaching themselves to the sialic acid receptors of cells. They can also prevent reinfection.

Because the influenza virus has a relatively high mutation rate, you may have the flu many times in your life. New strains of the flu virus are constantly generated, and these present new surface antigens. The reason is that, unlike almost all other living organisms, influenza has an RNA genome. Because RNA is a very reactive polymer, not only is it more unreliable than DNA for storing information but it mutates more rapidly, causing its progeny to diverge rapidly. In addition, there are no mechanisms for repairing RNA damage as there are for repairing DNA damage in cells. RNA genomes, therefore, retain more mistakes in their copies than do DNA genomes.

These slight mutations occurring in the HA or NA gene make it more difficult for antibodies generated by previous infections to bind to certain epitope sites. Hemagglutinin mutations often occur within four epitopes, or antigenic determinants, of a particular HA protein, with the mutations in at least two or more of the altered epitopes. These changes in surface antigens, known as *antigenic drift*, are small but significant enough to require a constant updating of vaccines.

In addition to its rapid mutation due to its RNA genome, the influenza virus has another characteristic that induces change: its genome consists of not one, but eight segments of RNA. A segmented genome increases the opportunities for mutation to create genetic diversity. Sometimes, segments are reassorted between two different viruses, causing a major change in the HA gene. It is thought that reassortment is probably a stronger force in generating viral variants in influenza than the minor changes involved in antigenic drift. These genetic reassortments result in antigenic shift (extensive variations in amino acid sequence that make the virus utterly unrecognizable to the immune system). The radically new flu viruses resulting from antigenic shift are thought to be the cause of devastating influenza pandemics, such as those experienced in 1918, 1957, and 1968. As Arnold Levine observes: "New pandemic strains are possible as long as there is a source of HA genes not previously encountered by living human hosts." (For more details, see Resource 2, "What We Now Know About the Influenza Virus.")

CONCLUDING COMMENTS

The immune response is a remarkable defense mechanism. Without it, we would be at the mercy of many pathogens that we now readily deflect. Nevertheless, the immune system can malfunction. In some diseases, such as rheumatoid arthritis, the body mounts an immune response against its own joints, causing inflammation, crippling pain, and destruction of bone and cartilage.

Some diseases involve lack of a proper immune response. The most notorious is AIDS (acquired immunodeficiency syndrome). In this disease, the human immunodeficiency virus (HIV) disables the immune response by infecting and destroying helper T cells and related cells. AIDS patients become suscepti-

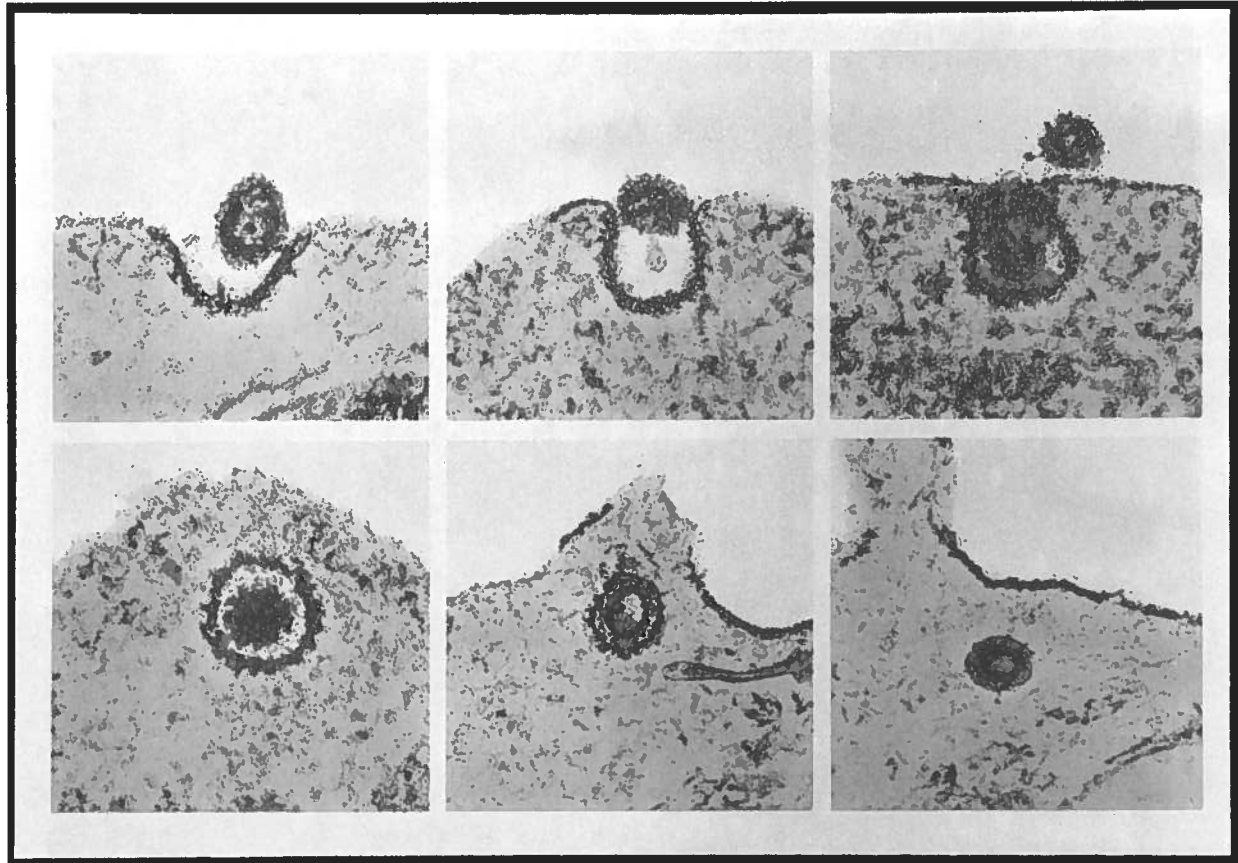
ble to infections that the immune response would normally prevent. The very horror of that disease alerts us to the routine complexity and efficiency of the immune system.

SUMMARY OF INFECTION AND DEFENSE

1. A macrophage, serving as a first line of defense against pathogens, engulfs the virus and digests it. Fragments of the partially digested pathogen are then displayed, in combination with MHC Class II markers, on the surface of the macrophage.
2. Helper T cell recognizes this antigen MHC Class II complex and binds to it. The antigen-presenting macrophage secretes Interleukin-1, which activates helper T cell.
3. Activated helper T cell secretes Interleukin-2, which leads to the proliferation of T cells and B cells.
4. Cytotoxic T cells recognize foreign proteins combined with MHC Class I molecules on the surface of virus-infected cells and destroy these cells.
5. Helper T cells also activate and clone memory helper T cells.
6. When B cells recognize the virus, their antibodies bind to it.
7. Most of the new B cells enlarge and differentiate into plasma cells that secrete large amounts of antibodies specific for the virus.
8. These antibodies are released into the bloodstream. When they meet the same type of virus, they recognize it, lock onto it, and tag it for destruction or neutralize it.
9. Other B cells become memory B cells, which stay in the system, prepared for any future infection by the same virus.

10. Suppressor T cells “shut off” the immune response once the pathogen has been controlled. Memory T cells and memory B cells

remain in the body for many years, ready to be activated by a subsequent infection.



Black and white reproduction of a colored Transmission Electron Micrograph of stages of a cell infection by an influenza virus. The virus appears rounded in shape, with a core of ribonucleic acid (RNA). It has a spiked outer coat that allows the virus to attach to host cells. Host cell cytoplasm appears granular. At top frames (3 images), the virus attaches to the cell, causing the cell membrane to fold around the virus. At lower frames (3 images), the virus penetrates the cell, infecting it and causing the production of more influenza viruses. This virus is contagious and invades mucous cells in the respiratory tract. **Magnification: x50,000 (for each inset) at 5x7cm size.**

Note

1. Levine, Arnold J., *Viruses* (New York: Scientific American Library, 1992), 169.

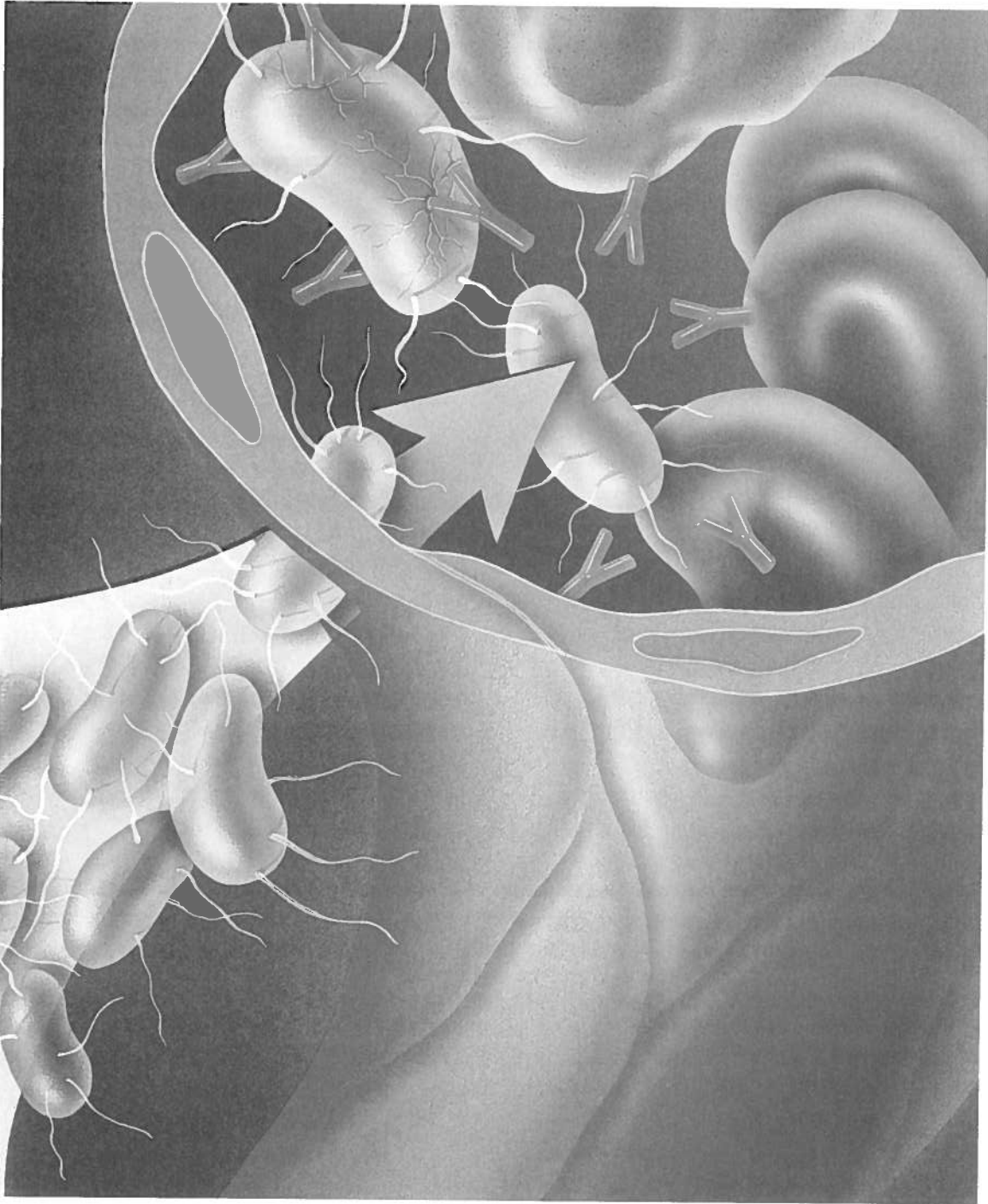


Diagram of antigen/antibody reaction. Antigens are substances that mobilize the immune system and provoke an immune response. Most antigens are large, complex molecules not normally present in the body. Antibodies are soluble proteins secreted by the plasma cell offspring of sensitized B-cells in response to an antigen and are capable of binding specifically with that antigen. This artist rendering shows the Y shaped antibodies attaching to surface antigens on bacterial cells as the cells enter the bloodstream. This attachment leads to bacterial cell lysis and phagocytosis. In this representation, the bacteria and antibodies are not drawn to scale.

Resource 4. Recovering a Killer

Ann H. Reid and Jeffery K. Taubenberger, M.D.

The March 21, 1997, issue of *Science* published a report by Ann H. Reid, Jeffery K. Taubenberger, and others at the Armed Forces Institute of Pathology (AFIP) entitled “Initial Genetic Characterization of the 1918 Spanish Influenza Virus.” On the same day, newspapers around the country announced the findings to the general public: the search for knowledge about the elusive 1918 killer flu had finally found some success. How, we wondered, had this team gone about its work? And what implications did its discovery have for controlling a new pandemic? In order to answer these questions, we turned to the scientists who made the discovery. The following is an interview with Reid and Taubenberger about their identification of the Spanish flu virus. The questions are in boldface.

Your discovery of direct evidence of the Spanish flu virus certainly made a lot of headlines. Why do you think this is so?

The influenza pandemic of 1918 killed more people in less time than any other infectious disease agent, making it the worst infectious disease episode in modern history. However, in 1918, medical technology was not advanced enough to isolate it. And, by the time the techniques necessary to study influenza viruses were developed, the 1918 strain had disappeared. Since new influenza strains continue to emerge, a better understanding of the most lethal strain in history may have ongoing public health benefits.

How were you able to locate it? I’m sure others have tried before.

The archives of the AFIP contain autopsy samples from over 70 victims of the 1918 epidemic. We decided to use techniques developed at the AFIP to try to isolate genetic material from the stored tissue. Then we studied their genetic sequence. It’s true that others have tried this before, but they haven’t been successful in extracting the genetic material from the preserved or frozen samples.

What did you do first?

When we began our work on the 1918 influenza virus, we first sought out what was already

known about the disease. While the virus itself had not been isolated, many descriptions were available of how the disease spread and its course in individual patients. In the 1930s, when both influenza viruses and the human immune system were better understood, studies of the serum of survivors of the pandemic gave indirect evidence as to the nature of the 1918 virus. Also, the biology and natural history of influenza viruses have been well studied. And, more recently, we have detailed genetic information for dozens of influenza strains.

You familiarized yourself with what was known about the flu, but how did that help you in deciding which of the 70 tissue samples or slides to choose?

We were looking for someone who died quickly after the onset of symptoms. From all accounts, the illness appeared to follow three possible courses. First, an acute illness for five to seven days followed by recovery. Second, lingering symptoms with complications leading to death by pneumonia after more than a week. Third, a precipitous decline to death within a week. The first and second courses are common to most influenza strains, but rapid death from influenza is unusual and indicates that the virus itself has caused lethal damage.

Also, we know that influenza viruses replicate very quickly in the lungs. After five to seven days, even if the patient remains sick

with secondary complications, the virus will no longer be present. Therefore, in order to have a chance at finding the Spanish flu virus, we had to find a case in which the victim had died within a week.

How successful were you?

Well, as I said, the AFIP archives contain both slides and preserved tissue from over 70 victims of the 1918 epidemic. We reviewed half of these cases. Several met our criteria and were chosen for further study. However, when the slides were examined for evidence of primary viral infection, only one of the cases had the appropriate pathology. This was a tissue sample from a 21-year-old army private who had been stationed in Fort Jackson, South Carolina. The case showed sparse acute inflammation of bronchioles with necrosis of the epithelial lining, and the victim died six days after the onset of symptoms.

You found a likely sample. What then?

We then had to extract genetic material from this 79-year-old sample of lung tissue. This was the most difficult part. Genetic information can be stored in two chemical forms. Most life-forms, including humans, store their genetic information in the form of DNA. Influenza viruses, however, store their genes as RNA, a form closely related to DNA but which more easily degrades.

How did you extract the RNA virus?

The tissue had been fixed in formaldehyde and embedded in paraffin wax. We first carved off a thick slice of the tissue, dissolved the paraffin in an organic solvent, and then digested away the proteins with an enzyme, leaving behind only the nucleic acids, DNA and RNA. The procedure that we then used to identify viral RNA is called *polymerase chain reaction* (PCR), a technique that mimics the process by which all cells reproduce. It was developed in the mid-1980s, and it allows the production of millions of copies of a specific fragment of DNA.

How did you go about this?

The first step in detecting influenza involved using an enzyme called reverse transcriptase to make a complementary DNA (cDNA) copy of the viral RNA. The DNA copy was then used for PCR.

Did this present any problems?

Well, the success of PCR depends on the ability of the primers to find and bind to their complementary sequence on the DNA. Obviously, in the case of the 1918 influenza virus, that sequence was unknown. So we had to design the primers ourselves, using what we could deduce about the 1918 strain.

What was involved in deciding how to design these primers?

We had to decide which genes to try to detect, which known strains to use for comparison, and how long a fragment to target. The influenza virus carries 10 genes on 8 RNA segments. Some of these genes mutate very rapidly, in order to evade detection by the immune system. Others, which are essential to the ability of the virus to reproduce itself, tend to remain more similar over time and across strains. Therefore, we reasoned that primers designed to detect these more stable genes could be made more precise and were more likely to succeed.

