

Introduction and Background.

Mr. Chairman and members of the Committee, it is a pleasure to appear before you to review our experience in attempting, for the first time in history, to prevent the possibility of widespread death and disability from a potential influenza pandemic. It was this Committee which, on March 31, 1976, heard the evidence of the emergence of a new strain of swine influenza-like virus (labeled A/New Jersey/76) and our concerns that this strain might produce an influenza pandemic. It was this Committee which helped to lead efforts throughout the summer months to resolve the impasse of liability protection for influenza vaccine manufacturers and health workers involved in the program. It was also this Committee which investigated our initial difficulties in providing an adequate supply of influenza vaccine to the States in hearings last September. It, therefore, seems appropriate to me that in this forum we begin a review of the past 18 months' arduous and in many ways frustrating experience. I hope this review can be constructively used to address issues which will confront any future attempt at a major national effort in preventive medicine. These issues include liability and the need for compensation for injuries resulting from vaccination, informed consent, public information and research, and their complicated interactions in the rapidly changing atmosphere of a potential epidemic. The challenge is to address these issues and resolve them in advance in such a way that national health emergencies can be met headon and in time.

In Act III, Scene 2, of Shakespeare's Julius Caesar, Mark Anthony eulogizes Caesar saying, "The evil that men do lives after them, the

good is oft interred with their bones!" One concludes that at the present moment those aspects of the National Influenza Immunization Program perceived as negative are still uppermost in the minds of the public. The successes accomplished by the program, if not "interred with the bones " are at least attracting far less attention than its problems.

Major Accomplishments.

Because of this, I would like to now cite some of the undersung positive accomplishments of the National Influenza Immunization Program of 1976.

1. The first is the immunity provided to our people, especially those at "high risk" of dying from influenza. In the light of the problems, delays, and controversies swirling around this program from its inception, a remarkably large proportion of Americans were immunized. Among the group of people considered to be at "high risk" of death and disability from influenza, approximately 40 percent received the bivalent vaccine providing protection against swine flu and A/Victoria flu (Fig. 1). This is about twice the coverage level ever previously achieved among this group of citizens. Furthermore, the protective effect of the bivalent vaccine against epidemics of A/Victoria influenza was documented in an outbreak in Florida; the vaccine was shown to be 83 percent effective in preventing potentially fatal A/Victoria influenza among

residents of a nursing home there. Among the total population, above the age of 18, 32 percent were immunized. This is several times higher than was accomplished in 1968, the only previous time when influenza immunizations were provided on a large scale. You will recall that in that instance immunizations had hardly begun when the full force of the Hong Kong influenza epidemic erupted throughout the country in October.

2. Second is the remarkable responsiveness of State and local health departments in implementing the national program. Perhaps the most encouraging aspect of the 1976 program was the performance of State and local health agencies throughout the country. They proved again that they are capable of a rapid, appropriate response, and massive efforts in the face of a clear national need. It has been popular in recent years in some quarters to criticize State and local health departments and to impugn their ability to move rapidly and effectively. However, despite delays in the availability of influenza vaccine, despite the complexity of the vaccine's immunologic behavior and hence the need for various complicated immunization recommendations, despite a shortage of the only vaccine formulation suitable for young people, and despite a continuous media barrage emphasizing these and other problems, the health departments established

programs which achieved an unprecedented success. More people were immunized in 2 1/2 months in the National Influenza Immunization Program than in any previous immunization program in this country's history, and that achievement is directly due to the efforts of State and local health departments (Fig. II).

3. Third, a major historic milestone in the practice of community preventive medicine was reached by implementing the principles of informed consent on a nationwide basis. This was achieved by requiring the use of information-consent forms and procedures for all swine influenza immunizations except those administered by private physicians to their individual private patients. Even in these settings, physicians frequently elected to use the informed consent procedure, and thereby to be afforded the liability protection provided by Public Law 94-380. I believe the principle of informed consent will remain an integral element in community immunization programs even though the legal significance of the documents may change. There is widespread acceptance of the notion that individuals presenting themselves or their children for immunization should understand the risks as well as the benefits of the procedure. Effective information documents must be developed to promote this growing understanding. This is much easier said than done, as I shall subsequently discuss.

