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1975–1976
Issued July 1977

CENTER FOR DISEASE CONTROL

INFLUENZA SURVEILLANCE

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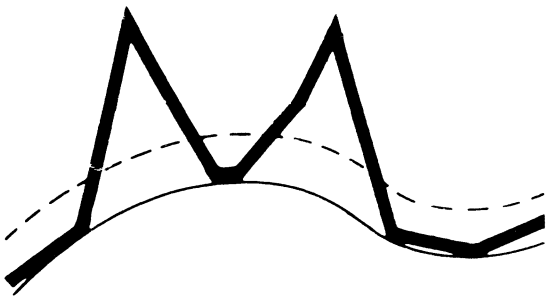

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE

P R E F A C E

Summarized in this report is information received from state and local health departments and other pertinent sources, domestic and foreign. Some of the information is preliminary. It is intended primarily for the use of those with responsibility for disease control activities. Anyone desiring to quote this report should contact the original investigator for confirmation and interpretation.

Contributions to the Surveillance Report are most welcome. Send them to

Center for Disease Control
Attention: Director, Immunization Division
Bureau of State Services
Atlanta, Georgia 30333

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Issued July 1977

Center for Disease Control.....William H. Foege, M.D., Director

This report was prepared by:

Bureau of State Services.....J. Donald Millar, M.D., Director
National Influenza Immunization Program,
Surveillance and Assessment Center.....Michael A.W. Hattwick, M.D., Chief*
Richard J. O'Brien, M.D.*
Information Systems.....Arthur C. Curtis, Chief
Immunization Division.....Alan R. Hinman, M.D., Director

Bureau of Epidemiology.....Philip S. Brachman, M.D., Director
Viral Diseases Division.....John A. Bryan, M.D., Director
Respiratory and Special Pathogens Branch.....Michael A.W. Hattwick, M.D., Chief*
Richard J. O'Brien, M.D.*
Barry Hafkin, M.D.*
Charles H. Hoke, Jr., M.D.**
Statistical Services & Evaluation Branch....Dennis J. Bregman, M.S., Chief
Editorial & Graphic Services.....Frances H. Porcher, M.A., Chief
Norma W. Strawn, Writer-Editor

Collaborators:

Bureau of Laboratories, Virology Division,
Respiratory Virology Branch.....Gary R. Noble, M.D., Chief
Alan P. Kendal, Ph.D.

World Health Organization
Collaborating Center for Influenza, CDC.....Walter R. Dowdle, Ph.D., Director

*Through June 1977
**Through June 1976

I. SUMMARY

The 1975-1976 influenza season was noteworthy because of several events. a) An H3N2 influenza virus (A/Victoria/3/75), isolated first in April 1975, caused a widespread epidemic late in the influenza season in the United States. Based on pneumonia- and influenza-associated mortality which peaked in February and March 1976, this was the most severe epidemic experienced by the United States since the 1968-1969 Hong Kong epidemic. b) In January and February an outbreak of influenza among recruits at Fort Dix, New Jersey, yielded 5 isolates of a virus resembling swine influenza strains. This discovery led to unprecedented investigations and to the recommendation for a nationwide influenza vaccination program in the fall of 1976. Furthermore, influenza surveillance activities were intensified and continued into the summer to search for any other evidence of infection of man by swine influenza-like virus. c) A total of 5 distinct strains of influenza A viruses were isolated in a single season--A/Port Chalmers/1/73, A/Victoria/3/75, A/England/864/75, A/Tokyo/1/75 (all H3N2 strains), and A/New Jersey/8/76, the HswlN1 virus from Fort Dix.

In the 1975-1976 season the Center for Disease Control (CDC) influenza surveillance data processing for the first time was done by computer. The data processing systems developed this season greatly augmented the capacity for handling multiple types of influenza surveillance data in large amounts from all sections of the United States.

A. H3N2 Influenza Virus Activity (September 1975 through June 1976)

A/Victoria/3/75-like virus was first isolated in the United States in Hawaii in November 1975 (1). The first documented outbreaks of influenza in the continental United States due to this virus were reported from a Portland, Oregon, nursing home and a Minneapolis, Minnesota, hospital in mid-January 1976 (2). Between February and April all regions of the United States experienced epidemic influenza activity due to A/Victoria virus. The New England, Middle Atlantic, Mountain, and Pacific divisions were the geographic areas most severely involved. Epidemic activity in the eastern and northeastern parts of the United States peaked in mid-February, and activity in the western part of the United States peaked in mid-March. Based on extrapolation of mortality data from 121 cities in the United States, an estimated 11,000 excess pneumonia and influenza deaths (see Section II A) and an estimated 20,000 total excess deaths were attributed to the A/Victoria epidemic. The least involved areas in the A/Victoria epidemic (West North Central, East South Central, and South Atlantic) were those areas of the country which had the greatest influenza activity due to A/Port Chalmers virus in the preceding 1974-1975 influenza season.

Between November 1975 and May 1976, 2,841 isolates of influenza A were reported by 53 World Health Organization (WHO) Collaborating Laboratories in 39 states throughout the United States. Of the 766 influenza A isolates received from the states by the WHO Collaborating Center for Influenza in Atlanta, all but 10 closely resembled A/Victoria/3/75. A/Victoria-like isolates were received by the WHO Center from all states except Colorado, Delaware, Montana, Nebraska, Nevada, South Dakota, and West Virginia. An isolate of A/Port Chalmers/1/73-like virus from Delaware, 2 H3N2 variants from Pennsylvania, 1 isolate of A/Tokyo/1/75-like virus from Hawaii (isolated from a Japanese traveler), and 1 isolate of A/England/864/75-like virus from Texas (isolated from a United States Air Force recruit) were also received.

Although epidemic influenza ended in April 1976, virus surveillance continued, and A/Victoria-like isolates from sporadic cases of influenza continued to be made through the summer.

B. Influenza B (July 1975 through June 1976)

In the 1975-1976 influenza season, 71 isolates of influenza B resembling B/Hong Kong/5/72 were reported by 8 WHO Collaborating Laboratories, and 23 isolates from 13 states were examined by the WHO Collaborating Center. Although some strains exhibited minor antigenic variation from B/Hong Kong/5/72, emergence of a significant new strain was not observed. The number of influenza B isolates was small in comparison with the number of influenza A isolates, but was a significant increase over the previous season when no influenza B isolates were reported within the United States. The first documented outbreak of influenza B was reported from Hawaii in November 1975, and isolates of influenza B were first reported from the continental United States in early

February 1976. Although isolates were reported from all regions of the country, activity was most pronounced in the western states.

C. Swine Influenza-like Virus (A/New Jersey/8/76)

In mid-January to early February 1976, coincident with an outbreak of A/Victoria influenza, an outbreak of influenza due to a swine influenza-like virus (A/New Jersey/8/76) occurred among military recruits at Fort Dix, New Jersey (3). A total of 5 isolates of this virus were obtained from clinically ill individuals, and an additional 6 cases were diagnosed by seroconversions (4). One of the individuals from whom this virus was isolated died of viral pneumonia, but the illness in the other 10 recruits was clinically indistinguishable from the A/Victoria influenza which was occurring at the same time. Epidemiologic investigation indicated that several hundred cases of infection from this virus may have occurred (5). Although virus surveillance activities increased in the United States and throughout the world, no additional isolates of this virus from man were reported through June 1976.

D. Reye Syndrome

Twenty-six cases of Reye syndrome in temporal association with influenza-like illness were reported to CDC between July 1975 and June 1976. The total number of reported cases with such association was small and significantly less than that reported for the 1973-1974 influenza season, during which an association was shown between Reye syndrome and influenza B infection (6). No cases of Reye syndrome in association with confirmed influenza B infection were reported to CDC in the 1975-1976 season.

II. SURVEILLANCE METHODS

A. Mortality

Deaths are reported to CDC each week by the Vital Statistics Offices of 121 United States cities with populations of approximately 100,000 or over and are published in Table IV of the Morbidity and Mortality Weekly Report (MMWR). Approximately 70 million people, or roughly one-third of the nation's population, live in the 121 reporting cities. The report is a count of death certificates filed each week and may include some deaths which occurred in preceding weeks. The number of delayed certificates usually increases during holiday periods, causing a drop in the number of deaths reported for those periods, followed by an increase when the delayed certificates are reported in succeeding weeks. Influenza epidemics usually are associated with a rise in mortality from all causes and in mortality due to pneumonia and influenza 2-4 weeks after widespread clinical illness is noted. The number of deaths due to pneumonia and influenza which exceeds the number expected provides the standard epidemiologic evidence of the extent and severity of epidemic influenza in large geographic regions. The expected number of deaths is determined by using weekly data for the previous 4 or 5 years, omitting data for the epidemic periods, and fitting the data to the following model by the least squares method:

$$\hat{Y} = u + rt + A_1 \cos\frac{2\pi t}{52} + B_1 \sin\frac{2\pi t}{52} + A_2 \cos\frac{4\pi t}{52} + B_2 \sin\frac{4\pi t}{52}$$

This procedure allows for a general mean, a standard error of the mean, a slope, and annual and semiannual cycles in the data. Omission of the epidemic data prevents an inflation of the expected level during the influenza season. An "epidemic threshold" is calculated as 1.65 x the standard error of the mean. Charts are prepared which show number of reported deaths, expected deaths, and the epidemic threshold for each area and the entire United States. These charts are scaled to make the distance between the expected and threshold levels constant for every curve, which allows visual comparison of influenza activity in different parts of the country (7-9).

B. Morbidity

Data reported by state epidemiologists provide the basis for nationwide surveillance of influenza morbidity. Statewide surveillance is maintained to some degree by all states. When influenza outbreaks are reported to state epidemiologists, this information is relayed to CDC by telephone, telegram, or letter, and confirmed outbreaks are reported in the MMWR.

Beginning in 1972, to develop more uniform nationwide data, CDC enlisted the cooperation of state and territorial epidemiologists to provide information routinely

about: 1) emergency room visits to large community hospitals in major cities within their states and 2) school and industrial absenteeism. Each week during the influenza season, these data are transmitted to the regional offices of the Department of Health, Education, and Welfare and then to CDC (10). During 1975-1976, 45 states and the District of Columbia participated in this institutional surveillance system, reporting data on 746 such institutions from 138 cities.

Twenty-five states included influenza among the list of reportable diseases in their morbidity reporting. These data are included in the states' morbidity reports and are utilized by CDC for influenza morbidity surveillance.

C. Laboratory Reports

Each of 58 WHO Collaborating Laboratories in the United States submits pre-addressed postcard reports to the WHO Collaborating Center for Influenza (CCI), Atlanta, on the numbers of specimens tested, influenza viruses isolated, and serum antibody rises detected. In addition, the CCI performs detailed antigenic analysis of representative influenza viruses which are submitted by laboratories throughout the Americas and elsewhere.

D. Surveillance at Airports and Ship Docks

After reports were received that A/Victoria-like strains of influenza were causing outbreaks of influenza in the South Pacific, CDC instituted influenza surveillance in early November at ports of entry in Honolulu, Anchorage, San Francisco, and Los Angeles in an attempt to document whether or not this strain of influenza may be imported into the United States. Passengers arriving from the Far East and South Pacific were questioned about influenza-like illness as they passed through immigration at airports. Throat swabs were obtained from those passengers found to have an influenza-like illness. Incoming cargo and passenger vessels from the Far East and South Pacific were asked to report the occurrence of outbreaks of influenza-like illness aboard ship at the time of docking. Vessels identified as having outbreaks of influenza-like illness were investigated, and throat swabs were taken from ill passengers and crew members.

E. International Reports

The WHO Weekly Epidemiological Record (WER) and surveillance reports from many countries are monitored for information on reported influenza outbreaks throughout the world. The antigenic characteristics of viruses and the epidemiologic patterns experienced in other nations are used as a guide to anticipate the nature of influenza outbreaks in the United States.

F. Epidemic Investigations

Data received through the surveillance system described above generally reflect influenza activity; however, because events other than influenza epidemics can cause fluctuation in the data, confirmation of reported outbreaks is sought and those of special interest are investigated. Most of the outbreaks described in this report are based on data from several sources.

III. SURVEILLANCE RESULTS, 1975-1976

A. Morbidity Surveillance

This year for the first time morbidity surveillance data (physicians' reporting of influenza-like illness, school and industrial absenteeism, and hospital emergency room visit data) were stored in a computer data bank and analyzed by mathematical algorithm for indication of evidence of influenza. A computer program used for evaluation of this year's morbidity surveillance data identified an institutional surveillance source as having abnormal activity when there was an increase in the data being reported (e.g., absenteeism) greater than 2 standard deviations above the baseline mean for a period of at least 2 consecutive weeks. After the A/Victoria epidemic state epidemiologists were asked to evaluate these data, and in nearly all cases in which the computer designated an institutional surveillance source as reporting data positive for an influenza outbreak, the state epidemiologists indicated that an outbreak did occur in the geographic area represented by the particular institution. These data are undergoing careful additional analysis.

Table 1 summarizes the results of the institutional surveillance system by division for the reporting schools, industries, and hospitals. Of the 746 reporting institutions, 538 (72%) reported data suitable for computer analysis. The other 208 institutions reported data too infrequently to be suitable for analysis by computer program. Sixty-six percent of the 388 schools, 77% of the 133 industries, and 80% of the 225 hospitals reported data suitable for analysis. Overall, data consistent with influenza were designated by computer in 69% of the schools reporting good data, 67% of such industries, and 79% of such hospitals.

Table 1

Influenza Morbidity, Institutional Surveillance System, 1975-1976

Division	Schools No.	Schools (%)*	Week of Peak Activity**	Industries No.	Industries (%)	Week of Peak Activity	Hospitals No.	Hospitals (%)	Week of Peak Activity
NE	17	(85)	31	10	(91)	32	8	(53)	34
MA	6	(86)	32	7	(88)	34	7	(78)	32
ENC	5	(33)	33	6	(40)	32	28	(85)	34
WNC	73	(67)	28	4	(57)	33	14	(74)	33
SA	24	(69)	31	17	(74)	30	28	(93)	32
ESC	11	(73)	33	10	(77)	34	11	(73)	33
WSC	16	(64)	34	7	(54)	34	23	(82)	33
MT	23	(92)	34	2	(29)	33	8	(53)	36
PAC	2	(40)	34	5	(100)	33	15	(94)	36
TOTAL	177	(69)		68	(67)		142	(79)	

*Number of institutions with epidemic activity (percentage with activity)
**Median week of peak activity (week 31 is week ending February 7, 1976)

The percentage of positive institutions varied from a low of 62% (39 of 63) in the East North Central Division to 85% (22 of 26) in the Pacific Division. The week of maximum peak activity generally was seen earlier in reporting schools and later in reporting hospitals. For all institutions considered by geographic division, those in the East had an earlier peak in their activity (weeks 32-34) than those in the West (week 36). For all reporting institutions, the mean peak in activity occurred 2.2 weeks before the average peak in pneumonia- and influenza-associated mortality. There was also some correlation seen between the percentage of institutions reporting data consistent with influenza-like activity in a given division and the magnitude of pneumonia and influenza deaths in that division. For example, 77% of the institutions in the New England, Middle Atlantic, Mountain, and Pacific divisions, the areas with the highest relative magnitude of pneumonia and influenza deaths, were positive for influenza-like activity, while 70% of the institutions in the other 5 divisions were positive.

Physicians' reporting of influenza-like illness also correlated with epidemic influenza. Ninety-two percent (175 of 191) of physicians' reporting units (e.g., sentinel physician reporters or routine county or state morbidity reporting) with adequate data for analysis reported data consistent with epidemic influenza. These data are undergoing analysis and comparison with similar physicians' reporting data from previous years in an attempt to determine the best means of evaluating this type of data.

B. Mortality Surveillance

Figure 1 shows pneumonia- and influenza-associated deaths reported from 121 cities in the United States for the entire country and for the 9 divisions. For the country, such mortality remained above the epidemic threshold from early February through early April. Geographically, pneumonia- and influenza-associated mortality first increased over the epidemic threshold in the New England Division in mid-January and remained above the epidemic threshold for a longer period than in any other division, not returning

to baseline until late March. Deaths caused by pneumonia and influenza in the Middle Atlantic Division also increased over epidemic threshold relatively early. Pneumonia- and influenza-associated mortality in all other divisions exceeded epidemic threshold for the first time in mid-February. Relative increases were most marked in the New England, Middle Atlantic, Mountain, and Pacific divisions.

Table 2 lists excess mortality due to pneumonia and influenza and total excess deaths from October 1957 through April 1976. For the nation an estimated 11,000 excess pneumonia and influenza deaths occurred during this epidemic. It should be noted that excess mortality in the last 2 years is based on extrapolation of mortality data from the 121 reporting cities rather than on data from the National Center for Health Statistics (NCHS), which were not available for this report.

