Influenza

R-file

Influenza Pandemic: Preparedness Plans of the Public Health Service*

L. E. Burney, M. D.
Surgeon General, Public Health Service
U. S. Department of Health, Education, and Welfare

I. Introduction

First, may I express my gratitude to the Advisory Committee on Influenza Research and to Dr. Loosli and the members of the Asian Influenza Committee for their fine work in conceiving and arranging this excellent program. The function of the session today is to take cognizance of the knowledge acquired during the 1957 Asian influenza epidemic, and all preceding experiences, in order that we may develop in this country a reasonable plan of action for a future pandemic of influenza. It goes without saying that knowledge and plans which may be helpful for a pandemic also will be of value in handling such a situation as now faces us when we are having numerous local outbreaks of influenza throughout the country.

Since the great pandemics occur at intervals of a generation or so, and since it is human nature to forget the disagreeable things of life, it is unfortunately true that we have approached each pandemic almost as if it were an entirely new problem. Our objective at this

---

*Presented at the International Conference on Asian Influenza, Bethesda, Md., February 19, 1960.

Conference is to crystallize the recent experience and to file the information in an available place (without forgetting where) in order that the next generation can at least begin its battle with the best plan that its predecessors could create.

The experience in the 1957 pandemic of influenza, which happened to originate in Asia, was unique in the history of this disease. For the first time, an epidemic was promptly recognized as being caused by a strain of influenza which differed significantly from those with which man had had any experience for the past 75 years. The build-up of this epidemic into a pandemic was followed, step by step, and its progress throughout the world was carefully plotted. Unlike previous pandemics, this one was identified by virological procedures as well as by clinical and epidemiological observation.

Like the other speakers this morning who will tell you what their organizations propose to do when the next pandemic reaches us, I shall spend most of my time outlining the preparedness plans of the Public Health Service. The efforts of the PHS will, of course, be integrated with those of other groups in the United States and in the world. Our efforts will likely fall into four broad categories, namely, (1) recognition of the pandemic; (2) preparation of vaccine; (3) use of vaccine, including problems of vaccine distribution and dissemination of information; (4) research.

II. Recognition of Pandemic

I shall not belabor the need for improving the reporting systems throughout the world, which serve as tracking stations for following epidemics of whatever cause. The Public Health Service's reporting system comprises our foreign quarantine division, with its officers stationed in various parts of the world and its liaison with private organizations such as transportation companies, plus our State and national health reporting systems. This network is integrally related with that of the World Health Organization. We shall strive to improve these services for the continuous monitoring of various types of infectious diseases. These improvements will automatically strengthen the total reporting system when pandemic influenza next occurs.

Since the beginning of World War II, the influenza diagnostic laboratory facilities in the Continental United States and in U. S. military installations overseas have constantly improved. The essential diagnostic procedures are no longer limited to virus research laboratories. On the contrary, they are broadly available in the laboratories of our cities, our states, and our overseas bases. All of these laboratories are ultimately tied in with the WHO surveillance system, and about 75 of them receive immediate support from the International Influenza Center for the Americas which is established

within the Public Health Service and is located at the Communicable Disease Center in Atlanta.

The Influenza Center maintains periodic correspondence with each collaborating laboratory, determining its current facilities and its need for standard influenza diagnostic materials which the Center prepares and supplies. The Public Health Service is proud of the constellation which includes the Influenza Center and the collaborating laboratories in State and City Department of Health and in University research centers.

We shall strengthen the facilities of the Influenza Center in order that it may increase its program of technical training in influenza typing and diagnostic procedures and augment its capacity to supply the collaborating laboratories with diagnostic materials. In addition, the Center and its associated laboratories must remain in readiness to initiate promptly, and carry through the completion, antigenic studies on newly isolated strains of influenza and serological assessment of immunity of a population. This latter was of great assistance in 1957 and will be invaluable in the future in predicting whether a local epidemic, wherever it occurs, is likely to progress into a severe epidemic among our people.

Over and above this, we must be prepared to put into the field small, mobile teams which will be able to establish the precise etiology of influenza outbreaks wherever and whenever they occur and

to return to their base laboratories with strains and materials that can be used for production of diagnostic reagents and vaccines.

Finally, we shall maintain a competent advisory group which will stay abreast of all types of information on influenza and which can advise the Surgeon General when a local epidemic shows possibilities of becoming a pandemic.

III. Preparation of Vaccine

In discussing the recognition and surveillance of the pandemic, I mentioned that the experience in 1957 was unique. I would be justified in using the same term "unique" to describe the development and production of more than 50 million doses of Asian influenza vaccine within seven months after the virus was first isolated by workers at the Walter Reed Army Institute of Research. In reviewing this record, it is difficult to see where time might have been saved. Each step, from the recognition of the outbreak in Hongkong to the preparation and distribution of the final vaccine and the supplying of information to the public and the medical profession, was taken at top speed, with all available resources mobilized. I think that everyone who participated in this effort can take pride in this outstanding achievement.