All right—take us through the process. Precisely which genes did you try to detect?

We began with genes for nucleoprotein and the two matrix proteins. These genes are relatively similar between strains and are abundant. In other words, the virus makes many copies of these genes during its life cycle. Also, these structural proteins are quite stable.

And how did you decide which strains you should make comparisons with?

By this time, there must be quite a number of influenza strains that have been identified.

Well, when we began our study of the 1918 viruses, one of the hypotheses concerning its origin was that an avian strain had recently emerged for which humans had little or no pre-existing immunity. Therefore, when we designed the primers to detect viral RNA fragments, we compared genes from avian, swine, and human strains and made mixtures of primers that would be able to find any of them. We tested the primers on two control virus strains, one human and one avian. We assumed that if the primers were able to find specific RNA fragments in both control strains, they would also be able to find the 1918 strain.

And how did you decide how long a fragment to target?

Well, the influenza virus genome contains over 13,000 bases of RNA. Each of its 10 genes is 1000 to 2000 bases in length. Even though PCR is capable of copying fragments of that length, the RNA that remains in preserved tissue samples is broken into much shorter pieces. Therefore, we designed primers that would flank fragments of less than 150 bases.

We first determined that we were able to design primers that allowed us to detect viral RNA in preserved tissue from a more recent influenza epidemic in 1957. Then we tried to do this with the more stable genes of the 1918 sample—the nucleoprotein and the two matrix proteins. Once we knew that we had success with them, we tried the more imprecise primers for hemagglutinin and neuraminidase.

These primers also identified specific fragments in the 1918 case. So, the PCR process had produced fragments of DNA that were copies of the original viral RNA.

Aside from the achievement of producing these gene fragments from the original virus, how did this help you learn more about the actual flu virus?

We were able to compare the genetic sequence of the 1918 virus fragments to the sequences of many other strains of the virus and look for similarities and differences.

How did you make these comparisons?

Through something like a genealogical chart.

You know, influenza viruses infect many different species, including birds, such as ducks and chickens, swine, horses, and humans. However, influenza does not produce symptoms in wildfowl and there does not appear to be an immune response in birds. As a result, the genetic code for the different subtypes in birds remains quite stable over time.

By contrast, those few subtypes of influenza that infect mammals provoke a strong immune response, which leads to rapid genetic change. Mutations in the RNA occur, which allow the virus to evade the new host's immune system, or to reproduce better in the new host's cells. These mutations will then be passed on to the next generation.

Because the process by which influenza virus reproduces its RNA is especially error-prone, new—possibly beneficial—mutations are introduced in each generation. Over many generations, enough mutations accumulate to justify our calling the virus a new strain. When the sequences of many strains are compared, the change pattern in the genetic sequence reflects the evolution of the virus and shows how strains are related.

There are computer programs that analyze the sequence differences between strains and generate a “family tree” that shows which strains are likely to be ancestral and where different strains branch out into new host species and their subsequent adaptation.

How did you use these family trees?

The first question we asked ourselves about the newly generated 1918 sequences was whether they were unique. With a technique as sensitive and powerful as PCR, there is a significant danger of contamination causing millions of copies of the wrong DNA fragment. Most of the 1918 sequences, while clearly very similar to other influenza strains, were not an exact match to any known influenza sequences—and none of them matched the sequences of the control influenza strains used in our laboratory.

We then compared the sequence fragments of each gene to the same fragments of known strains. The fragments of nucleoprotein and the two matrix genes indicated that these genes were more similar to strains infecting mammals than those infecting birds. However, the amount of information that could be gained from these genes was limited, both because the fragments were short and because these genes do not change very fast. So there was less genetic variation to evaluate.

The short fragment generated from the neuraminidase gene perfectly matched an early human influenza strain isolated in 1933. While we were able to determine that the neuraminidase was of the N1 subtype and that it belonged to the group of strains infecting humans, little more could be deduced without sequencing a longer fragment.

We then concentrated our efforts on the hemagglutinin gene, making copies of several short fragments and linking them together to compare with known hemagglutinin sequences. The sequences clearly indicated that the 1918 virus contained a hemagglutinin gene of the H1 subtype.

The family tree of the H1 hemagglutinin sequences showed three groups—human, swine, and avian—with the 1918 sequence falling into the swine group. The 1918 sequence appeared to be most similar to the strains circulating in pigs in the 1930s.

In other words, all the information gained from sequencing the 1918 virus fragments was consistent with what had already been deduced about the virus.

Which was...?

The studies of survivors' antibodies in the 1930s had indicated that the 1918 strain was of the H1N1 subtype and that it was apparently very similar to classic swine flu. The sequences that we found in the 1918 case matched best to H1 and N1 sequences, with H1 appearing most closely related to swine strains. What the sequence information did not give us was an answer to the question of why the 1918 strain was so deadly.

Did you come any closer to answering that question?

Well, we eliminated some hypotheses. For example, one hypothesis proposed that the strain had recently emerged from birds and was completely novel to humans, and, therefore, there was no prior human immunity. The sequences showed adaptation at least to growth in mammals. However, it must be said that when it comes to predicting which influenza strains will be most deadly, current knowledge is inadequate. Certainly, when new strains emerge—as happened in 1957 and 1968—they tend to be extremely infectious, although they do not necessarily cause more severe symptoms.

Did you test any other hypotheses about the Spanish flu?

Yes, we were able to test another hypothesis about its virulence. This hypothesis was based on the finding that a characteristic mutation in hemagglutinin genes of two subtypes—H5 and H7—results in strains that are particularly lethal in birds. In this mutation, extra bases are inserted into an important functional site of the hemagglutinin gene. While it has never been found in an H1 subtype hemagglutinin,

nor in a mammalian strain, it has been suggested that its appearance in the 1918 influenza might explain why the strain was so lethal. However, sequences across the suspected site in the 1918 hemagglutinin gene revealed no additional bases.

Do you have any other hypotheses about why the 1918 flu was more lethal than any before or since? This seems to be an important public health question.

As we learn more about the effects of specific genetic changes on the virulence of the influenza virus, we should be able to see whether the 1918 virus has those changes. It may even be possible to learn from the 1918 sequence itself what makes an influenza virus lethal.

For example, there was a pronounced wave of influenza in the spring of 1918. Many millions of people were infected and more than average numbers died, especially in the young adult age group. However, neither the spread nor the severity of this first wave was unusual enough to gain wide attention until the second, more severe, wave in the fall caused people to wonder about the origin of the killer virus.

In retrospect, it seems likely that the spring wave was caused by the emergence of a novel influenza virus, just as novel strains caused the pandemics of 1957 and 1968. Then, between the spring and the fall, a mutation occurred that drastically increased the virulence of the emergent strain. It would be fascinating to compare the sequences of the spring and fall

strains. Even if a spring case is never located, it is possible that comparing the sequence of the fall 1918 case to subsequent H1N1 strains will provide clues to the strain's virulence.

On the other hand, we still don't know whether the 1918 virus caused such severe illness because of some quality inherent in the virus, or whether the human population in 1918 was peculiarly susceptible to this virus, perhaps because an H1N1 subtype virus had not circulated for an unusually long time. We need a more detailed understanding of how the genetics of the virus affect specific species and which cells it can infect, which genetic changes provoke the most extreme immune response, and which changes might produce the type of damage seen in the lungs of 1918 victims.

That's quite an order! What do you think you'll tackle next?

Our first priority is to continue to sequence the viral RNA in the already identified case. The sequence will be useful to influenza researchers as they try to understand what made that strain so lethal. We also hope to immortalize the positive case by creating a DNA library of all of its RNA.

We will also be contacting pathology departments around the world. And, we will be examining the remaining cases in the AFIP archives in the hopes of finding other cases that will contain the 1918 influenza virus.

Thank you and good luck!

Resource 5. Preparing for the Worst

Peter A. Patriarca and Michael Williams of the Food and Drug Administration

The following is an interview with Peter A. Patriarca and Michael Williams about the flu, the workings of the FDA, vaccines, and other topics.

What are the factors that determine whether or not there is a pandemic?

An influenza pandemic means that there is a worldwide epidemic of influenza virus infection. This is caused by a strain of the virus that has changes on its surface so major that it “escapes” from the antibodies that are present in the human population. Since it is new, people have little or no protection against it. Pandemics are very difficult to predict because there is no real understanding about why these changes occur. Sometimes, pandemics result in rather mild illness, but the ones that we worry about are those that are virulent, as in 1918. And there is no way to predict virulence before the disease is actually full-blown.

Who makes the decision on whether or not to declare a pandemic?

The Centers for Disease Control (CDC) and the World Health Organization (WHO) make the call jointly. For us in the United States, it is the CDC, but it is not clear-cut. CDC does the epidemiology and testing. It will find a strain that has no serologic response to any current antisera. That will be the first clue that something may be going on and will set the system on alert. Of course, eventually, it will be the president who will make the “official” call. This will be based on both political and legal reasons to invoke certain laws and statutes on the books.

How do pandemic virus strains originate?

This is the real 64,000-dollar question. On a simple level, you can say a pandemic virus is a mutation in a strain of virus. For the one virulent pandemic we have had—in 1918—we have no valid scientific data about the virus. It is clas-

sified as the H1N1 strain, but that does not explain why it was so bad. Its only other reappearance was in the Fort Dix epidemic in 1976.

There are three basic strains of the influenza virus in humans—H1, H2, and H3. There are a total of 17 variants of these viruses that are being studied extensively by Dr. Robert Webster of St. Jude’s Medical Center. He believes that there is very little change in animal viruses, and so the current thinking is that the next pandemic will come from either H4, H7, or H2. The reason for these guesses is that both H4 and H7 can now be cultured in mammalian cells. H4 has been creating some “problems” in China. We’ve also talked a lot about H7, and this virus may be “on the move.” These and other strains may be brewing in China.

Why is there usually a second wave of flu following the first?

No one really knows what is happening here. It might be logical to assume that there is a small mutation that enables the virus to hit people who were not susceptible the first time around. The “Asian flu” skipped whole age groups the first time around, and then on the second time through, it got those groups that it had skipped the first time.

What are the procedures and timetable for determining and producing vaccines?

There are basically four drug companies that make flu vaccines for use in the U.S. Three are here and one is in England. They work closely with one another even though each company has its “own” techniques for purifying the vaccine and some other differences. These com-

panies actually begin to produce vaccine in December by beginning to grow some of the viruses. Because they use hundreds of thousands of eggs per week, they are very dependent upon chicken farm contracts. They need fertile eggs, and it is best to inoculate them when they are 9 to 11 days old. Many of the eggs come from Pennsylvania where two of the firms are located.

Because the current vaccine in the U.S. is a trivalent vaccine that is good for H1N1, influenza B, and H3N2, the firms know which viruses to begin with. In January, a team from FDA and CDC meets to make a determination about which strains they think are going to be significant for the upcoming flu season. You might note that they have not been wrong in the last six or seven years. Usually in February, this same team will go to Geneva to meet with WHO people. This is when the final decisions are made regarding which “beasts” may be problems in the upcoming season. Meanwhile, Mike has been growing these variants and supplying them to the drug companies so that they can begin to narrow down their vaccine. Remember that these companies have to grow enough viruses for 80 million doses for the U.S. (They also make vaccine for foreign countries, to some extent.) And, since there are three different strains, they are really growing 240 million doses. This is why we feel that if we have a pandemic we could make enough monovalent vaccine for the U.S. population.

After the WHO meeting, there is just enough time. The companies are furiously producing and storing antigen from the viruses grown in the eggs. The FDA is furiously producing antisera from sheep so that the companies can test their vaccines for potency and standardize the amounts of each of the viruses that you have to add together to make this trivalent vaccine.

The next problem is distributing and inoculating the population. In this decade, there has been a huge jump in the number of doses. In

the late 1980s, companies were producing in the range of 25 million doses. Now, it's in the 80 million range. Interestingly enough, the basic technology for producing the vaccines has not changed in 20 years. The big improvement has been in purifying them. There are many fewer contaminants in the current vaccines compared with 20 years ago, especially in terms of extraneous proteins that could generate a local immune response near the site of the injection. Since these purification techniques have improved, fewer people have had adverse reactions to the vaccine. This is also a factor in the increased number of doses. Generally, we believe that we are reaching about 60 percent of the population who need the vaccine. A lot of others get it as a preventive—especially health care givers and others at risk.

What will be the next step in vaccine production?

The big advance has been the increase in vaccine purity. The next big step will be to develop vaccines that don't require eggs as the substrate but are just as effective as (or more effective than) those we currently produce in eggs. Also, right now we use up most of the virus for vaccines. However, vaccines that contain viruses grown on tissue culture containing only critical “pieces” of the virus can probably be produced in much greater quantities and more quickly. Those developments will help in the rapid production that will be crucial to deal with the next pandemic.

How do the FDA and manufacturers ensure quality control?

No one wants lawsuits. So avoiding them becomes a very powerful driving force basically. The manufacturers (or at least their procedures) must be approved to manufacture the vaccines. They are primarily responsible for testing the purity, safety, and potency of the vaccines. They have to submit samples of their vaccines to the FDA. The FDA requires samples from each lot

that the company produces. These we test for purity, safety, and potency on a random basis. Quality control is generally not a problem!

Why do you use animals for study?

We use animals to produce antisera that we then use in the field to identify new strains of the virus. We use animals because many of these studies cannot be done on humans—at least on any large scale!

What about the liability issue?

That's another big problem, although there are previous models to work with. You might look at vaccine as a "no fault" situation, but it is possible for people to develop complications, such as Guillain-Barré, and these people are truly innocent victims.

The risk problems really lie with the insurance companies, not the vaccine makers. The solution is for the federal government to buy the vaccine at bargain basement prices and then distribute it. That way the government is responsible for liability. This is a big expenditure even at a good price. Most of the money could come through budgeted items, such as FEMA's (Federal Emergency Management Agency) disaster money and public health money. In any case, it is doable—assuming the powers that be work out the price now, not in the middle of a flu epidemic.

Are there any conflicts between scientists and politicians in facing these issues?

No conflicts. The basic problem is that politicians often do not have enough understanding of science to act responsibly. Science administrators need to constantly educate Congress and keep them "up" on what is happening.

Do you see any problems with delivering the vaccines?

The drug companies claim they have an effective "delivery" system in place already. So there is no need for the federal government to worry about this end of the process. We're not so sure. We worry that the companies will not know how many doses to send to different locations. The vaccine needed in one area may end up in another, and once local health people have the vaccine, they may be reluctant to share. Of course, when you get into third world countries, distribution becomes a major headache. We all agree that this is a big issue that needs to be addressed soon.

What are the ethical issues involved in a pandemic?

The first is volume. Either we cannot produce enough vaccine for the U.S. or we can produce just enough. Two hundred forty million doses is reasonable, but this is the limit for production in the U.S. France can probably produce enough for itself. The same is probably true of Japan. But production is really limited to those countries that have vaccine-producing facilities.

As other countries produce vaccines, we might be able to conserve some of our doses, but then who gets them? For instance, many developing countries have virtually no companies that can produce large volumes of vaccine. Any decision to restrict the distribution of U.S.-produced vaccine outside the U.S. would have to be made on the basis of national security considerations.

Issues surrounding vaccine production are exceedingly complex. The World Health Organization is trying to get a better handle on this through an international working group on pandemic influenza. Meanwhile, there's no clear answer!

Resource 6. Lessons from the Swine Flu Episode

By Diana B. Dutton

The material in Resource 6 is largely based on the author's *Worse Than the Disease*, Chapter 5, "The Swine Flu Immunization Program," published by Cambridge University Press (and used by permission).

THE BACKGROUND

When Private David Lewis, an army recruit, reported for sick call at Fort Dix, New Jersey, in early February, 1976, he complained of mild, flu-like symptoms. No one dreamed he would be dead within a week. Nor would anyone ever have imagined that his death would launch an unprecedented episode in U.S. public health: a federally funded campaign to immunize every man, woman, and child against a feared "killer" epidemic of swine flu.

At first the reasoning seemed clear: if the epidemic came, the nation would be protected; if it didn't, mass immunization would still have been a prudent investment. "Dollars for lives" became the byword of federal officials. Yet from the outset almost nothing seemed to go right. The program was mired in controversy and beset with unending problems. It fell further and further behind schedule. Moreover, there was no epidemic. Indeed, from the shots themselves came the most serious illness—Guillain-Barré syndrome (GBS), a rare but paralyzing and sometimes fatal condition.

This misguided venture cries out for the clarity of hindsight. How and why did things go so wrong? Was it, like the classic Greek tragedy, simply the playing out of inexorable events over which the actors, whoever they might have been, had no control? Or could things have turned out differently? In the recounting that follows, it will be apparent that at many points, different decisions could have been made that might have changed the course of events. Indeed, it is striking how many of the problems actually were foreseen but were downplayed or ignored. Had decision makers been willing to confront more openly the

issues critics tried to raise, this sad tale might have ended more happily.