Table 2
Excess Mortality Due to Pneumonia and Influenza
October 1957-April 1976

Period of Excess Mortality	Population (1,000's)	Estimated Number of Excess Deaths Due to Pneumonia and Influenza	Rate of Excess P and I Deaths Per 100,000	Estimated Total Excess Deaths	Rate of Total Excess Deaths per 100,000	Type of Influenza
Oct. 1957-Mar. 1958	173,232	18,500	10.7	69,800	40.3	A(Asian)
Mar.-Apr. 1959	176,420	1,400	0.8	7,900	4.5	A(Asian)
Jan.-Mar. 1960	179,323	12,700	7.1	38,000	21.2	A(Asian)
Jan.-Mar. 1962	185,890	3,500	1.9	17,100	9.2	B
Feb.-Mar. 1963	188,658	11,500	6.1	43,200	22.9	A(Asian)
Feb.-Mar. 1965	193,818	2,900	1.5	14,900	7.7	A(Asian)
Feb.-Apr. 1966	195,875	3,700	1.9	15,900	8.1	A(Asian)
Jan.-Feb. 1968	199,846	9,000	4.5	23,800	11.9	A(Asian)
Dec. 1968-Jan. 1969	201,921	12,700	6.3	33,800	16.7	A(HK)
Jan.-Feb. 1970	203,736	3,500	1.7	17,300	8.5	A(HK)
Jan.-Feb. 1972	208,232	5,600	2.7	24,600	11.8	A(HK)
Jan.-Feb. 1973	209,851	6,700	3.2	24,800	11.8	A(HK-Eng)
Jan.-Feb. 1975*	211,390	4,800	2.3	17,400	8.2	A(HK-PC)
Feb.-Apr. 1976*	213,000	11,000	5.2	19,800	9.3	A(HK-Vic)

*Estimates based on pneumonia and influenza mortality data collected from 121 U.S. cities by CDC. Mortality data in earlier years based on data obtained from the National Center for Health Statistics

Figure 2 shows a comparison of pneumonia- and influenza-associated deaths with 1) total deaths from all causes for all ages and 2) deaths from all causes by age groups. The total number of excess deaths estimated to have occurred during this epidemic was 20,000. Again this number is based on extrapolation of data from 121 cities and is not directly comparable with the data reported for earlier years. Nonetheless, it can be seen that excess mortality occurred mainly in persons over age 65.

C. Laboratory Report from the World Health Organization Collaborating Center for Influenza, Atlanta

1. Virus Surveillance. During the 1975-1976 influenza season 58 WHO Collaborating Laboratories reported to CDC once a week the results of influenza diagnostic studies. Between November 15, 1975, and May 15, 1976, 13,296 specimens were tested for the presence of influenza virus; 2,841 isolates of influenza A and 71 isolates of influenza B were made (Figure 3). Within the same period these laboratories performed hemagglutination inhibition (HI) or complement fixation (CF) tests on 10,387 paired blood samples. Diagnostic antibody titer rises ($\geq$4-fold) were found for influenza A in 2,171 pairs and for influenza B in 182 pairs (Figure 4). Influenza A isolates were reported from all but 3 states, and 16 states reported influenza B isolates (Figure 5).

2. Antigenic Analysis of Influenza A Viruses. From July 1, 1975, to June 30, 1976, a total of 1,177 influenza viruses were studied, comprising 1,125 influenza A strains and 52 influenza B strains (Table 3).

Fig. 1 PNEUMONIA-INFLUENZA DEATHS IN 121 UNITED STATES CITIES

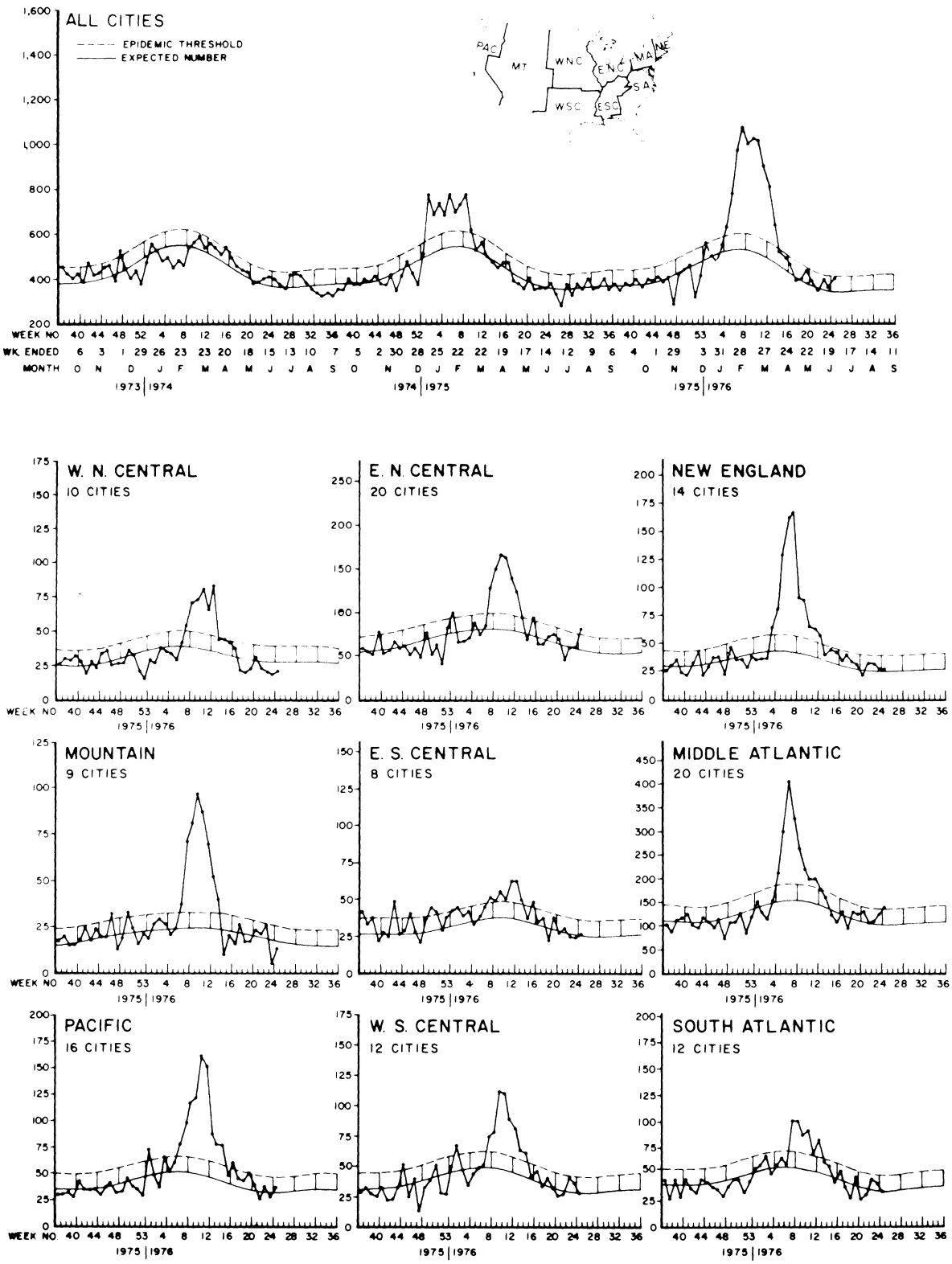


Fig. 2 MORTALITY IN 121 UNITED STATES CITIES

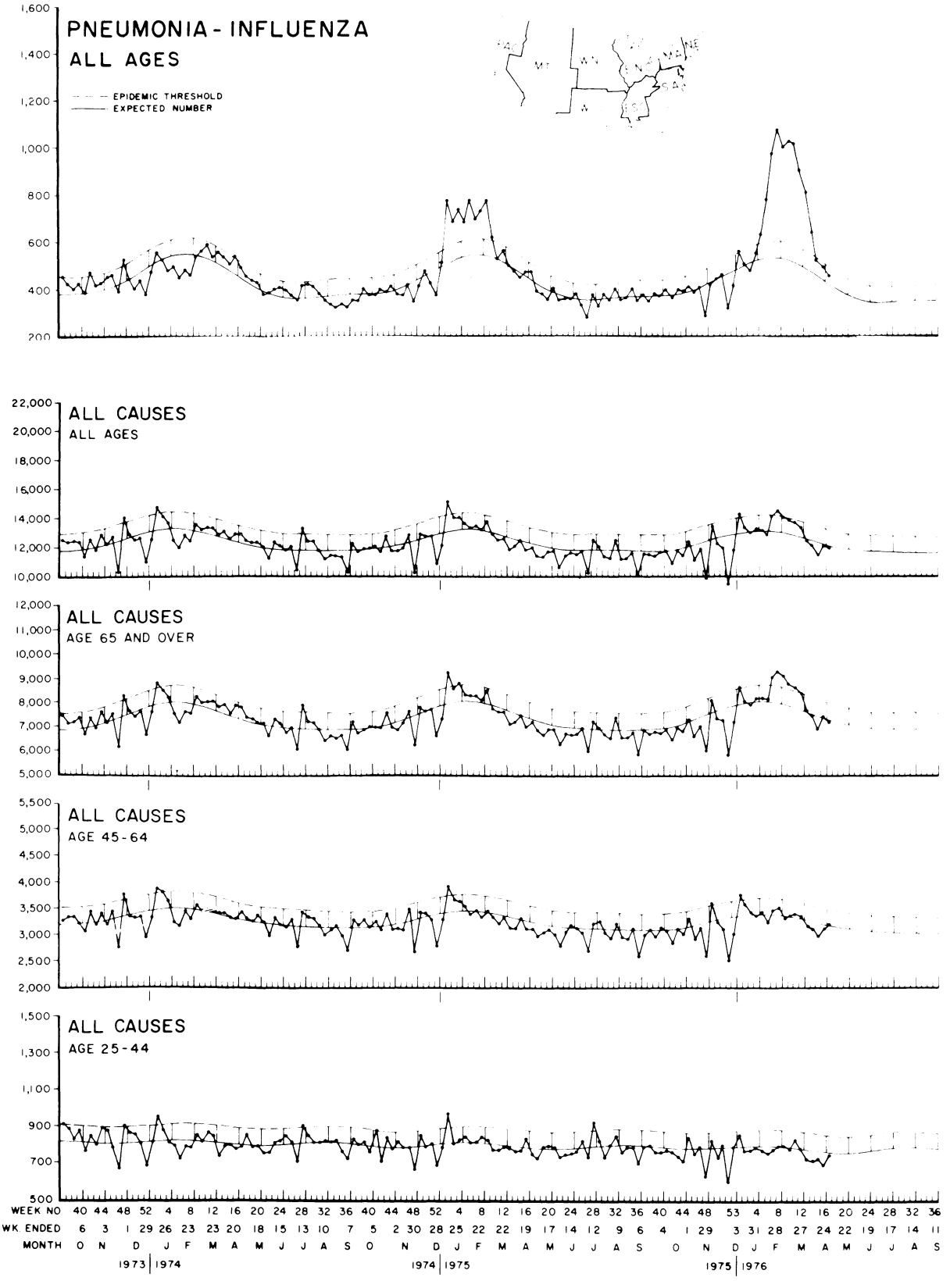


Fig. 3 DIAGNOSTIC STUDIES FOR INFLUENZA VIRUS ISOLATION, WHO COLLABORATING LABORATORIES IN UNITED STATES, BY WEEK, NOVEMBER 15, 1975 - MAY 15, 1976

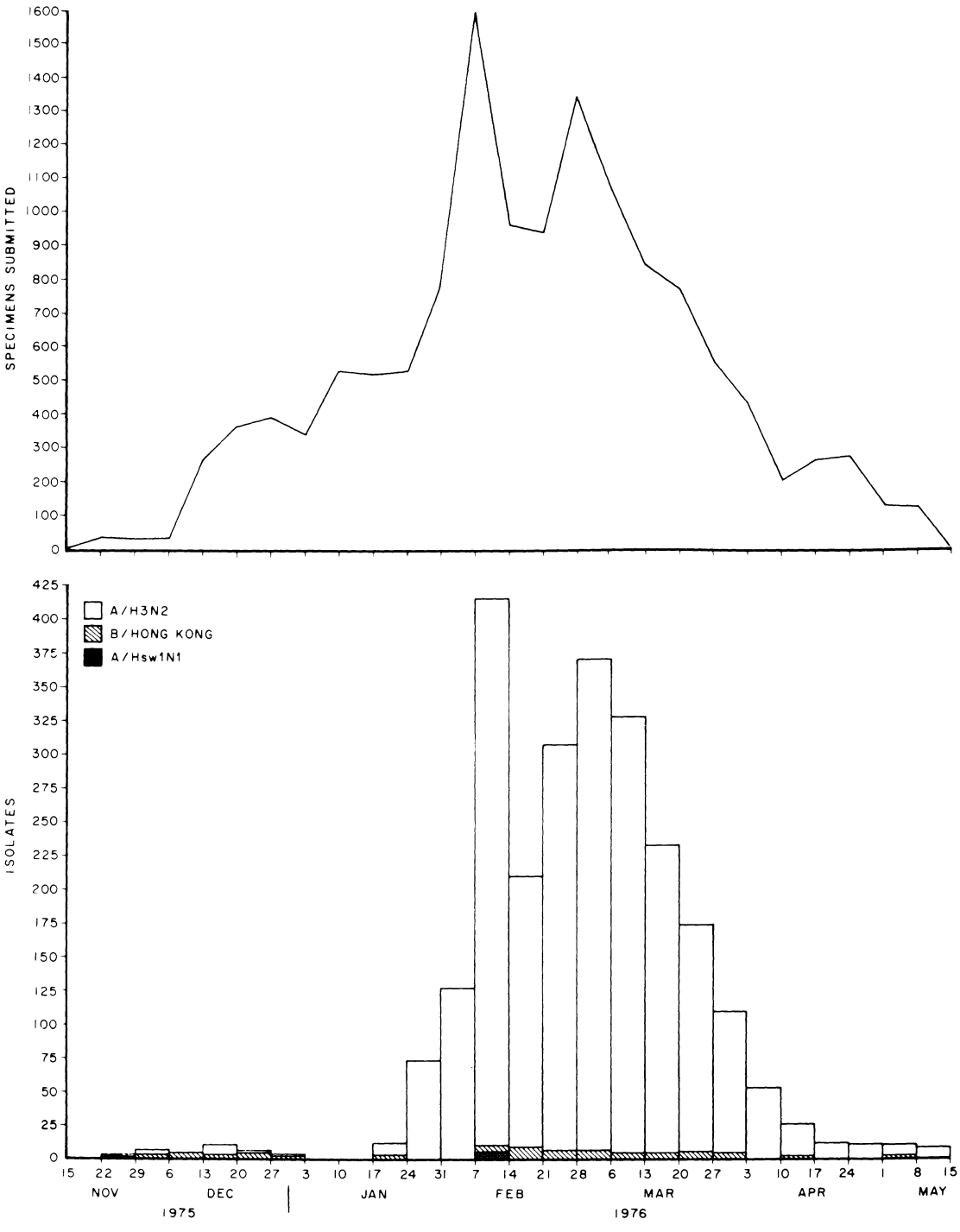


Fig. 4 DIAGNOSTIC STUDIES FOR SEROCONVERSION TO INFLUENZA VIRUS, WHO COLLABORATING LABORATORIES IN UNITED STATES, BY WEEK, NOVEMBER 15, 1975 - MAY 15, 1976