Had the main force of the epidemic struck late in the fall, as we expected on the basis of previous experience, this major effort in which the pharmaceutical industry played so important a part would have

been even more successful. Despite the early arrival of the epidemic, there was some vaccine on the market before the first local outbreaks were reported. But only 4.6 million ccs were available by the fifth of September, when the epidemic wave was breaking. By the first of November, when 42.6 million ccs were available, the week of highest incidence had passed. Thus the supply was limited during the period when it could have been most useful.

No one can reasonably deny, however, that the production schedule was impressive, nor that the vaccine which was used had an effect in reducing the impact of the epidemic. It is easy to enumerate quickly certain of the essential points which made the achievement possible. First was the prompt isolation, in a foreign land, of an agent producing an epidemic which did not reach our shores immediately and which developed into epidemic proportion here only after several months. Second, the fact was quickly recognized that our people did not possess antibodies against this hitherto unknown strain. A third factor was the continual interchange of scientific and professional information between the governmental agencies and the vaccine producers; an indispensable fourth was the full cooperation of the manufacturers, including their sizable investment of risk of capital. Finally, the decision was made, long before the disease reached epidemic proportions in the U. S., to use a monovalent Asian strain vaccine standardized for potency by a

simplified, rapid technique which was employed simultaneously on each batch by the Division of Biologics Standards and the manufacturer.

It would be wishful thinking to assume that when the next pandemic invades the U. S., we will be so fortunate as we were in 1957 in having a long lead time. Further, it seems unlikely that the same kind of approach used in 1957 would appreciably decrease the interval of four months which elapsed from the time the new virus reached American laboratories until 5 million ccs of vaccine were delivered for use. Therefore, we must find alternate approaches if we are to succeed in producing a vaccine in the teeth of an epidemic.

One of the significant time consumers in 1957 was the adaptation of the strain to the point where it would provide crude material sufficiently rich in virus to produce a vaccine containing 200 or 400 CCA units of antigen per cc. Should the next pandemic be caused by a previously known strain, or by one with an antigenic complex that can be simulated by using a polyvalent vaccine containing several laboratory strains each of which has one or more antigen of the new pandemic strains, then the time can be shortened appreciably. If one could only improve the efficiency of a given unit of antigen in eliciting antibodies and immunity in man, then smaller quantities and less potent material would be required in order to get vaccine production under way. It is to be hoped that our research efforts before the next pandemic will provide a solution to this problem. At the moment I would not hazard a guess as

to whether this solution will come through the use of adjuvants, through the use of live virus rather than the killed material used in 1957, or through new methods of immunization.

IV. Use of the Vaccine

Whether or not a vaccine is available in time to immunize the population in advance of a spreading pandemic will depend upon chance as well as on thorough preparation. In any case, we can assume that available stocks of vaccine will be in extremely short supply during at least the initial phase of any preventive medicine operation. Consequently, advance planning must provide lists of types of persons who should receive vaccine on a priority basis. These categories of persons will fall into two general classes. One will include those who might be considered medical risks and whose immunization might prevent death, among whom will be the aged, the debilitated, and pregnant women. The second will comprise those persons who should be kept healthy because of their essentiality to the nation and the community. Included among the last group are persons in the military services and, in the civilian community, those concerned with preventive medicine, the care of the sick, communications in all forms, transportation, utilities, fire and police forces, and certain essential industries.

I am happy to report that the planning of the PHS, as part of an exercise during the influenza epidemic of 1951, provided a list of essential civilian occupations which included some six million Americans,

and this list was promptly put into use in the planning for the 1957 Asian influenza outbreak. In the future, we should keep such lists up to date and, in addition, prepare comparable estimates of the numbers of people who belong in the medical risk categories. As an ancillary value, such lists would provide the manufacturers with an estimate of the minimal amount of vaccine which would be required in an emergency.

Such a conference as this must not only recognize successful procedures and arrange for their continuation and augmentation, but also acknowledge deficiencies in order that they may be corrected. I regret to say that our experience with the distribution and use of influenza vaccine during the early days of Asian influenza in this country left much to be desired. After careful consideration and with the advice of health officers and of industry, the decision was made to distribute the available stocks without restrictions. Dependence was placed on informing the health professions and the public of the categories of persons who should receive vaccine in the first priority. The manufacturers cooperated in 1957 by distributiong their stocks to the States on the basis of population. But beyond this point the priority system in many instances was not followed.

We have time before the next pandemic to work out with the various health groups concerned a better method for voluntary control of influenza vaccine when it is in short supply. I feel confident that plans which promise to meet the problem will materialize and that the necessity for compulsory allocation will consequently not arise.

One of the significant contributions to knowledge gained during the 1957 epidemic was the demonstration that success or failure of a vaccination program in a given community was largely dependent upon the attitude of the local medical society and its individual members. It is not enough to have fine policies and words from the Federal and state health officials and the national medical and health organizations. Unless the local medical community is informed, and ready and willing to act, any program seems doomed to failure.

