INTRODUCTION

Wagers and Unexpected Outcomes

It all started with a bet.[1]

On 5 January 1976, the U.S. Army base at Fort Dix, in south-central New Jersey, rapidly filled with a mixture of new recruits, advanced recruits, and military and civilian personnel and dependents. The camp barracks and quarters—which had been nearly deserted over the Christmas and New Year's break—quickly crowded with about 19,000 people. Quarters were tight, and none more so than those for the approximately 6,000 basic trainees. These new recruits were grouped into units of fifty and assigned to eight-person rooms. In addition to sharing a common mess hall and repeated training processes, the men were restricted to their barracks for the first two weeks and to the camp for the following two weeks. The combination of close proximity, physical exertion, sleep deprivation, and high stress prompted the rapid circulation of infectious disease, a phenomenon military leaders have long observed.[2] To help forestall such infections, the U.S. military routinely inoculates new recruits against a host of diseases, including influenza, during their initial three-day stay at the reception center. Despite these precautions, the post's medical officer, Colonel Joseph Bartley, anticipated a surge of illness reports, especially of respiratory problems, which readily spread among those housed in close quarters. Col. Bartley was particularly vigilant for adenovirus, which causes mild flulike symptoms. The infection had been reported at a base in Missouri prior to the Christmas break and, more recently, at Fort Meade, just down the highway in Maryland.

In the weeks following the repopulation of the camp, recruits began to complain of fevers and coughs, and a surprising number were put to bed in the camp hospital. In casual conversation with Martin Goldfield, chief epidemiologist for the state of New Jersey, Colonel Bartley reported the suspected outbreak of an adenovirus infection at the camp and warned Dr. Goldfield to watch out for it in the civilian population. Dr. Goldfield listened to the description of the symptoms and suspected that the sudden rise of cases, rapid onset, high fevers, and large number of hospitalized recruits signaled influenza rather than an adenovirus infection. In the course of their friendly banter, Dr. Goldfield wagered Col. Bartley that the illness was influenza. To settle the bet, Col. Bartley sent nineteen samples from sick recruits to the Division of Laboratories and Epidemilogy, New Jersey Department of Health for identification on 29 and 30 January. Eleven samples tested positive for influenza, winning Goldfield the wager. Of these eleven, seven readily reacted to antigens for the prevailing strain of influenza, A/Victoria.[3] The other four positives appeared to be influenza, but of a type that the state laboratory could not identify. Standard procedure called for unidentified viral material to be sent to the Atlanta office of the Centers for Disease Control (CDC) for typing. Goldfield dutifully arranged to have the specimens sent to Atlanta by airplane on 6 February.

Meanwhile, Fort Dix continued to undergo what was now identified as a mini–influenza epidemic. Even so, despite the increased numbers hospitalized on the base, the epidemic had proved to be of minor consequence. All the soldiers had recovered and reported back to duty. However, this status was about to change.

Private David Lewis, a nineteen-year-old recruit from Ashley Falls, Massachusetts, had been fighting what he believed was a bad cold for about a week before he visited the camp dispensary on 3 February. He was given cold medicine and ordered to his bunk for the next forty-eight hours. The next morning—either feeling better or fearful of having to repeat basic training if he missed too much time—Lewis formed up with his unit for a five-mile march to the shooting range. After training all day, the unit reformed for the march back to camp. On the return march Lewis fell farther behind and collapsed, gasping for air. Sergeant Good, who was walking "drag" on the march, came to his aid. Lewis stopped breathing, and Sgt. Good administered mouth-to-mouth resuscitation while the senior drill sergeant rushed Lewis to the base hospital by car. By the time they arrived at the hospital, Lewis was dead. Postmortem testing provided another sample of the unidentified influenza, and this specimen, too, was sped to Atlanta.

The Lewis sample added to the urgency in identifying the unknown influenza strain. Five examples of a new flu strain had been found, one of which killed an apparently healthy nineteen-year-old man. The CDC's testing on 11 February revealed the virus from Fort Dix to be type H1swN1. Retesting confirmed it; the influenza strains were a type of swine flu, the same type believed to be the cause of the infamous Spanish flu, which had killed millions in 1918 and 1919.

The investigation of events at Fort Dix seemed to confirm health officials' worst fears of a pandemic. Goldfield's bet had set in motion what would become a massive immunization program designed to protect every "man, woman, and child in the United States" from a pandemic of swine flu (in 1976 the only protective option against contracting influenza was vaccination).[4] The National Influenza Immunization Program (NIIP)—commonly dubbed the "Swine Flu Program"—sought to produce, purchase, and distribute a protective vaccine for the entire population of the United States (over 200 million doses) before the onset of the next flu season the following September. Despite numerous setbacks, the program successfully injected over 42 million people, more than 31 percent of the population, twice the percentage achieved by any previous influenza program.[5] The program continued until it was stopped in mid-December because of concerns that it might be prompting an obscure neurological disease known as Guillain-Barré syndrome (GBS).