FORT DIX IN WINTER

Private Lewis was only one of many soldiers at Fort Dix that winter who had come down with respiratory illnesses after their Christmas holidays. Because of the grueling conditions of boot camp, illnesses were common at that time of year, and army doctors assumed they were due to the usual adenoviruses, like those that cause the common cold. They reported the situation to the county health officer, who in turn alerted the state's chief epidemiologist, Dr. Martin Goldfield. To Goldfield, it sounded more like an outbreak of influenza. He bet the Fort Dix doctors that throat cultures from the sick soldiers would prove him right.¹

Sure enough, of the 19 specimens tested, 11 revealed A/Victoria strain of flu, the most common type of human influenza. But the other eight revealed flu isolates that could not be identified, and were sent to the federal government's Centers for Disease Control (CDC) in Atlanta for further investigation.² Goldfield was worried. If these really were new strains of flu, a major epidemic could be in the offing. What, he joked grimly, if it turned out to be the infamous "swine flu," the most deadly influenza ever known?³

Meanwhile, back at Fort Dix, Private David Lewis had died. Sick for more than a week with a headache, sore throat, and low-grade fever, Lewis had ignored doctors' orders to stay in the barracks and had joined fellow recruits on a strenuous five-mile march in the snow. On the return trip, he collapsed. He was rushed to the hospital but was dead on arrival. Doctors immediately sent throat and lung specimens to CDC for identification.

Swine Flu Appears

By February 12, CDC had confirmed Goldfield's half-facetious fear. The unidentified virus from the earlier specimens, as well as that from Private Lewis, was indeed swine flu.

Dr. David Sencer, head of CDC, hurriedly called a meeting of experts from various federal agencies for February 14 to discuss this disturbing finding. Everyone recognized that the news was ominous. Although influenza is not normally very serious, in 1918-19 a devastating flu pandemic (or worldwide epidemic) had swept the globe. Over 20 million people had died, including approximately 500,000 Americans. It was the worst medical catastrophe in modern history. Later, research confirmed that a similar virus had also infected and killed large numbers of pigs, and the 1918 pandemic came to be called "swine flu."⁴ Although the disease had died out among humans by the late 1920s, it continued to circulate among swine, emerging occasionally among humans in contact with pigs. Since then, there had been no known cases of "human-to-human" transmission of swine flu, such as had now apparently occurred at Fort Dix. If it were now returning to humans, no one under age 50 would have built up antibodies from previous infection. The toll in morbidity and mortality could be enormous.

Pandemic Possibilities

What was even more alarming was that all the conditions necessary for a pandemic seemed to exist. First, prior pandemics had all been preceded by smaller, localized flu outbreaks. The 1918 pandemic itself had come in two or more waves, the first much milder than the second. The Fort Dix cases could be the precursor of a new pandemic in the next flu season. Second, the Fort Dix virus had two key surface proteins, called *antigens*, that differed from those of the dominant strains of influenza viruses. Experts call this an "antigenic shift."⁵ The prevailing view at this time was that an antigenic shift left the population without immunity to the new strain of flu and invariably led to a

major pandemic. Third, previous pandemics seemed to come about every 11 years, having occurred in 1946, 1957, and 1968. Another one was due soon. Based on an influenza virus "recycling" theory then current, some experts had even predicted that the next pandemic would be caused by a swine virus. This theory postulated that earlier forms of flu virus would resurface when a large enough group of people without immunity had accumulated.

Everyone agreed that more data were needed to determine the extent of the outbreak in and around Fort Dix. They decided that since the significance of the Fort Dix cases was still unclear, there should be no publicity. A few days later, however, fearful of uninformed press leaks, CDC Director Sencer changed his mind and held a press conference. The conference made headlines. On February 20, the *New York Times*, in a front-page story, reported: "The possibility was raised today that the virus that caused the greatest world epidemic of influenza in modern history—the pandemic of 1918-19—may have returned."⁶

During the following weeks, intensive surveillance of influenza activity revealed no new swine flu cases at Fort Dix or, for that matter, anywhere else. There was plenty of flu at Fort Dix, but it was all A/Victoria. Had Goldfield made his bet just a week later, swine flu might never have been discovered.

In the meantime, the news from Fort Dix was not good. Human-to-human transmission had been confirmed. None of the sick soldiers had had any contact with pigs, and laboratory contamination of the cultures had been ruled out. The number of proved cases of swine flu had risen to 13. Moreover, swine flu antibodies had been found in blood samples from some 500 recruits, suggesting that they too could have been infected with swine flu, with or without clinical symptoms.⁷

SENCER DECIDES

On March 10, Sencer held another meeting, this time including the Advisory Committee on

Immunization Practices (ACIP), a group of outside experts that advises CDC on immunization efforts, to consider whether plans for vaccine production should be changed in light of Fort Dix. Manufacturers had already begun production of A/Victoria strain flu vaccine for the coming fall. If they were now to be asked to produce a new vaccine for swine flu in time for the 1976-77 flu season, the ACIP would have to act almost immediately. The press was there. Everyone understood that important decisions were at hand.

No one at the meeting would even hazard a guess at the chances of a pandemic occurring. Privately, most seemed to consider it quite unlikely. Because it could not be ruled out, however, participants agreed that steps should be taken to produce enough vaccine for the entire population. Many were no doubt remembering the painful lessons of the last two flu pandemics, in 1957 and 1968, when the federal government had been unable to mobilize immunization campaigns in time to do much good.⁸ The 1957 pandemic had caused 70,000 deaths; the 1968 pandemic, about 28,000. The message was clear: to make any headway against the next pandemic, the government would have to be directly involved in vaccine procurement and administration. Fort Dix seemed to present the perfect example.

One member of the group, Dr. E. Russell Alexander, an ACIP member and professor of public health, argued that the decision on mass immunization should be delayed until swine flu resurfaced. He urged that the vaccine be produced but then “stockpiled” until another outbreak of swine flu occurred *somewhere*. Alexander felt, as he later put it, “that you should be conservative about putting foreign material into the human body... especially when you are talking about 200 million bodies. The need should be estimated conservatively. If you don’t need to give it, don’t.”⁹ This was clearly not the majority view. Most experts at the time, including the other ACIP members,

considered flu vaccines essentially free of major risks—“just like water,”¹⁰ in the words of CDC’s chief virologist.

Alexander also asked the question that would turn out to be pivotal: “At what point do we stop going on with our preparations to immunize everybody and turn to stockpiling instead—what point in terms both of progress of our preparations and progress of the disease?”¹¹ Unfortunately, that question was never answered. Sencer and his staff had apparently concluded that stockpiling was not feasible logistically. Inoculation took two weeks to provide immunity. If the virus reappeared, it could spread rapidly around the country via air travel (“jet spread”), gaining a foothold before the vaccine could be distributed, shots administered, and immunity built up. Besides, CDC staff had pointed out, stockpiling made little sense if the vaccine really had no risks; better to store it in people’s arms than on refrigerator shelves. And what if a pandemic occurred? As one official put it:

Suppose...it comes out: “They had the opportunity to save life; they made the vaccine, they put it in the refrigerator...” That translates to “they did nothing.” And worse, “they didn’t even recommend an immunization campaign.”¹²

Sencer did not press for unanimity at the March 10 meeting. He told the group to “sleep on it,” and he would call them in a few days. But, in a closing pun, he made his position clear: “It looks like we’re going to have to go whole hog.”¹³

Two days later, Sencer called ACIP members. Two were reportedly in favor of going ahead with immunization. Two, including Alexander, favored stockpiling. This left Sencer with the tie-breaking vote. There was little doubt as to how he would cast it.

The Memorandum

Sencer immediately began preparing a memorandum titled “Swine Influenza—ACTION.” It would become the decision paper in the

case. It was forceful and persuasive, designed to sell the program to the Department of Health, Education, and Welfare (HEW), the White House, and Congress. It began with evidence that a swine flu epidemic was a “strong possibility.” The second “fact” listed was, so to speak, the killer: “The virus [isolated at Fort Dix] is antigenically related to the influenza virus which has been implicated as the cause of the 1918-1919 pandemic which killed 450,000 people—more than 400 out of every 100,000 Americans.”¹⁴

The memo contended that the only way to halt a possible pandemic was to immunize the entire population. A more conservative effort would be little better than none at all; 1957 and 1968 had proved that. This conclusion was based on a critical (and highly debatable) assumption: “The situation is one of ‘go or no go.’” Noting that “there is barely enough time to assure adequate vaccine production and to mobilize the nation’s health care delivery system,” the memo concluded that a decision on mass immunization “must be made now.”¹⁵ The memo did acknowledge that immunizing an entire population would be expensive (with total cost estimated at \$134 million) and that some people might be “needlessly reimmunized” (those over 50, who might still have swine flu antibodies). Actually, to many politicians, \$134 million for a nationwide anything sounded pretty cheap.

Two separable decisions (producing sufficient vaccine and embarking on mass immunization) were thus rolled into a single “go or no-go” decision that had to be made in the next two weeks. Despite many attempts, they would never again be separated.

Mathews Endorses

That weekend, David Sencer flew to Washington, memo in hand, for a meeting Monday morning, March 15, with HEW Secretary David Mathews and other federal officials. Mathews’ principal question, and the one that most frequently would be posed to him over

the next days and weeks, was: “What is the probability of an epidemic?” Sencer’s answer: “Unknown.” According to one official, the example of 1918-19, where half a million lives were lost, hung like a “ghastly vignette” over the discussion.¹⁶

Mathews also inquired about vaccine safety. Sencer’s response was reassuring. Flu vaccines had been used for a quarter of a century, with no major problems—sore arms, fever and chills, but no serious side effects. That same morning, Mathews wrote a memo to the head of the Office of Management and Budget (OMB), the White House federal budget watchdog, strongly endorsing mass immunization: “There is evidence that there will be a major flu epidemic this coming fall...that we will see a return of the 1918 flu virus that is the most virulent form of flu...The projections are that this virus will kill one million Americans.”¹⁷

An Even Bet

Gone were all the caveats and qualifiers that even Sencer had included in his hard-hitting ACTION memo. Gone was the ambivalence reflected in the ACIP’s split vote only five days before. The higher up the federal chain of command, the greater the sense of urgency and alarm. ACIP participants had considered the odds of an epidemic very low (in the range of 2 to 20 percent they later said). Sencer’s ACTION memo called the epidemic a “strong possibility.” Mathews’ memorandum referred to “evidence that there will be a major flu epidemic.” The impression that filtered up to the HEW General Counsel’s office was that the chances seemed to be 1 in 2 that swine flu would come. An unknown but low probability had been translated into an even bet.

Mathews also exaggerated the epidemic’s likely severity. ACIP members had explicitly noted that it was impossible to know whether a new swine flu epidemic would be as virulent as the 1918 pandemic. Mathews assumed it would be and, because the population had since doubled, simply doubled the casualty

level of 1918 (ignoring the fact that antibiotics would now prevent many of the pneumonia deaths that had occurred in 1918).

President Ford and Politics

It was generally assumed that the final decision would come from President Gerald Ford. Simply as a procedural matter, he would have to sign the request for a supplemental budget appropriation. If a major national emergency really was looming, he would sooner or later have to be involved. Furthermore, a presidential election was coming up that November and Ford, running for a second term in office, could ill afford a massive outbreak of swine flu just before the election. Viewing an epidemic as likely and believing the risks of the vaccine to be negligible, government officials saw the program as politically inevitable under any circumstances, especially given the upcoming election. As an HEW assistant secretary put it:

People at the top of the department came pretty quickly to a belief that inaction...was simply untenable.... And people were mindful of the fact that it was a presidential election year and that made the thing dreadfully more difficult in a sense—the consequences of doing nothing and having it later come to light.¹⁸

THE WHITE HOUSE DECIDES

If scientific concerns suggested it could, perhaps should, be done, political concerns dictated that it would be done. All this came at a busy time for Ford and his advisers. Ford was not doing well in the polls and was widely viewed as uninspiring. The swine flu program gave him a chance to seize the initiative, to take the helm of a nationwide campaign in what experts said could be a genuine public health disaster. It looked like a political windfall.

White House staff recognized that the president would have to act promptly, even though some had “real questions” about the whole program. “There was no ‘rush to judgment,’” recalled the White House deputy chief of staff. “We’d put the issue on a fast-track for

decision but be damned sure we’d gotten a full staff review.”¹⁹ By this time the press had learned of the decisions that were brewing. On Sunday, March 21, swine flu made its second appearance on the front page of the *New York Times*: “Flu Experts Soon to Rule on Need of New Vaccine.” The article described Fort Dix as “a single scream in the night and then silence.” It reported that the government, based on the recommendations of Sencer and other advisers, was expected to decide in favor of mass immunization. “It’s a choice between gambling with money or gambling with lives,”²⁰ one official was quoted as saying.

The time had come for the president’s decision. On March 22, Ford met with high-level advisers for a final briefing. Upon learning that no new scientific review body had been set up specifically to deal with swine flu, Ford agreed that such a review should now take place at the presidential level. It would serve not only as a final opportunity to ferret out any remaining objections, but also as a way of extending responsibility for the decision beyond the federal bureaucracy. It would provide graphic proof that the president was acting on sound advice. Ford asked his aides to assemble a group of the “best” scientists and experts, representing a spectrum of views, to meet with him in two days. Although Ford did not announce a final decision at the meeting, most participants emerged convinced that mass immunization was now a near certainty.

The Review Group

In putting together the new review group, White House staff relied mainly on lists drawn up by Sencer and other agency heads. The group included many familiar faces, some new ones from state health departments and the AMA (American Medical Association), and sundry public figures. Also invited were Jonas Salk and Albert Sabin, the fathers of the polio vaccine, whose names had become almost synonymous with vaccination. Notably not on the list were critics such as Alexander and Goldfield, both of

whom had expressed doubts at the ACIP meeting two weeks before. White House staff didn't know them. The others did not propose them.

The Meeting

On the day of the meeting, March 24, the invited experts assembled in the Cabinet Room. President Ford welcomed the group, and Sencer summarized the background and facts. Salk and Sabin then followed with strong statements of support for mass immunization. None of the experts present had a disparaging word for the program, even though everyone agreed that no figure could be placed on the probability of an epidemic. The 1918 disaster was a recurring topic. When Ford asked how many were in favor of mass immunization, all hands went up. He also asked whether anyone had any reservations. (One participant later compared this to asking for objections at a wedding: "Does anyone object, or forever hold your peace.") There was a long silence. "Later," one participant acknowledged, "I regretted not having spoken up and said, Mr. President, this may not be proper for me to say, but I believe we should not go ahead with immunization until we are sure this is a real threat."²¹

Around 4:50 p.m., Ford appeared in the White House press room with Salk and Sabin on either side. Sencer and HEW officials stood respectfully in the background. The president said that the "very outstanding technicians" who had just met with him had advised that a swine flu epidemic was a "very real possibility." Consequently, he continued,

I am asking the Congress to appropriate \$135 million prior to the April recess to inoculate every man, woman, and child in the United States...I am asking each and every American to make certain he or she receives an inoculation this fall.²²

Ford was no doubt pleased. He had launched an ambitious and seemingly noncontroversial program to safeguard the public's health. And he might have gained some political mileage in the process. Congressional aides thought he had.

The Controversy

His pleasure was short-lived. No sooner had the announcement been made than controversy erupted. That night CBS News reported that "some doctors and public health officials...believe that such a massive program is premature and unwise, that there is not enough proof of the need for it...But because President Ford and others are endorsing the program, those who oppose it privately are afraid to say so in public."²³ A local CBS reporter in Atlanta had called sources inside CDC, and had been told on "deep background" that, based on present evidence, nationwide immunization was unjustified, "a crazy program."²⁴

The next day, all three networks aired criticisms from various sources, notably among them Dr. Sidney Wolfe of Ralph Nader's Health Research Group, a frequent critic of the medical establishment. Walter Cronkite reported that the World Health Organization had "expressed surprise at the president's decision." A WHO spokesperson said "there is no evidence of an epidemic and no plans in other countries for massive inoculations."²⁵ A CBS insider later revealed that what they learned from CDC convinced them early on that it "was a rotten program, rotten to the core. We thought it was politically inspired...it certainly was awful in technical terms...unwarranted...unnecessary."²⁶

This barrage of criticism apparently took White House officials by surprise. They had been assured by Sencer and others that support for the program was nearly unanimous. They checked again at CDC for internal dissent and again found none. The wheels were in motion.

A SHAKY START

Congress responded speedily to the president's call for funds. The Senate Appropriations Committee added a supplemental appropriation of \$135 million to a pending bill, and the two key figures in health matters, Edward Kennedy in the Senate and Paul Rogers in the

House, promptly scheduled subcommittee hearings for March 31. Both men were firm believers in preventive medicine and convinced that the threat of swine flu was real. Kennedy also saw the program as a way of promoting children's vaccination against other, potentially more serious diseases such as measles and rubella.