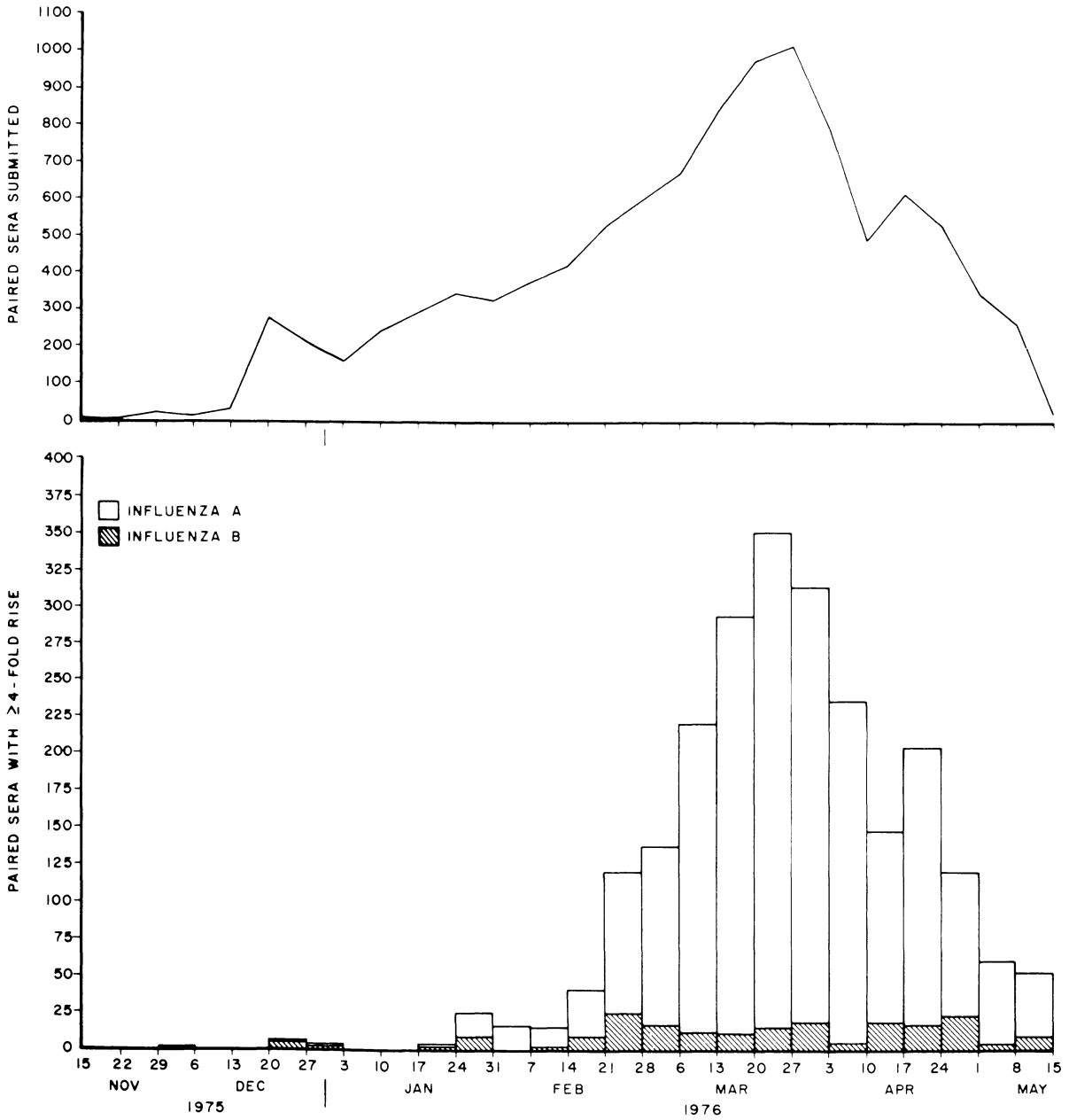


Fig 5 STATES REPORTING ISOLATES OF INFLUENZA VIRUS, JULY 1975-JUNE 1976

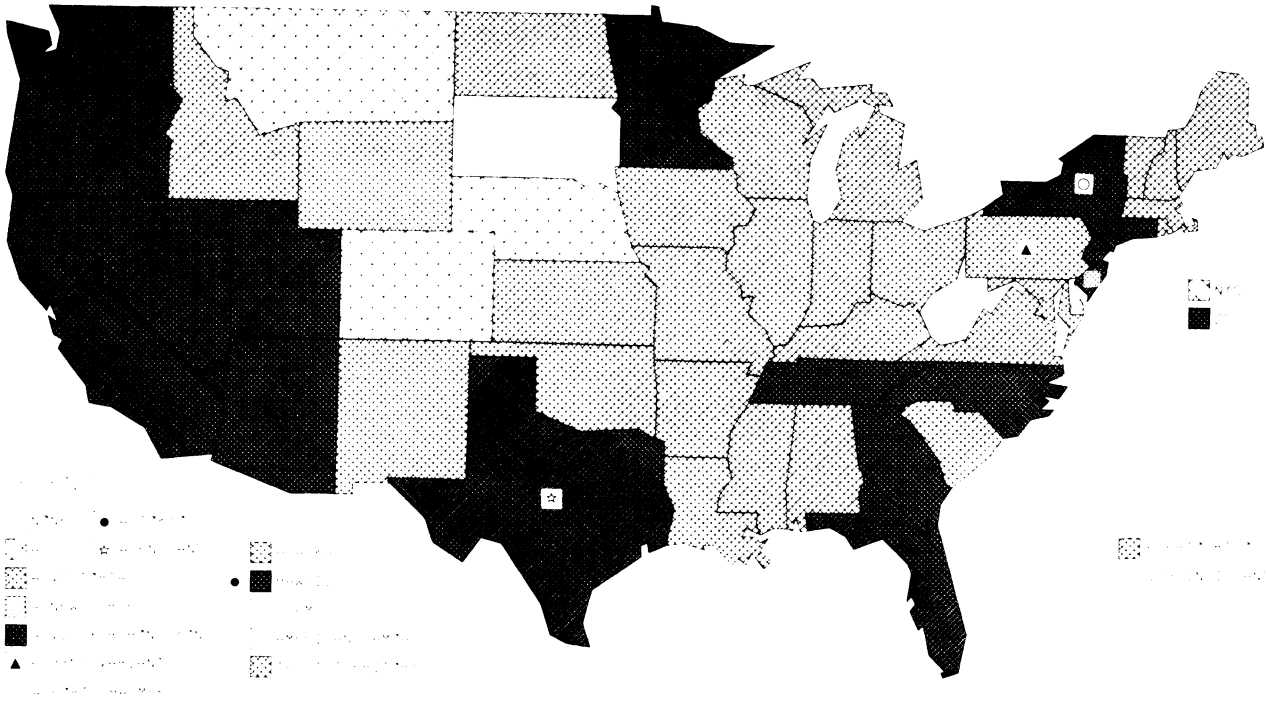


Table 3
Human Influenza Isolates Examined at the World Health Organization
Collaborating Center for Influenza, Atlanta, Georgia
July 1, 1975-June 30, 1976

North America	A/Victoria/3/75	Other Influenza A	Influenza B
Alabama	5		
Alaska	14		
Arizona	34		1
Arkansas	2		
California	43		1
Connecticut	40		2
Delaware		1-A/Port Chalmers/1/73-like	
District of Columbia	3		
Florida	2		
Georgia	34		1
Idaho	8		
Illinois	10		
Indiana	4		
Iowa	14		
Kansas	2		
Kentucky	20		
Louisiana	5		
Maine	7		
Maryland	15		
Massachusetts	33		
Michigan	25		
Minnesota	4		1
Mississippi	10		
Missouri	35		
New Hampshire	2		
New Jersey	7	5-swine influenza-like	1
New Mexico	30		
New York	34	1-A/Port Chalmers/73-like	1
North Carolina	25	5-A/Port Chalmers/73-like	3
North Dakota	16		
Ohio	12		
Oklahoma	6		
Oregon	15		4
Pennsylvania	47	2 H3N2 variants	
Rhode Island	2		
South Carolina	9		
Tennessee	10		1
Texas	90	1 A/England/864/75-like	5
Utah	10		1
Vermont	11		
Virginia	30		
Washington	11		1
Wisconsin	13		
Wyoming	2		
Canada	4		3
Mexico	6	—	—
TOTAL	761	15	26

Table 3 (Continued)

Caribbean	A/Victoria/3/75	Other Influenza A	Influenza B
Antigua	3		
Barbados	3		
Curacao	1	1 A/England/864/75-like	
Dominica	1		
Jamaica		13 A/England/864/75-like	
Puerto Rico	14		
Santa Lucia	10		
Santo Domingo	3		
Trinidad	53	—	1
TOTAL	88	14	1
Central America			
Guatemala	1	30 A/Port Chalmers-like	—
TOTAL	1	30	0
South America			
Argentina	56		
Brazil	49	8 A/Port Chalmers-like	1
Chile	4		
Colombia	3		
Uruguay	3		3
Venezuela	6	—	—
TOTAL	121	8	4
Pacific and Far East			
Australia	2		1
Fiji Islands	1		
Hawaii	20	1-A/Tokyo/1/75-like	7
Hong Kong	4	1 Intermediate Port Ch./Vic.	2
Japan	1	5-A/Tokyo/1/75-like	1
New Guinea	2		
New Zealand			1
Philippines	22	1-A/Port Chalmers/73-like 2-A/England/864/75-like	
Singapore	3	3-A/England/864/75-like	
Taiwan	9	1-A/Port Chalmers/73-like	9
Thailand	1	—	—
TOTAL	65	14	21
Europe	6	1-A/England/864/75-like	—
TOTAL	6	1	0
Africa	—	1-A/Port Chalmers/73-like	—
TOTAL	0	1	0
TOTAL	1,042	83	52

HI tests with ferret antisera showed that many viruses isolated in Singapore and Hong Kong (April-May 1975), in the Philippines and Taiwan (June-July 1975), and in Australia and New Guinea (August-October 1975) appeared to be closely related to each other. These isolates were variants from A/Port Chalmers/1/73 and A/Scotland/840/74 strains, prototypes which represented the predominant viruses reported during the winter of 1974-1975.

HI tests of A/Victoria/3/75, selected as a prototype of the new variants, are shown in Table 4, which also demonstrates the cross-reaction of 2 additional influenza A variants, represented by A/England/864/75 and A/Tokyo/1/75. All of the new variants--while still related to A/Hong Kong/68, the original prototype H3N2 virus--are inhibited to only low titers by antisera to prior H3N2 strains.

Table 4
Hemagglutination Inhibition Test Reactions of Prototype H3N2 Viruses

	Ferret Serum*						
Antigen	A/Hong Kong/8/68	A/England/42/72	A/Port Chalmers/1/73	A/Scotland/840/74	A/Victoria/3/75	A/England/864/75	A/Tokyo/1/75
A/Hong Kong/8/68	1,280**	2,560	320	160	80	80	40
A/England/42/72	160	1,280	1,280	320	160	80	40
A/Port Chalmers/1/73	40	320	2,560	160	80	80	40
A/Scotland/840/74	10	160	640	640	40	20	20
A/Victoria/3/75	20	80	320	80	2,560	160	80
A/England/864/75	80	160	320	80	160	2,560	80
A/Tokyo/1/75	20	80	160	40	640	80	1,280

*Serum to recombinant containing Neq1
**Underscoring indicates results of homologous reaction

Examination of the neuraminidases of the new variants showed that A/England/864/75- and A/Tokyo/1/75-like viruses possessed neuraminidases similar to that of A/Port Chalmers/1/73 (Table 5). The neuraminidase of A/Victoria/3/75, however, was found to be inhibited relatively poorly by antisera to the A/Port Chalmers-like neuraminidase, even though antisera to A/Victoria/3/75 was broadly reactive. In its reaction, the A/Victoria neuraminidase was thus characterized as either being non-avid for antibody, or exhibiting asymmetric antigenic drift from the A/Port Chalmers neuraminidase. However, the neuraminidase antigen from thirty 1975-76 influenza A isolates which were examined from Europe, Asia, and North and South America all resembled the A/Port Chalmers/1/73 neuraminidase. This included 1975-76 isolates having hemagglutinin antigens of A/Port Chalmers/1/73, A/Victoria/3/75, A/England/864/75, or A/Tokyo/1/75. Thus, widespread antigenic drift of neuraminidase of H3N2 virus does not appear to have occurred.

Table 5
Neuraminidase Inhibition Test Reactions of 1975 Influenza Prototype Strains

	Rabbit Serum*						
Antigen	A/Japan/305/57	A/Hong Kong/8/68	A/England/42/72	A/Port Chalmers/1/73	A/Victoria/3/75	A/England/864/75	A/Tokyo/1/75
A/Japan/305/57	11,100**	910	<10	200	20	<10	12
A/Hong Kong/8/68	2,900	37,900	260	1,860	220	200	900
A/England/42/72	510	3,760	5,850	6,800	290	760	1,830
A/Port Chalmers/1/73	70	530	270	10,800	940	1,960	5,730
A/Victoria/3/75	160	640	<100	2,660	920	300	3,160
A/England/864/75	150	720	140	9,300	540	2,580	5,600
A/Tokyo/1/75	150	490	120	7,400	720	1,540	5,760

*Serum to recombinant containing hemagglutinin Heq1
**Underscoring indicates results of homologous reaction

The 5 isolates of swine influenza-like virus from Fort Dix, New Jersey, were shown by HI tests to consist of at least 2 virus subpopulations. These could be differentiated by 1) whether or not they were inhibited by ferret serum to A/swine/Cambridge/39 (HswlNl) virus, and 2) the magnitude of their inhibition by antiserum to A/swine/Tennessee/1/75 and/or A/New Jersey/76 ferret sera. Analysis of different passage-level antigens and of recombinant viruses prepared by using a/New Jersey/8/76 or A/New Jersey/11/76 virus as hemagglutinin gene donors showed that at least these 2 isolates initially contained a mixture of the 2 antigenically distinguishable subpopulations of swine influenza-like viruses. One subpopulation of A/New Jersey/76 viruses resembles swine influenza isolates from at least 1957 to the present, whereas the other subpopulation of A/New Jersey/76 viruses resembles swine influenza isolates first seen in about 1973 and isolated in 1975 and 1976 (11). HI reactions of viruses representing the 2 New Jersey/76 and swine influenza virus subpopulations are shown in Table 6.

Table 6
Hemagglutination Inhibition Test Reactions of Hsw1N1 Influenza Viruses Isolated from Man and Pigs

	Ferret Serum				
Antigen	A/swine/Iowa/15/30	A/swine/Cambridge/39	A/swine/Wisconsin/1/67	A/swine/Tennessee/1/75	A/New Jersey/8/76
A/swine/Iowa/15/30	640*	<10	80	20	80
A/swine/Cambridge/39	80	2,560	20	320	1,280
A/swine/Wisconsin/4/57	80	<10	640	80	320
A/swine/Wisconsin/1/67	80	<10	640	40	320
A/swine/Tennessee/12260/76	80	<10	640	80	320
A/New Jersey/11/76**	160	<10	640	40	640
A/swine/Iowa/1/73	80	320	640	1,280	2,560
A/swine/Tennessee/1/75	80	320	320	2,560	2,560
A/New Jersey/8/76	80	160	320	640	2,560

*Underscoring indicates results of homologous reaction
**Cloned by 3 terminal dilution passages

3. Antigenic Analysis of Influenza B Viruses. Only a small number of influenza B isolates were received for antigenic analysis. Although some isolates appeared to have undergone slight antigenic drift from the B/Hong Kong/5/72 reference strain, this was not a consistent finding, and no clear evidence was obtained for the emergence of a new influenza B variant.

4. Comparison of HI and CF Tests for the Serodiagnosis of Influenza Infection. During the 1975-76 influenza season, both HI and CF tests were used for the serodiagnosis of influenza. Influenza A/Port Chalmers/1/73 (H3N2) and B/Hong Kong/5/72 were the antigens used throughout the season in the HI test; A/Victoria/3/75 (H3N2) was added in January, and 3 swine influenza-like antigens, A/swine/1976/37*, A/Mayo Clinic/103/74, and A/New Jersey/8/76, were added in February. When a comparison was made of all paired sera tested by both methods during the year, a greater number of significant antibody rises was detected by the HI test than by the CF test (Table 7). Of 188 paired sera showing an antibody rise by 1 or both tests, 163 (87%) were detected by HI, and 133 (71%) were recognized by CF testing. The greatest number of HI rises occurred with A/Victoria/3/75 virus, although occasionally an anamnestic rise to A/Port Chalmers was seen without a concomitant rise in A/Victoria antibody. As noted below, a low frequency of heterotypic rises in Hswl antibody was also seen when an A/Victoria infection occurred.

*Previously identified as A/swine/1976/31 (11)

Table 7
Results of Hemagglutination Inhibition and Complement Fixation Tests
for the Serodiagnosis of Influenza A,
June 1, 1975-July 31, 1976

Serologic Test	Diagnostic Rises* No.	Percent
HI† and/or CF§ (totals)	188	100
HI	163	87
CF	133	71
HI (CF negative)	55	29
CF (HI negative)	25	13

*≥4-fold rise in antibody titer
†A/Port Chalmers/1/73 and/or A/Victoria/3/75
§Influenza A ribonucleoprotein

5. Serologic Studies of Antibody to Swine Influenza-like Virus in Man. After the outbreak of swine influenza-like virus infection at Fort Dix, New Jersey, CDC performed several prevalence studies of HI antibody to Hswl viruses. The results of these studies are shown in Table 8, which also includes results from 2 earlier serosurveys. In every study the presence of antibody to Hswl viruses is uncommon in young persons, it increases as age increases, and it approaches 100% in those over age 50. The high prevalence of antibody to these viruses in older persons presumably reflects exposure to human Hswl influenza viruses between 1918 and the late 1920s.

