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I. Overview of the Swine Influenza Program

On January 27, 1976, an outbreak of respiratory disease was identified at Ft. Dix, New Jersey. On February 12 the CDC influenza laboratory notified the CDC Director that a swine influenza virus strain had been isolated from patients that possessed hemagglutinin and neuraminidase subtypes that had not circulated for more than 50 years. Experience had led scientists to conclude that introduction of a new strain inevitably resulted in a pandemic. An emergency interagency meeting was held on February 14, and state health officials were notified on February 18. On March 10, the Advisory Committee on Immunization Practices (ACIP) reviewed available data and concluded that person-to-person transmission of swine influenza had occurred but there was no way to determine whether or not a pandemic would occur. CDC notified the Department of Health and Human Services and recommended mass immunization. On March 24 President Ford met with CDC, FDA, and NIH representatives and other experts. There was a unanimous recommendation to initiate mass immunization.

On April 2, CDC held meetings with state health officials. Proposals to stockpile vaccine until there was more evidence of virus spread were dismissed primarily on logistical grounds – because of the time needed to plan and implement a mass vaccination campaign and stockpiling vaccine until there was evidence of disease would substantially delay the protection that a vaccine would provide. States began planning their vaccination programs with the recommendation and support of CDC. In addition to planning logistics and providing guidance to states, federal activities included passing an appropriations bill to support vaccine purchase; contracting with manufacturers; conducting clinical trials to determine vaccine dose and schedule in adults and children; and developing consent forms and other materials to support the vaccination program. Following guarantees of federal purchase, manufacturers began production of vaccine to the pandemic strain but fewer doses of vaccine were produced than anticipated because of low per-egg yield of vaccine virus.

Liability protection for manufacturers emerged as an issue in April. The administration requested that Congress pass legislation indemnifying manufacturers against vaccine associated injuries. Without insurance, manufacturers threatened to stop production. Legislation was required but there were concerns in Congress. On August 1, the press reported an outbreak of severe respiratory disease among attendees at an American Legion convention in Philadelphia (later was identified as a bacterial infection, called Legionnaire's Disease). Although the disease did not resemble influenza clinically and it would take four days before swine influenza could be ruled out and Congress moved forward with passage of the swine influenza Tort Claims Act. President Ford signed the Act on August 12.

The first vaccine was shipped to State Health Departments on September 22 and the first injections were given on October 1. Vaccination programs proceeded based on state plans and capacities, with some aggressively implementing mass vaccination and others implementing more limited programs. Overall, between October 1 and December 16, more than 40 million civilians were vaccinated; 85% by public sector providers (this

compares with ~10 million persons vaccinated during the previous influenza season). Several million more were vaccinated in Veterans Administration and Department of Defense programs.

Less than two weeks after vaccination began, three elderly Pittsburgh citizens with pre-existing heart disease died within several days after vaccination. Local health authorities attributed the deaths to the vaccine. Pittsburgh suspended its program on October 12 and nine other states also halted vaccinations. CDC calculated the risk of death among elderly persons expected within a several day period regardless of vaccination and results suggested that the cluster was coincidental, not causally related to vaccine. On October 14, the President and his family received shots on prime-time television to reassure the public of the vaccine's safety and most states that had suspended vaccinations restarted their programs.

In November, several cases of Guillain-Barré syndrome (GBS) – a severe neurological condition associated with paralysis that may include the respiratory muscles and may be fatal – were reported from Minnesota. Cases were also reported from several other states (by the time the vaccination program ended, 532 GBS cases and 32 deaths had been reported). CDC surveyed neurologists in several states and calculated the GBS risk among vaccinated and unvaccinated persons. The results suggested an increased risk among those who were vaccinated. On December 16, based on CDC's recommendation and after consultation with the President, the Assistant Secretary for Health announced the suspension of the swine influenza vaccination program. Although some persons at high-risk for severe influenza complications received the swine influenza vaccine subsequently, the large-scale vaccination program was not resumed. Neither a swine influenza pandemic nor focal outbreaks following the one initially identified at Fort Dix occurred.

The first vaccine dose was given 7.5 months after the virus was identified. By 9.5 months, 150 million doses of vaccine had been produced under a federal contract. Overall, 45 million persons were vaccinated in a two and one-half month period. Coverage varied widely from state to state and within states, reflecting differences in perceptions of the risk of a pandemic and to strategies and capabilities for program implementation.