The Hearings

Many of the problems that were to plague the swine flu program over the coming months were raised at these subcommittee hearings. The epidemic's uncertainty was acknowledged. Subcommittee members asked about vaccine side effects and were assured they would be "minimal."²⁷ One medical leader testified that it was "questionable whether adequate informed consent is possible, indeed practical, in a mass immunization program of this magnitude."²⁸ The drug industry's trade association president warned that the "probabilities" were that drug companies could not produce enough vaccine to inoculate all Americans (213 million doses) until well into the fall. He also noted the "major product liability problems associated with mass immunization programs" and called for government indemnification of vaccine manufacturers. "Quite frankly," the trade association vice president told a Senate subcommittee, "the liability is so enormous here, we doubt whether we could obtain the necessary insurance coverage."²⁹

The Appropriation Approved

Despite such indications of brewing trouble, most members of Congress favored the swine flu program. They believed the experts who said that it was a sensible insurance policy against the possibility of a devastating pandemic. Like Ford, they undoubtedly feared what would happen in the November elections if swine flu became rampant in October and Congress had denied the president's request for funds. The supplemental appropriation was

approved handily in the House and Senate and signed into law April 15.

THE CAMPAIGN BEGINS

Meanwhile, planning efforts were getting underway. On April 2, a week after the president's announcement, CDC held a giant meeting in Atlanta to acquaint state health officials and private physicians with the program and to coordinate local planning. To the chagrin of the meeting's leaders, many of those attending apparently viewed the whole enterprise with suspicion if not outright hostility. Dr. Martin Goldfield, the New Jersey epidemiologist whose hunch had uncovered swine flu at Fort Dix, expressed his opposition to the program in no uncertain terms, focusing especially on the risks to pregnant women. "When we talk emotionally about gambling with lives, we must also remember that we are gambling with lives, health, and welfare if we throw around 200 million doses of the vaccine,"³⁰ he warned. Although specialists discounted Goldfield's concern about pregnant women, all the network TV news shows that evening gave him feature coverage. "There are as many dangers to going ahead with immunizing the population as there are with withholding the vaccine," he declared prophetically on national television. "We can soberly estimate that approximately 15 percent of the entire population will suffer disability reaction."³¹

Some experts were glad that someone had finally expressed the doubts they had secretly been nursing. One CDC official told Goldfield confidentially, "Marty, keep it up. I can't say anything."³² Most scientists, however, were dismayed at what they saw as a breach of professional conduct. One senior epidemiologist chastised Goldfield privately: "Marty, you have some good points. I agree with much of what you say. But the decision's made. Now is the time to close ranks. You are wrong to go public."³³ By all accounts, Goldfield was never forgiven for breaking rank and expressing his doubts in public.

On April 6, four days after this rather unsettling meeting in Atlanta, CDC officials got another jolt, this time from a stinging editorial in the *New York Times*. The editorial questioned whether the swine flu threat was real, whether vaccine production could be completed in time, whether the benefits of the vaccine would outweigh its medical and financial costs, and whether the vaccine would be effective. It stated:

The president's medical advisers seem to have panicked and to have talked him into a decision based on the worst assumptions about the still poorly known virus and the best assumptions about the vaccine...A convincing case for the president's proposal...cannot be made until those who support it debate publicly with the medical and scientific skeptics who are already voicing their doubts.³⁴

This editorial was written by Harry Schwartz, a longstanding foe of public medicine. Schwartz was convinced that the program was without scientific merit and that Ford's endorsement was pure "politics." It was a view that would appear repeatedly in the *New York Times* editorials throughout the summer. Other newspapers, although favorable at the outset, also became more dubious as the spring wore on.

The reaction in other countries to the swine flu threat was cautious and politely skeptical. In early April, the World Health Organization held an international meeting of experts to consider appropriate responses. Noting that "extensive investigations in the United States have revealed no further infections since [Fort Dix]," the meeting concluded that it was "entirely possible that this may have been a unique event in a military recruit population and will not lead to widespread epidemics."³⁵ WHO recommended increased surveillance and production of vaccine for stockpiling or immunization, depending on a country's resources and priorities. American experts claimed that other countries were not respond-

ing as aggressively as the United States because they lacked the funds and facilities. Most foreign observers thought that the United States was overreacting.

MORE PROBLEMS AND OPPOSITION

The field trials of swine flu vaccine began on April 21. They were the largest ever conducted in the history of influenza, involving more than 5,000 people spread over different age groups. Each person got a single shot.

Vaccine production had also begun, but it was behind schedule because the eggs were yielding roughly one dose of vaccine per egg instead of the expected two. (To some critics, this low yield suggested that the swine flu virus was not very virulent and hence an unlikely agent of a pandemic.) In mid-June, vaccine manufacturers announced that the first 80 million doses would probably not be ready until October. Another 60 million would follow in December or later. This was already way behind the original timetable, which had full-scale immunization starting in July and being substantially completed by October.

Evaluating Trial Results

The results of the field trials were reported June 21-22 at a huge meeting at the National Institutes of Health (NIH). The news was mixed. The vaccine appeared to be effective in adults, based on antibody responses, and to have few side effects. But it worked poorly in children, either causing too many adverse reactions or failing to confer immunity.³⁶

What this meant (although officials certainly didn't want to publicize it) was that children were out of the program unless a pandemic erupted. (If it did, children would get single doses of adult-strength vaccine regardless of adverse reactions.) The exclusion of children had to be kept quiet, officials felt, because it would have sounded crazy to most Americans, who, after polio, considered shots for kids the

heart of preventive immunization. Everyone knew that children were prime spreaders of influenza in schools and child care settings. How could any self-respecting national campaign leave out the nation's children?

The Stockpiling Issue

The second day of the NIH meeting was devoted largely to the question of stockpiling, a topic that Sabin, surprisingly, had put on the agenda. With no trace of swine flu anywhere in the world, including the southern hemisphere where flu season was nearing its peak, Sabin now favored watchful waiting. The likely exclusion of children from the program only reinforced his views. Sabin maintained that with proper planning, they could still inoculate in time if signs of a major epidemic appeared by using brigades of local volunteers to conduct assembly-line inoculations in each community. Such an approach, he insisted, fueled by a sense of national emergency, could drastically reduce the time required for immunization. Alexander, also at the meeting, strongly supported Sabin's appeal.

Sencer and other CDC officials responded with the standard arguments against stockpiling.³⁷ Furthermore, state inoculation plans were now well underway and could not easily be revised without a serious loss of momentum. To some participants, even those sympathetic to stockpiling, this was a key point. Besides, if the vaccine was in fact perfectly safe as most experts believed, then stockpiling made no sense.

That evening, all three TV network news shows featured the debate over stockpiling, and two offered wry comments about the ambiguous status of children in the program. Sabin led the dissenters and was joined by others, including Alexander, who had finally decided to go public with his doubts. "[A]s time goes on," Alexander told the nation, "most people think that the probability is there will not be an epidemic in the 1976-77 season due to swine influenza."³⁸ The *New York Times* renewed its attack on the program.³⁹

Bad Press for Pork

CDC officials were not the only ones smarting under these attacks. Touchy pork producers complained that all the talk about "swine flu" might give the industry a bad name and suggested that the flu be renamed "New Jersey flu." (New Jersey officials politely declined the honor.) The pork industry did convince federal officials not to consider a mass immunization program for the nation's pigs, which one veterinary expert had proposed.

The growing criticism, and especially the defection of key scientific supporters like Sabin, was beginning to worry many members of Congress. Their concerns were soon eclipsed by news of a new blow to the program: The insurance industry would not insure the companies producing swine flu vaccine.

THE IMPASSE OVER LIABILITY

On June 25, Leslie Cheek, head of the American Insurance Association's Washington office, called CDC and the White House to announce that the manufacturers of swine flu vaccine would not get liability coverage. The insurers were simply too worried about the potential liability of a nationwide immunization program to be willing to underwrite vaccine producers, Cheek said. Existing coverage would terminate June 30. And manufacturers would not bottle or release the vaccine without insurance.

This issue had been looming for some time, although Cheek's call still came as a shock. Ever since the initial congressional hearings, vaccine manufacturers had been talking darkly about liability problems. Now the government was trapped. If private insurers would not provide coverage, then the government would have to do it instead. Reluctantly, HEW lawyers set about drafting an indemnification bill, which, still more reluctantly, OMB approved.

In defense of their position, insurers pointed to the side effects that inevitably accompany vaccinations and to the possible breakdown of

quality control under the pressures of a “crash” program. But what they feared most of all, they stressed, were the costs of defending against all the damage claims (groundless as well as valid) that would be entailed in a program this size. The number of frivolous claims alone could be enormous, not to mention damage awards and out-of-court settlements.

DOUBTS AND MORE DOUBTS

Meanwhile, doubts about the program continued to grow. Flu season in the southern hemisphere was at its height, with no sign of swine flu. Studies questioning the program began to appear in respected medical journals.⁴⁰ In late July, the assistant director of CDC acknowledged publicly that there had been no reason to “raise the specter of 1918” in connection with Fort Dix. “We have nothing on which to base a similarity of behavior between the two viruses,” he admitted in a congressional hearing.

HEW and White House staff again raised with President Ford the possibility of abandoning the foundering program. Ford asked whether his advisers still considered the pandemic possible. They did. This Ford apparently viewed as decisive, and he turned his energies toward persuading Congress, due to recess shortly, to act.

Caught in a deadlock between Congress and the insurance industry, with vaccine production on hold and doubts widespread, the swine flu program was in real jeopardy. Then, by a fluke, outside events intervened. On August 1, newspapers reported a mysterious respiratory ailment among people attending an American Legion Convention in Pennsylvania. At least eight died. Swine flu was suspected as the culprit. A few days later, CDC announced that the infectious agent, although not yet identified, was definitely not swine flu. But this scare had a big impact on Congress. President Ford seized the opportunity to do some more arm-twisting. At a nationally televised press conference, he told Congress:

These tragic deaths were not the result of swine flu. But let us remember one thing: they could have been. The threat of swine flu is still very, very genuine...I am frankly very dumbfounded to know that the Congress...has failed to protect 215 million Americans from the threat of swine flu...Further delay in this urgently needed legislation is unconscionable.⁴¹

With an election coming up shortly, this was more pressure than members of Congress could stand. Both houses bowed to the president's wishes and hastily drafted a new swine flu liability bill, passing it on the eve of the convention recess. Many legislators still resented giving in to what they saw as the greed of the insurance industry and were uneasy about getting the government into the insurance business. “I hate this bill,” Senator Ted Kennedy was quoted as saying, “but suppose there is a swine flu epidemic? They'll blame me.”⁴²

The bill assigned legal liability to the federal government for everything except negligence. HEW was to draft a written consent form informing vaccine recipients of risks and benefits. Manufacturers would be freed from the duty to warn and from the costs of defending against most suits. All claims would be filed against the government, which in turn could sue manufacturers to recover damages caused by negligence. Manufacturers could then collect from their insurers. (As it turned out, because recoveries for negligence were minimal, insurers ended up pocketing as pure profit nearly all of the roughly \$8.6 million that manufacturers had paid in premiums.) Ford signed the bill into law on August 12.

The swine flu program had been snatched from the jaws of defeat. President Ford, Sencer, and other top program leaders were jubilant. Some lower-level officials, on the other hand, were secretly sorry. By late summer, with no sign of swine flu anywhere in the world, many felt, as CDC's chief virologist recalled, that “there wasn't much point in going on.”⁴³ Now they had no choice. It was

their job to resurrect a program that was by then hopelessly behind schedule, beset by legal and logistical uncertainties, castigated by the news media, and quite possibly totally unnecessary. Their candid reaction? “Oh no.”

IMMUNIZATION BEGINS

The new swine flu law did not go into effect until October 1, the new fiscal year, and insurers refused to permit the vaccines to be used before then. Production was also falling further and further behind schedule. Manufacturers were now projecting that only 20 million doses (a quarter of what they had promised back in June) could be delivered by October. Public confidence was also flagging. A national poll in late August showed that while almost all Americans had heard of the swine flu program, only 53 percent intended to get shots.

On October 1, mass immunization finally got underway in states that had the vaccine; others joined in as they received supplies. In the first 10 days, over a million adult Americans got swine flu shots. (Children were still on hold.)

Bad News

Then a new bombshell hit. On October 11, three elderly people, all suffering from heart disease, died shortly after receiving swine flu shots from the same clinic in Pittsburgh, Pennsylvania. The story quickly made national headlines. The local coroner suggested that maybe a bad batch of vaccine had been responsible. Many local health officials panicked, and nine states quickly suspended the program. The *New York Times* fired off another searing editorial, calling for President Ford to “order a halt” until there had been “a second hard look at the costs and benefits of what is being done to forestall the disease that isn’t there.”⁴⁴

For three days, the news media featured scare stories from around the country on vaccine recipients who had died, regardless of cause. CDC officials did their best to reassure an anxious nation that these deaths were in all likelihood simply coincidental (“temporally

related deaths” occurring soon after flu shots but not caused by them).⁴⁵ The panic subsided a few days later when laboratory results exonerated swine flu vaccine in the Pittsburgh deaths, and Ford and his family got flu shots on national TV. Five states announced resumption of mass immunization; four others soon followed. Federal officials heaved a sigh of relief. CDC resumed its promotional efforts but decided to drop one tag line from the planned advertising: “The swine flu shot. Get it. Before it gets you.”⁴⁶

Vaccinations Continue

In spite of all the negative publicity, 2.4 million people were vaccinated during the week of the Pittsburgh deaths. As state plans got underway, vaccination rates continued to rise, reaching a peak of 6.4 million people in mid-November. Then the rates declined as the sense of crisis receded with swine flu still nowhere in sight. Federal officials finally announced appropriate dosages for children (two shots of half-strength vaccine, a month apart), but disclosed that available vaccine supplies would cover only 7 percent of eligible children (roughly 2 percent ended up getting shots). Vaccination rates varied widely. Delaware, at the high end, immunized almost 90 percent of its population, Louisiana only 12 percent. Altogether, more than 45 million people got flu shots between October 1 and December 16 (twice the number ever immunized before in a single season, but still less than a quarter of the total population).

THE PROGRAM ENDS

In mid-November, CDC got a call from Minnesota reporting that someone who had recently gotten a swine flu shot had developed an ascending paralysis called *Guillain-Barré Syndrome* (GBS). At first this received little notice. Throughout the fall, CDC’s surveillance center had been investigating thousands of reports of serious reactions and fatalities following flu shots. These had all been judged to

be “temporally related,” like the Pittsburgh deaths—chance events not caused by the shots. But within a week, three more cases of GBS, one fatal, were reported from Minnesota, plus three from Alabama and one from New Jersey. Program officials now grew alarmed. CDC staff began contacting neurologists and other specialists around the country to try to find out if GBS was indeed occurring at a higher rate among swine flu vaccine recipients.

The data that began to accumulate were disturbing, though not conclusive. Trends toward higher rates of GBS among vaccinees were unmistakable, but officials were still not convinced that the flu shots were actually *causing* the GBS cases. Nevertheless, they agreed that surveillance efforts should be expanded. The mere hint of such a risk, after nine long months of doubts and problems, was enough to frighten even the staunchest program advocate. For some embattled officials, it was the final straw.⁴⁷

On December 14, CDC announced publicly that it was investigating a possible association between GBS and swine flu shots, but it added that “there was no evidence to link the reported cases to vaccination.”⁴⁸ Two days later, CDC recommended suspension of the program pending further investigation of GBS. Sencer and other officials told Ford, who, sighing, concurred. That afternoon HEW leaders announced that the swine flu program was being suspended “in the interests of safety of the public...of credibility, and...of the practice of good medicine.”⁴⁹ They emphasized that this was only a temporary step while further investigation of the GBS data was being conducted. But most program officials, already battle scarred and weary, knew in their hearts it was “the death knell for the program.”⁵⁰ They were right. The epidemic never came, and the mass immunization campaign was never reinstated.

EPILOGUE

But the swine flu story was not quite over. In January 1977, Joseph Califano, newly ap-

pointed secretary of HEW under President Jimmy Carter, was informed, after little more than a week in office, that an outbreak of A/Victoria flu had swept through a nursing home in Florida, causing three deaths. He was informed that the only vaccine available to prevent further spread was a combined A/Victoria-swine flu vaccine. The ACIP thought it should be used, Califano was told, since A/Victoria flu generally poses a much greater danger to the frail elderly than the very slight risk of getting GBS. But how would the public react to the news that a vaccine that could cause paralysis or even death was to be used on this vulnerable population? It was a potentially treacherous situation, especially for a political newcomer.

Califano decided to confront the issue. He told Carter he planned to “ask other experts to join the [ACIP] so that we will have as broad and objective a base as possible.” He wanted people outside CDC and ACIP, he later explained, since both agencies had “a strong interest in promoting immunization programs and in vindicating their earlier judgments on this one.”⁵¹

The group met for an all-day session February 7 in front of TV cameras and a roomful of spectators, including previous critics of the program. Califano himself was present for much of the discussion. Many were expecting a real donnybrook given the divergent views of the various participants. What ensued instead was, in the words of a *Washington Post* editorial, “a full day of reasoned, wide-ranging and extraordinarily comprehensive discussion, and ultimately a consensus.”⁵²

At the end of the day, the group recommended the release of the combined vaccine and the voluntary inoculation of groups at high risk for A/Victoria flu. Secretary Califano concurred.