Table 8
Summary of Serologic Investigations of the Prevalence of
Antibodies to Swine Influenza Virus in Human Populations

Year	Location	Population	Age Groups at the Time Blood Was Drawn				
			≤15	16-29	30-45	>45	
1966[1]	Illinois	General public	1/200(.5)[4]	1/247(.4)	39/242(16)	116/151(77)	
		Persons occupationally exposed to swine	-	17/182(9.3)	81/413(20)	251/345(72)	
			≤16	17-31	32-46	>46	
1971[2]	Atlanta, Ga.	Community members	1/161(.6)	14/163(8.6)	43/112(38)	217/250(87)	
			≤20	21-30	31-40	41-50	>50
1976[3]	Atlanta, Ga.	Community members	1/37(3)	2/25(8)	9/33(27)	9/25(36)	27/27(100)
			≤15	16-29	30-49	>50	
1976	Sheboygan, Wis.	Community members	0/156(0)	1/25(4)	2/19(11)	33/88(37)	
			≤15	16-29	30-49	>50	
1976	Fayettesville, Pa.	Community members	0/60(0)	5/38(13)	9/52(17)	46/52(88)	

[1]Schurrenberger PR, Woods GT, Martin RJ: Serologic evidence of human infection with swine virus. Am Rev Respir Dis 102:356-361, 1970
[2]Courtesy of William Marine, M.D., Professor and Chairman, Department of Preventive Medicine and Comprehensive Health Care, University of Colorado Medical Center
[3]Courtesy of Gary Noble, M.D., Chief, Respiratory Virology Branch, Virology Division, Bureau of Laboratories, CDC
[4]Numerator = number having titers, denominator = number tested, ( ) = percentage of population

Several factors must be taken into account in interpreting results of studies made of younger persons. It has been suggested that individuals having occupational exposure to swine may have a higher age-adjusted prevalence of HI antibody to Hswl viruses (12). This might result from symptomatic or asymptomatic infection or from immunization without infection after a person has been exposed to Hswl viruses shed by swine. Antibody may also result from prior immunization with influenza vaccine containing Hswl antigen. Between 1955 and 1969 influenza vaccines administered to U.S. military personnel and affiliated groups contained Hswl antigen, and between 1956 and 1958 influenza vaccines prepared for civilian use contained that antigen (13). Finally, antibody to Hswl viruses may result from a heterologous response to H3N2 virus infection or immunization (Table 9).

Table 9a
Swine Influenza Virus HI Titer Rises Among
Serologically Confirmed Influenza A (H3N2) Infections[1]

	Swine Virus Antibody[2]			
	Acute Phase		Convalescent Phase	
Age	Titer	No.	≥4-fold Rise	Percent
≥50	<10	2	0	4
	≥10	22	1	
<50	<10	89	2	3
	≥10	13	1	
Total		126	4	3

Table 9b
Swine Influenza HI Titer Rises Among 1973-74
and 1975-76 Vaccine Recipients[3]

	Swine Virus Antibody[2]			
	Prevaccination		Postvaccination	
Age	Titer	No.	≥4-fold Rise	Percent
≥50	<10	2	0	16
	≥10	29	5	
<50	<10	41	2	8
	≥10	9	2	
Total		81	9	11

[1]All subjects had ≥4-fold rises to A/Port Chalmers 1/73 or A/Victoria/3/75 in interval January 1975 to March 1976
[2]Number with titers or rise to 1 or more swine virus-like strains: A/swine/1976/31, A/Mayo Clinic/103/74, or A/New Jersey/8/76
[3]All subjects had ≥4-fold rise to A/England/42/72 (1973-74 vaccine, 18 recipients) or to A/Port Chalmers/1/73 (1975-76 vaccine, 63 recipients)

Thus the interpretation of HI antibody to Hswl viruses in an individual is difficult. Age, exposure to swine, past immunization, military service, and recent H3N2 infection or immunization must be considered.

D. Summaries by Geographic Areas

Figures 6-13 reflect reported influenza outbreaks by states, by 2-week periods.

1. New England Division. Influenza was first reported from this area in Boston, where an outbreak of influenza-like illness began on January 19, 1976, at West Roxbury Veterans Administration Hospital. Within the next few weeks influenza became widespread in eastern Massachusetts, and many hospitals in the Boston area reported nosocomial influenza. All of the isolates from these outbreaks were characterized as A/Victoria/3/75-like. A/Victoria-like isolates from Connecticut were first reported on January 27. Influenza remained widespread throughout the New England area during the early part of February and then gradually decreased, although all states in this division were reporting sporadic cases of influenza-like illnesses as late as the first of April. As noted above, pneumonia- and influenza-associated deaths increased above epidemic threshold for this area for the first time in the third week of January, suggesting that influenza was occurring here before the first reports were made to CDC of influenza in this division.

2. Middle Atlantic Division. The first reports of epidemic influenza in this area were from New York, where an outbreak of influenza began on January 19 at Riker's Island Prison. The following week influenza A isolates, subsequently shown to be similar to A/Victoria, were reported from several outbreaks in the metropolitan New York City area and from outbreaks of influenza in schools in Cumberland County, New Jersey, and Camden, New Jersey. Influenza rapidly became widespread throughout New Jersey and New York. Syracuse, Rochester, and New York City were the most severely affected areas in New York State. Influenza activity peaked in mid-February in New Jersey and within a week later in New York. The first Pennsylvania influenza isolates, subsequently shown to be A/Victoria/3/75-like, were reported on January 27 from Philadelphia. Pennsylvania experienced widespread influenza somewhat later than New Jersey and New York, with the peak occurring in early March. Mortality due to pneumonia and influenza peaked in the Middle Atlantic states in mid-February but remained elevated over epidemic threshold until the end of March.

In addition to the A/Victoria epidemic, the New Jersey Department of Health in early February reported several isolates of influenza A from military recruits at Fort Dix, New Jersey. These isolates subsequently were shown to be swine influenza-like viruses.

3. South Atlantic. Influenza activity in this division began somewhat later than influenza in the Middle Atlantic and New England divisions, and with the exception of the northern portion (Delaware, Maryland, District of Columbia, and northern Virginia) this area was relatively spared from widespread influenza. The first reports of influenza received from this division were in early February from Washington, D.C., where scattered outbreaks of influenza-like illness had been noted in late January, and from Maryland, where 2 isolates of A/Victoria-like virus were made from sporadic cases in late January. Influenza epidemics peaked in the northern part of this division in mid- to late February; epidemic influenza in the southern portion peaked in mid- to late March and was never widespread in North Carolina, Georgia, or Florida. Outbreaks of influenza in institutions were documented as late as the first part of April (see Section IV, A6).

4. East South Central. Influenza in this area, as indicated by pneumonia- and influenza-associated mortality, was the least severe for any area of the country, although confirmed influenza outbreaks were reported from all 4 states in this division. The first recognized outbreak of influenza began on January 24 and involved members of a ski club from Nashville, Tennessee, traveling to North Carolina for a weekend ski trip. A/Victoria-like virus was isolated from ill patients in this group as well as from patients at Vanderbilt University, where an outbreak of influenza began about the same time. The first isolate of A/Victoria influenza from Mississippi was reported in mid-February from a patient who was ill in late January. An outbreak of influenza began in early February among members of a tour group from Jackson, Mississippi, and Memphis, Tennessee, who became ill shortly after arrival in Las Vegas. Within a week

widespread outbreaks of influenza due to A/Victoria were reported from Memphis, and by the first week in February influenza was recognized in Kentucky, Mississippi, and Alabama. Widespread influenza was not prominent in this region, and influenza activity peaked in late February and early March.

5. East North Central. Influenza from this division was first reported from Illinois, where outbreaks of influenza due to A/Victoria were recognized on January 21 among students at Northwestern University and among naval recruits at Great Lakes Naval Training Station. An outbreak of influenza among university students in Lansing, Michigan, began in late January, and A/Victoria-like virus was isolated. Isolates of A/Victoria-like virus were reported from Wisconsin in early February. Outbreaks of A/Victoria influenza were reported from Cleveland, Ohio, in late February. Widespread influenza was reported only from Michigan and Indiana, and epidemic influenza for the entire division peaked in mid-March.

6. West North Central. One of the earliest reported outbreaks of influenza due to A/Victoria in the continental United States this season was from Minneapolis, Minnesota, where an outbreak of influenza involving teenagers in an alcoholism unit began about January 1. On January 13 an outbreak of influenza was recognized in a St. Paul, Minnesota, high school, with a 33% attack rate. Approximately January 19, 2 outbreaks of influenza in Iowa began, 1 in a Lansing high school, and another in Iowa City involving students at the University of Iowa. The first reported outbreak of influenza from Missouri was in late January, when the A/Victoria virus caused epidemic influenza among students at Washington University in St. Louis. The first recognized influenza outbreak in Nebraska, where influenza A isolates were reported in mid-February, involved approximately 25% of the students attending a primary-secondary school in Wilber. Mortality due to pneumonia and influenza in this division peaked in late March and was not so marked as that seen in other regions.

7. West South Central. Isolates of A/Victoria influenza virus were first reported from Houston, Texas, from sporadic cases in late January. In the first week of February scattered outbreaks of A/Victoria influenza were reported from Arkansas and Louisiana, and widespread outbreaks of influenza were noted in both Dallas and Houston. There was a moderate increase in pneumonia- and influenza-associated mortality, which peaked in early March.

8. Mountain. In this area isolates of A/Victoria influenza were first reported from Arizona in the third week of January. That same week outbreaks of A/Victoria influenza occurred at Carlsbad, New Mexico, and at an Air Force Base near Las Vegas, Nevada. One of the first reported isolates of influenza B virus in the continental United States was made at the time of the A/Victoria outbreak at the Nevada Air Force Base. In Colorado outbreaks of influenza A were first noted in late January. The number of deaths due to pneumonia and influenza was greater than usual for this area, with elevations being above epidemic threshold from mid-February through early April and peaking in early March.

9. Pacific. Oregon reported both the first influenza A/Victoria and B/Hong Kong virus isolations for the continental United States in this influenza season. Two outbreaks of A/Victoria influenza were recognized in early January and affected patients of 2 nursing homes in Portland, Oregon. Oregon also reported 4 isolates of influenza B from sporadic cases; all patients involved had had onsets of illness in late January, and they were from 4 separate cities in the west central portion of the state. Isolates of A/Victoria influenza were reported from California and Washington the third week in January. Despite the early reports of A/Victoria influenza isolates from this division and several localized outbreaks, truly epidemic influenza--which ultimately was widespread in this area--did not begin until mid-February and did not peak until a month later. Pneumonia- and influenza-associated mortality, again fairly marked for this division, was elevated between mid-February and early April and peaked in mid-March. Hawaii, as noted earlier, reported isolates of A/Victoria influenza and influenza B in November; these were associated with localized outbreaks in schools. Influenza activity increased, it peaked in December, and it was still reported through mid-March. A/Victoria influenza activity was also noted in Anchorage and peaked in late February.