Such an incongruously large response to a comparatively minor influenza epidemic in a military encampment demands explanation. The key to this dramatic response lay not in the events at the camp themselves but in the potential portents of this flurry of infections. The infections at Fort Dix had been seen as a possible opening act to an ensuing influenza pandemic. Public health officials readily acknowledged that the infections might be no more than a curiosity, but the miniepidemic at the camp fit some predictive models indicating a potential for a significantly wider spread. Knowledge of the virus and its transmission pattern suggested that the events at the camp were not likely to remain isolated. Medical researchers were confident in their predictions of a worst-case scenario because of their faith in the science that underlay their assessments. The influenza virus still retained much to confound scientists, but by the early 1970s researchers believed that the tools and techniques of science had cracked the code on the virus and its pandemic spread. And who could doubt their assurance? Influenza researchers in the 1970s were the inheritors of the scientific revolution, and the scientific revolution had provided so many fantastic breakthroughs and solved so many puzzles that no one could suggest their faith was misplaced.

The scientific revolution, as any schoolchild knows, was a dramatic change in understanding how the world works. But this time-worn retelling often overlooks the fact that the revolution, without which our modern technical world simply could not exist, is of surprisingly recent vintage. The value of this new approach was not necessarily self-evident to our ancestors; in fact, it is still not universally accepted today. At the heart of this new science-based model lies the primacy of evidence. In some cases, evidence is produced through carefully controlled experimental manipulations; in others, however, the evidence results from close observations of uncontrolled events to detect changes and determine causal connections. Simply put, many natural phenomena remain too complex to re-create in the laboratory, a problem as true today as it was for our intellectual ancestors. Such systematic observation, whether in poking through cadavers or peering at the heavens at night, has generated data to bolster rational explanations for events. Absent visible data, whether in controlled or uncontrolled settings, it remained difficult to craft a compelling scientific rationale to supplant magical thinking, and competing theories long retained strong acceptance among the learned and unlearned alike.[6] Accepting a rational rather than a mystical explanation for the world required a radical break with the accepted worldview, a true paradigm shift.[7]

Although the term *revolution* generally carries connotations of suddenness, or rapid change, the science-based model for the world developed in fits and starts over centuries. Societies and even individuals held competing interpretations for the world they inhabited.[8] Part of the reason for this comparatively slow transformation from a magical to a science-based orientation (beyond sheer inertia) was the difficulty of uncovering clear evidence to support the new interpretation, and the messy world of biology presented some of the greatest difficulties in demonstrating rational explanations, with scientific accounts of health and illness perhaps being the most difficult to produce.

The question of disease causation was a vexing problem for would-be medical researchers for many years. The failure of observation to explain disease onset—especially rapid and generalized disease onset—hindered the development of effective disease-specific responses until nearly the end of the nineteenth century. Compounding these explanatory difficulties was the fact that a system reliant on the observation of illness—symptomology, in effect—created catch-all categories, such as "fevers" or the "bloody flux," that masked the origin of various sicknesses. Even distinctive diseases such as smallpox were occasionally misdiagnosed as measles or some other dire skin-erupting infection.

This is not to say that close observation did not lend itself to the discovery of some useful strategies for mitigating diseases in the days before the scientific revolution. The feared Black Death prompted quarantine practices whose later use successfully interrupted epidemic spread in some cases. And as was discovered in China (and likely independently in India) as early as the tenth century C.E., variolation offered protection from epidemics of smallpox.[9] But while the proponents of these responses recognized the contagious nature of these infections, they could not fully delineate why their tactics worked in some cases but not in others. Quarantine boosters could not explain why holding suspect ships in the harbor did not prevent cholera from afflicting their cities in the nineteenth century. And if the sanitarians were correct in suggesting that cleaning up the accumulated filth of a town was a healthy idea, it was not because doing so prevented the development of the deadly invisible miasmas for which they were perpetually alert. A truly satisfying determination of disease onset would be able to explain any patterns a disease exhibits and identify its cause.

It is the ability to identify the origins of diseases that made Pasteur and Koch's "germ theory" of disease revolutionary. The germ theory addresses the questions of illness transfer and onset with a testable model that can produce evidence. This radically new concept—namely, that a specific sickness is caused by a discrete microscopic organism and that distinctive illnesses arise only though contamination with particular entities—offered a compelling explanation for observed events. Variolation worked in part because it transferred the smallpox germ from arm to arm. Quarantine worked for the plague but not for cholera because it prevented the transfer of some unknown substance that caused the former but failed to block whatever element was responsible for the latter. The new theory did not immediately supplant the competing narratives for disease outbreaks, but it did provide an empirically verifiable method for describing illnesses. Interested observers were keen to detect evidence to prove or disprove this new theory of disease onset.

In many ways, the story of the promotion and acceptance of a scientific model for disease causation intertwines with the history of influenza pandemics. The first pandemic in the mode of the twentieth century appeared in 1889, when the germ theory of disease was still a matter of fierce scientific debate, generating much study and argument. The identification of Pfeiffer's bacillus as the causative agent behind the flu and the perception of the disease as the mild "old person's angel of mercy" bred complacency over the disease. This complacency was shattered by the catastrophic Spanish flu. Physicians' inability to counteract the disease represented a signal failure in the scientific approach to health. Compounding this failure was the fact that researchers could not even identify the agent causing the pandemic. Strangely, the unmitigated global public health disaster of Spanish flu did not result in the founding of research institutes dedicated to studying the illness. Instead, research on influenza during the interwar years became the province of individual scientists largely working alone. These researchers not only discovered the agent responsible for influenza but also helped propel scientific understanding of the invisible filter-passing elements we now call viruses. Interest in or knowledge about these scientific breakthroughs regarding influenza remained largely confined to a small circle of researchers.