A. What Went Well

- Laboratory testing and epidemiological investigation identified the swine influenza outbreak in Ft. Dix and documented person-to-person spread of infection. U.S. and international surveillance also was adequate to document that swine influenza strains did not cause disease subsequently in the U.S. or elsewhere globally. Surveillance in the Southern Hemisphere during the summer of 1976 did not identify circulation of swine influenza and contributed to debate over whether a pandemic was likely to occur.
- The government was able to contract for pandemic vaccine with all of the nation's influenza vaccine manufacturers, obtain needed appropriations, and pass

indemnification legislation. Despite lower yield than anticipated, manufacturers were able to produce 150 million doses of vaccine. (Note that in 1976 annual influenza vaccine use and production capacity were much less than exist currently.)

- States effectively established mass vaccination programs and immunized more than 40 million people in 10 weeks. This was a substantial accomplishment given the much lower annual influenza vaccination rate and the differences in program participation between states.
- Reporting, investigation and response to cases of GBS detected in several states was rapid and appropriate. By calculating the risk of this adverse event among vaccinated and unvaccinated persons, CDC was able to identify it as being vaccine-associated. Combined with surveillance data indicating no swine influenza disease, health officials and decision-makers were able to assess the risks and benefits of vaccination and to suspend the program.

B. What Went Wrong

- Program decisions made early in the process were not modified based on new information – e.g., the absence of any Swine influenza cases detected by surveillance following the Ft. Dix outbreak – because of concerns over logistical obstacles and impact on program support by the medical community, policy-makers, and the public.
- Implementation of the program by state health departments varied – possibly because perceptions of the risk of a swine influenza pandemic occurring differed or because of differences in state infrastructure. If a pandemic had occurred, preparedness would have been low in many states.
- Vaccine production was less than expected and ultimately would have been insufficient to protect the entire U.S. population, especially as clinical studies, conducted after manufacturing contracts had been established and after program plans were developed, showed that children would require two doses for protection.
- Liability issues – the need to indemnify vaccine manufacturers before they would release pandemic vaccine – threatened the availability of vaccine and delayed program implementation.
- Unexpected, severe adverse reactions occurred associated with vaccination.
- Adverse events that were only coincidentally related to vaccination resulted in substantial publicity and led to a suspension of the vaccination program in several states. Although it was predictable that some elderly persons would die shortly after vaccination by coincidence alone, health officials were unprepared to address the issue and had not developed appropriate communications strategies.

II. Lessons from the Swine influenza program

- For policy decisions and in communication, making clear what is not known is as important as stating what is known. When assumptions are made, the basis for the assumptions and the uncertainties surrounding them should be communicated. To the extent possible, key data needs should be anticipated and infrastructures developed that will provide information that limits the number of assumptions.
- The program should include mileposts for periodic re-evaluation so that necessary changes can be made, including potentially stopping the program, based on new information.
- External reviews of the program should be conducted periodically to invite objectivity and improve decision-making and the credibility of decisions that are made. These reviews may include those by chartered federal advisory committees and of independent scientists empanelled through existing mechanisms such as the Institute of Medicine.
- Ensure that all states are able to respond to a pandemic and implement mass vaccination programs effectively. Providing funding to states for preparedness and infrastructure development should be supplemented by guidance and technical support given the key role of state decision-makers in implementation. Federal oversight and assistance will be important to assure nationwide protection and consistency of the response.
- Adverse event surveillance systems should be in place before starting the program. Expected rates of serious health events (e.g., cardiac events) should be calculated in advance to facilitate appropriate evaluation of potentially coincidental events. Communications materials on risks and benefits of vaccination should be developed to educate health care providers and the public. These materials should make clear that adverse health events will inevitably occur shortly after vaccination, make clear the difficulty in separating coincidental from causally-related events, and highlight that investigation of events that may be linked with vaccination takes time.
- Expect and plan for the unexpected. Although it was not possible to foresee the occurrence of GBS, specifically, it is possible to prepare for policy and communications issues that would arise from the occurrence of unexpected adverse events.

III. Conclusions by other reviewers of the Swine influenza experience

- Drs. Feinberg and Neustadt were asked by the Carter administration to review the swine influenza program, focusing specifically on the decision-making process. They concluded in *The Epidemic That Never Was*, "Decision-making for the swine flu program had seven leading features. To simplify somewhat, they are:
    - Overconfidence by specialists in theories extrapolated from meager evidence.
    - Conviction fueled by a conjunction of some preexisting personal agendas.
    - Zeal by health professionals to make their lay superiors do right.