In developing plans for informing and educating practicing physicians, cognizance should be taken of the difference in points of view of the physician and the health officer. The physician is primarily concerned with his individual patients, particularly those in the medical risk category, and what the vaccine will do for them. In contrast, the health officer looks at the community and aims his immunization program at the health protection of those segments of the population whose continued activities are essential for the community. We cannot expect to change the points of view of the physician and the health officer, but we can hope, by appropriate educational measures to help each understand the other.

An important corollary to the information that reaches the public through its medical and health authorities, is the information that reaches them through lay sources: the press, radio, TV, magazines, meetings of clubs, business, church and other groups. If our story is clear, convincing and told in simple, specific and understandable terms, it can and will be quickly disseminated through national channels. A public opinion survey, conducted shortly after the 1957 Asian flu story broke, indicated that almost 90 percent of the people had heard about it.

But hearing about it obviously is not enough when specific action is desired. Like the professional public, the general public must also get information from local sources before it is ready to act. Here again, failure to develop effective local information programs has been our Achilles heel. It is unrealistic to expect that all local medical societies, health departments and other key agencies will be staffed with information specialists who can team up to organize local promotion programs. However, much can be accomplished when representatives from the local press, radio and TV stations are included as members of the local planning committee. Too often, I fear, they are not only omitted from committee membership but even barred from covering the planning meetings.

We must keep constantly in mind that it is only the local channels that can provide information about the availability of local supplies, the time and place of clinics, the priority that will be given to various classes of eligibles, and the other details that people must have before they can act effectively. The PHS will therefore give primary attention to ways in which State and national agencies, working cooperatively, can help communities develop strong information programs.

V. Research

What I have said thus far has largely concerned the practical aspects of the influenza problem -- how best to apply our present knowledge and resources in combating epidemic disease. As this audience well knows, significant progress against influenza in the years ahead will depend on how successful we are in shrinking our present areas of ignorance.

The importance and urgency of influenza studies are, I trust, evident in the priority given this area by the Public Health Service. We have created a National Advisory Committee on Influenza Research. And we have set up a Subcommittee of Investigators to enable the parent group to operate with maximum efficiency and dispatch. We look to the Subcommittee to stimulate and maintain long-term research interest in influenza, to assess research needs, and to help establish the general climate which is indispensable to productive study.

The major gaps in our present knowledge of influenza are painfully evident to all of us. We shall foster research on the mutagenic capacity of influenza viruses, on the nature of the virulence factor, on detailed analyses of the full spectrum of antigens of all known prototype strains of the viruses, and on the pathogenesis and physiological abnormalities of the disease in man. In brief, we shall look to the subcommittee of investigators to encourage basic studies on the virus and on the abnormalities it produces in man in order that this knowledge may be used during the next pandemic.

In the area of applied or developmental research we should sponsor research on chemotherapy and chemoprophylaxis of influenza and improve the methods for lengthening the protective period afforded by vaccines. In the latter category, research should be pushed on the development of adjuvants -- materials which, when added to vaccines, are capable of greatly boosting the antibody levels produced by immunization. Experimental results to date are sufficiently encouraging to warrant extensive exploration of the whole problem.

Many other areas might be cited in which research could profitably be initiated or expanded. I will mention only a few: the use of germ-free animals to explore the relationship between single bacterial infection and influenza virus infections; neurological research on the causes of myalgia and post-influenzal myasthenia; and studies relating to the cardiopulmonary complications common to influenza. These examples

and many others one might name suggest that influenza is still very much an unfinished business.

The kinds of research I have in mind, and which we shall foster, will be valuable not only for the scientific knowledge acquired but also because they will provide a nucleus of intelligent trained people who will be available at a moment's notice to provide the Surgeon General of the Public Health Service in 1980 with the kind of essential advice that he will require if faced with a pandemic of influenza.

In preparing the legacy for my successor who will hold office when the next pandemic strikes, I hope to provide him with three different kinds of sound investments. These are (1) a finite set of operating plans based on the experience of 1957; (2) a continually accumulating body of scientific information resulting from sound research on influenza carefully fostered by a dedicated cadre of investigators; and (3) a group of senior scientists and health officers who have maintained cognizance in the field and who can serve as his advisors.

Conclusion

These actions, if carried out in the inter-pandemic period, will be of great value not only to the U. S., but to other countries as well. Information which we obtain from our state and national surveillance and from field teams outside the borders of the U. S. as well as from

our research laboratories and biological houses within the USA, will be of as much value to others as to ourselves. Where the next pandemic will start no one knows. If it starts in our own country we would nevertheless expect to accumulate -- and disseminate -- the information necessary for effective control measures, even though it would be obtained too late to be of value to us. We would do this because it would help others -- a motive that is a tradition of our Nation and the Public Health Service.