SWINE FLU LESSONS

The swine flu story did not end happily. Critics have called it the “most misguided vaccination

program ever attempted,” a “fiasco,” a “debacle.”⁵³ What can we learn from this sorry saga?

One obvious lesson is that no proof of risk is not the same as proof of no risk. Even though swine flu vaccine was tested in the largest field trial in vaccine history, the risk of GBS was too low to be detected. Swine flu shots caused several hundred cases of GBS, some resulting in permanent disability or death. Subsequent investigations revealed that the rate of GBS was roughly seven times higher among people who had been vaccinated, but even this relatively strong association was not picked up in the field trials because GBS was so rare (1 to 10 cases per *million* people). Clinical trials, however well designed, provide some protection against unsuspected effects but offer no guarantees against risks that are very small (albeit potentially deadly) or effects whose onset is delayed.

The swine flu story also offers vivid testimony to the tension between promoting a medical procedure and providing adequate information to patients about the risks it entails. In accepting liability for vaccine-related injuries, Congress had insisted that written consent be obtained from all those vaccinated. However, this requirement was at odds with the goal of immunizing as many people as possible, and the consent procedures actually left much unsaid. The problem for HEW was how, in one official’s words, “to protect without discouraging.”⁵⁴

It was a delicate balance to strike, but HEW’s consent form did not come very close. The initial documents made no mention of any uncertainty about the pandemic occurring. They stated flatly that the vaccine “can be taken safely during pregnancy,” yet it had never been tested on any pregnant women. Several members of the National Commission for the Protection of Human Subjects, after reviewing the forms, suggested discarding them and starting over.⁵⁵ Even after some of the commission’s recommended changes were included in a cover sheet, the contents remained strongly tilted toward the benefits of vaccination.

Such failures of communication are not uncommon. Many physicians avoid disclosing the risks of medical procedures to patients for fear of producing imaginary symptoms among “suggestible” patients or of undermining faith in the physician’s curative powers. Even less likely to be communicated are the numerous uncertainties involved in many medical procedures.

As it turned out, the swine flu consent procedure achieved neither an informed, immunized public nor a legally reliable consent document. People signed a consent form after they had come in to be vaccinated and had, presumably, already made up their minds. A majority of those who had signed a form, when questioned subsequently, were unaware of the information it provided. Fifteen percent said they did not even remember signing a form.

Another lesson we can learn from the swine flu story is how easy it is to underestimate the full costs of public programs. President Ford sold the mass immunization program to Congress as a \$135 million insurance policy against a major public health threat. The final price tag was probably closer to \$600 million, considering federal, state, and local spending on immunization, damages for injured victims, and the cost of program management and adjudication.

The final reckoning of this ill-fated chapter in public health history must also include the opportunities lost to use swine flu funds more productively. Immunization levels among children had been falling since the early 1970s, and by 1976, more than a third were without adequate protection against preventable diseases such as polio, measles, rubella, and whooping cough. Yet the Ford Administration, while allocating \$135 million to swine flu, refused to budget more than \$5 million to help states immunize children against these other, more serious diseases. Indeed, the all-out effort required for swine flu forced many states to divert resources away from these other programs, leading to further declines. Not surprisingly, the number of rubella, measles, and

whooping cough cases nationally rose in 1977 by anywhere from 39 to 115 percent.

Another lesson from the swine flu story reveals how hard it is to get effective disease prevention services to the disadvantaged. Influenza is well known to be more prevalent and more severe among poor and minority groups.⁵⁶ In an effort to reach these groups, the government targeted special media appeals for urban ghettos and other poverty areas. Nevertheless, vaccination rates in these areas remained well below average. This is the standard pattern in health care. One analyst called it the “inverse care law”: the greater the medical need, the less care available. Poor and minority groups have lower rates of virtually every preventive service, even access to vitamins. Had a swine flu epidemic come, the country’s most disadvantaged citizens would have been hurt the most.

Exactly why influenza strikes the poor and minorities harder than others is not fully understood, but hardships such as stress, crowding, poor nutrition, and environmental pollution probably all play a role. With these factors unchanged, purely medical interventions like flu shots will inevitably be inadequate.

Improving social conditions is not normally within medicine’s purview, of course. “Prevention,” in the medical model, is generally confined to technical interventions in the disease process, while the precipitating social circumstances remain unaddressed. Yet the close relationship between poverty and most health measures suggests that fully effective disease prevention is impossible without major changes in the structure of society itself. It is far easier (and less threatening politically) to focus on the consequences of that structure. As one medical observer lamented: “We have conquered polio but not poverty, tuberculosis but not truancy, syphilis but not slums. Somehow, we seem condemned to triumphs of biological wizardry and failures of social management.”⁵⁷

The swine flu story also offers valuable insights into the problems of handling vaccine-

related injuries through the courts. With proper planning and anticipation, the mass immunization program could have furnished an ideal opportunity to design a model compensation program for a limited purpose that avoided the pitfalls of current litigation—a kind of national experiment in social insurance. What emerged, however, was a hybrid approach that gained few of the advantages of social insurance while retaining all of the delays, costs, and moral ambiguities of our present, tort-based legal system.

One thing was clear: The swine flu law was a good deal for the insurance companies. Vaccine producers were liable only for negligent injuries, a risk insurers were quite willing to bear since producers’ negligence had rarely been a factor in prior vaccine litigation (nor was it in most swine flu suits). Some angry members of Congress accused insurers of corporate blackmail. In reality, the problem lay at a deeper level, in the uneasy mix of private insurance and public legal justice.

Should the federal government have assumed liability for injuries caused by swine flu? Almost all vaccines produce a few adverse reactions, no matter how careful the production and testing. There is a plausible rationale for expecting the government to assume liability for these rare, but sometimes serious, injuries. The government regulates vaccine production and is heavily involved in the funding and administration of most immunization programs. Moreover, society has a collective interest in widespread immunization in order to increase the population’s immunity, and it is arguably the government’s responsibility to compensate people who take risks that benefit society as a whole. Furthermore, in the swine flu program, the government itself had tested the vaccine and claimed that side effects would be minimal. And the government had implored all citizens to get shots. In the words of one GBS victim paralyzed from the waist down, “president [Ford] got on TV and made it seem like my patriotic duty.”⁵⁸

Soon after the program was suspended, injury claims began pouring in. In the first year alone, the government received over 1,200 claims seeking damages totaling over \$608 million. Government lawyers were swamped.

Lawyers representing swine flu victims called the government's legal battles against "crippled American citizens" "hard-nosed," and lacking "any real sense of humanity."⁵⁹ They charged that the government spent more money fighting cases than it would have cost to settle them out of court. The government was in a ticklish position. As the chief federal attorney heading swine flu litigation put it, "You can't expect us to give somebody one million dollars because he was sick for a month."⁶⁰ One can just hear the cries of boondoggle, especially for claims that appeared dubious. In relying on the courts to resolve disputed claims, the swine flu law in effect guaranteed controversial and inconsistent judgments. The family of one man who died from GBS agreed to a settlement of \$285,000, while another family won \$5 million in damages.⁶¹ Moreover, contrary to the program's stated goal, compensation of swine flu claims was anything but "prompt." Predictably, case-by-case litigation proved to be a slow and inefficient way to handle generic questions of fact, and trials and appeals took a decade or more to complete.

The swine flu compensation program's problems (protracted trials, delayed awards, uneven amounts, and huge legal costs) are characteristic of the present legal system. Built into its very design is the fundamental incompatibility between tort law doctrine, with its emphasis on punishing wrongdoers, and the view that society has a moral duty to compensate innocent victims, especially those injured in pursuit of a collective goal. That duty is increasingly recognized both here and abroad. Many other industrial countries provide "no-fault" compensation through publicly funded social insurance as well as private sector programs. A number of European countries provide publicly funded no-fault compensation

for vaccine injuries. Most no-fault systems are less generous than American juries tend to be in personal injury suits, but they generally compensate a much higher proportion of all covered injuries.⁶² In 1988, the United States finally adopted a federal no-fault compensation program for children injured or killed by mandatory vaccines. This program was established with the aim not only of providing equitable compensation for children and their families but also to try to curb the sharp escalation in vaccine prices and to halt the exodus of drug companies from the business of producing vaccines—both of which manufacturers blamed on their expanding liability.

WAS THE PROGRAM JUSTIFIED?

Suppose an epidemic had come. Would the swine flu program then have been judged a success? The answer must be, for the most part, no. For, as we have seen, much of what went wrong would have been even more serious had the epidemic come. The program suffered a seemingly endless series of logistical and legal problems for which there had been little if any contingency planning: lagging production, special children's dosages, temporally related deaths, inadequate informed consent, and the impasse over liability. As a result, its future was continually in doubt, undermining public confidence, disrupting state plans, and causing major shortfalls in vaccine supply. Because of such problems, less than a quarter of the population (and almost no children) had been vaccinated by mid-December—in all likelihood too few people to provide any meaningful protection against an oncoming epidemic. Had a major outbreak of swine flu erupted that fall or winter, the program would surely have been judged at least as harshly for being too little too late.

The epidemic did not come, however, and the main question that has haunted the swine flu program is whether it was an unnecessary and avoidable waste of resources or, rather, a prudent insurance policy against a threat that

just happened never to materialize. The initial response following the Fort Dix events seems reasonable. All the ingredients for a pandemic appeared to exist, including a virus similar to that implicated in the deadly 1918 pandemic. In view of these circumstances, it made sense to arrange for the necessary vaccine to be obtained from manufacturers and to begin planning for its distribution—but not to commit irrevocably to a mass immunization campaign. Yet that is just what happened once Sencer's ACTION memo compressed these two separable steps (preparation and immunization) into a single “go or no-go” decision.

If a commitment to mass immunization so early seems premature, it is even harder to defend the persistent refusal to back away from that commitment as the summer wore on with no sign of swine flu. Despite a swelling chorus of doubt and criticism, program leaders, convinced that an epidemic was possible, plowed doggedly on. By the fall, with swine flu still nowhere in sight, many officials clearly wanted to shift course and retreat to stockpiling, but they were afraid to say so publicly. By then, there was too much face to be saved (and too much potential political fallout) for such a step to be taken.

If doubts and dissent had been aired openly from the outset (as Califano did in deciding to release the combined A/Victoria-swine flu vaccine for high-risk groups), the story might have been different. At some point, the obstacles might have seemed simply too overwhelming, and the payoff too unlikely, to proceed with immunization. Instead, warnings were ignored, and program leaders pushed ahead with plans based on best-case assumptions:

- The vaccine would be *effective*.
- It would cause *few if any side effects*.
- Production would occur *on schedule*.
- There would be *no unusual liability problems*. Plainly such optimism was not justified. Optimism shifted to pessimism

when it came to the perceived need for the program.

- A pandemic was a “*strong possibility*.”
- *Most of the population* would be vulnerable.
- The toll in death and disease would be *comparable to 1918-19*.

This split perspective (overestimating the benefits of technological intervention on the one hand and inflating the dangers of not intervening on the other) is characteristic of experts in many fields. We might call it “technological optimism.”

Technological optimism went largely unchecked in the swine flu program for at least three reasons. One was the substantial influence of medical scientists in aspects of the program that fell outside their expertise.

Another reason why optimism prevailed over realism undoubtedly had to do with Ford's role. Once the prestige of the presidency had been thrown behind the program, officials had substantially less maneuvering room to modify their course of action as problems multiplied and the chance of an epidemic dwindled.

The third and perhaps most important reason for the optimism that pervaded swine flu planning was its insulation from the probing scrutiny of public discussion. Throughout, critics complained that decisions were being made by a small clique of government officials and their handpicked scientific advisors and that these leaders refused to debate publicly with challengers either inside or outside the government. All of the major participants, critics charged, had something to gain from the program:

1. Government bureaucrats would get funding for their agencies and some yearned for public limelight.
2. Scientists would be able to test immunization theories and develop new vaccines.
3. Drug companies would reap essentially risk-free profits and useful publicity about their liability problems.

4. Private physicians would be able to expand their patient clientele.
5. Government officials could claim to be champions of public health.

Broader public dialogue might have provided the needed filter for uncritical and seemingly myopic expert advice. President Ford's decision may have been partly political, but it was a choice pressed upon him by his most trusted scientific advisers.

Indeed, the real problem lay not so much in the decision to go ahead with immunization as in the way the decision was made. By refusing to confront openly and candidly the charges of the critics, decision makers left themselves open to precisely the kinds of attacks and suspicions that arose. Had they done as Califano did (encouraging full public debate and inviting critics and the press into the inner sanctum to partici-

pate in policy discussions), events might have gone quite differently. More important, however they turned out, there might have been less rancor and suspicion surrounding the program.

In short, the swine flu story was not inevitable. There were alternative actions and decisions that might have produced a happier ending. Many were steps that critics tried in vain to bring about. That they did not succeed highlights the dangers of overconfidence in the safety and efficacy of medical intervention (even in the name of prevention), of overreliance on a narrow group of experts for the formation of national health policy, of mixing partisan politics with public health decisions, and, most of all, of deliberately excluding dissent. The lessons seem clear in hindsight. Harder will be knowing how and when to apply them next time.

Notes

1. Interview with Martin Goldfield, M.D., by Ralph Silber, November 7, 1979.
2. CDC is the federal government's "preventive medicine" organization. It has responsibility for tracking the course of diseases through the population, offering recommendations as to whether a new vaccine is needed (and, if so, what kind), and dealing with state and local health departments.
3. Lawrence Wright, "Sweating Out the Swine Flu Scare." *New York Times* (June 11, 1976): 30.
4. There were, to be sure, several important qualifications. The virus responsible for the 1918-19 pandemic had never been identified with absolute certainty. It was not until 1931 that laboratory techniques were able to isolate and identify the swine virus from that year's pig population. Based on the similarity between this virus and the antibodies still in the blood of people who had survived the 1918 pandemic, virologists concluded that this was the same virus that had caused the pandemic. Although most experts accepted this conclusion, a few scientists remained doubtful. Moreover, some virologists took the fact that the virus isolated at Fort Dix did not spread to the surrounding community and turned out not to grow well in eggs to indicate that it was a relatively weak pathogen and hence only distantly related, if at all, to the lethal virus of 1918-19.
5. Influenza viruses are identified by their surface proteins or "antigens." When a virus appears with antigens differing in composition from those of the virus previously circulating in the population, an "antigenic shift" is said to have occurred. Although it is still widely believed that antigenic shifts produce influenza pandemics, some experts, such as Albert Sabin, cite contrary evidence.
6. Harold M. Schmeck, Jr., "U.S. Calls Flu Alert on Possible Return of Epidemic's Virus." *New York Times* (February 20, 1976): 1.
7. The most definite way to identify a virus is by isolating it from a throat culture. A second method that is nearly as certain is to show an increase in antibody levels in successive blood samples, which increase presumably reflects the body's response to the virus. Five of the 13 cases positively identified at Fort Dix were based on throat cultures, and another 8 on rising swine antibody levels in two successive blood tests. The third and least reliable method is simply to measure the absolute antibody concentration in a single blood sample, with high concentrations being interpreted as evidence of previous infection.