4. Many other positive aspects of the program of 1976 must be recognized. The vaccine manufacturers produced 150 million doses of influenza vaccine, more than seven times their usual production. Before being offered to the public, the influenza vaccines of 1976 were subjected to the largest field trials in the history of influenza vaccines. As part of the National Influenza Immunization Program, a system was established for the first time to monitor illnesses which occurred following immunization, a mechanism which was sufficiently sensitive to identify a condition of very low incidence. The existence of the national program produced a profound increase in surveillance for influenza disease and finally, the implementation of the program directly involved an impressive range of American institutions, public, private, and voluntary.

Significant reviews and evaluations of the 1976 program will continue to provide productive interpretations of the program. You have discussed the intensive and concurrent review performed by the Government Accounting Office (GAO). As the historical evidence emerges, I feel that the National Influenza Immunization Program will prove to have been a highly significant and appropriate effort or in the words of the GAO Report, "an unprecedented venture in preventive medicine."

Major Problems.

There were numerous well publicized legal, logistical and contractual problems in implementing the National Influenza Immunization Program.

Some of these were brought to this Committee as they emerged as obstacles to timely completion of the program.

Special criteria and procedures for determining costs for vaccine contracts were required because, under Public Law 94-380, monovalent swine influenza vaccine was to be provided to the Government at cost, and a reasonable profit was permitted on the A/Victoria/75 component of the bivalent vaccine. Like so many other aspects of this program, we and the manufacturers were faced with uncommon situations which required special solutions, and these took time. It should be emphasized, however, that negotiation of these issues did not affect the supply of vaccine, once the basic problem of liability protection was resolved in August 1976. Letter contracts were signed in September 1976 with all four manufacturers, and production and distribution of vaccine proceeded. The signing of definitized contracts to replace the letter contracts was delayed by a combination of reasons, one being a ruling by the Internal Revenue Service regarding the taxability of the manufacturers' Self Insurance Retention Fund. The vaccine manufacturers' accounting mechanisms were not designed to meet the requirements of the Government's cost accounting standards. Therefore, a waiver was requested. Once the waiver was granted, three finalized contracts were signed. The fourth contract is still being delayed because of a dispute about who pays for the production of several lots of vaccine made from the wrong seed virus.

There are two major developments which must be viewed as serious negative outcomes of the program. In the long run, however, even these may result

in significant benefits in clearly defining problems of vaccination campaigns or in producing understanding of previously mysterious disease processes.

1. Guillain-Barre Syndrome and other illnesses following vaccination.

The most dramatic unexpected problem which arose during the program was the discovery of an apparent statistical association between influenza immunization and the Guillain-Barre Syndrome (GBS). The Guillain-Barre Syndrome is an uncommon condition of unknown cause characterized by a transient "ascending paralysis," i.e., the paralysis begins in the legs and later involves the trunk, the arms, and the neck. For most people this condition is transient. However, it is fatal in 5 percent and produces rare residual paralysis in another 5 percent. Although the cause of GBS has never been known, two-thirds of persons with this condition report some health event, disease or accident in the weeks preceding onset; at least 150 different such "antecedent conditions" have been described. To the point here, however, is the fact that we identified an apparent statistical association between influenza immunization and the Guillain-Barre Syndrome. While a specific causal link between immunization and GBS has not been defined, the epidemiologic and statistical associations are significant.

As part of the National Influenza Immunization Program, we established at the outset a system to encourage individuals

and physicians to report any health problems occurring after immunization. These reports were made to local and State health authorities and from them to us. In mid-November we received a report from the State of Minnesota of a person who developed the Guillain-Barre Syndrome following influenza immunization. An investigation was carried out by health officials in Minnesota to identify all cases of the syndrome which had occurred there in recent months. No evidence for an association with immunization was found. On December 2, an Alabama physician reported three cases of the Guillain-Barre Syndrome, all among persons living in close proximity to each other. An investigation was initiated in Alabama and the investigation in Minnesota was reopened; a week later another inquiry was initiated in New Jersey when a case was reported there. At about the same time we asked eight other States to initiate similar investigations although no cases had been reported at that time in those States. By December 16, we had considerable data from four of the States; and in consultation with a number of outside experts, we decided to recommend suspension of the influenza immunizations until a nationwide investigation could be completed.