Considering the role influenza research played in the history of science and the drama of global pandemics, it is surprising that, with one notable exception, the topic has drawn little scholarly attention outside the fields of public health and medicine. Some historical geographers focused on the 1889 Russian flu to construct models of disease transmission, and one of these researchers followed the pattern up through the 1957 Asian and 1968 Hong Kong pandemics.[10] But these pandemic years received little examination outside the historical epidemiology focus or medical researchers' studies of the outbreaks.[11] The 1976 Swine Flu Program, however, generated significant interest in understanding how this "fiasco" could have occurred. The incoming secretary of health, education, and welfare ordered a study of the decision-making chain that led to the massive program. The report by the Harvard colleagues Richard Neustadt and Harvey Fineberg was subsequently published as a book, *The Swine Flu Affair,* and it remains a touchstone for any discussion of the program. Its characterization (or mischaracterization) of the decisions and the individuals involved in the ill-fated vaccination program prompted Arthur Silverstein to rebut Neustadt and Fineberg's evaluation in his book *Pure Politics and Impure Science*.[12] Aside from these examples, the story of influenza pandemics and the science surrounding them has been principally the domain of the medical community, with Spanish flu being the sole exception.

In the 1990s and 2000s, Spanish flu became a topic of intense investigation. In fact, if one were to graph the number of books and articles on Spanish flu that appeared in these decades, the result would mirror the steep epidemic rise of the illness they describe. Such a flourishing of interest stands in stark contrast to the relative lack of attention paid to the pandemic in previous decades, at least in published discussions of the event. The 1920s saw a spate of articles and reviews on the disease, including the monumental survey of medical literature undertaken by Edwin Oakes Jordan. In the ensuing decades, however, a curious silence descended on the subject, with little discussion of the event outside the specialist literature, and even there the disaster received scant attention. In 1976 Alfred Crosby's book *Epidemic and Peace, 1918* appeared. To the publisher's good fortune, the book was placed on shelves just as the debates over the Swine Flu Program were dominating the news.[13] Crosby's book retained some interest in the following years and sparked renewed attention when it was purchased and reissued by the Cambridge University Press under the title *America's Forgotten Pandemic* in 1989. However, it was the dramatic recovery of the virus in 1997 and the appearance of bird flu that galvanized interest in Spanish flu. In short order a number of books and articles appeared recounting aspects of the pandemic, including a popular history; a collection of papers from a scholarly conference; a documentation of the U.S. military's encounter with the virus during the war; and even a biographical account of the attempt to recover the virus from frozen, entombed victims of the pandemic.[14] In the present day, any discussion of influenza epidemics is certain to contain some reference to the Spanish flu pandemic.[15]

Reflecting a similar apathy, research foundations, both public and private, seem early on not to have placed a high priority on studying the virus and the pandemics it periodically sparked. Institutional support came comparatively late to the study of the influenza virus. But the model of focused work on the infectious agent was championed by government investment, as has been the case in many other programs of scientific research. It is a matter of no small coincidence that the first well-financed research effort on the diagnosis, treatment, and prevention of the disease came originally as part of the military effort during World War II. Similar to that on other topics of scientific interest, research on the influenza virus was initially part of a government-science partnership that dominated postwar science, especially in the United States. Such focused research efforts produced a number of technologically driven strategies that could be rapidly deployed to safeguard against influenza and a host of other infectious diseases. The state began to shoulder an increasing role in protecting the public's health, and these treatment and prevention programs and practices were at first so successful that they seemed to herald a new age.

As befits federal efforts, the public health plans were national in scope. Protection against infectious diseases, including influenza, was to be obtained by quickly delivering a protective vaccine to those at risk. Emblematic of a heady, optimistic time in public health, massive inoculation campaigns were undertaken to intervene in emerging influenza pandemics in 1957 and 1968. Such large-scale state-directed efforts culminated in the Swine Flu Program of 1976, one of the most dramatic national vaccination campaigns ever undertaken. This universal interventionist approach fell out of favor as the sole option against infectious disease in subsequent years, and attention to influenza infections dissipated as new and newly reemerging afflictions commanded scientific and medical research and dollars. After being crowded out by attention to dramatic new and resurgent afflictions, however, pandemic influenza reappeared as a focus for concern in the twenty-first century, now recast as an emerging disease. Emerging influenza pandemics and research into the virus illustrates the scientific and medical conceptualization of disease that remains the dominant paradigm.

Conceptualizing illnesses as new or reappearing threats that endanger not only individuals but the state itself was an idea that rapidly gained favor in health and policy-making circles. Vigorously promoted by Stephen Morse and Joshua Lederberg at a National Institutes of Health conference in 1989, the model of seeing infectious diseases as both a health and a security problem quickly found traction among a variety of science and policy committees.[16] Studied from this vantage point, the 1976 Swine Flu Program was in fact a preview of this later model.

The 1976 Swine Flu Program can also be read as the climax of a century's worth of investigation into infectious diseases; in addition, the program crystallized a number of public health and scientific issues that had not been contemplated previously. The massive response initiated by the U.S. Public Health Service (USPHS) resulted from a number of trends that came together at this critical moment in history. The first trend was a dramatic series of breakthroughs in scientific knowledge about the virus and its behavior. This knowledge, which centered on the intricacies of the virus's genetic code, exemplified the staggering increase in knowledge produced by the scientific revolutions of the twentieth century—revolutions fueled by dramatically expanded government investment in scientific research. Powerful new tools, technologies, and approaches were unlocking a multitude of mysteries across the scientific disciplines. Armed with new information and technical approaches, medical researchers applied their scientific know-how to controlling and eradicating the numberless bacteria, viruses, parasites, and rickettsias that afflict humankind.