Fig. 6 STATES REPORTING INFLUENZA OUTBREAKS, DECEMBER 16-31, 1975

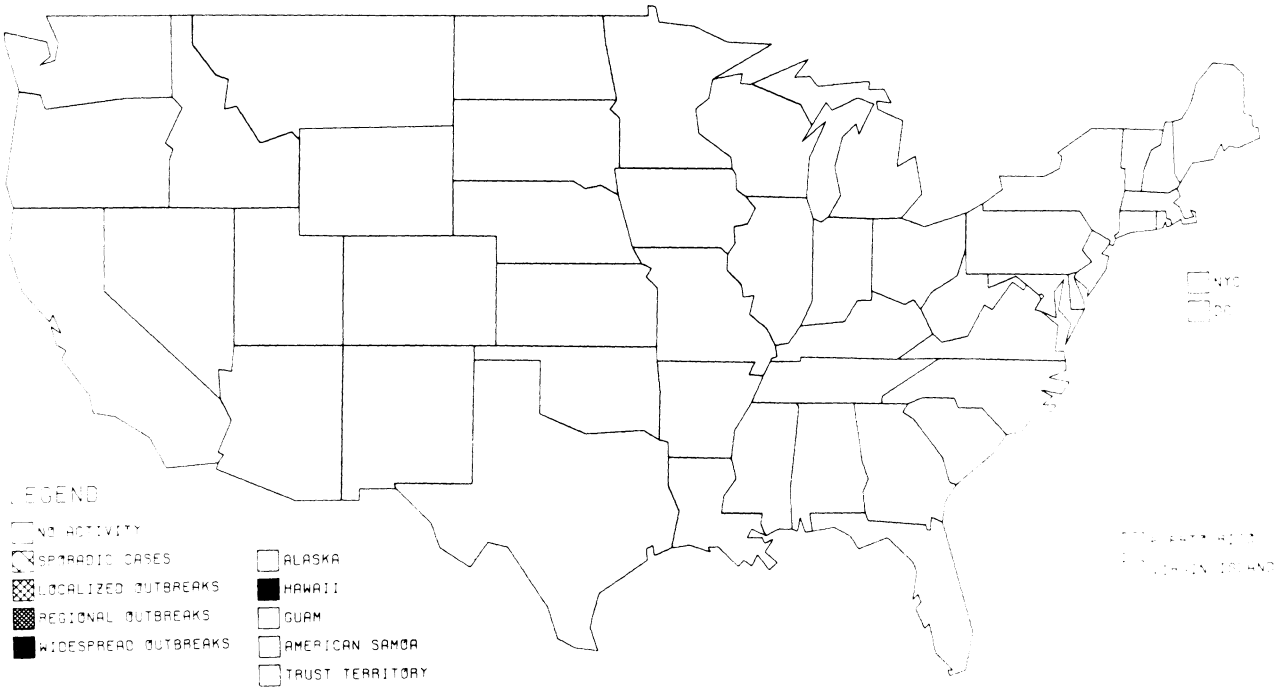


Fig. 7 STATES REPORTING INFLUENZA OUTBREAKS, JANUARY 1-15, 1976

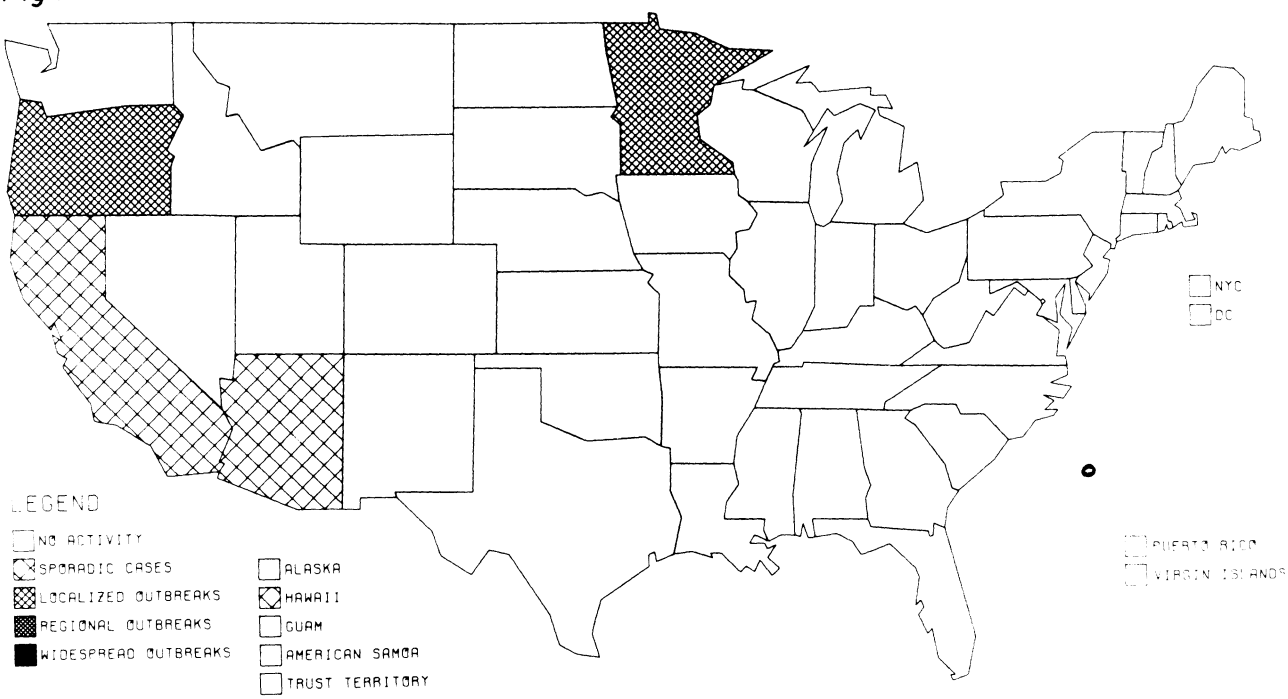


Fig. 8 STATES REPORTING INFLUENZA OUTBREAKS, JANUARY 16-31, 1976

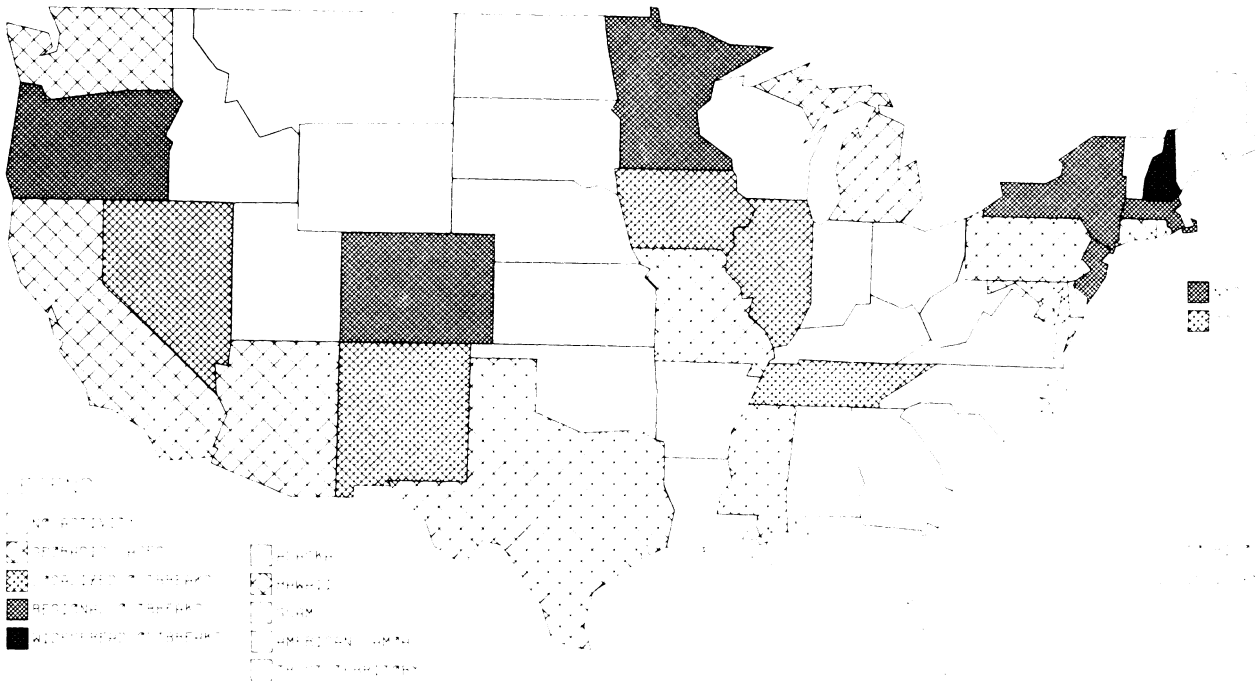


Fig. 9 STATES REPORTING INFLUENZA OUTBREAKS, FEBRUARY 1-14, 1976

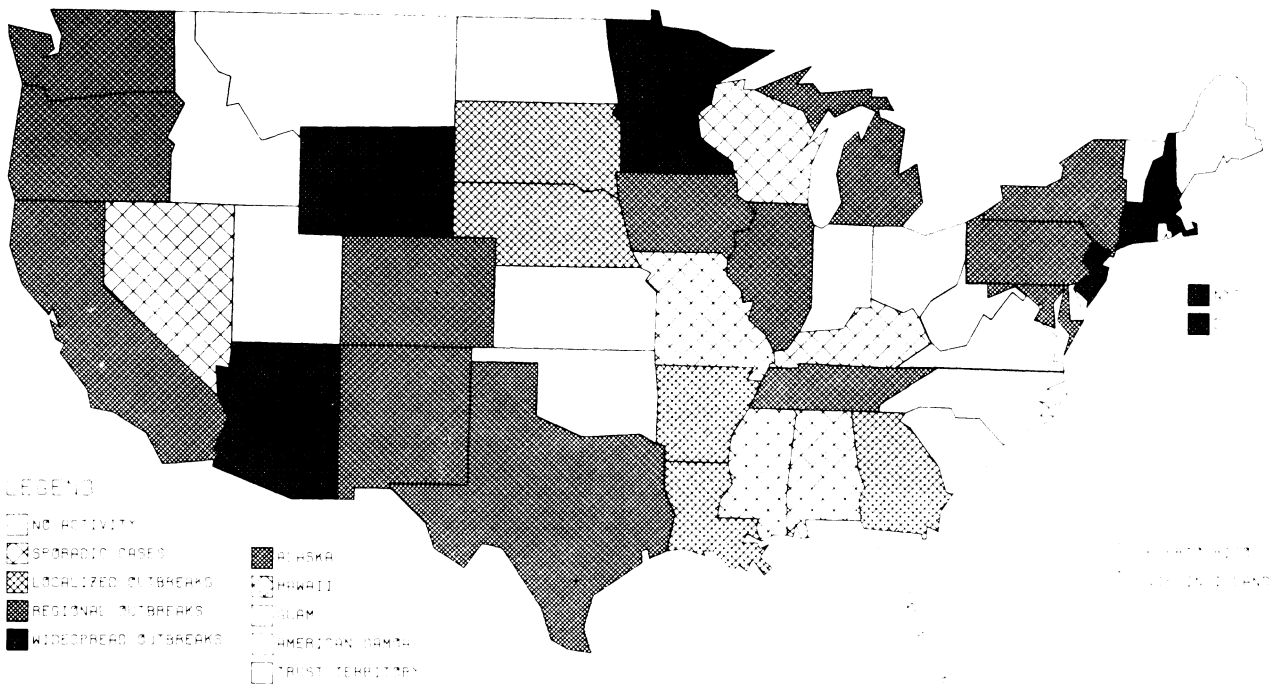


Fig. 10 STATES REPORTING INFLUENZA OUTBREAKS, FEBRUARY 15-29, 1976

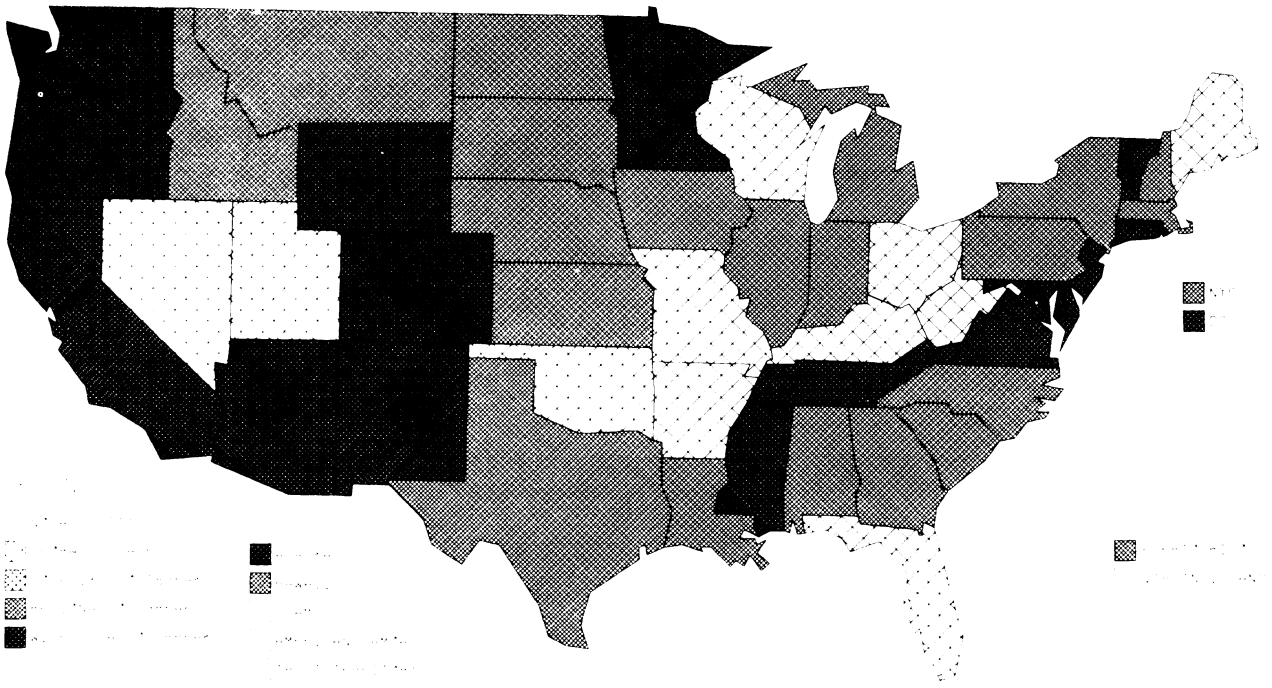


Fig. 11 STATES REPORTING INFLUENZA OUTBREAKS, MARCH 1-15, 1976

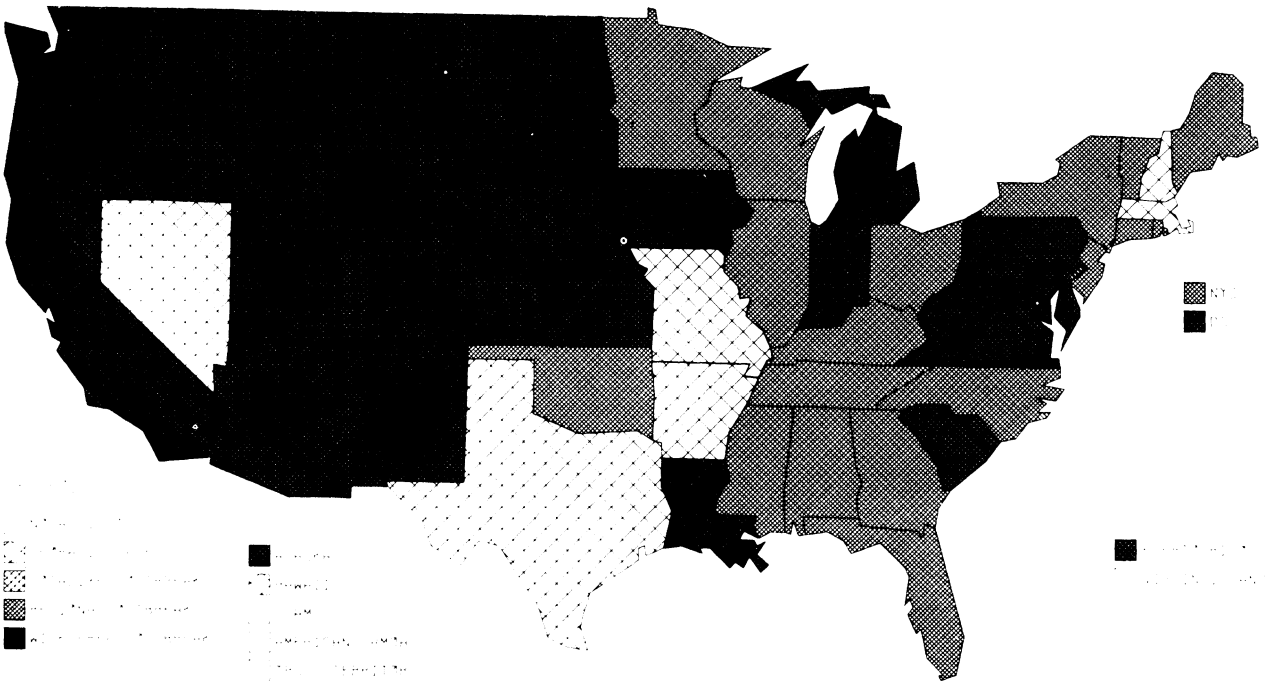


Fig. 12 STATES REPORTING INFLUENZA OUTBREAKS, MARCH 16-31, 1976

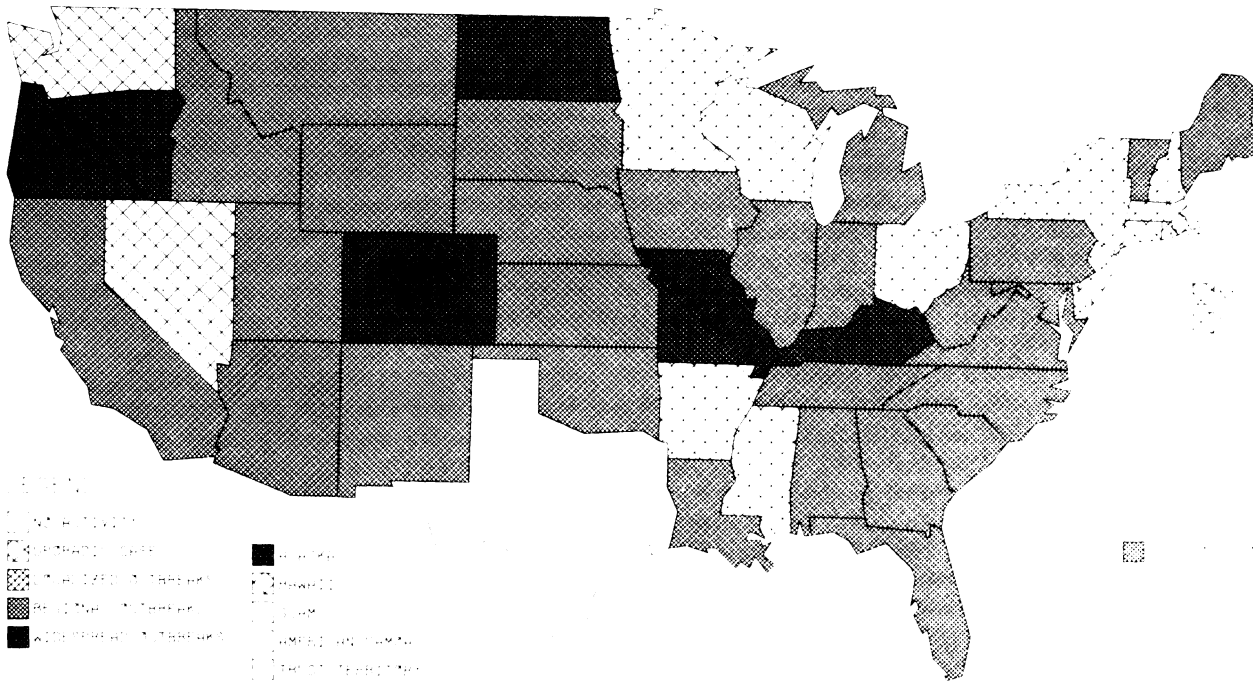
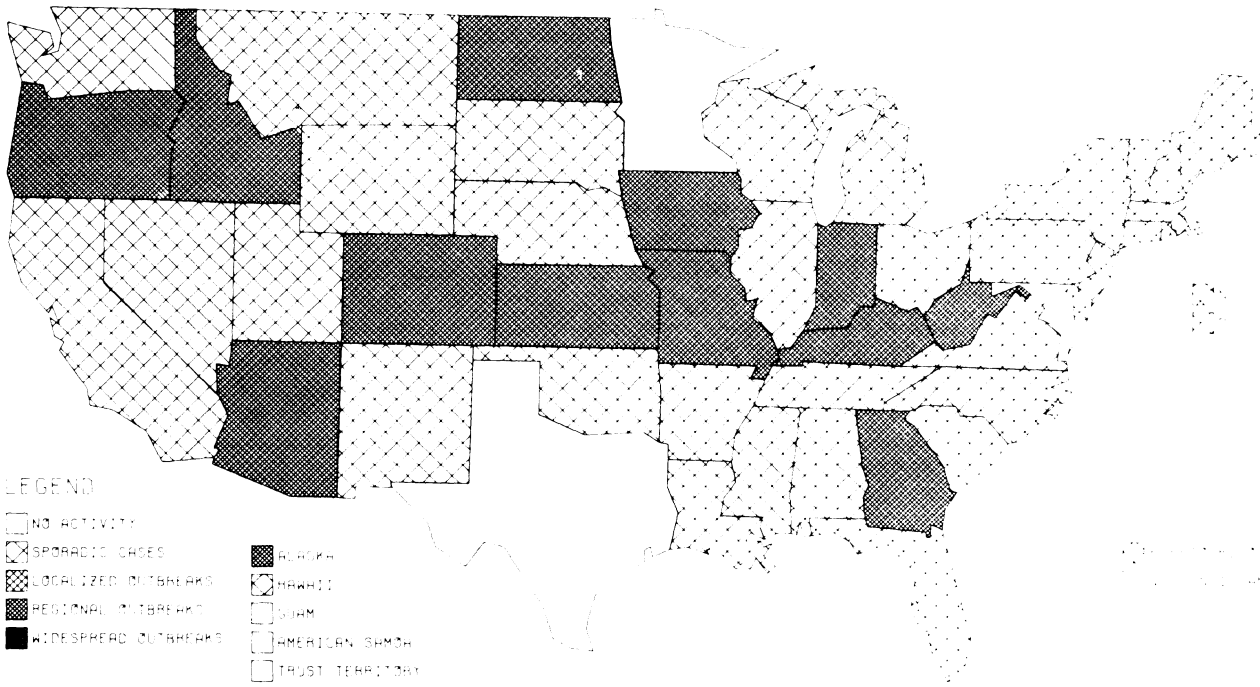


Fig. 13 STATES REPORTING INFLUENZA OUTBREAKS, APRIL 1-15, 1976



IV. SUMMARIES OF EPIDEMIC INVESTIGATIONS AND SPECIAL STUDIES

A. A/Victoria Influenza

1. Kwajalein Atoll, Trust Territory of the Pacific Islands. As previously noted, A/Victoria/3/75 virus was first isolated from sporadic cases in Singapore in April 1975. The first epidemic due to A/Victoria-like virus occurred in September 1975 in Papua, New Guinea. Over 600 deaths due to influenza were attributed to that outbreak, and the case-fatality ratio reportedly was high. In mid-October an outbreak of influenza-like illness affected nearly all of the approximately 800 residents on Christmas Island in the South Pacific. About the same time a similar outbreak of influenza-like illness was reported to be affecting the United States population on Kwajalein Atoll Missile Range in the Trust Territory of the Pacific Islands. Because of the suspicion that this outbreak might be due to A/Victoria influenza, CDC initiated an epidemic investigation.