An intensive nationwide epidemiological investigation was initiated to determine if there was a significant association between influenza immunizations and the Guillain-Barre Syndrome.

The primary phase of this investigation consisted of a survey of neurologists in each of the 50 States to identify all cases of the Guillain-Barre Syndrome they had seen during the period October 1976 through January 1977. A second phase of the investigation, currently underway, includes the intricate study of immunological factors which may be associated with the disorder.

The first phase of the investigation, which began in mid-December, resulted in reports from all 50 States, the District of Columbia, and Puerto Rico. These reports yielded a total of 1,104 cases of the Guillain-Barre Syndrome with onsets during the surveillance period. Five hundred and thirty-five cases occurred in persons who had recently received swine influenza (A/New Jersey/76) vaccine, either by itself or in combination with A/Victoria/75 vaccine; and five hundred and thirty one cases occurred in persons who had received no influenza vaccines. Fifteen additional cases occurred in persons who had received other flu vaccines. The vaccination status in 8 cases remains unknown. Analysis of these data (Figs. III, IV, V) revealed that persons who received swine influenza vaccines experienced the Guillain-Barre Syndrome during the 10 weeks following immunization at a rate about 10 times higher than ordinarily expected (i.e., about one case per 1,000,000 persons per month). Viewed in another way, one extra case of the Guillain-Barre Syndrome above the expected incidence was observed for each 100,000 influenza immunizations. Because so

little was known previously about the frequency of the GBS, a clear interpretation of these findings is very difficult. One thing is clear, however; if we had not established a monitoring system and if 40 million doses of vaccine had not been given in so short a time, an apparent association of this low order of magnitude would not have been discovered.

The second phase of the investigation includes a detailed immunologic study of randomly selected patients in specific geographic locations. The study involves a sample of 150 previously identified GBS patients, all over 15 years of age, who are being compared with persons with similar characteristics who did not develop the condition. Immunologic tests will be performed to detect any perceptible differences. The epidemiological observations will also be extended by use of a more detailed interview concerning specific information on allergy, previous neurologic disorders, other immunizations, injections, surgery, or acute illnesses immediately prior to the onset of the Guillain-Barre Syndrome and to other questions suggested by the available surveillance information.

Thus, even the apparent association of influenza vaccine with the Guillain-Barre Syndrome, unexpected and undesirable though it is, has opened important avenues of research on the basic causes of the Guillain-Barre Syndrome. These may help in unraveling the nature of this mysterious syndrome, which has frustrated physicians for over 50 years.

In addition to the reports of the Guillain-Barre Syndrome, we received reports on other instances of health problems which occurred subsequent to immunization. With the exception of the expected occurrence of fevers, muscle aches, tenderness at the site of the injection, and one non-fatal case of an anaphylactic reaction, there is no evidence that any other conditions were associated, except temporally, with immunization. In no cases did any of these other health events occur at rates exceeding normal expectations in the population.

2. Liability and Claims.

The second major negative outcome of the program is a series of claims due to illnesses or deaths following vaccination. Many of these are associated with the occurrence of unexpected cases of the Guillain-Barre Syndrome. Because of the pressing need for swift action in initiating the program, the Federal Government assumed, via Public Law 94-380, unprecedented responsibility for liability in the event of injury or death due to immunization. Unquestionably, by assuming primary responsibility for claims filed as a result of the program, the Federal Government will be involved in a long and costly process of reviewing, litigating, and settling these claims. It is highly unlikely, however, that the costs will approach the billion dollar figure, which has been widely quoted. Since the Justice Department will be appearing before you today, I am sure they will provide a summary of the current situation related to claims.