In a second trend, a string of successes throughout the twentieth century gave health officials a powerful and abiding faith that science held the key to the imminent extinction of infectious diseases. Many health officials believed that the most important questions surrounding epidemic diseases would be ones of logistics: specifically, how to get the life-saving magic cures into the hands of all. Public health officials sought to create large-scale programs not just to protect against but to permanently eradicate a number of infectious diseases. By 1976 smallpox was well on its way to global elimination, and other massive vaccination programs were under way or on the drawing board.

The events at Fort Dix in 1976 also occurred at a time of long-term change in the field of global public health. As medical science began to demonstrate the extent to which infectious diseases had affected populations in the nineteenth century, nation-states began to recognize the true costs of epidemic disease. National governments realized that the ad-hoc local and regional authorities that sprang up in response to periodic epidemics of yellow fever and other diseases were ineffectual in protecting the public. Governmental officials also disliked quarantine, often suggested as the proper response to pandemics, because it disrupts trade. Accordingly, some state governments began to create more permanent public health organizations, and although not particularly powerful initially, these boards began to strengthen by the end of the nineteenth century.

National governments also began to recognize that threats at home might be better combated by keeping diseases far offshore and that the safety of their populations might be best maintained by cooperating with other states for mutual protection. To some degree this cooperative approach was evident in quarantine responses to plague infections. But such combined approaches were minimal and often evaded by any party that found itself aggrieved in the process. In the nineteenth century, only the arrival of the dreaded cholera truly galvanized interstate coordination. Cooperative action in preventing the interstate spread of the disease was initially hindered by disagreements over the mode of transmission and by stout resistance—especially by the British—to regionwide quarantine efforts in places presumed to be undergoing cholera outbreaks. But the gradual acceptance of the germ theory of disease led to effective international anticholera programs by the century's end. In 1907 a number of powerful (and mainly European) states sponsored an international organization to manage the barricade effort of public health. The Office International d'Hygiène Publique (OIHP) was charged with overseeing quarantine programs designed to keep diseases common to the colonial world—cholera, yellow fever, and plague—from infecting the founders' home states.

Although theoretically an international organization, the OIHP sought resolutely national goals: to keep the sicknesses of "others" away from the home populations. This philosophy also undergirded the creation of a regional organization in the Americas; founded in 1902, the Pan American Sanitary Bureau was implicitly mandated with keeping diseases out of the United States. Such organizations may have been on the pathway to international public health, but they remained staunchly national in focus. This nation-centered emphasis continued up through World War I.

In the wake of the Great War, an internationalist spirit infiltrated the field of global public health. The newly formed League of Nations established its own body, the League of Nations Health Organization (LNHO), whose mandate was to facilitate improved public health for all league members. This internationalist goal contrasted with the nation-centered philosophy of the

OIHP. The powerful European states that benefited from the workings of the OIHP jealously guarded this organization's assets and resisted its incorporation into the LNHO. Starved for resources, the LNHO coexisted uneasily with the OIHP and was forced to rein in its more ambitious global health plans. The LNHO was able to establish a reputation for technical proficiency—especially in the arenas of epidemiology and vaccine standardization—but its fortunes were tied to the League of Nations itself, which succumbed to the bitter nationalist passions that spurred World War II. The dislocations resulting from that war temporarily thwarted the development of a number of international organizations. But, as Akira Iriye points out, not even the caustic nationalist sentiments of the two world wars could reverse the trend toward an increase in the number of intergovernmental and international nongovernmental organizations. An intricate network of state, quasi-state, and private international organizations continued to develop.[17]

As the planet recovered from the trauma of World War II, a reinvigorated spirit of internationalism bloomed anew. Just as the LNHO had been a manifestation of global health concerns for the League of Nations, so too was the World Health Organization (WHO) an outgrowth of the United Nations. Like the LNHO, the WHO was unable to completely separate itself from nation-centered health organizations. But unlike the LNHO, it was able to carve out sufficient revenue streams to pursue broader international health goals and to fold national or regional health systems into a global health system.[18] The method of achieving international health goals by relying on national health resources resulted in some tensions, but generally issues of global health harmonized with those of national health, for, as national public health officials realized, quarantine or barricade efforts were impractical in an era of rapid and widespread global commerce and travel. Also like the LNHO, the WHO adopted technical solutions to health issues, a hallmark of its predecessor's approach. Such technical methods suited the interests of the WHO's primary backer, the United States, which provided the largest share of financing and was also the major source of the organization's leaders and experts via the Centers for Disease Control. In the early decades of its existence, the CDC strongly favored technical approaches to safeguarding health.

The CDC evolved from coordinated programs created during World War II to protect troops against malaria, a deadly and debilitating infection. In the postwar period, the organization continued its mosquito eradication programs around the nation to break the chain of malarial infection. Having stamped out malaria in the continental United States, however, the CDC was left without a clear mandate. Under its two eminent leaders—Joseph Mountin and Alexander Langmuir—the organization reinvented itself as the nation's epidemiology and public health laboratory par excellence. Under the leadership of David Sencer, its director during the 1960s, the CDC had steadily increased its global reach, its staff members working sometimes as experts invited by other states but more often within WHO programs. The CDC provided the leadership and expertise in the smallpox eradication effort; it also reorganized malaria control after the failed global malaria eradication effort of the 1950s and 1960s.[19] The CDC's technical solutions to health objectives meshed well with, and in some respects dominated, many WHO programs.