The outbreak occurred between October 11 and November 1, and approximately 30% of the population was affected (total pop. 3,400). Cases were clustered in families and evenly distributed among adults and children. The illness was typical of influenza, and no severe complications or deaths were noted. Serologic studies indicated that an influenza A virus was the cause of the outbreak. Two A/Victoria/3/75-like strains of influenza virus were isolated from asymptomatic persons who were passing through Hawaii from Kwajalein at the time of the outbreak. (Reported by Ned H. Wiebenga, M.D., State Epidemiologist, and David J. Oblon, M.D., EIS Officer, Field Services Division, Hawaii State Department of Health, Honolulu, Hawaii)

2. A/Victoria Outbreak in Portland Nursing Homes, January 1976. The first outbreak of A/Victoria influenza in the continental United States this season reported to CDC was from Portland, Oregon, where outbreaks of influenza in 2 nursing homes began the first week in January. Since additional information was desired on the source of the virus, the possible effect of the epidemic on the community, the clinical spectrum of disease caused by A/Victoria, and the protection afforded by vaccine, an investigation was undertaken.

The first nursing home cared for 91 patients on 2 floors. The complex also included a retirement home where 143 residents lived on the third floor of the nursing home and in a large adjacent building. The index patient, a nurse's aide who became ill on January 2, had contact in late December with a clinically ill friend from Germany. On the 3 days of her illness the aide worked on the second floor of the nursing home. The outbreak began approximately January 7 on the second floor of the nursing home, ultimately affecting 26 of the 50 patients on that floor. Only 1 of the 41 patients on the first floor of the nursing home became ill, possibly because of quarantine measures instituted shortly after the outbreak was recognized. Illness spread rapidly through the staff and to the adjacent retirement home. The attack rate in the nursing home was 30% (27/91), in the retirement home 31% (45/143), and among the staff 46% (50/109). Of the 153 patients and residents who had been given influenza vaccine (A/Scotland, A/Port Chalmers, and B/Hong Kong) the previous fall, 44 became ill (29%); 23 of 72 (32%) unvaccinated persons became ill. There was 1 death, an 88-year-old woman with severe cardiovascular disease who had received influenza vaccine in the fall of 1975 and reportedly had recovered from an influenzal illness at the time of her death.

The outbreak at the second nursing home was of similar magnitude. The index patient worked in the kitchen for approximately 1 week after onset of an upper respiratory illness. Twenty-seven of 104 patients (26%) and 27 of approximately 100 staff members (27%) became ill. There were 2 influenza-related deaths; the deceased were elderly women with severe heart disease who had received influenza vaccine in November 1975. Nineteen of 74 (26%) vaccinated patients and 6 of 21 (29%) unvaccinated patients became ill.

Overall 176 of 547 (32%) persons from both institutions had influenza-like illness. The attack rates were 28% for vaccinated patients and residents (63/227) and 32% for unvaccinated patients and residents (29/90), a difference which was not statistically significant. Although respiratory illnesses other than influenza may have been occurring in the vaccinated and unvaccinated groups during the outbreaks, an isolation rate of A/Victoria-like virus of 82% (18 of 22 throat washings yielding virus) suggested

that this was unlikely. Four vaccinated ill patients from whom paired sera were collected had 4-fold or greater rises in hemagglutination inhibition antibody titer to A/Victoria from titers of 1:10 found in blood samples taken in the acute phase of illness. The "acute" titers to A/Port Chalmers ranged from 1:40 to 1:160. These data illustrate 1 of the limitations of influenza vaccines--namely, that as new strains of influenza A emerge, the vaccine administered may not provide significant protection against illness.

Clinical illness in this outbreak was typical of influenza. Fever, malaise, headache, myalgia, and respiratory symptoms were prominent. Approximately 2 weeks after the outbreaks at the nursing homes, an increase was noted in visits for influenza-like illness to sentinel reporting physicians in Portland, and the first virus isolation of A/Victoria was made from a patient living in the community. Epidemiologically, the 2 outbreaks at the nursing homes could not be linked, and the index patients at each nursing home could be linked to contact with different individuals with influenza-like illness who resided outside of Portland. (Reported by John A. Googins, M.D., Oregon State Epidemiologist; the Oregon State Health Department Laboratories; and the Virology Division, Bureau of Laboratories, and the Viral Diseases Division, Bureau of Epidemiology, CDC)

3. Influenza A/Victoria at a Ski Club--Nashville, Tennessee. On January 23, 75 persons aged 20 to 36 left Nashville by 2 buses for a ski trip to North Carolina. The following afternoon several tour members had symptoms of influenza, and by the next day it was obvious that an epidemic of influenza-like illness was occurring. The clinical attack rate was high (70%) among those 63 tour group members who completed a questionnaire on the outbreak. Clinical symptoms were those of typical influenza, and the age and sex distribution was similar in ill and not ill individuals. Two of 44 (5%) ill persons had been vaccinated, and 4 of 19 (21%) well persons had been vaccinated. Five tour group members were hospitalized on January 25 as they were returning to Nashville, and chest x-rays showed that 3 of these had diffuse bronchopneumonia. One person in the group became ill the day of departure and coughed frequently on the bus during the travel to North Carolina. A/Victoria-like virus was isolated from 4 ill persons in the tour group. A few isolates of A/Victoria influenza were also obtained from students at Vanderbilt University in Nashville the week before the tour. (Reported by David S. Folland, M.D., Assistant State Epidemiologist, and the Division of Laboratory Services, Department of Public Health, Nashville, Tennessee)

4. A/Victoria Outbreak at a Nursing Home--Pinellas County, Florida. In early March CDC learned of an outbreak of influenza-like illness in residents of a nursing home at St. Petersburg, Florida. Since preliminary data suggested that the illness was unusually severe, with 24 deaths reported among 41 patients who had clinical illness, an investigation was conducted. The outbreak began in the first week of February and continued through the first part of March. Of 124 nursing home residents, 54 (44%) had clinical illness. Twenty-two of the 54 residents (41%) with an influenza-like illness died. The patients had not received influenza vaccine the previous fall. Thirty-one of 67 employees (46%) also reported having an illness compatible with influenza, later determined to be typical influenza. No employees died. Illness in both employees and residents began almost simultaneously.

Several factors may have contributed to the significantly high mortality rate. The patients who became ill were elderly (median age 83) and often bedridden with a severe chronic disabling disease. The prevalence of diabetes and chronic heart disease in both groups was similar. Survivors were more likely to have received antibiotics or cough suppressants than were patients who died and less likely to have been receiving corticosteroids. No isolates of virus were made, but serologic studies indicated that influenza A was the cause of the outbreak. (Reported by Robert M. Lumish, M.D., EIS Officer, Dade County Department of Public Health, Miami and Bureau of Laboratories, Florida State Division of Health, Jacksonville, Florida)

5. A/Victoria Influenza Outbreak at a Community Hospital--Durham, North Carolina. Between February 25 and March 5, 1976, an outbreak of influenza confirmed by isolation of A/Victoria-like viruses occurred in personnel and patients on a medical ward of a community hospital in Durham. A nurse had the first case, with onset occurring on February 25. The first hospital patient became ill on February 27, and by March 1 an

influenza-like illness had developed in 14 of the 30 patients on that ward (46%). A total of 7 of the 24 nursing personnel on this ward also became ill with typical influenza-like illness. On March 2 control measures were instituted which may have been effective in preventing illness from spreading to other sections of the hospital. The control measures were: 1) no new patients were admitted to the ward unless they had clinical influenza, 2) visitors to the ward were restricted, 3) patients were confined to their rooms, 4) all ill patients were placed in respiratory isolation, 5) all ill personnel were instructed to remain at home until well, 6) there was no interchange in nursing staff on this ward with other staff in the hospital, and 7) masks were worn by ill patients if they had to leave the ward, by employees who worked on the floor and left for other parts of the hospital, and by those practicing respiratory isolation procedures. (Reported by Peter D. Rogers, M.D., M.P.H., EIS Officer, Epidemiology Section, and Division of Laboratories, North Carolina Division of Health Services, Raleigh, North Carolina)

6. Influenza Outbreak at an Institution for the Mentally Retarded in Florida. In mid-April an outbreak of febrile upper respiratory illness was noted in mentally retarded patients at an institution in Florida. The prominent symptoms were fever, pharyngitis characterized by erythema and vesicles on the posterior oral pharynx, and occasionally pulmonary rales. Review of clinic and hospital records indicated that this syndrome had developed in approximately 400 of the 680 patients at the center between April 1 and 16. Approximately 100 chest x-rays were taken during this period, and one-third of these indicated pneumonitis. Diagnostic rises in antibody titers to influenza A were found in 4 of 5 paired sera tested, while no rises were found to influenza B, parainfluenza 1 or 3, adenovirus, or mycoplasma. One isolate of A/Victoria/3/75-like virus was made from an ill person. All other throat cultures were negative for bacterial pathogens. This outbreak was unusual because 1) pharyngitis was the prominent symptom associated with the illness, 2) vesicles were noted in many of the patients with pharyngitis, 3) most patients were not acutely ill and remained ambulatory throughout their illness, and 4) the outbreak occurred late in the influenza season. (Reported by Edward W.P. Smith, M.D., Acting State Epidemiologist, and Bureau of Laboratories, State Department of Health and Rehabilitative Services, Jacksonville, Florida)

7. West Coast Airport Surveillance. In early November after reports were received that A/Victoria/3/75-like virus isolations had been made in association with recognized outbreaks of clinical influenza, CDC initiated influenza surveillance at 4 ports of entry into the United States (Honolulu, Anchorage, San Francisco, and Los Angeles). The primary purpose of the program was to determine if incoming travelers might be bringing influenza into the United States. At the airports Immigration Service personnel questioned incoming travelers about respiratory illness, and quarantine officers obtained throat swabs for virus isolation from persons found to have an upper respiratory illness characterized by fever, headache, myalgia, or malaise. Maritime surveillance relied on travelers' voluntary reporting of any influenza-like illness they may have had aboard incoming vessels. State and local health departments provided laboratory support. The program was begun in early November and was terminated the last part of February, a period in which approximately 640,000 passengers passed through immigration at 1 of the 4 airports. A total of 60 throat swabs for virus isolation were obtained from ill persons, and only 1 virus isolation was made. The isolate, resembling A/Tokyo/1/75, was from a traveler from Japan who passed through Honolulu in the first week of January.

Maritime surveillance was carried out in Honolulu, Los Angeles, and San Francisco. Fewer than half of the incoming vessels reported data on influenza-like illness. Influenza-like illnesses on 3 vessels were investigated, 2 passenger ships in Los Angeles and 1 cargo ship in San Francisco. No isolations were made from the 7 throat swabs taken from passengers and crew members who had suspected influenza-like illness aboard these vessels. (Reported by the Hawaii State Department of Health Laboratory and the Quarantine Division and the Viral Diseases Division, Bureau of Epidemiology, CDC)

8. Reports of Respiratory Illness in Vaccinated and Unvaccinated Groups. In November 1975 CDC studied serum HI antibody response to commercial influenza vaccine containing A/Port Chalmers, A/Scotland, and B/Hong Kong in 160 adult subjects in Atlanta.

Only 3% of this group had a preexisting HI titer to A/Victoria of ≥1:40, but after vaccination 35% had a titer of ≥1:40 to A/Victoria, and approximately 80% had a titer of ≥1:40 to the antigens contained in the vaccine (A/Port Chalmers and A/Scotland). These data suggested that the vaccine being used might be partially protective against A/Victoria influenza but by no means was an ideal vaccine against that virus.

In the influenza season CDC received several reports of respiratory illness rates in vaccinated and unvaccinated groups. Retrospective evaluations of vaccine efficacy have many problems and pitfalls because of uncontrollable selection bias and the occurrence of illnesses mimicking influenza in vaccinated and unvaccinated groups. The following reports should be interpreted cautiously with these problems kept in mind.

a. United States Air Force. A study of illness in vaccinated and unvaccinated personnel at a U.S. Air Force Base near Las Vegas, Nevada, was conducted when an outbreak of A/Victoria influenza was detected in late January. Of 55 vaccinated servicemen, 10 had clinical illness; of 15 unvaccinated persons, 11 were ill. This difference is statistically significant ($p<.001$, $x^2=14.5$), suggesting that the vaccine was partially protective. (Reported by Epidemiology Division, School of Aerospace and Medicine, Brooks Air Force Base, Texas)

b. Seattle-King County, Washington. In October 1975 free influenza vaccine was made available to employees in a school district of suburban Seattle, an area where significant influenza activity occurred due to A/Victoria in the winter and spring of 1976. In April, after the influenza epidemic, a questionnaire was administered to all employees. Of those 75 respondents who had had influenza vaccine the previous fall, 47% (35/75) had an illness compatible with influenza. Of those 542 who did not receive influenza vaccine, 241 (44%) had symptoms compatible with influenza ($p>.05$). Of those individuals who were ill and had received vaccine, an average of 2.80 days' absence was recorded, whereas for those unvaccinated individuals who were ill, an average of 2.78 days' absence was recorded. (Reported by Max Bader, M.D., M.P.H., Epidemiologist, Seattle-King County Department of Public Health, Seattle, Washington)

c. Bank Employees--Chicago, Illinois. A large private bank in the Chicago area through its medical department offers free influenza vaccine to all its employees each fall. In 1976 a follow-up study of absenteeism due to influenza-like symptoms among the vaccinees and the nonvaccinees was conducted. Of the 6,354 employees, 2,275 received vaccine. For this study 225 vaccinated employees and 225 unvaccinated employees were randomly selected, and personnel records were reviewed for absenteeism due to respiratory disease during the past year. All employees who had been absent for more than 10 days because of illness were eliminated from the study. During the year there were 110 days of absence due to influenza-like illness among the vaccinated group, compared with 115 days of absence due to influenza-like illness among the unvaccinated group. This difference was not statistically significant. (Reported by Charles E. Thompson, M.D., Chicago, Illinois)

B. Investigations Related to A/New Jersey (Swine Influenza) Virus

1. Fort Dix, New Jersey. In the latter half of January and the early part of February 1976, an influenza epidemic occurred among Army recruits and military personnel at a large Army post at Fort Dix, New Jersey. Throat swabs from clinically ill recruits with respiratory illness were obtained by Army hospital personnel and forwarded to the New Jersey State Department of Health for attempted virus isolation. Among the first virus isolates from Fort Dix were several viruses that later were shown to be A/Victoria-like and 2 viruses that were not inhibited by antisera to current influenza A and B strains. The latter 2 isolates were received at CDC on February 4 and by the following week were identified as influenza A viruses with hemagglutinin and neuraminidase antigens similar to swine influenza virus (11). On February 14 representatives of CDC, New Jersey State Department of Health, United States Army, National Institute of Allergy and Infectious Disease, and Bureau of Biologics met at CDC to review the laboratory findings, to evaluate the epidemiologic information and significance of the findings, and to plan for special studies.