8. In 1957, although Asian flu had been reported in China six months before it peaked in the United States, vaccine production and distribution fell far short of needs, despite federal exhortations. In 1968, with almost five months of warning, vaccine supplies were again inadequate and an even smaller fraction of the population was immunized.
9. E. Russell Alexander, M.D., quoted in Richard E. Neustadt and Harvey V. Fineberg, *The Swine Flu Affair: Decision-Making on a Slippery Disease* (Washington, D.C.: Government Printing Office, 1978), 13.
10. Interview with Walter R. Dowdle, M.D., by Ralph Silber, November 1, 1979.
11. Alexander, quoted in Neustadt and Fineberg (n9), *The Swine Flu Affair*, p. 13.
12. John R. Seal, M.D. or Harry M. Meyer, Jr., M.D., to David J. Sencer, M.D., quoted in Neustadt and Fineberg (n9), *The Swine Flu Affair*, 14.
13. Also, by some accounts, the ACIP was practically a house organ and generally satisfied Sencer's wishes. Quote is from interview with David J. Sencer, M.D., Director of CDC, by Ralph Silber, November 6, 1979.
14. Memorandum signed by Dr. James F. Dickson on behalf of Dr. Theodore Cooper to David Mathews, Secretary of HEW, March 18, 1976, 1, reprinted in Neustadt and Fineberg (n9), *The Swine Flu Affair*, 147-55.
15. *Ibid.*, 2, 9.
16. Dickson, quoted in J. Bradley O'Connell, "Swine Flu," case study prepared for the Kennedy School of Government Case Program under the supervision of Laurence E. Lynn, Jr., Professor of Public Policy at the John Fitzgerald Kennedy School of Government, Harvard University, Cambridge, Mass., 1979, 9.
17. Memorandum from David Mathews, Secretary of HEW, to James T. Lynn, Director of OMB, March 15, 1976, reprinted in Neustadt and Fineberg (n9), *The Swine Flu Affair*, 156.
18. Arthur M. Silverstein, *Pure Politics and Impure Science: The Swine Flu Affair* (Baltimore: Johns Hopkins University Press, 1981), 43. Quote by HEW Assistant Secretary William Morrill is from O'Connell (n16), "Swine Flu," 14.
19. James Cavanaugh quotes are from O'Connell (n16), "Swine Flu," 16-17.
20. Harold M. Schmeck, Jr., "Flu Experts Soon to Rule on Need of New Vaccine." *New York Times* (March 21, 1976): 1, 39.
21. Quoted in Neustadt and Fineberg (n9), *The Swine Flu Affair*, 28.
22. "Swine Flu Inoculations, The President's Remarks Announcing Actions to Combat the Influenza, March 24, 1976." *Weekly Compilation of Presidential Documents* 12 (March 29, 1976): 484.
23. Robert C. Pierpoint, quoted in Neustadt and Fineberg (n9), *The Swine Flu Affair*, p. 30.
24. Neustadt and Fineberg (n9), *The Swine Flu Affair*, 29.
25. "Excerpts from Cronkite Show Of 3/25/76," quoted in Barton J. Bernstein, "The Swine Flu Immunization Program." *Medical Heritage* 1 (July-August 1985), 247.
26. Quoted in Neustadt and Fineberg (n9), *The Swine Flu Affair*, 30.
27. Testimony of Theodore Cooper, M.D., in *Proposed National Swine Flu Vaccination Program*, hearing before the Subcommittee on Health and the Environment of the Committee on Interstate and Foreign Commerce, U.S. House, 94th Congress, 2nd Session, March 31, 1976, 13-22.8. Testimony of Merritt Low, M.D., in Swine Flu Immunization Program, hearings before the Subcommittee on Health of the Committee on Labor and Public Welfare, U.S. Senate, 94th Congress, 2nd Session, April 1 and August 5, U.S. Senate, April 1976, 57.
28. Testimony of Merritt Low, M.D., in *Swine Flu Immunization Program*, hearings before the Subcommittee on Health of the Committee on Labor and Public Welfare, U.S. Senate, 94th Congress, 2nd Session, April 1 and August 5, U.S. Senate, April 1976, 57.
29. Testimony of Bruce Brennan, *Ibid.*, 73. Stetler quote is from p. 72.
30. Goldfield, quoted in Wright (n3), "Sweating Out the Swine Flu Scare," 36.
31. Goldfield, transcript of CBS Evening News, April 2, 1976, quoted in Neustadt and Fineberg (n9), *The Swine Flu Affair*, 40.
32. Interview with Goldfield (n1), November 7, 1979.
33. Quoted in Neustadt and Fineberg (n9), *The Swine Flu Affair*, 40.

34. "Flu Vaccine" (editorial). *New York Times* (April 6, 1976): 34.
35. "Influenza," *Weekly Epidemiological Record of the World Health Organization* 16 (April 15, 1976): 123.
36. "Whole" vaccine produced immunity in children but caused many adverse reactions, ranging from sore arms to high fevers. "Split" vaccine, on the other hand, caused few side effects, but failed to confer immunity. ("Whole" and "split" vaccines refer to two different methods of preparing killed-virus vaccine.)
37. These arguments rested on the questionable assumption that if a swine flu pandemic occurred, it would spread too quickly to allow time to move from stockpiling to immunization. In fact, what little was known about the speed of an influenza pandemic came from past pandemics and suggested that there might be enough time to move from stockpiling to immunization if the pandemic spread at the same rate as in 1968, but not if it spread as quickly as in 1957. (The pandemics of 1957 and 1968 were the only ones for which data existed.) However, if immunization could be done on a crash basis, as Sabin was proposing, it might still be possible to intervene in time even if the pandemic spread as rapidly as in 1957.
38. Alexander, transcript of CBS Evening News, June 22, 1976, quoted in Neustadt and Fineberg (n9), *The Swine Flu Affair*, 46.
39. "Swine Flu Scare" (editorial). *New York Times* (July 3, 1976): 20.
40. A paper in the respected British journal *Lancet* reported that six volunteers exposed to swine flu virus had shown only "mild" symptoms, implying that the virus was less virulent than many other flu viruses and was unlikely to cause widespread disease. Another article in the same issue, by the leading British influenza expert, concluded that preparing for mass immunization was "highly questionable," even in the United States, "until the shape of things to come can be seen more clearly."
41. "Swine Flu Immunization Program: The President's Remarks Urging Congressional Enactment of the Program, August 6, 1976." *Weekly Compilation of Presidential Documents* 12 (August 9, 1976): 1249
42. Senator Ted Kennedy, quoted in "Shots in the Arm." *Time* (August 23, 1976): 41.
43. Interview with Dowdle (n10), November 1, 1979.
44. "Phantom Flu" (editorial). *New York Times* (October 14, 1976): 36.
45. Program planners had actually foreseen the problem of temporally related deaths, but they had decided not to discuss the likelihood of such deaths publicly for fear of discouraging people from getting shots. In fact, the panic and misunderstanding caused by the Pittsburgh deaths were undoubtedly much greater than they would have been had adequate information been provided in advance.
46. Philip H. Dougherty, "Flu-Shot Ad Campaign Ready to Go." *New York Times* (November 17, 1976): D12.
47. Lawrence B. Schonberger, M.D., letter to Diana Dutton, June 16, 1987.
48. Quoted in Philip M. Boffey, "Guillain-Barré: Rare Disease Paralyzes Swine Flu Campaign." *Science* 195 (January 14, 1977): 156.
49. Cooper, quoted in Lawrence K. Altman, "Swine Flu Program Suspended in Nation; Disease Link Feared." *New York Times* (December 17, 1976): A1.
50. Interview with Lawrence B. Schonberger, M.D., Viral Diseases Division, Bureau of Epidemiology, CDC, by Malcolm Goggin, February 11, 1980.
51. First Califano quote is from Neustadt and Fineberg (n9), *The Swine Flu Affair*, 74. Second quote is from Joseph A. Califano, Jr., *Governing America: An Insider's Report from the White House and the Cabinet* (New York: Simon and Schuster, 1981),176.
52. "Swine Flu: Letting the Sunshine In" (editorial). *Washington Post* (February 13, 1977): C6.
53. See, for example, Harry Schwartz, "Swine Flu Fiasco." *New York Times* (December 21, 1976): 33; George A. Silver, "Lessons of the Swine Flu Debacle." *Nation* (February 12, 1977):166-69; Cyril H. Wecht. "The Swine Flu Immunization Program: Scientific Venture or Political Folly?" *American Journal of Law & Medicine* 3 (Winter 1977-78): 425-45.
54. Silverstein (n 18), *Pure Politics and Impure Science*, 109; also Greenberger testimony, *Ibid*.
55. EVIST interview with Professor Jay Katz, Yale Law School, January 15, 1980.
56. Influenza is almost twice as common among poor adults as among the affluent, and age-adjusted

death rates for influenza and pneumonia are about 50 percent higher among nonwhites than whites.

57. Gerald Weissmann, "AIDS and Heat." *New York Times* (September 28, 1983): 25.
58. "Big Award in Swine Flu Vaccine Case." *San Francisco Chronicle* (February 2, 1983): 2.
59. Mark P. Friedlander, Jr., Attorney, Friedlander, Friedlander and Brooks, Arlington, Virginia, letter to Barton Bernstein, July 25, 1983.
60. Jeffrey Axelrad, quoted in Philip Taubman, "Claims of Flu Shot Victims Unpaid Despite U.S. Pledge." *New York Times* (June 10, 1979): 30.
61. "\$285,000 for Swine Flu Death," *San Francisco Chronicle* (August 30, 1979): 5. In the Cardillo (1984) case, a wrongful death suit, damages of \$5 million were awarded; that judgment was also appealed (Jeffrey Axelrad, personal communication, July 10, 1986).
62. However, this country's closest analogues, the workers' compensation system and the federal Social Security Disability program, have both been widely criticized, underscoring the political and economic vulnerability of nonjudicial systems in the United States.

Resource 7. Hearing Before House Committee on Appropriations

The following exchanges are excerpts from a hearing on Monday, January 12, 1919, before the subcommittee of the House Committee on Appropriations, consisting of Messers. Thomas Upton Sisson, James McAndrews, James A. Gallivan, Charles R. Davis, and William R. Wood.

TOPIC: RELIEF TO ALASKA

Statements of Mr. Thomas Riggs, Jr., Governor of Alaska, and Mr. P. P. Claxton, Commissioner of Education

MR. SISSON. You have before this committee a joint resolution for relief in Alaska, which passed the Senate a few days ago, enabling the Secretary of the Interior to pay \$100,000, which is necessary to cooperate with the Public Health Service to combat influenza in Alaska, and in addition to combating influenza, to relieve the indigent natives that may be affected by influenza of their wants.

MR. RIGGS. Yes, sir.

MR. SISSON. Will you explain the situation in Alaska?

MR. RIGGS. The influenza epidemic reached Alaska through the regular channels of transportation and affected practically all of the coast of Alaska....Those most affected were the natives; about 90 percent of the indigency and the deaths have been among the natives...in places which were not ice free and which do not have winter transportation. The epidemic worked great havoc. There we have had deaths of approximately 1,000 Eskimos, whole communities having been wiped out. We have at one place alone 90 orphans as the result of the influenza epidemic. We had no funds with which to combat the disease....

The surgeon general of the Public Health Service, who had an appropriation of \$1,000,000 to combat influenza, authorized me to engage doctors and nurses where I could get them and that was done as to the ice-free portion of Alaska, but, of course, we could not reach the ice-bound portions. I have authorized, where I have had any funds to do it, the

sending of relief expeditions for the gathering up of these orphans and have contracted for their keep: I have authorized the purchase of provisions for the indigent natives because they are not allowed to travel and trap, and, as a matter of fact, most of them are dead. For instance, at Cape Prince of Wales, of a population of 300 natives, 5 adults were left alive: at Kodiak probably 50 percent of the natives died: and all along the line I have been controlling travel among the natives so that the disease would not get to the more isolated natives and affect the white population....

If it were merely for the relief of the white population I should not come to Congress for 1 cent. I should put that on the territory where, I think, it rightly belongs, but when it comes to what we consider the wards of the Nation, who are not taxpayers and who, in other parts of the United States, are attended to by the Government, I consider that our small treasury should not be diminished by the sum necessary.

We need that for our schools and roads; we have not a very large treasury, and we can not handle it ourselves: it has gone beyond our control. There were approximately 2,000 deaths, as I figure it, in Alaska from influenza, which are scattered all over the Territory. The Territory is two and a quarter times the size of Texas, and many places there are without any means of communication. I sent one doctor 400 miles by dog team, an expensive trip. He got to the afflicted community and died.

MR. WOOD. The doctor died?

MR. RIGGS. Yes; of influenza....We probably have 1,000 natives unburied, and the best price I have been able to get is \$30 to bury a native. You have to thaw the ground in order to make an excavation, and these Indians have

got to be buried. It is progressing all along the isolated settlements of the Aleutian Islands.

MR. SISSON. Have you any information from Alaska by telegram or otherwise?

MR. RIGGS. Yes; I have....A telegram from Mr. Evans, the school teacher at Nome, which is as follows:

Nome, Alaska. January 2, 1919
Hon. P. P. Claxton
Commissioner of Education,
Washington, D.C:

Ten villages this district affected. Three wiped out entirely, others average 85 percent deaths. Majority of children of affected villages saved by relief parties sent by the Bureau of Education. Teachers in stricken villages all sick, two dead, rest recovering. Total number of deaths reported 750, probably 25 percent this number frozen to death before help arrived. Over 300 children to be cared for, majority of whom are orphans. Am feeding and caring for surviving population of five large villages. Seven relief hospitals operated in affected villages: no trained nurses or physicians available, but splendid work done by white people in charge. Cost to date estimated \$70,000 for native relief alone; will need about \$15,000 this month. May be necessary to send relief to several quarantined villages owing to regulations preventing natives from trapping, and cannot purchase necessities. Impossible at this time to lift quarantine zones in outlying affected villages. Appalling and beyond description. Am giving 90 orphans to mission at Nome to care for at \$10 per month, but hope department will plan for large industrial training school this district next summer. Splendid opportunity for educational advancement for the Eskimos.

Evans

MR. SISSON. Why are these Eskimos not trapping?

MR. RIGGS. Most of them are dead, and those who are not dead are ill, and they must be controlled in their villages in order to keep them from going to other villages.

MR. SISSON. Did you stop the trapping and traveling around in order to prevent the spread of the disease?

MR. RIGGS. Yes, sir: I asked those in charge to take such steps to prevent a spread of the disease to outlying districts.

MR. SISSON. How did you get the supplies and materials—buy them from individuals who would sell to you on that account?

MR. RIGGS. On my personal credit, my word that it would be paid.

MR. RIGGS. The United States government, in the United States proper, has always taken care of the Indians. They are wards of the government.

MR. SISSON. In the United States we have been taking care of the Indians largely out of their own revenues. Of course, there has been a certain appropriation made for educational purposes, for hospitals, and things of that sort, but the Indians have a fund of their own—the Indians in Oklahoma, the Five Civilized Tribes—and pay their own expenses. Then there is a certain fund of the Indians in the Dakotas and Montana, which is administered by Congress, but the Government, while acting as guardian for the Indians, is using Indians' funds. We took the Indians' lands and those lands were sold; a fund was created and that fund has been divided among some of the civilized tribes, where Congress has decided that they are capable of administering their own affairs.

MR. CLAXTON. May I say, on the other hand, that the natives of Alaska have no funds at all; we bought them, apparently, with the Territory, and have never recognized that they had any rights.

MR. SISSON. You cannot say that every nontaxpayer in the country is not a very useful part of society.

MR. CLAXTON. He is a very useful part of society; but the point is that these natives of Alaska only get the money that is appropriated to them, and there is no fund in the banks for their use.

MR. WOOD. The United States has never recognized any land holdings by the Alaska Indians?

MR. CLAXTON. No, sir. It is also true, in addition to the funds the government adminis-

ters for the Indians, the direct appropriations for two years are as much per capita as the total appropriations per capita for 40 years in Alaska.

MR. RIGGS. I wanted \$200,000 in the first place. The Senate cut it down to \$100,000. Now we have obligations amounting to \$107,000. We are asking for this \$100,000 to pay these obligations and to pay the rest of our obligations out of the Territorial funds when the legislature shall meet and appropriate it.

MR. RIGGS. There are at present only about 20,000 white people in Alaska. Twelve percent of the population went into the Army. For their quota they led all the States and Territories in subscriptions to the Liberty loans, and in the war-saving stamps they headed the list. Ninety-four percent of the people are members of the Red Cross, and they headed the list in subscriptions to the Red Cross. It is pretty hard on 20,000 taxpayers of the Territory of Alaska to take care of the wards of the Government who were inherited from Russia....

MR. SISSON. You have more Indians than white people?

MR. RIGGS. Yes, sir. About 27,000.

MR. SISSON. Do they own land?

MR. RIGGS. Some have secured allotments, but very little is done to the land. Very few of them pay any taxes.

MR. CLAXTON. They simply pay to live on the land.

MR. RIGGS. These are our own people; they are not from Austria, Turkey, Belgium, or Serbia; our own American people, who belong to us. It is a very serious situation.

MR. CLAXTON. May I add for these Eskimos and Indians that they never have been a charge upon the Treasury, and I do not think anything done now will be taken as a precedent in a large way. The only time when any appropriation has been definitely made for that purpose has been when there was some great calamity like a flood or the eruption of a volcano, and the appropriations for these cases have been very small. The sum total of money expended in Alaska annually for the relief of want has been less than \$2,000 a year.

MR. SISSON. I do not think that this is a condition that we should complain about.

MR. CLAXTON. We are not complaining about it. I simply give it as a fact. Under ordinary circumstances they do care for themselves, and they have not been a charge for any large amount for their support.

Resource 8. Medical Report From the A.E.F. in France and England

By Ward J. MacNeal, M.D.

The following account is excerpted from the *Archives of Internal Medicine*, Vol. 23, No. 6, June 1919. The subject is the influenza epidemic of 1918 in the American Expeditionary Forces (A.E.F.) in France and England.

INTRODUCTION

In the spring of 1918 reports of an epidemic disease in various parts of Southern France, Italy, and Spain appeared. Greater publicity was given to these reports in Spain, doubtless, in part, because that country was not engaged in war. By midsummer this disease had spread widely throughout Europe, and in the autumn had involved South Africa and America.

Numerous reports dealing with outbreaks of this disease have accumulated in the office of the Chief Surgeon, A.E.F., and in several instances special investigations of the epidemiology and bacteriology of these outbreaks have been reported. Manifestly, available reports are in many instances fragmentary, and the world's literature is not at hand for consultation, even if the necessary time could be devoted to it. Especially unsatisfactory are the reports of the disease in the military and civilian population of the belligerent countries, reports which one reads always with a suspicion that scientific accuracy may have been sacrificed to military or political considerations. It is intended to present here the known facts in regard to the disease, without regard to censorship, and it is expected that this paper will not receive publicity until the necessity for military or political censorship shall have ceased to exist. It may then become possible to obtain a sufficient number of reports from different countries so as to obtain a broad view of this pandemic and perhaps to arrive at clear and definite conclusions in regard to features now obscure.