Summary of Current Costs of the National Influenza Immunization Program.

I would like to briefly summarize the costs of the program to date. Of the \$135,064,000 appropriated by Congress to carry out the National Influenza Immunization Program, approximately \$101 million have been obligated. In addition, \$12 million have been reappropriated by Congress for use in other public health programs. The balances available from the original appropriation occurred primarily because both the amount and provisional unit cost of the vaccines were less than originally estimated. While the final cost of vaccine and storage have not been determined, we anticipate that sufficient funds will be available.

Only with respect to claims that may or may not be allowed in the future, is there any possibility of significant cost to the Government beyond what was budgeted for the program. It should be remembered that at the start of the immunization program, serious complications were not known to be associated with influenza immunization. Hence, major financial claims logically were not expected. As noted, earlier, the combination of a system for monitoring illnesses after vaccination and a prodigious output of immunizations in a short time was required to bring the low risk of GBS to light. The discovery of this apparent statistical association during the campaign has been primarily responsible for many of the claims filed.

The Future.

I would like now to turn to four aspects of the National Influenza Immunization Program which have distinct implications for future

programs against potential epidemics.

1. The Decision-making Process.

Given the imprecise nature of our understanding of influenza, what lessons are there for us in making decisions in the future? HEW Secretary Joseph Califano is publicly committed to looking very carefully at this question. The GAO has examined the decision process in 1976 and makes one concrete recommendation: That formal decision points be preestablished at which the basic policy decision is to be periodically reevaluated in light of new information (or lack of it). Such reevaluations were made in effect for the National Influenza Immunization Program through a series of Congressional hearings; and also they were made almost daily by CDC professionals trying to operate the program in view of the limited occurrence of influenza, particularly swine influenza, in the early fall and the seemingly unending implementation problems. Nonetheless, serious consideration should be given to formalizing a system of preplanned policy evaluation as suggested by GAO.

2. Compensation and Liability.

The most pressing questions requiring resolution in the wake of the National Influenza Immunization Program are those which provoked the special legislation in August of 1976; i.e., who is liable if someone is injured by immunization and what recourse does a person have to obtain compensation for that injury?

Public Law 94-380 established a program to cope with these issues in the particular context of the threat presented by swine flu, but at the same time made it clear that examination should be made of alternative approaches so that a more carefully considered permanent solution to these questions could be found. The law calls upon the Department of Health, Education, and Welfare to report to Congress on alternative methods of allocating liability and compensating the injured. Since that time these issues have received careful attention by individuals both inside and outside the Government. An interim working draft has been submitted to Congress and a final document will be produced by October 15.

I will not attempt to trace the background which led up to the legal situation that now faces us, nor to summarize the various alternatives which are potentially available. Instead, I would like to draw your attention to certain policy objectives which must be pursued if changes in the existing system are to be made.

First, and most importantly, it must be our objective to insure that sufficient vaccines continue to be manufactured, distributed, and administered in the face of increased concern by manufacturers over their liability for vaccine-related side effects. The manufacturers' refusal to supply vaccines without assurance that their liability would be limited was the primary impetus for last years' legislation protecting them against losses in the swine flu program. While this issue is currently being adequately addressed in the routine immunization programs by the Federal Government's assumption of the duty to warn vaccinees about risks and benefits, it is entirely possible that the liability issue

will surface again in the future as an impediment to vaccine supply. In addition, health care professionals and administering agents who also fear increased liability must be assured that if they perform their tasks carefully, they will not be held responsible for injuries resulting from immunization programs.

Secondly, since individuals who participate in immunization programs benefit not only themselves, but also the community at large, we must develop some means of assuring compensation for those who suffer vaccine-related injuries and have no other means of recovery. The Department is currently examining the structure and cost of a number of compensation plans, and these will be in our October 15 report.

Finally since no medication or biological is free from some degree of inherent risk, we must continue and expand our efforts to identify the inherent risks associated with vaccination and to develop ways to anticipate and prevent them in order to minimize the number of persons injured. Although CDC gathers a substantial amount of data concerning immunization programs, these efforts could be broadened and made more systematic. States administering the vaccine under Federal influenza immunization grants were asked to report to CDC illnesses and injuries occurring after vaccination. Modifications of this system are being developed to encompass all immunization programs.