- Premature commitment to deciding more than had to be decided.
- Failure to address uncertainties in such a way as to prepare for reconsideration.
- Insufficient questioning of scientific logic and of implementation prospects.
- Insensitivity to media relations and the long-term credibility of institutions."

Source: Neustadt RE, Fineberg HV. *The Epidemic That Never Was. Policy-Making and the Swine Flu Scare*. Vintage Books, 1982, p. 12. (Dr. Fineberg is the current President of the Institute of Medicine.)

- Dr. Walter Dowdle participated in the Swine influenza program at CDC, and subsequently became CDC Deputy Director. In 1997, from a position with the Task Force for Child Survival and Development at the Carter Center, he published his observations on the Swine influenza experience. Dr. Dowdle states, "Numerous lessons of 1976 are critical to pandemic planning." He highlights the importance of separating "risk assessment" which is a scientific activity from "risk management" which is a political process. A formal process of risk assessment would include assessing the probability of a pandemic; defining the options available for control and their risks and benefits; and reassessing the situation as new data become available or new events occur. These analyses would provide the best possible scientific guidance to the political process of making risk management decisions.

  Source: Dowdle WR, The 1976 Experience, J Infect Dis 1997;176(suppl 1):S69-72.

IV. Conclusions

The swine influenza program provides a benchmark for decision-making and public health response to the threat of an influenza pandemic. Yet, how relevant are the experiences and lessons of 1976 for a pandemic response today? Substantial changes in public health preparedness and infrastructure, in vaccine manufacturing and delivery, and in society have occurred which will affect a pandemic response. U.S. and international surveillance for influenza and the strains that cause infection is much stronger than in 1976. The additional surveillance data available today will provide a much stronger basis for assessing the likelihood of a pandemic. Experience has shown that new influenza strains can cause clusters of human disease without becoming widespread.

Improvements also have been made in public health preparedness planning, and communications between federal, state, and local levels. Conversely, the ability of the public sector to provide mass vaccinations may be less, as vaccine delivery has increasingly moved from the public to the private sector. Children who once were vaccinated in public clinics now receive publicly funded vaccines from private providers. Institution-based or community-wide mass vaccination for meningitis by some state and

local health departments is the only recent U.S. experience in providing mass vaccination.

Whereas U.S. influenza vaccine manufacturing capacity is greater now than in 1976, only two vaccine companies currently supply the majority of influenza vaccine for the U.S. compared with four that made vaccine for the swine influenza program. Although the total number and proportion of persons vaccinated annually against influenza has increased from about 10 million to nearly 90 million, this is just 50 percent of total number of doses needed to protect the entire population.

Despite these changes, many of the lessons from the swine influenza experience remain relevant and, as demonstrated by the experience implementing smallpox vaccination, remain as significant challenges. The need to identify adverse events following vaccination as coincidental or causal also remained problematic. Separating risk assessment and risk management, conduct of external program reviews, improved communications planning, and strong surveillance for vaccine safety all are areas where the lessons of swine influenza were appropriately applied in the smallpox program.

Lessons from swine influenza also were considered in developing the national pandemic influenza preparedness and response plan. The importance of planning by state and local health departments during the inter-pandemic period, of strengthening key infrastructures, and of exercising response plans are emphasized. Several sections of the plan highlight critical decisions that can be made before a pandemic occurs and those that can only be made after a pandemic begins. Recommendations are made for periodic review of program decisions at multiple levels including by chartered federal advisory committees or independent scientific groups. A section of the plan highlights legal authorities and issues – including liability protection for manufacturers and those administering vaccine – that must be addressed before or at the time of a pandemic. Adverse event surveillance and communications planning also are highlighted. Work is ongoing to increase influenza vaccine manufacturing capacity and increase the speed with which vaccine can be produced.

Improved ability to assess risk through expanded U.S. and international surveillance, increased knowledge regarding the transmission and spread of influenza, and experience investigating influenza clusters and outbreaks should improve the ability make optimal risk management decisions. The swine influenza experience, however, is silent regarding the effect of risk management decisions on disease, the decisions that would be needed during a pandemic, and the effectiveness of pandemic response activities – because swine influenza was a pandemic that never occurred.