Data from the Army's epidemiologic investigation of the Fort Dix outbreak indicated that the virus probably was introduced onto the post in the early part of January (5) and that the outbreak of swine influenza-like illness occurred coincident with a larger outbreak of A/Victoria influenza (14). A total of 5 isolates of swine influenza

virus were made, including 1 from a patient who died of influenza pneumonia, and 8 other cases were confirmed by serologic studies (4). A comparison of the 10 nonfatal cases of swine influenza with a similar number of A/Victoria influenza cases in military recruits at Fort Dix indicated that the illnesses were clinically similar. A serologic survey of military personnel at Fort Dix conducted by the Army in the latter part of February showed that the prevalence rate of HI antibody titers $\geq$10 to swine influenza virus was 28% in training companies in which confirmed cases of swine influenza had occurred. The prevalence rate was 8% among those soldiers in companies in which no confirmed cases had occurred, a prevalence rate not significantly different from that for the general population of the United States in this age group (Table 8). It was estimated that several hundred cases of swine influenza occurred in military recruits at Fort Dix in this outbreak (5).

The United States Army also conducted a serosurvey of dependents and retirees at Fort Dix, New Jersey, and the antibody prevalence rate (HI titer to swine influenza) by age was the same as that found in other general population groups (5). Coincident with the investigations at Fort Dix, the New Jersey State Department of Health instituted intensive surveillance in the counties surrounding Fort Dix. As part of the surveillance network, nearly 100 isolates of influenza A virus were obtained from individuals with influenza-like illness. All of those isolates were characterized as A/Victoria-like. Serologic studies on blood specimens from civilians in New Jersey showed no indication of virus spread to the civilian population. (Reported by Colonel Philip Russell, Epidemiology Department, Walter Reed Army Hospital; Martin Goldfield, M.D., New Jersey State Department of Health; and the Virology Division, Bureau of Laboratories, CDC)

2. Sheboygan, Wisconsin. Approximately 3 weeks before the isolation of A/New Jersey (HswlN1) virus from Fort Dix, CDC in cooperation with the Wisconsin State Department of Health and Social Services made a serologic diagnosis of swine influenza in an 8-year-old boy from rural Sheboygan County, Wisconsin. In February CDC dispatched 2 medical epidemiologists to Sheboygan, Wisconsin, to gather epidemiologic information on that case. Over a 2-day period the patient and his family were interviewed, and blood specimens were obtained from the family members and families living in the area, from school contacts of the patient, and from other school and community controls. Approximately 250 serologic specimens and 5 throat swabs were obtained and brought back to CDC for testing.

The patient's illness in October 1975 had been a febrile upper respiratory infection. Coincident with his illness, an outbreak of respiratory disease occurred among swine on the farm where the patient lived. No similar illness occurred in any family member, and a review of school absenteeism and hospital emergency room visits revealed no indication of any significant influenza-like activity between October and February. Five of 7 household members of the index patient had HI antibody to swine influenza virus, and none had serologic evidence of A/Victoria infection. The seropositive individuals included the patient's father, aged 33, and 4 siblings, aged 3, 4, 7, and 9. None of 24 classmates of the index patient who were exposed in class during the early part of the patient's illness had antibody to swine virus. The antibody prevalence rate by age in the general population was similar to that found in other serosurveys (Table 8). Subsequent investigation by the University of Wisconsin School of Veterinary Medicine indicated that the swine at the farm where the patient lived had antibody to swine influenza virus, while 2 swine herds nearby did not have antibody. It was concluded that the patient's illness resulted from exposure to swine which were ill with influenza at that time and that the other members in the family had asymptomatic infection either directly related to exposure to the ill swine or from intrafamilial spread of viruses. There was no evidence that person-to-person transmission of this virus occurred outside of the family (15). (Reported by the Wisconsin State Department of Health and Social Services, the University of Wisconsin School of Veterinary Medicine, and the Virology Division, Bureau of Laboratories, and the Viral Diseases Division, Bureau of Epidemiology, CDC)

3. Fort Dix Recruit Family Study in Fayetteville, Pennsylvania. Soon after the outbreak of swine influenza at Fort Dix, the United States Army provided CDC with a list of 22 Fort Dix recruits, all of whom had a history of swine contact before

induction, had HI titer to swine antibody, and had first come to Fort Dix in early January. With the cooperation of state and local health departments, histories and blood specimens were obtained from 171 family members and close contacts of these recruits. Of these 171 persons, 19 had HI antibody to swine influenza, and 14 of these were in age groups in which antibody is commonly found. However, of the other 5 younger seropositive persons, 4 were in 1 recruit's family who lived in Fayetteville, Pennsylvania.

An epidemiologic investigation was undertaken of this family and their community. Family members were interviewed, and blood specimens were obtained from other close contacts of the recruit, community controls, and individuals with a history of recent influenza-like illness. Most of the family members of the recruit gave a history of having influenza-like illness in February, at a time when A/Victoria influenza was present and confirmed; none had a history of exposure to swine. No relationship was found between the illness in the family and the recruit, who had been at Fort Dix since early January. Furthermore, most of the family members had elevated HI titers to A/Victoria, including 2 of the 4 who also had antibody to swine influenza virus. The prevalence rate of HI antibody to A/New Jersey among the 200 serologic samples obtained from area residents was no different from that found in other serosurveys (Table 8). None of 60 individuals under age 15, including 41 classmates of 2 of the seropositive recruit's siblings, had antibody to swine influenza virus. Five of 38 individuals (13%) between ages 16 and 29 had antibody to swine influenza virus; 4 of these persons gave a history of having had close contact with swine, and the other person was a teacher who frequently visited the recruit's household. Although inconclusive, the evidence suggests that the 4 seropositive individuals in this family may have been infected with swine influenza virus which was transmitted person to person. Subsequently, 55 serum specimens from swine in the county were tested for the presence of HI antibody to A/New Jersey. Titers $\geq$40 were found in 18 (33%) of the specimens, and several titers $\geq$1,280 were seen, suggesting that swine influenza had occurred recently in the area. (Reported by Grayson B. Miller, Jr., M.D., and Ernest J. Witte, V.M.D., M.P.H., Pennsylvania State Department of Health; Field Services Division, Bureau of Epidemiology; and Virology Division, Bureau of Laboratories, CDC)

4. Pneumonia Cases--Charlottesville, Virginia. On February 27 a report was received from Charlottesville, Virginia, of antibody rises to swine influenza virus in 2 patients who had been hospitalized in December. As requested, CDC immediately dispatched 2 medical epidemiologists to Charlottesville to assist in the study of the circumstances surrounding these reported cases. The first patient was a 40-year-old woman who was hospitalized on December 5 with typical pneumococcal pneumonia. Before her illness she had had close contact with swine at home. None of her 5 children and none of 6 other close contacts had HI antibody to swine influenza virus. The second patient was a 55-year-old man from New York City who was hospitalized in Charlottesville, December 27, with severe viral pneumonia. He had no history of contact with pigs and had been in the Charlottesville area for 1 week before his illness. Before that he had been living in New York City. None of 5 close contacts under age 55 had antibody to that virus, and 1 person over age 55 had antibody. Further investigation indicated that an outbreak of A/Victoria influenza had occurred there in late January and persisted during February. Four isolates of A/Victoria were obtained from individuals ill at the time of the February investigation (16). Precise interpretation of the serologic data for these patients is difficult without virus isolation, particularly when other influenza strains are present which might cause heterotypic antibody rises to HswlN1 viruses in persons of their age group (17). (Reported by the Virginia Department of Health; the Department of Medicine, University of Virginia, Charlottesville, Virginia; the Field Services Division and Viral Diseases Division, Bureau of Epidemiology, CDC; and the Virology Division, Bureau of Laboratories, CDC)

5. Investigation of Seropositive Naval Personnel, Norfolk, Virginia. In the early part of 1976 the U. S. Navy investigated several outbreaks of influenza-like illness aboard ships in the North Atlantic. In 1 of these investigations paired blood samples from a 36-year-old man showed an HI titer rise to A/Mayo Clinic (HswlN1) of from 1:10 to 1:80. Subsequent investigation indicated that 3 family members and 6 work associates of the patient were seronegative for A/Mayo Clinic. However, 9 of 11 other

men aboard ship with whom the patient had frequent contact had antibody to A/Mayo Clinic. Among this group of 17 men aboard ship, all 6 under the age of 21 were seronegative, but only 2 of 11 men over age 28 were seronegative.

Later a random serosurvey of personnel aboard the vessel was conducted, and 98 additional blood specimens were obtained. There was a striking age difference between those with and without antibody to A/Mayo Clinic in this group. Six of 57 men aged 19-29 had an antibody titer to A/Mayo Clinic of 1:10; none had higher titers. However, 31 of 41 men aged 30-44 had a titer of 1:10, and 15 had a titer of $\geq$1:20. The serologic tests also indicated that many of these persons had a recent H3N2 infection. The evidence suggested that the Hswl antibody in the older individuals resulted from either a crossing of antibody to H2 influenza A viruses or prior immunization with influenza vaccine containing swine influenza virus (13, 17). (Reported by Naval Environmental and Preventive Medicine Unit #2, Norfolk, Virginia; and James M. Veazey, Jr., Fellow, Infectious Diseases and Epidemiology, University of Virginia Hospital, and formerly an EIS Officer located at the State Department of Health, Richmond, Virginia)

V. WORLDWIDE INFLUENZA SURVEILLANCE--THE A/VICTORIA PANDEMIC

Table 10 summarizes worldwide influenza activity for the period July 1975-June 1976. There was relatively little influenza A reported in the summer and fall, while influenza B caused scattered cases and localized outbreaks throughout the Pacific region and Far East. In the period from April through August 1975 and before the epidemic of influenza in Papua, New Guinea, in September 1975, sporadic cases due to A/Victoria/75 occurred in Hong Kong, Singapore, Philippines, Taiwan, Australia, and Thailand. As the year drew to a close A/Victoria had spread across the Pacific Islands (Fiji, Kwajalein, and Hawaii) to South America, where it was isolated in Argentina and Chile. The virus also appeared in Europe late in the year; it was isolated from specimens collected during a mid-December outbreak at a military camp in Finland and also from a patient in England who became ill in late December.

Table 10
Influenza in the World
July 1975-June 1976*

Continent/Country	Time of Occurrence	Virus	Remarks
AFRICA			
Algeria	1976	A/England	6 isolates reported
Central African Republic	Aug-Sept 1975	A/Port Chalmers	5% attack rate in Bangui
Egypt	1976	A/England	11 isolates reported
Kenya	Feb 1976	A/Port Chalmers, A/Victoria	3 A/PC and 8 A/Vic isolates reported
Morocco	1976	A/Victoria, A/England	5 A/Eng and 1 A/Vic isolates reported
South Africa	Dec 1975-Jan 1976	A	Sporadic outbreak in Johannesburg Community outbreak in Transvaal
	May-Jun 1976	A/Victoria	Epidemic influenza
Senegal	1976	A/Victoria, A/Port Chalmers	14 isolates of A/Victoria and 8 isolates of A/Port Chalmers
Tunisia	1976	A/Victoria	
ASIA			
Hong Kong	Jul-Aug 1975	B/Hong Kong	Sporadic cases initially resulting in generalized outbreak
	Nov 1975-Jun 1976	A/Victoria	Sporadic cases during entire period except for epidemic April-May 1976
India	1976	A/England	
Japan	Nov 1975	B	Outbreak in school
	Nov-Dec 1975	A/Tokyo	Outbreak in school
	1976	A/Tokyo, A/Victoria	
Korea, Republic of	Dec 1975-Jan 1976	A/Victoria, A/England	Scattered outbreaks (single isolate of A/Eng, most isolates A/Vic)

*Summarized from Weekly Epidemiological Record 50(33,34,36,38,41-43,45,48,49,51), 1975; 51(1-5,7-17,19,20,22-29,31,34), 1976, with annotations by the WHO Collaborating Center for Influenza, Atlanta, Georgia.

Table 10 (Continued)

Continent/Country	Time of Occurrence	Virus	Remarks
Malaysia	Nov-Dec 1975	A	Outbreak in Kuala Lumpur
	May-Jun 1975	A	Small outbreaks
Singapore	Nov 1975	A/Victoria	Single isolate reported
	Apr 1976	A/Victoria	Epidemic influenza
	1976	A/England	
Taiwan, Republic of China	Jun-Aug 1975	A/Victoria, A/Port Chalmers	Sporadic cases and localized outbreaks
	Dec 1975-Mar 1976	B/Hong Kong	Sporadic cases
	Mar-May 1976	A/Victoria	Sporadic cases
Thailand	Jul-Sept 1975	A/Victoria	Sporadic cases and localized outbreaks in Bangkok
	Jun 1976	A/Victoria	Increase in sporadic cases
Sri Lanke	1975	A/England, A/Port Chalmers	1 isolate of A/Eng and 10 isolates of A/PC reported
AUSTRALIA (Including South Pacific)			
Australia	Jun-Aug 1975	A/Port Chalmers	Sporadic cases
	Aug 1975	B/Hong Kong	Outbreak in Queensland
	Apr-Jun 1976	A/Victoria	Sporadic cases initially leading to epidemic influenza
Christmas Island	Sept 1976		High attack rate of influenza-like illness
Fiji	Feb-Mar 1976	A/Victoria	Epidemic involving all age groups
Kwajalein Atoll	Oct-Nov 1975	A/Victoria	Epidemic with 30% attack rate
New Guinea	Sept 1975	A/Victoria	Outbreak with high mortality
New Zealand	Jul-Sept 1975	B, A/Port Chalmers	Outbreaks with high attack rates in schools, most of isolates B virus
	Feb-Jun 1976	A/Victoria	Sporadic cases with epidemics peaking in March and June

Table 10 (Continued)

Continent/Country	Time of Occurrence	Virus	Remarks
Philippines	Jun-Aug 1975	A/Victoria	Sporadic cases
	Jan-Apr 1976	A/Victoria, A/England	Sporadic cases and localized outbreaks; most isolates A/Victoria
EUROPE (Including Middle East)			
Austria	Feb-Mar 1976	A/Victoria, A/England	Epidemic influenza--6 isolates of A/Vic and 1 A/Eng reported
Belgium	Jan-Feb 1976	A/Victoria, A/England	Epidemic influenza with increased mortality in elderly; most isolates A/Victoria
Bulgaria	Feb 1976	A, B	Localized outbreaks
Czechoslovakia	Jan-Mar 1976	A/Victoria	Epidemic influenza
Denmark	Feb-Mar 1976	A/Victoria	Epidemic influenza
Finland	Dec 1975-Jan 1976	A/Victoria	Epidemic widespread
France	Jan-Apr 1976	A/Victoria, A/England, A/Tokyo, B/Hong Kong	Epidemic influenza A with most isolates A/Victoria; sporadic cases of influenza B
Germany Democratic Republic	Jan-Mar 1976	A, B	Epidemic influenza A
Germany Federal Republic	Feb-Mar 1976	A/Victoria, A/England, B/Hong Kong	Epidemic influenza A, most isolates A/Victoria
Greece	1976	A/England	
Hungary	Jan-Mar 1976	A/Victoria	Localized outbreaks
Iceland	Feb 1976		Sporadic cases
Italy	Feb-Mar 1976	A/Victoria	Epidemic influenza
Israel	Jan-Mar 1976	A/Victoria, A/England	Sporadic cases and localized outbreaks

Table 10 (Continued)

Continent/Country	Time of Occurrence	Virus	Remarks
Netherlands	Feb-Mar 1976	A/Victoria, A/England	Epidemic influenza
Norway	Feb-Mar 1976	A/Victoria	Epidemic influenza
Poland	Feb-Apr 1976	A/Port Chalmers	Scattered epidemics
Portugal	1976	A/Victoria	
Romania	Jan-Feb 1976	A/Victoria	Widespread outbreaks
Spain	Jan-Mar 1976	A/Victoria, B/Hong Kong	Localized outbreaks
Sweden	Feb-Mar 1976	A/Victoria, B	Epidemic influenza
Switzerland	Feb-Mar 1976	A/Victoria, B/Hong Kong	Epidemic influenza
United Kingdom	Nov 1975-Mar 1976	A/Victoria, A/England, B/Hong Kong	Widespread epidemics peaking in late February; total of 200 isolates of A (150 of A/Vic and 50 of A/Eng)
USSR	Nov 1975	A/Victoria, B	Localized outbreaks with low attack rates
	Feb 1976	A	
Yugoslavia	Feb-Mar 1976	A/Victoria	Scattered outbreaks
NORTH AMERICA (Including Caribbean)			
Canada	Nov 1975-Feb 1976	B	School outbreaks in Western Provinces spreading eastward
	Jan-Apr 1976	A/Victoria	Widespread epidemics of influenza
Caribbean Islands	Jan-Mar 1976	A/England	Hospital outbreak and scattered cases in Jamaica
	Jan-Mar 1976	A/Victoria	Outbreaks in Trinidad, Tobago, St. Lucia, and Barbados. Isolates reported from Antigua, Dominica, Puerto Rico, and Santo Domingo
	Jan-Mar 1976	A/England, A/Victoria	Single isolate of each virus reported from Curacao

Table 10 (Continued)

Continent/Country	Time of Occurrence	Virus	Remarks
Caribbean Islands (Cont'd)	Jan-Mar 1976	B/Hong Kong	Single isolate reported from Trinidad
	Apr 1976	A	Martinique
Guatemala	Feb 1976	A/Port Chalmers	Outbreaks following February earthquake
Mexico	Mar 1976	A/Victoria	Outbreak of influenza in Mexico City
United States	Nov-Dec 1975	A/Victoria, A/Tokyo, B/Hong Kong	Outbreaks in schools in Hawaii, primarily A/Victoria
	Jan-Mar 1976	A/Victoria B/Hong Kong A/New Jersey (Hswl)	Widespread epidemics Sporadic cases Outbreak on army post
SOUTH AMERICA			
Argentina	Sep 1975	A/Victoria	Sporadic cases
	May-Jun 1976	A/Victoria	Epidemic influenza
Brazil	Apr 1976	A/Victoria, A/Port Chalmers, B/Hong Kong	Scattered outbreaks, most of isolates A/ Vic, 1 isolate B
Colombia	1976	A/Victoria	3 isolates reported
Chile	Nov 1975	A/Victoria	
French Guiana	Apr-May 1976	A	Epidemic influenza
Uruguay	Jul 1975	A/Victoria, B/Hong Kong	Sporadic cases
	Apr-May 1976	A/Victoria	Increased sporadic cases
Venezuela	1976	A/Victoria	6 isolates reported

Beginning in January 1976 outbreaks of A/Victoria influenza occurred throughout the United States and Europe. The epidemics which followed in the United States and in many countries of Europe were the most severe since the 1968-69 Hong Kong pandemic. In the spring and summer of 1976, as epidemic A/Victoria influenza was ending in the northern hemisphere, it caused severe widespread outbreaks in many additional countries in South America. Finally, it reappeared in epidemic form in that part of the world where it was first recognized.