Because of the difficulty in gathering data concerning the costs of various alternatives for addressing the liability and compensation issues, and because the Office of Management and Budget would require cost information

on any recommendations involving an additional expenditure of Department funds, the Department is unable at this time to recommend a specific solution for these problems. We intend to present the alternatives in detail in our October 15 report and to outline available cost estimates. We hope that the data available then will be sufficiently reliable to allow us to recommend a particular approach to this problem.

3. Benefit-Risk Information

Irrespective of solutions to the compensation and liability issues, persons receiving vaccines must receive meaningful information as to the benefits and risks of immunization. A method of accomplishing this is by no means simple or straight forward. One aspect of the problem is the need to distill very complex medical information into language understandable by a wide array of persons without medical backgrounds. Another aspect is the need to present a balanced picture of both risks and benefits, including the risks of not being immunized. At the present time, these two needs are compounded by a third: The need to provide this information in a way which minimizes a litigant's ability to prove in court that he or she was not adequately warned about the risks of immunization. It goes almost without saying that few people sue, if, after failing to be immunized, they subsequently become ill. I do not want to minimize the need to avoid costly financial losses associated with immunization. However, I believe our primary responsibility to the public is to conduct preventive health programs free of an overly defensive posture because of fear of lawsuits.

One of the difficulties with the GAO report is the narrow-gauge discussion of our implementation of informed consent requirements. They proceed almost exclusively from the position that the function of the information-consent process is to defend the Government in court. Their criticisms derive from probes at the adequacy of our procedure in respect to this one function while under emphasizing adequacy in providing information on which a reasonable person can make a reasonable choice. We must regain a balanced perspective on the use of informed consent documents. Otherwise, the construction of statements to serve as adequate documents for legal defense will fail completely to provide a lucid understandable summary of the information needed by the parent or individual to be immunized. We have recently carried out field tests of information and consent procedures for other vaccines. Results are being tabulated and analyzed. I regret to report that we have not yet found totally satisfactory ways to adequately serve these conflicting needs.

4. Understanding the epidemiology of influenza.

An outcome of significant ramifications for the future is the fact that we carried out a most extensive preventive health program against an epidemic which did not occur. We knew full well that this outcome was possible and said so repeatedly. Our understanding of the behavior of influenza virus was far from complete when the decision was made. The continued absence of epidemic swine flu unfortunately has contributed very little to our ability to predict the behavior of influenza. In the past all discoveries of major variations of influenza viruses were made in association with pandemics; we now have one example in which a major

new variant of influenza appeared, produced one sizeable human outbreak at Fort Dix, and did not spread in the ensuing influenza season. That knowledge doesn't help us a great deal.

However, we do know that influenza pandemics take a large toll in loss of life and large financial outlays for medical care and income loss. We also know that inevitably there will be another pandemic of some sort. If this pandemic is not due to swine influenza, we will have learned that not every type A influenza virus which mutates its surface antigens is explosive even when it has shown the ability to spread from man to man in environments such as military bases. It is too early to make any such presumptions regarding the next few years. Therefore, we are taking the necessary steps to maintain the existing supplies of the swine influenza vaccine for future use if needed.

In closing, Mr. Chairman, I would like to note my commitment to the importance of learning from our recent experience with the National Influenza Immunization Program of 1976. However, in doing this, the program must be viewed in the context of other preventive efforts, especially previous responses to threats of influenza pandemics. In 1957 and again in 1968, this country moved cautiously but the influenza virus did not; in 1976 the country moved quickly and decisively but the influenza virus did not. Some say the score is 3 to 0 in favor of the influenza virus, although for quite different reasons. Nevertheless, faced with a similar possibility in the future, I hope we will not hesitate to take necessary prudent, decisive, defensive action. If we wait until all questions are answered and all implications are clear, we will always find ourselves too late with too little in the fight against influenza.