In the 1970s and continuing through the 1980s, the WHO roiled with debate as more and more member states pushed for broader public health programs rather than technically based, disease-specific approaches. Such debates over the WHO's proper emphasis in improving health led to fractious coalitions and bitter funding clashes. Further complicating matters in the late twentieth and early twenty-first centuries was the appearance of richly funded private organizations, such as the Bill and Melinda Gates Foundation, that sought to craft independent programs of global health. In the present day, responses to infectious diseases still highlight the sometimes contradictory goals of national and international health, a legacy of the comparatively recent change in health protection models.[20]

The convergence of these trends in 1976 helps to explain why the United States responded so quickly to a novel influenza strain at Fort Dix. But that does not explain why it was virtually the *only* government to respond with a massive vaccination program. Like all highly transmissible infectious diseases, influenza does not respect borders or nationalities. Since vaccination was the only protective option against influenza in 1976, it is surprising that no other nation joined the United States in immunizing its citizens against this new flu. Only Canada took steps to create any type of crash immunization program. Experts at the WHO evaluated the same evidence as did those at the USPHS but recommended a policy best described as watchful waiting. The U.S. program was labeled a "fiasco" when no swine flu pandemic occurred, and this assessment remains the popular perception of the effort, while the cautious WHO recommendation has been held up as the wiser course of action.[21]

A close examination of the Swine Flu Program illustrates one of the key themes of public health and this book. Events in 1976 laid bare questions that public health policy makers continue to face in the present day. What should be done? What can be done? What should not be done? In 1976, influenza scientists and USPHS officials weighed the likelihood of a pandemic, the capabilities of the nation's surveillance and vaccine manufacturing capacity, and the cost of a pandemic in human and economic terms and then recommended a massive vaccination campaign to protect the nation's citizens. Officials at the

WHO, drawing on the same evidence, addressed the same issues and recommended a "wait-and-see" policy for their member states. Both groups based their decisions on partial and contradictory evidence, and in both cases, the answers to what *could* be done shaped the assessment of what *should* be done.

The USPHS and WHO officials in 1976 were addressing the problem of risk analysis, a component of every health decision. In the case of influenza, weighing the various options is further complicated by the unpredictable behavior of the virus. Misjudging the pandemic potential of the particular strain had tremendous potential costs to be measured both in the sickness or deaths of millions of people and in billions of dollars in health expenses and lost income. Mounting a large but unnecessary vaccination campaign can waste millions of dollars in itself, but further potential costs lie in adverse reactions to the vaccine and disruptions both to everyday life and to other public health programs. An additional complication in predicting the possible course of any novel influenza strain is the fact that a decision must be made quickly because of the highly transmissible nature of the virus and the laborious vaccine-manufacturing process. Judging the likelihood of adverse reactions to be low, U.S. public health officials in 1976 believed that the worst outcome would be the expenditure of public funds to prevent a pandemic when no such threat ever truly existed. The officials at the USPHS opted to risk the dangers of an unneeded vaccination campaign, which they viewed as gambling with dollars, not lives. Officials at the WHO, however, had wagered that the virus would not develop into a pandemic, at least not in the near future. When the fall came and there was no pandemic, the U.S. program was condemned, and the WHO decision lauded. Nonetheless, such a simple summation of the actions pursued in 1976 fails to acknowledge the complex elements that formed the calculated decisions. The Swine Flu Program was labeled a fiasco not because of mismanagement or a failure to develop the program but simply because the pandemic never developed.

The USPHS's and the WHO's conflicting policies regarding the new influenza strain illustrate the core weaknesses of national health programs that attempt to serve both national and international health goals. Events in 1976 also illustrate the WHO's uneven mixture of international and national capacities. The surveillance program for detecting novel influenza viruses was a truly global entity, with national organizations providing data for an international constituency. Founded in the days after World War II, the system had steadily increased its reach and sophistication as more national programs entered into sentinel roles. The surveillance system was an exemplar of the technical approach to health. National health laboratories around the world collected samples, but the process of typing the strains was done at a small number of labs (two in 1976, since expanded to four) that possessed the technology to differentiate between the viral types. However international the surveillance system might have been, though, the response to novel influenza strains remained a resolutely national program. The WHO had no resources for producing or distributing vaccine. Any vaccination campaign would be a purely national affair and thus limited to those states with the resources to mount crash immunization efforts. Such limited national responses to universal pandemic threats clashed with "health for all" mandates that were attracting the interests and attention of a number of delegations to the WHO. What good was a global health net if it benefited only a handful of states?