CLINICAL MANIFESTATIONS

General Considerations

The clinical signs and symptoms of the disease are not entirely uniform and are similar to the manifestations of the group of acute infectious fevers. Were it not for the epidemiological evidence it would be difficult to characterize the disease as a distinct and definite clinical entity. Nevertheless, when it appears in the epidemic form, the early signs and symptoms are strikingly similar. At such times the most common and dangerous mistake is the designation of early cerebrospinal fever and of various respiratory infections as influenza because of the existence of an epidemic of the latter disease.

Course and Outcome

In the early months, May, June, and July, rest in bed and a purgative were followed by subsidence of the fever and amelioration of all symptoms in twenty-four to seventy-two hours, and prompt recovery without further manifestations, except slight weakness and depression. Complications were so rare as to be considered nonexistent and the relatively few cases of pneumonia observed were subsequently regarded as instances of mistaken initial diagnosis.

In the later months, from about the beginning of September, the disease has been perhaps less sudden in onset, but the course has been distinctly more malignant and a complicating fatal bronchopneumonia has become alarmingly frequent; so frequent, indeed, as to suggest a new epidemic of an entirely different disease.

In these more severe cases, distinct evidence of the tracheobronchitis and bronchopneumonia appeared, sometimes within the first forty-eight hours, but usually at about the end of the third or fourth day. Pleural effusion occurred in some cases; emphysema occurred rarely. Gradual unconsciousness for some hours before death, with considerable extension of the thoracic dullness in the last forty-eight hours, were commonly observed in the fatal cases.

The death rate in these pneumonias has been high, varying from 5 to 100 percent in different epidemics. During July this rate varied from 11.4 to 22.0 percent in the different weeks, but for the last week in October it reached 75 percent and continued high during November. The bulk of these deaths resulted from the bronchopneumonia of the influenza epidemic.

PATHOLOGIC ANATOMY

General Considerations

In the early months of the epidemic the disease was so benign in character that deaths which did occur were invariably ascribed to other causes. Since about August 15, 1918, deaths have become much more frequent and records of necropsy in this disease have become numerous.

The Respiratory Organs

The larynx, trachea, and larger bronchi showed swelling, edema, injection, and infiltration of the mucous membrane, which was covered by frothy mucopurulent, often bloodstained exudate. The smaller bronchi and bronchioles were also involved in the same process and some of them plugged with mucus.

On section, the cut surfaces were very moist, dripping a bloody, frothy fluid; the color was somewhat variegated, often showing a few firmer grayish patches of older consolidation centrally located. Invariably the lower lobes were more severely involved. The whole process in the lungs might be designated as an example of massive, pseudolobar form of bronchopneumonia of a very malignant type.

Pathology of Particular Cases

Clinical histories are available in some instances so as to permit a determination of the exact duration of the disease before death occurred.

Case 5002: Patient had a slight cold on Saturday, October 5, but took dinner with friends on that date. He was admitted to American Red Cross Military Hospital I from the Hotel Neurice at 6 p.m. on October 7 in a dying condition; died October 8 at 8:30 a.m. Duration of illness was therefore about 60 hours. Pleural cavities contain a few cubic centimeters of cloudy fluid. There are no adhesions. Lungs are both of the size of full inspiration. There is practically no exudate on either pleural surface. The right lung shows the upper two thirds of the upper lobe, the apex of the middle lobe and scattered patches throughout the lower lobe containing solid bluish-red areas, which have ill-defined margins. On section these areas are dark red in color and comparatively airless, the surfaces being bathed with a very large amount of bloody fluid. The remaining portions of the lungs are heavy with congestion and edema, except for a few of the anterior portions, which are dilated and feathery. The outer middle portion of the upper lobe and the outer half of the lower lobe of the left lung are in a similar condition; otherwise it resembles the right. The bronchi of both lungs are deep red in color, bathed with abundant bloodstained frothy mucus and covered with a thin, closely adherent, grayish-yellow, fibrinous pseudomembrane. The peribronchial lymph nodes are not markedly swollen. The sinuses at the base of the skull show some thickening of the mucosa and a small amount of mucoid fluid in the left sphenoid and left frontal. Smears and cultures from the lungs show streptococci and gram-negative bacilli (*B. influenzae*?). Smears from frontal sinus show staphylococci, gram-negative bacilli (*B. influenzae*?) and a short gram-positive bacillus; cultures from the same place show staphylococci. *Prosector: Major H. E. Robertson.*

Case 2920: Patient entered Base Hospital 17 Sept. 2. 1918, having been in France one week. He had been sick since landing, and had been riding in a baggage car for several days. He died September 12 at 11:50 p.m. The necropsy was performed at 3:25 p.m., September 13. The mediastinum is well covered with fat, the right visceral pleura hemorrhagic and injected and covered with fibrinous deposits. The pericardial cavity contains about 70 c.c. of a straw-colored fluid. The left lung weighs 1 pound 13.5 ounces and shows irregular consolidated areas. The right lung weighs 2 pounds 12.5 ounces. The left lung floats in water; on section it shows irregular consolidated areas from which frothy mucus exudes. The lobular type is more evident to the sense of touch than of sight. The entire right lung floats in water as do portions from the most nearly consolidated portions. Bronchi are red and inflamed. Cultures from the brain and from the heart blood are negative; cultures from the right lung show *B. influenzae* and *Streptococcus viridians*. *Prosector: Capt. Henry W. Cattell.*

BACTERIOLOGY

Clinical

The interest in many instances has centered on the question of Pfeiffer's bacillus and reports in regard to it have shown the very widest variety. Cultures made on blood-agar or on hemoglobin-agar have revealed, in the large majority of cases, pneumococci, streptococci, influenza bacilli, staphylococci, and gram-negative cocci. Attempts to detect a filterable virus have been reported, but experiments of this kind have not been carried out in the American Expeditionary Forces.

At Necropsy

At necropsy, also, the bacteriological findings have been variable and have usually shown a mixture of various species of microbes. Influenza bacilli, pneumococci of various types, hemolytic and non-hemolytic streptococci have occurred most frequently in the infiltrat-

ed lungs....These findings suggest that the disease has been essentially due to an invasion of the respiratory tract by influenza bacilli, followed by and associated with other pharyngeal organisms, and that the fatal outcome, in most instances, has been brought about particularly by these secondary invaders, in some instances streptococci, in others pneumococci.

ETIOLOGY

Susceptibility

The disease was distinctly milder in the nurses and officers than in the enlisted men. The relative care possibly explains this difference. Older men, particularly those beyond the age of 50, appear to have escaped to such an extent as to suggest a real immunity. Men of this age in the A.E.F. have been relatively few in number and have probably enjoyed better living conditions than most of the younger men, so that the evidence of their immunity should not be too readily accepted as conclusive. Of the soldiers, a very large proportion has been found susceptible. In some companies as many as 90 percent have been stricken within a period of ten days, and occasionally from 30 to 50 percent of a company have reported sick within a period of two days. High incidence of the disease has been observed in organizations performing exhausting duties and in those exposed to cold and wet, and without proper nourishment, particularly in units arriving on crowded transports, making long journeys in troop trains and in those undergoing severe training. Fatigue evidently plays a part in increasing susceptibility, and the influence of exposure to cold and wet is clearly indicated.

Specific Organism

In its epidemiologic, clinical, bacteriologic, and pathologic features, the disease is everywhere recognized as being identical with influenza as it was observed in the pandemic of 1889-90. The bacterial findings are those of influenza. In the A.E.F. the bacillus of Pfeiffer has been demonstrated in a very large percent-

age of the cases properly examined; in several series it has been demonstrated in every case. The other bacteria isolated, namely, streptococci, pneumococci, gram-negative cocci, although undoubtedly the cause of death in many cases, can be excluded from consideration as the primary cause of the epidemic disease, because of the inconstancy with which any one specific type has been encountered. The possible causative relation of the bacillus of Pfeiffer cannot be similarly excluded. On the other hand, the causative relation of this organism cannot be accepted as proven. During this epidemic, as during previous epidemics of influenza, a considerable proportion of throats of persons not suffering from the disease have been found to harbor this organism or organisms indistinguishable from it by the methods employed.

In order to settle in a convincing fashion the relation of the bacillus of Pfeiffer to the disease it would be necessary to carry out a series of very carefully controlled experiments on a group of thoroughly segregated men, preferably those confined in a prison which has entirely escaped the epidemic. It will not be sufficient to produce by the inoculation of pure cultures the clinical manifestations of influenza merely in the individual inoculated, but a critical demonstration should include the reproduction of the disease with its characteristic epidemic feature.

A limited number of experiments have been reported by various investigators suggesting that the causative organism may be a filterable virus. More detailed reports of experiments on a considerably larger scale will be required before the results can be accepted as conclusive. In addition to the numerous sources of error which require attention in all investigations of filterable viruses, there is here the special confusing element of the filterable virus of common colds, which appears to be capable of causing the signs and symptoms of influenza in the individual inoculated, but has not been proved to be connected with the genuine pandemic disease.

Until conclusive experiments have been carried out to decide the claims of the bacillus of Pfeiffer and of the filterable virus as the cause of influenza, one should keep an open mind in regard to the matter. It appears fruitless to attempt to settle the question by debate.

EPIDEMIOLOGY

General Considerations

The origin of the great pandemic of influenza of 1918 is involved in considerable obscurity, and it may never be possible to elucidate the question in a convincing manner. It seems certain that the epidemic outbreaks first appeared in Europe, apparently either in France, Italy, or Spain, and that the disease subsequently spread northward to Belgium and England and across the sea in ships to America and Africa. It is known that the disease also prevailed in Germany and Austria during the summer and fall, and special meetings of the medical societies of Berlin and of Munich were devoted to it in July 1918. In August and September the disease was carried across the sea to America and to South Africa, where it has spread extensively. The conditions for its incubation probably bear a relation to the great war and the altered living conditions dependent on it, but the relation is far from clear. Theoretical considerations must enter largely into the discussion of its origin because of the incompleteness of accurately recorded observations.

Origin of the Epidemic

From the preceding discussion, it is evident that the possibility that the epidemic actually originated in France has to be considered. The alternative possibility is that the disease first became epidemic elsewhere and was introduced into France in the epidemic form in the spring of 1918. The problem is made more complex because of lack of absolute certainty in regard to the nature of the disease and the identity of the epidemic disease with the influenza which was endemic in France in previous years.

The condition favoring influenza in France, in addition to the ordinary hardships of a country at war and the large amount of cold, damp weather, has been the fuel shortage, which has been peculiarly severe in France during the war. The evidence indicates that influenza has been very prevalent and that small epidemic outbreaks of it were recognized in the British Army in France in 1916 and 1917.

The arrival of American troops in France has been a factor of possible importance in relation to this disease. Attention may be directed to the sudden increase in mean strength from March to April, 1918, when 150,000 men were added to the 287,000 already in France. This increase of more than 50 percent required in many places, the crowding of three or even four men into the quarters previously occupied by two, thus increasing enormously the opportunity for the rapid transmission of respiratory infection. Furthermore, it furnished a large group of newly arrived susceptible individuals and brought them into close association with the influenza endemic among the American soldiers who had preceded them.

One is tempted, therefore, to account for the origin of the epidemic by assuming an increase in virulence of endemic influenza, depending, first, on war conditions in France, especially the lack of fuel; second, the introduction of Americans in 1917 and the spread of the disease among them during the following fall and winter; and third, the greater influx of susceptible American troops, beginning in the latter part of March, following which the disease assumed epidemic proportions. The evidence in favor of this conception appears

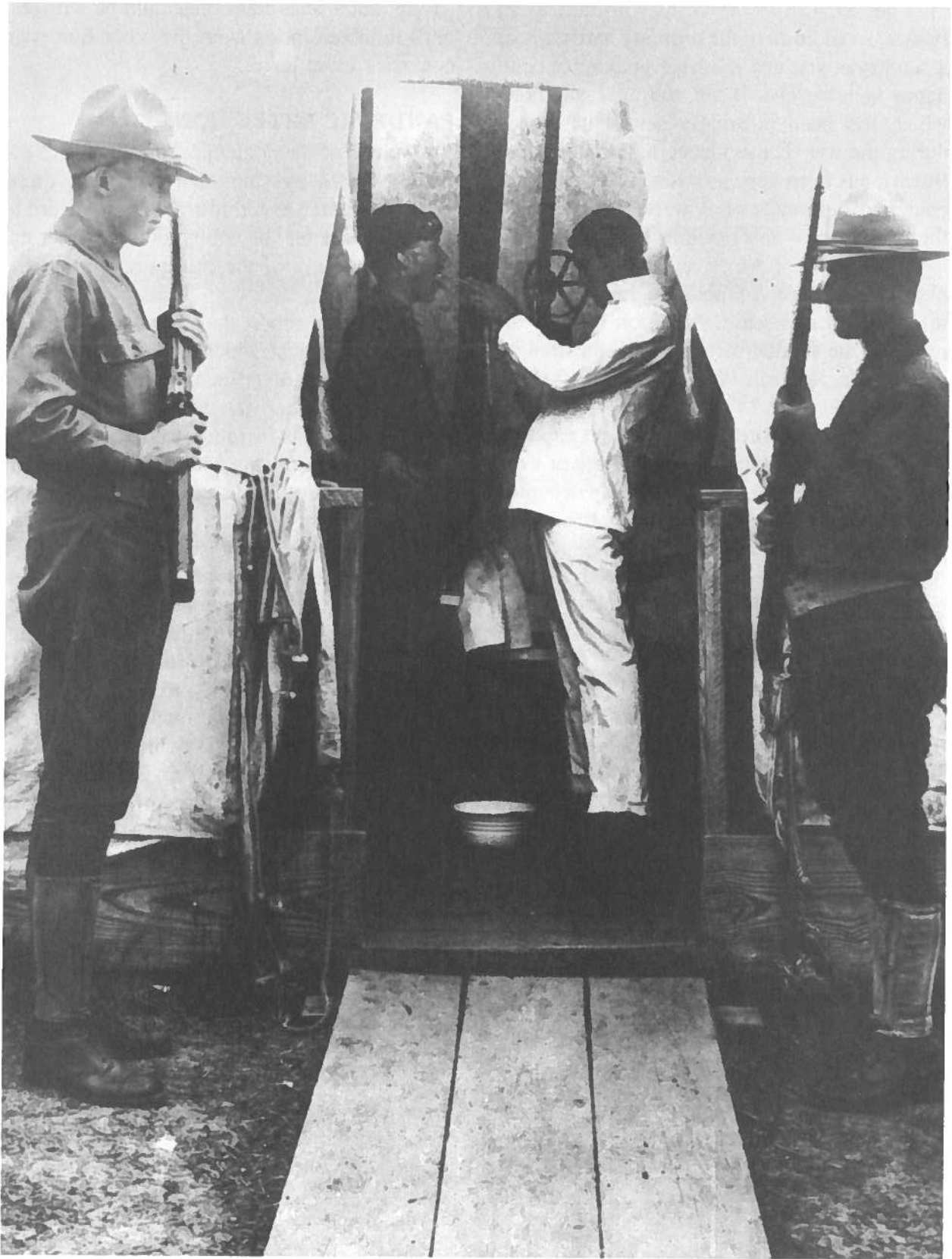
strong, but a final decision should be withheld until reliable reports from the other European countries are at hand.

PANDEMIC EXTENSION

The spread of the epidemic from France to the United States by ships can hardly be questioned, although exact information in regard to this may better be obtained in America. Doubtless many of the transports carried the infection.

A written report has been rendered in regard to one boat which had an outbreak of forty-two cases of influenza among the crew during the voyage to the United States in August, 1918. On its return to France this ship brought a part of the 64th Infantry. An epidemic of about 100 cases of influenza broke out on this boat again two days before reaching France, about September 1. The disease evidently spread rather rapidly in the United States, so that after September 15, nearly every transport arriving in France or in England, came in with a serious epidemic of influenza onboard, which could be traced back to cases existing in the military organizations before embarkation in the United States.

Reports from the United States indicate very clearly that the disease spread westward from the Atlantic seaboard. Although the disease must be regarded as identical in essential nature with influenza, which has been endemic in many parts of the United States since 1890, it is necessary to recognize that the virus brought over from France had acquired an epidemic quality to a degree which that previously existent in America no longer possessed.



Spraying throats was recommended as a treatment to prevent Spanish flu.

Resource 9. Report of the Spanish Flu in India

The following account has been adapted from I. D. Mills's "The 1918-1919 Influenza Pandemic—The Indian Experience," *Indian Economic and Social History Review*, 23, 1 (1986): 1-40.

The 1918-19 influenza pandemic is unique in terms of the sheer scale of the mortality it caused. Newly corrected figures suggest that a total of 17.4 million people died in its short sweep through the country. Rivers became clogged with corpses because available firewood was insufficient for the cremation of Hindus.

The first wave of influenza arrived in Bombay City, India, on May 29, 1918. Aided by the movements of troops, the postal workers of the Railway Postal Service, and panic migration of sick people by the railway from infected areas, it then spread through the whole of India by August.