The Swine Flu Program remained a cautionary tale for public health officials throughout the later twentieth century and dampened the enthusiasm for interventionist pandemic flu response for nearly two decades. That changed when a series of headline-grabbing events prompted a reassessment of influenza pandemic preparedness. In the spring of 1997, Jeffrey Taubenberger announced that his laboratory had successfully recovered and sequenced a portion of the genetic code of the infamous Spanish flu.[22] Hot on the heels of Taubenberger's announcement, health officials uncovered cases of human infection with an avian influenza strain (H5N1). Eighteen people were infected by contact with live poultry, and six died. In dramatic fashion, local health officials ordered the slaughter of all poultry in Hong Kong and banned the importation of chickens from surrounding areas. The Hong Kong wet markets were supplied with live poultry both produced in farms within Hong Kong territory (subsequently to be termed the Special Administrative Region when sovereignty was transferred to the Chinese by the British) and imported from Guangdong and other provinces in the People's Republic of China. In fact, roughly 80 percent of the birds supplied to the market came from mainland Chinese farms. After bird importation had been halted, the birds on hand destroyed, and the markets closed for several weeks for cleaning and disinfecting, Hong Kong government officials—working cross-border with PRC officials—developed an import and farm inspection plan to detect a reoccurrence of the deadly virus. The procedure appeared to break the chain of infection from birds to humans.[23]

The combination of these two events—new research into Spanish flu and the pandemic threat posed by avian flu in 1997—galvanized both national and international public health officials to reexamine their plans for countering influenza pandemics. Shortcomings in the two major components of pandemic responsiveness, surveillance and manufacturing, provided additional spurs to this reexamination early in the twenty-first century. On 11 February 2003 China reported to the WHO that it was experiencing an outbreak of "atypical pneumonia." This illness, subsequently dubbed severe acute respiratory syndrome (SARS), had been occurring for over two months before the Chinese reported it.[24] The SARS virus spread globally before it was controlled, ultimately infecting over 8,000 people and killing at least 774.[25] The outbreak and reaction cost billions of dollars and illustrated the weakness in global disease surveillance. If a nation could not or, as in the case of China, would not report an epidemic, the infection might spread widely before it could be stopped.

The second major component of pandemic planning is manufacturing protective vaccines. In 2004 the limitations of influenza vaccine production were starkly illustrated. That year vaccine regulators in the United Kingdom condemned the entire production lot of influenza vaccine from Chiron, one of two influenza vaccine producers for the U.S. market. The loss of almost half the vaccine supply for the United States prompted a shortage and desperate attempts to make up the shortfall.[26] Only limited amounts of vaccine were available to the United States, because the remaining global producers of influenza vaccine had already been operating at basically full capacity; they could produce no more.

Also in 2004, Vietnamese officials reported observing an avian influenza similar to the strain that had appeared in Hong Kong in 1997. This highly pathogenic virus circulated through domestic poultry flocks throughout Southeast Asia. Most alarming, the virus had periodically infected humans, with a high percentage of mortality. At last count, 565 people have been positively identified as being infected with avian influenza, and 331 of those infected have died.[27] Adding to the concern about the spread of avian influenza was the fact that the virus had been detected in migratory waterfowl whose migration routes link all the continents to one another. Combined with the international poultry trade, this meant that the avian influenza virus would have ample opportunity to spread globally.[28]

In the light of these events, national and international health organizations quickly moved to assess response plans for an influenza pandemic. The results were not encouraging. Few nations had any concrete plans to respond to an influenza emergency. Recognizing the "general lack of preparedness," the World Health Assembly called on nations to create national response plans, and the WHO pledged to strengthen global surveillance.[29] The WHO realized that reliance on purely national programs had failed in the past and would not be of interest to nations that could not participate in such vaccination efforts. A new approach was needed to complement national vaccination programs. In response to these new demands, the WHO created its "Global Influenza Preparedness Plan" in March 2005 to coordinate national and global response to an emerging influenza pandemic. This vital document provides a blueprint both for responses to influenza pandemics and for the future of global public health.

In 2005 the WHO also issued its revised International Health Regulations (IHR), a plan that radically transformed the reporting duties of states facing epidemic threats. As Lorna Weir and Eric Mykhalovskiy point out in their study *Global Public Health Vigilance,* the new regulations discard the mandatory disease-specific reporting mechanism—limited to cholera, plague, smallpox, and yellow fever in a 1969 revision—for a broader requirement to report "public health events" that could provoke an "international public health emergency." Previous IHR plans going back to the founding of the WHO gave sovereign states the responsibility for reporting their incidences of these "notifiable" diseases. As Weir and Mykhalovskiy demonstrated, the short list of reportable diseases combined with a state's desire to hide these inconvenient outbreaks—cholera being the most common example—meant that the WHO was notified of outbreaks only rarely, and even then, the reports were not filed in a timely fashion. These factors combined to give the WHO only a limited role in epidemic disease prevention. Drawing on the work of the international law expert David Fidler, Weir and Mykhalovskiy argue that the new regulations have broadened the effectiveness of the WHO reporting mechanism and, combined with powerful new surveillance systems (they favor the Internet-based Global Public Health Intelligence Network), have created a "global emergency vigilance system" and a "world on alert." This new reporting system holds out the promise of a more active and effective role for the WHO in epidemic prevention.[30]

While there is much to recommend in Weir and Mykhalovskiy's examination, their focus on a formal top-down approach fails to capture the workings of the WHO below the level of officially reported disease outbreaks. For example, from the organization's founding in 1948 up through the IHR revisions of 2005, influenza was not classified as a reportable disease. Despite this gap in the prevailing IHR guidelines, however, the WHO influenza surveillance system was an active international health organization and, as I will show, much more than just a clearing house for information. Moreover, the officials monitoring influenza constituted just one of a number of expert groups dedicated to crafting WHO policies for threats to global public health that did not fall under the mandated reporting requirements. Under Weir and Mykhalovskiy's approach, even the massive WHO-coordinated malaria eradication program of the 1950s and 1960s would not appear as a WHO-sponsored assault on epidemic outbreaks, for malaria was not a reportable disease. The WHO's international health programs involve more than just the official interstate relations created by its constitution. The WHO operates at a variety of levels in detecting and protecting against epidemic diseases. An examination only of the officially notifiable diseases misses much of the organization's work in communicable disease protection. That said, revamping the IHR to broaden the WHO's role as an epidemiological clearinghouse for global health issues was long overdue.

The reassessment of public health preparations for pandemic influenza and the revision of the IHR immediately proved their value when an emerging pandemic strain of influenza did appear, even though it was not the one to which the global influenza plans had been geared. In the spring of 2009, the WHO's pandemic plan got its first real-world challenge. While participating in a test of enhanced influenza surveillance, USPHS officials in San Diego detected a new influenza strain infecting two children with no apparent connection to each other. On 21 April 2009 the CDC announced that the children were infected with a novel strain of influenza, typed as H1N1 swine flu. By 24 April 2009 the CDC was able to link the novel strain with an influenza-like illness that Mexican health officials had observed in March and early April of that year. Faced with the information that a novel influenza strain was circulating in their country, Mexican health officials quickly installed social distancing measures, closing schools and restaurants and banning public gatherings in the hopes of forestalling a wider spread. It was too late. By 6 May 2009 the swine flu had been identified in twenty-one additional countries aside from the United States and Mexico. The WHO quickly escalated its influenza pandemic alert system to level 6, its highest, which confirmed that the virus was causing "sustained community level outbreaks" in countries in "two or more WHO regions." In short, the virus was a pandemic.[31]

The sudden appearance of H1N1 confounded influenza experts. The virus's surprising genetic makeup, its unusual pattern of summer spread in the Northern Hemisphere, and its explosive infection rate in the Southern Hemisphere prompted a desperate race to produce protective vaccines for the Northern Hemisphere's coming fall flu season. The pandemic turned out to be mild, although at this writing its full impact cannot yet be gauged. In any case, the programmatic responses to this novel epidemic strain taken by national and international health organizations have unquestionably been shaped by responses taken and not taken during more than a century's worth of experience with pandemic influenza, and as it has in the past, the virus behaved in unexpected ways.[32]

Contemporary public health officers and policy makers struggle with the same sets of questions about influenza that have bedeviled their predecessors: Will the new virus prompt a pandemic? How deadly will the pandemic be? How will the pandemic affect things economically? Socially? Politically?

What can be done to mitigate or stop it? The answers to these questions are necessarily tentative, since formulating them requires us to predict an unpredictable virus. In 1918 medical researchers were unable to detect the organism responsible for the pandemic. In 1976 USPHS officials weighed the available evidence, assessed their capabilities, and judged a massive vaccination campaign to be both necessary and possible. In 2011 the public health landscape has again changed. Our ability to detect and describe novel influenza viruses has increased dramatically; conversely, our ability to protect the public through the production of vaccines and antivirals has failed to keep pace with burgeoning populations. Consequently, public health officials have had to develop new strategies to deal with influenza pandemics.

The new approach developed by the WHO builds on successful elements of the organization's influenza surveillance system while recognizing the limits of nation-based vaccination efforts. The key element that thwarted previous vaccination campaigns was the mismatch between a speedily transmissible virus and a laborious and slow manufacturing and distribution process. Simply put, the virus infected populations before a vaccine could be developed, manufactured, and delivered in any quantity. The increasing volume and speed of travel and trade are likely to further widen the gap between pandemic and protection for the foreseeable future. In response, the new approach seeks to reverse the process of surveillance by giving sentinel sites powerful new tools for rapidly identifying new strains. And once a strain is identified, the new plan—enshrined in the WHO's Pandemic Preparedness Plan (the new name for the Global Influenza Preparedness Plan) and facilitated by a new version of the International Health Regulations—calls for the delivery of influenza experts to the site of the new viral strain.

The new WHO influenza pandemic plan represents a reversal in the traditional surveillance structure because instead of waiting for the satellite laboratories to send samples from the outbreak to the experts, the experts are to rush to the site of the outbreak and immediately begin a program of pandemic disruption. The WHO influenza experts would be armed with either "barricade" vaccines—a small stockpile of general, family-wide vaccines that offer at least partial immunity—or rapidly produced doses of experimental vaccines against the specific new virus. These vaccines would be combined with widespread antiviral treatments given with the intent of choking off the new strain before it efficiently adapts to its new human host.[33] Such a program relies on effective surveillance for quick detection of a new virus and international cooperation of influenza experts and resources. The new model creates a hybrid approach to public health that may finally move the WHO closer to its idealistic health mandate. It harnesses technical sophistication to identify a potential pandemic but relies on a combined global approach rather than a nation-centered solution. As the 2009 H1N1 swine flu pandemic demonstrated, this new approach is hardly foolproof, but it offers the current best hope for protecting against an emerging influenza pandemic.

The story of influenza pandemics is ultimately a story about the natural world, too. The preceding decades of study and observation of the virus have revealed many of its secrets. While no scientist could claim mastery over the subject, medical researchers became increasingly confident of their ability to predict the behavior of the virus, and with prediction came the ability to control its impact. Nevertheless, as the virus demonstrated in 1976 and over the ensuing decades, the infection operates in random, unexpected ways. This is hardly unusual, however, for the natural world still offers much to surprise and confound us. The emergence of new diseases, such as AIDS and SARS, and the reemergence of old infections, including tuberculosis, suggest that the long-running war between humans and the infections that plague us has no foreseeable end. The search for deeper understanding of infectious diseases continues, but perhaps with a greater appreciation of the difficulty of the task.