In August, a second wave began again in Bombay Presidency and was well established by the month of September. Within India, the general direction of spread was from west to east, with an October peak in the Bombay Presidency, a November peak in the Center and North, and a December peak in Bengal. Thus, the pandemic was a highly concentrated phenomenon, with the severe second wave sweeping a given area in a period of only two to three months. In India as a whole, the second wave lasted for a matter of four months only, and yet it accounted for the lives of around 17-18 million people in that brief period.

AGE EFFECT

In influenza epidemics since 1918-19, as in those before, the common conclusion is that influenza extinguishes the life of the aged or those who have chronic disease. In marked contrast to this general pattern, the concentration of deaths in the age range of 20 to 40 was a spectacular departure from the common influenza pattern. Only 20 percent of excess deaths occurred to those over the age of 50, while 42 percent of deaths were in the age range of 20 to 40.

Another notable feature was that infants appeared to escape relatively lightly, having an excess mortality figure that was considerably lower than that for children aged one to four. This is a surprising feature in a society where the normally high infant mortality rate suggests that infants had a particularly precarious grasp on life.

Why this particular pandemic should have departed so radically from the usual influenza mortality age pattern is a mystery. However, several suggestions have emerged. One of these is that the older age groups had immunity conferred upon them from the last influenza pandemic in 1889-90 and from intervening influenza prevalence. Several points can be put up against this argument. First, as mentioned earlier, influenza retains its power to arise in epidemic form due to the ability of the virus to mutate. Thus "the degree and extent of...acquired immunity is slight, transient, variable and incomplete." Second, with the last epidemic occurring some 28 years previously, it would be logical to expect those aged 30 and above (and not those under it) to exhibit immunity. However, those aged 30 to 40 were particularly hard hit, while those in the 5 to 15 age range escaped lightly.

A further set of explanations revolve around the fact that the pandemic occurred at the end of a world war. For example, the grouping together of young and middle-aged adults in the armed forces or the munitions factories may have allowed the disease an unprecedented opportunity to fasten upon these age groups. Linked to this argument is the idea that adolescents and adults were suffering from the debilitating influences of war (from strain and exposure). While conditions of this nature could be expected to increase both transmission rates (as the disease is spread by

air-borne droplets) and susceptibility to the disease, the fact that the pandemic overran populations far removed from the war, with the same effects, means that this can only be a partial explanation.

A more purely biological hypothesis is proposed by Burnet and Clark and summarized by Crosby.¹ Burnet and Clark argue that the mutated 1918-19 virus was particularly virulent, and in the absence of any resistance in the general population, it was able to permeate rapidly through the entire respiratory tract of people of all ages. The particular age incidence of mortality is, then, a function of the way the body's defense mechanisms change with age. They argue that, in a person of any age, the response to infection is inflammation of the infected area, by which means a quantity of blood, fluid, antibodies, and white blood cells infuses the affected tissue. In a child, the inflammation process is geared to respond to widespread infections (the diseases of childhood). By adolescence, this stage is past, and the body generally suffers localized injuries, such as wounds and broken bones. For this reason, the young adult is able to produce intense localized inflammation to deal with localized injury. Thus, with the sudden large-scale invasion of the mutated influenza virus, "the intense local inflammation becomes intense general inflammation. The inflammation...is so massive that a springtide of fluids overwhelms the lungs." The young adults' bodies "reacted so vigorously to the threat of influenza that the reaction drowned them." With the aging of the body, the ability to summon up such massive reaction fades, and thus the mortality level declines, until the physical degeneration of old age once again enhances the risk of death.

As well as being strongly selective by age, the pandemic also displayed a tendency to attack women more severely than men. The particular virulence of the disease for women of reproductive age was noted at the time in

India. The explanation offered being that "in addition to the ordinary tasks of the house, on them fell the duty of nursing the others even when they themselves were ill."

EFFECTS OF CLASS

For low-caste Hindus, influenza mortality was higher than mortality from all causes for any other subgroup. This raises the question of whether the observed differences were due to different rates of transmission of the disease among different races/castes or whether the differential is rooted in varying levels of mortality, once infected.

Mills reports that answers to this question are suggested from other sources. For example, data for the army in India has shown that British troops had an influenza incidence rate almost twice the rate of Indian troops. The Indian death rate was 15.23 per 1000 compared with 8.81 per 1000 for British troops. Furthermore, among the general population, the Sanitary Commissioner for Bombay stated that "the divergence in the mortality of nursed and unnursed cases is very apparent...I have been told unofficially that it is about eightfold." This suggests that the level of access to medical treatment among different classes was likely to differ.

Another reason may lie in the infection itself. The 1918-19 influenza virus paved the way for bacterial invasions leading to pneumonic complications. Furthermore, a link has been found between pneumonia and malnutrition. It is to be expected that those at the lower end of the social spectrum would be more prone to malnutrition and thus to pneumonic complications. This is supported by the fact that in 1918, the South-West monsoon failed in several parts of India, causing crops to fail. The areas hardest hit by this crop failure were those that suffered the most severe influenza mortality. It appears that the greatest mortality was experienced by those classes that normally had the weakest grip on life, with malnutrition acting as an intervening variable in the contraction of usually fatal complicating disease.

In addition to the failure of crops affecting the influenza mortality through the mechanism of malnutrition, the influenza pandemic in its turn affected agricultural production in the most severely stricken regions. In Bombay Presidency, the severe second wave came at the time of the harvest of early crops and the sowing of the late crops. With morbidity estimated to be in excess of 50 percent of the general population and with the concentration of severe attacks in the most productive age range (20 to 40), the effect on agricultural production was extreme. The effects of rain failure and a work force incapacitated by illness combined to result in a 19 percent decrease in the area under food crops in 1918 compared with 1917 and a 15 percent decrease in the area under nonfood crops. Staple food prices rose by 100 percent as a result of this reduction of area, coupled with failure of growth and the scanty yield. Famine or scarcity was declared over the greater part of the Presidency.

The Bombay Health Officer's Report for the third quarter of 1918 states that "there has

been a large influx, especially of poorer people, into the city...from districts affected with scarcity and cleanness of food." Another report mentions "thousands of refugees from famine stricken areas in a weakened and destitute condition." Such reports of distress migration into Bombay City attest to the condition of the poor in the rural areas of Bombay Presidency and strengthen the argument that this was a factor, not only in the interclass mortality differentials, but also possibly in the geographic distribution of mortality.

Mills concludes: "Thus, it would appear that the famine and the pandemic, in the Indian context, formed a set of mutually exacerbating catastrophes. While the synergistic effects of malnutrition and infection are well recorded at the individual level, this suggests that such relationships, though brought about by somewhat different mechanisms, also occur at the societal level [and may explain] India's position as the country with the highest recorded mortality during the pandemic."

Note

1. Crosby, Alfred W., *America's Forgotten Pandemic: The Influenza of 1918* (New York: Cambridge University Press, 1989).

Resource 10. Using the Case in Postsecondary Education

By Louise A. Paquin

I have long used materials about disease and its impact on our society in my own teaching at the college level and beyond. When I have occasionally taught a course in bioethics as an interdisciplinary enterprise, I have regularly used case materials.

When I was invited to attend a 1994 conference of the College Board, which eventually led to this account, I was immediately caught up in the possibility of using case studies not only for the teaching of disease, but also in other courses. I was most pleased to have been included in a variety of ongoing meetings during the development of *The Spanish Flu and Its Legacy*. This was a rewarding, stimulating, and challenging opportunity. However, since I am a college professor, I wanted to find ways to use these materials with my college students and, eventually, with adult students in a master's program in the liberal arts.

I am a geneticist and teach at Western Maryland College, a small private liberal arts college in north central Maryland. While my primary responsibilities are as department chair and teacher of genetics to biology and biochemistry majors at various academic levels, I also share in the teaching of nonscience majors, each of whom is expected to take at least two science courses. I have also been the coordinator of, and still teach in, the Master of Liberal Arts (MLA) program in which adult learners with very varied backgrounds are each expected to take at least two of the offerings demarcated as *contemporary issues* courses. These are frequently related to the sciences but no special science background can be expected from students. It is for these two audiences that I have especially used the materials on the Spanish flu, polio, the black death, and the 1976 cases of swine flu and Legionnaire's Disease with which the College Board initiative has worked. I have found that, while the materials were originally intended for a high school setting, they are very readily adapted to

almost any audience, with only a small amount of creativity required from the instructor. Furthermore, I have adapted the approach to using case studies with my genetics students as well.

Like the rest of us, college students love stories. Perhaps none of us ever outgrows a particular fondness for a good story, whether that fondness is translated into a love of reading, the theater, or stand-up comics. But, since most of us as professors have limitations of expertise, we tend to tell stories from our own experience unless we have a preformulated story at our disposal.

I always tell students in my genetics classes true stories (albeit with confidentiality restrictions) from my own previous clinical practice. They relate to the individuals or families involved, their imaginations are fired, and they are motivated to learn more — no surprise. Students in a liberal arts context also love the interplay of forces in a story: the effects of history, politics, the arts, economics, on a particular piece of science. I use the interplay of art and genetics, of economics and cancer, and of literature and the concept of evolution. Many of my nonscience students have major interests or are simultaneously taking courses in these areas, and the juxtapositions enable them to interact with the science material in unexpected ways. I shamelessly use their current interests and what they know from other disciplines in order to involve them in the understanding of scientific thought and process.

I have used sections of *The Spanish Flu* as they became available (in different draft forms and for varying amounts of time in the courses). In each instance, they have represented what might be referred to as a unit

(although they are not so designated in my syllabi). During a recent semester I used drafts of Cases 1 and 2 in two courses: one course was a special freshman seminar of 15 students and the other an MLA program with 9 adults. In each situation, the class was small enough to avoid subdividing the students into small groups for work or discussion. (I would have used small groups for a larger class.)

In each of these two courses on the social impact of disease, the semester was divided into four segments: infectious disease, genetic disease, cancer, and a minor segment on some things we treat, perhaps inappropriately, as if they are disease (for example, pregnancy, old age, sexual preference). Since it was the first segment and acted as a model for the other segments, I gave infectious disease the greatest amount of time. In each of these areas, scientific findings have changed human conduct. At the same time, society has had considerable influence on the course of research. That division, and the use of the cases, were about the only similarities between the freshman and MLA courses. In every other respect, they were very different from one another, as were the students who participated.

In each course, students were first given the narrative to read. The freshmen were given the cases separately. In the following class period(s), students were expected to arrive with questions for discussion and with a list of more areas they would like to explore. The discussions took a number of twists and turns, but some of the more productive areas included discussion of

- Koch's Postulates.
- Differentiation among cause, effect, and correlation.
- Treatment versus cure versus prevention.
- Suggestions on what kinds of experiments might have been performed with the level of knowledge and technology of the time.

Using the information presented, the class also calculated infection and mortality rates.

After the initial discussion, the freshmen were given follow-up questions. These included, for example,

Explain the problems that the 1918 scientific community had that we no longer have today.

Describe the means by which bacteria and viruses were originally distinguished.

How would that be accomplished today if the CDC were to be faced with a new disease?

What is the role of technology then and now?

Why did people die of flu in 1918?

Why was this not recognized as a severe epidemic for quite some time?

Does anyone die of it today? Who? Why?

What is the status of current flu vaccines?

Specifically, what strains of flu will this year's vaccine protect us from?

How and why were these chosen?

Why does knowing the genetics of a particular virus help?

Each of these questions, and others like them, led the students to explore either the 1918 scientific or social context or the ways in which science and medicine today deal with similar issues. They used books and articles on reserve or in their readings packets (used in lieu of a textbook for this course), and they made considerable use of the resources on the Internet. They found several CDC-related sites most useful. After further discussion and lectures on the nature of the virus and on the immune response, students reported to the class on what they had found. I was especially pleased with their willingness to search for additional material on their own. They were, as ever, remarkably resourceful.

Having been guided through this experience on the subject of infectious disease and its history, each student then had to choose a topic for a brief paper (five to six pages) on a related

topic. The paper could be about the human impact or the epidemiology of a particular human infectious disease. It could be on a particular pathogen, vaccine, antibiotic, or treatment. Or it could be on a broader subject (such as the political impact of malaria). Students did indeed choose a wide variety of topics, according to their own interests and backgrounds. For example, one of my students who had been born in an African country chose to write about the impact of infectious disease on life expectancy in that region. Others researched the social impact of tuberculosis and the prospect for an effective vaccine for malaria.

The class of adults used the materials somewhat differently. Their auxiliary reading lists were far more extensive. We had previously examined the social, demographic, and economic impact of the bubonic plague. So the class had some idea of the extent to which such an exploration could go. In a two-week period, we examined materials on the Spanish flu and also on the polio epidemics of the 1940s and 1950s. We spent a good deal of time on the similarities and differences between epidemics. The readings for these students included the following:

1. Colwell, R. "Global climate and infectious disease: The cholera paradigm." *Science* 1996; 274: 2025-31.
2. Dove, A. and Racaniello, V. "The polio eradication effort: Should vaccine eradication be next?" *Science* 1997; 277:779-80.
3. Doyle, R. and Lee, N. "Microbes, warfare, religion, and human institutions." *Canadian Journal of Microbiology*. 1986; 32:193-200. Engelhard, V. "How cells process antigens." *Scientific American*. 1994; 271:54.
4. Gould, T. "A planned miracle." Excerpt from *A Summer Plague: Polio and its Survivors*. New Haven: Yale University Press, 1995.
5. Halstead, L. "Post-polio syndrome." *Scientific American*. 1998; 278:42-47.
6. Risse, G. "Revolt against quarantine: Responses to the 1916 polio epidemic." Oyster Bay, N. Y. *Transactions of the College of Physicians of Philadelphia* 1992; 5(14):23-50.
7. Taubenberger, J.; Reid, A.; Krafft, A.; Bijwaard, K.; Fanning, T. "Initial genetic characterization of the 1918 Spanish influenza virus." *Science* 1997; 275:1793-95.

The adult learners brought to class their own areas of expertise: one was a musician, one a physics teacher, one in allied health, one a literature teacher, another a fund-raiser, and so on. They tended to want to explore the ways in which disease affects or is affected by the disciplines from which they come. So, for example, the musician wrote a paper on the portrayal of infectious disease in *La Boheme* and in *Rent*. In our discussion, the physics teacher brought out some of the comparisons between the impact of medical/biological breakthroughs versus those in his own field. The health professional was able to supply current observations on the impact of disease sequelae on her patients. All of these and many more ideas enriched the discussion and the context for what students were learning about the biology of the subject. This was a group who, like my freshmen, were initially "science phobic." However, when set in the historical context of the case studies, the integration of the basic biology of pathogens and of the immune response made sense to them.

Student reactions were very positive from both groups. All of them appreciated the interdisciplinary approach. All of them were more tuned in to the science content because they saw it as relevant. The freshman students liked the fact that they could read about "real people." The adults felt they had been given "permission" to explore not only the scientific literature but a variety of other sources. Their papers and their test scores demonstrated that the use of the materials had not in any way lessened the amount of biology they had learned —

quite the contrary. The case studies had served as a stepping stone. Since then, I have also heard from some members of the class (who are themselves teachers) that they had tried similar methods in their high school classes.

I also learned from these experiences to make yet another use of case studies. In my genetics course for biology majors, I had for many years had students write their first brief paper on a human genetic condition. Each year, students are provided with a particular list of assorted single-gene conditions from which to choose, most of which they have never heard of before. They had until last year written a brief review on the topic. I decided after my initial work with case studies in science to change this requirement and, instead, have the students prepare case studies on the conditions they chose. I had them work initially in pairs. However, each student had to prepare a narrative from a different perspective: sometimes one a geneticist and one a parent, or one a primary care physician and one a specialist, and so forth. They provided data and, incidentally, a brief review of the literature along with their narratives.

The result has been extraordinary. Students learn far more about the condition, how to test for it, how to diagnose and treat it, and how much is or is not known about its causes. I

believe that this comes from their taking the subject far more personally. They actually begin to care about the individuals, usually purely fictitious, about whom they write. They also write better. I don't have to convince them that the passive voice doesn't sound more "scientific," and so their use of language about science tends to be less stilted. At another level, the case study approach allows students to make connections between what they have learned as theory and what they might one day encounter either personally or clinically. In his essay "Professing the Liberal Arts," Lee Shulman says: "Connections between theoretical principles and case narratives are established when we not only ask, *what's the case?* but more critically, *what is this a case of?*"¹

Using case studies began for me as an experiment, but I will continue (with some permutation of the requirement) because it has been so successful. In summary, a case study approach in general, and the materials on the Spanish flu in particular, have been of great benefit to my teaching and to my students. I realize that the instances I have described are only the beginning of the ways in which the material might be used, and I expect that any creative professor can find many more designs for their use.

Note

1. Shulman, Lee S. "Professing the Liberal Arts." In R. Orrill, ed., *Education and Democracy: Re-imagining Liberal Learning in America* (New York: College Entrance Examination Board, 1997), 160.

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