The struggle between science's ability to understand and predict nature and the natural world's stubborn unpredictability played out across the long twentieth century. This back and forth between science and nature forms a second theme of this study. Emerging influenza pandemics and institutional responses to real or perceived pandemics present a unique window on a number of processes evolving over the course of the twentieth century. The 1889 Russian flu appeared during the ascendancy of the germ theory, and the tracking and tracing of the infection bolstered those who asserted this model of pandemic spread, even though researchers had mischaracterized the agent responsible for the illness. The catastrophic Spanish flu shook the complacent confidence of the medical establishment, eventually leading to the proper identification of the virus responsible for the affliction. Sustained, institutionally supported research has unraveled many mysteries of the virus, leading to the point where extinct strains can be resurrected and every letter of a current strain's genetic code can be scrutinized for hints of future behavior. But even our increased knowledge of the influenza virus has proven unequal to the task of protecting the public from influenza pandemics.

In a related fashion, the narrative of influenza outbreaks from the 1870s onward reveals the increasingly interconnected world we inhabit. Russian flu was truly an international affair exploiting transportation networks to infect residents of every region of the world. Spanish flu roared around the planet in four months, its speed of transmission amplifying its devastating impact. In 1957 and 1968 small localized outbreaks of a new influenza strain were uncovered around the world. Scientists call this process of low-level distribution "seeding," and when conditions are right, a seeded virus can burst into epidemic spread around the globe. In recent times the rapid cycling of 2009's H1N1 swine flu into pandemic status underscored the reality that we are all citizens of one global disease environment.

A final theme of this book is that a close study of influenza pandemics casts light on the evolving role of organizations and their responses to health emergencies. Weak public health organizations had little to offer in 1889, and a lack of accurate knowledge and techniques rendered medical responses to Spanish flu useless at best and dangerous at worst. Mirroring a pattern of research support across many fields of science, military investment in influenza prevention generated some important protective breakthroughs. The wedding of governmental support and academic research that evolved from the war effort built on these advances and continued to contribute to increased scientific knowledge of the virus and its properties. A reincarnated global health agency, now known as the World Health Organization, expanded on the approaches first developed by its predecessor, the League of Nations Health Organization. In some arenas the WHO managed to foster the development of truly global approaches that combined national and international goals, the influenza surveillance system being a notable example. But the organization remained fundamentally reliant on national health organizations and the resources they were willing to extend to achieve global health. Such a reliance on national resources carries with it the seeds of conflict, for priorities and capabilities may differ markedly among states. The national vaccination campaigns of the 1957 and 1968 pandemics illustrate the great mix of capabilities and resources found in various health programs. In the fallout from the 1976 Swine Flu Program and (as will be detailed) the accidental and artificially produced epidemic of 1977, interventionist pandemic planning was placed on the shelf, soon to be eclipsed by new global health emergencies. The overall effect of twentieth-century responses to influenza pandemics was to illustrate the limitations of national responses to international health threats. Successful programmatic responses would need to draw on new models.

Any new approach to international public health must recognize the central conundrum at the heart of previous antipandemic programs. Quickly detecting spreading infections demands a global surveillance net, but the technical capability for responding rapidly to detected threats is limited to a mere handful of states. Accordingly, any effective new program would permit a greater variety of nation-states to participate and benefit from the new system. High-tech approaches favored by technologically advanced states remain key, but low-tech systems have their value, too. The surveillance system adopted to track bird flu embodies this hybrid approach: the sudden die-off of domestic chicken flocks serves as an early indicator that bird flu may be circulating and that enhanced strain surveillance is needed. Such a blending of high- and low-tech tools can serve as a template for new international health tactics that offer greater chances for success and the ability to utilize the capabilities of an increased number of states.

This book's central thesis is that the new influenza pandemic response model represents a template for a truly global public health system. This new model, promoted by an assertive WHO, was crafted by drawing on successes and limitations in earlier epidemic years. As increasing scientific knowledge of the mutability of influenza virus suggested, and the failed national interventionist efforts of 1957, 1968, and 1976 demonstrated, nation-centered vaccination efforts cannot protect citizens from influenza pandemics. For the foreseeable future, only the close international cooperation of health experts and organizations manifested in the WHO Global Influenza Preparedness Plan offers the hope of thwarting an emerging pandemic and protecting the public's health. National health programs will continue to play an important role in protecting citizens' health, but protection against epidemic diseases in this interconnected, global world requires greater investment of time, talent, and money in health programs with a global focus. Such a rapid, collaborative approach offers the only opportunity to derail pandemic threats and so provide safety for all.

In a very real and demonstrable sense, any individual's health is intimately tied into the health of all. Influenza pandemics starkly illustrate this reality. Influenza experts can tell us that the virus has periodically mutated into pandemic strains that caused massive illness, suffering, and death. Based on that history, it is highly probable the virus will do so again. But as events in 2009 remind us, they cannot tell us when; that determination is up to the virus. Only by acknowledging the shared nature of the threat and strengthening rapid international responses can we hope to limit the impact of an influenza pandemic.