Although A/Victoria was certainly the predominant strain of influenza for this season, 3 other related strains were also isolated. A/Port Chalmers/1/73-like strains, which had been prevalent throughout the world for the previous 2 years, were reported from several countries and were the only influenza A isolates reported from the Central African Republic, Poland, and Guatemala. In addition, in both England and Tokyo, antigenically distinct strains of influenza A appeared coincidentally with A/Victoria/3/75-like viruses. The early A influenza activity in England was due primarily to A/England/864/75, which was subsequently isolated in several countries throughout the world, especially in Europe and North Africa. Notably, it was the only influenza A virus isolated in Algeria, Egypt, India (where isolates were obtained before the prototype strain), Greece, and Jamaica. In Japan the virus designated A/Tokyo/1/75 was especially prominent during the first influenza A epidemics in that country but subsequently exhibited very limited spread beyond Japan.

Influenza B was reported from countries throughout the world, and widespread outbreaks due to influenza B were reported from Western Canada and the United Kingdom.

VI. METHOD FOR DIAGNOSING INFLUENZA OUTBREAKS

Two prinicpal procedures are available to establish the occurrence of influenza: 1) isolation of the virus, and 2) a rise in titer of influenza antibody between serum specimens collected in the acute and convalescent phases of illness.

As the public generally believes that all febrile upper respiratory disease is the "flu," laboratory confirmation of influenza is important to document the true cause of influenzal illness. The diagnosis of influenza initially must be made either serologically or by virus isolation. Facilities for such diagnosis are available in almost every state and large city, and private practitioners are encouraged to use these facilities if they suspect an outbreak of influenza. Only when a virus has been isolated during an outbreak can the type of influenza virus causing the outbreak and its relationship to previous types be established with certainty. Even though multiple virus isolates obtained from the same epidemic will undoubtedly confirm that the epidemic is caused by a specific influenza virus, virus isolation is not always a practical means of laboratory documentation of influenza. Theoretically it should be possible to isolate and identify an influenza virus in as little as 48 hours, but in practice it may take a week or more before an isolate is obtained and identified because of the need for host tissue in which to grow virus and the necessity to undertake a blind passage of the specimen before a negative result is accepted. It is much easier to demonstrate a diagnostic rise in antibody than to isolate a virus from a single infected person.

Serologic diagnosis of influenza infection is made most readily by the HI or by the CF tests. Although CF or HI tests can be run within a 24-hour period, there is a considerable time lag in making a serologic diagnosis, since collection of acute- and convalescent-phase blood samples from the same individual takes 2 to 3 weeks. To minimize this time lag, serodiagnosis of an epidemic may be possible by comparing groups of acute- and convalescent-phase samples taken from different persons during the epidemic (18-20).

By the time an epidemic has been confirmed, there are usually some individuals in the community who are already convalescent from the illness, while others are in the early acute stages. At a specific time, 10 or more acute-phase specimens and 10 or more convalescent-phase specimens usually can be collected easily. Since influenza antibody levels vary according to a person's age and influenza vaccination status, the acute and convalescent groups should be made up of equivalent age groups and preferably should consist of unvaccinated individuals.

The same serologic test (CF or HI) is performed in a single run on each of the blood samples in each group. A geometric mean titer (GMT) is then calculated for the acute and the convalescent groups. Although 1 individual's 4-fold rise in titer constitutes a diagnostic rise, a 4-fold rise in GMT is clearly too stringent a criterion for documenting an epidemic. For example, if 6 of 10 persons involved in the same outbreak had exactly a 4-fold rise in influenza antibody and the other 4 had no rise, one would not hesitate to make the diagnosis of an influenza outbreak, even though the GMT rise for the group of 10 was less than 4-fold.

The statistical significance of a comparison between acute and convalescent GMTs must be made by using log titers because of the geometric increase in titer values. A conventional Student's t test is then performed on the log titers.

The comparison of blood samples taken at the acute and convalescent phases can apply to most epidemic illnesses for which a diagnosis can be made serologically. In instances where acute-phase specimens are not available, one may be tempted to compare persons who did not become ill with persons who are convalescent. It is possible, however, that persons who did not become ill may have had preexisting high titers, and they may not have become ill because they were already immune to the agent. In this event the "not ill" group will have a high GMT and will not differ significantly from the convalescents.

VII. GUIDELINES FOR THE CONTROL OF NOSOCOMIAL INFLUENZA

Several characteristics of influenza infection make control of nosocomial influenza difficult. Influenza virus is commonly shed for several days before the onset of clinical illness and continues to be shed for 3 or more days after symptoms begin (21). Thus an individual with influenza may be infectious to others for a period of 5 or more days, including several days during which the infection is not recognized. Furthermore, in an influenza epidemic a sizable number of individuals infected with influenza virus, estimated to be as high as 30%, never have symptoms (22). Because of viral shedding before illness, asymptomatic infection, and high transmissibility in close populations, the measures commonly employed to limit nosocomial spread of other infectious diseases generally have not proven efficacious when applied to influenza. Thus, the Public Health Service has not issued formal recommendations for controlling nosocomial influenza. Many hospitalized patients, however, fall into the high-risk category for influenza, and it is prudent to attempt to protect them against hospital-acquired influenza. The following guidelines, which are based partly on measures of proven benefit and partly on theoretical considerations, are suggested.

In approaching the problem of nosocomial influenza, 3 possible control measures--immunization, chemoprophylaxis, and isolation--must be considered in relation to 3 possible sources of infection: hospital staff, visitors, and patients.

Under ideal circumstances persons in the high-risk groups would receive influenza vaccine in the fall before the beginning of the influenza season. Except in the case of vaccine against a potentially pandemic strain of influenza (e.g., swine influenza), vaccine generally has not been recommended for other individuals. However, if sufficient vaccine is available after the high-risk population has been vaccinated, then immunization of hospital staff may be considered, since staff members are likely to play a significant role in introducing and spreading nosocomial influenza.

Since 2 weeks may be required for protective levels of antibody to develop after vaccination (23), vaccinations administered during a confirmed nosocomial influenza outbreak often will be too late to be effective. However, vaccinations may be worthwhile if they are given to susceptible patients and staff as soon as the possibility of nosocomial influenza is recognized (i.e., at the first indication of influenza in the community).

Amantadine hydrochloride has been shown in several studies to be of prophylactic value for both H2N2 (Asian) strains and H3N2 (Hong Kong) strains of influenza (24, 25), and its value in preventing nosocomial influenza has been suggested (26). According to

R.R. Grunert, M.D., E.I. du Pont de Nemours and Company, Newark, Delaware, in vitro and animal studies have also suggested that it would be equally efficacious against HswlN1 (swine) strains. The Food and Drug Administration has recently broadened the indications for the prophylactic use of amantadine hydrochloride to include recent human strains of influenza (H3N2) as well as swine influenza.

Consideration may be given to the administration of amantadine hydrochloride to patients (especially those in the high-risk group and those who have not received vaccine) and staff both before and at the time of the first indication of nosocomial influenza.

There are several drawbacks to chemoprophylaxis with this drug, however. These include the expense of the drug, the side effects (especially in the elderly), and the length of time required for administration. To be effective prophylactically the drug must be given during the entire period of epidemic influenza, because early withdrawal has often led to influenza in persons who formerly were receiving the drug (27). Since amantadine hydrochloride does not interfere with production of antibody to killed virus vaccine, consideration may be given to initiating amantadine hydrochloride prophylaxis at the same time a person is vaccinated, then terminating the drug 2 weeks later.

Quarantine and isolation measures may also be of value in preventing introduction and spread of influenza in the hospital, as was suggested by 2 reports summarized above (Section IV, A, 2 and 5). In a confirmed community influenza outbreak hospital staff members should leave work as soon as they have the first sign of a respiratory illness or other indication of influenza (fever, myalgia, malaise, or headache) and not return until they are recovered. When nosocomial influenza is suspected, complete segregation of staff by work area may be valuable if visitors are also restricted.

Patients with confirmed or suspected influenza may be segregated in 1 area of the hospital or in 1 ward when possible. If possible, patients with suspected influenza requiring admission to the hospital should be admitted to 1 area or ward. During a nosocomial influenza outbreak all patients should remain in their rooms to a reasonable extent. Elective admissions to the hospital probably do not need to be restricted unless there is a shortage of beds, actual or anticipated.

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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

INFLUENZA VACCINE — PRELIMINARY STATEMENT*

INTRODUCTION

Influenza occurs in the United States every year, but there is great variation in its incidence and geographic distribution. Periodically, influenza becomes epidemic, apparently when the antigens of prevalent influenza viruses have changed enough to render the population susceptible. More epidemics are caused by influenza A viruses than by influenza B viruses, and influenza A epidemics are generally more severe. Furthermore, only influenza A viruses undergo abrupt antigen changes which result in worldwide epidemics, or pandemics.

Thousands have died of influenza in epidemics in the United States in the past 20 years. In the 1957-1958 influenza season, when a new influenza A virus (Asian strain) appeared, nearly 70,000 deaths occurred in this country alone. In 1968-1969, when the Hong Kong variant caused widespread epidemics in the United States, there were an estimated 33,000 excess deaths. In the intervening years, whenever influenza A epidemics involved most of the country, 10,000 to 20,000 deaths resulted.

Efforts to prevent or control influenza in the United States have generally been aimed at protecting those at greatest risk of having serious illness or dying. This has involved emphasizing the need for annual vaccination of high-risk groups. In interpandemic periods, general vaccination of the entire population has not been a reasonable public health objective for several reasons, including the limited duration of protection from influenza vaccines, the relatively low attack rates of influenza in community outbreaks, and the small number of serious complications of the disease in healthy people.

When, however, an influenza virus with major antigen differences from prevalent strains appears, one to which the population has little or no immunity, a far more aggressive approach may be needed to prevent a possibly extensive epidemic. Such is the case this year.

INFLUENZA A/NEW JERSEY/76 (SWINE INFLUENZA VIRUS)

In February 1976 a new strain of human influenza A virus, A/New Jersey/76 (Hsw1N1),** was isolated in an outbreak of influenza among United States Army recruits at Fort Dix, New Jersey. Retrospective serologic studies show that several hundred personnel on the post were infected; but apparently cases did not spread beyond Fort Dix. This virus is related antigenically to the virus that is believed to have caused the severe influenza pandemic of 1918-1919 and to that which has been circulating in swine since then. There is no evidence that the swine influenza virus has regularly infected human beings since 1930, except in rare instances when human disease was directly related to contact with swine. (Those few persons born since 1930 who have low level of swine influenza antibody most likely encountered somewhat related strains in nature or in influenza vaccines.) The outbreak at Fort Dix thus represents the first documented human-to-human transmission of swine influenza virus since before 1930.

Influenza virus A/New Jersey/76 (Hsw1N1), so-called swine influenza virus, represents a major change from the A/Hong Kong (H3N2) influenza viruses prevalent since 1968. (A current variant of these H3N2 viruses, A/Victoria/75, was epidemic in many parts of the world, including most of the United States, in 1975-1976.) Experience indicates that when a major antigen change occurs in prevalent influenza A viruses, the new virus will rapidly spread worldwide. This sequence of events was particularly notable in 1957 and 1968 when the Asian and Hong Kong strains first appeared.

NATIONAL INFLUENZA IMMUNIZATION PROGRAM

Based on the prospect that the new swine influenza virus will persist and cause extensive disease, health officials in the Federal Government, after consulting with specialists in public health, preventive medicine, and influenza research and with vaccine manufacturers, began planning a nationwide vaccination campaign to protect against this possibility. Comprehensive immunization is feasible this year because the swine influenza virus appeared in time for the United States biologics' producers to prepare enough vaccine to meet the anticipated need. Congress has made funds available to purchase vaccine for all those in the population who are recommended for vaccination. This massive public health effort, unique in our history, is already underway.

The current plan is to distribute swine influenza vaccines at no cost to State agencies for use in State and local programs. National, State, and local public information efforts will make people aware of the availability of vaccine, emphasize the importance of being vaccinated, and describe the associated benefits and risks. The Center for Disease Control will oversee the formulation of national plans, distribute vaccines, maintain epidemiologic and laboratory surveillance of influenza, and assess overall effectiveness of the immunization effort.

Success of the nationwide program depends not only on the proportion of the population vaccinated but also on the potency and safety of the vaccines to be used. Therefore, studies have been underway to test prototype vaccines with several thousand volunteers of different ages. These investi-

*A final statement including results of field trials of vaccines to be used in the United States in 1976-1977 will be published in early July.

**The World Health Organization nomenclature for influenza A viruses includes their strain designation and a description of the 2 surface antigens, hemagglutinin (H) and neuraminidase (N).

gations are sponsored by the National Institute of Allergy and Infectious Diseases (National Institutes of Health), the Bureau of Biologics (Food and Drug Administration), and the Center for Disease Control. Results will be compiled in late June to provide a sound basis for specifying vaccine dosage, age, expected side effects, and contraindications.

INFLUENZA VIRUS VACCINES FOR 1976-1977

The National Influenza Immunization Program provides for two vaccine formulations: a bivalent vaccine for the traditionally identified "high-risk" groups and a monovalent vaccine for the rest of the population. The bivalent vaccine will contain both A/Victoria/75 and A/New Jersey/76 (the swine influenza virus) because the A/Victoria strain which was prevalent in 1975-1976 may persist to some extent in 1976-1977. The monovalent vaccine will contain only the A/New Jersey/76 strain. Vaccines will begin to become available during the summer.

In addition to the influenza A vaccines provided in the National Influenza Immunization Program, there will be a monovalent influenza B vaccine. It will be available through regular commercial channels for persons in the high-risk groups for whom annual influenza vaccination is regularly recommended.

SWINE INFLUENZA VACCINE USAGE

General Recommendations

High-Risk Groups: Bivalent influenza A vaccine is recommended for persons of all ages who have such chronic health problems as 1) heart disease of any etiology, particularly with mitral stenosis or cardiac failure, 2) chronic bronchopulmonary diseases, such as asthma, chronic bronchitis, cystic fibrosis, bronchiectasis, tuberculosis, and emphysema, 3) chronic renal failure, and 4) diabetes mellitus and other chronic metabolic disorders.

Bivalent influenza A vaccine is also recommended for older persons, particularly those over age 65 years. This is because excess mortality in influenza outbreaks is seen among those in the older age groups as well as among patients with chronic illnesses.

General Population: Monovalent A/New Jersey/76 (swine influenza virus) vaccine is recommended for all persons not in the high-risk groups who can safely and effectively be vaccinated. Age criteria for vaccine recipients will be derived from the field trials being conducted at the present time and will be included in the final ACIP influenza statement to be published in July 1976.

Information for Vaccinees: Influenza vaccination should be preceded by informing all potential recipients or the parents of children to be vaccinated of the general characteristics of the vaccine, what its benefits are, and what side effects it has. Comparable procedures for providing this information should be used. There should be ample opportunity for recipients to have their questions answered, and there should be documentation that information was received and vaccination desired. Documentation could be by the signature of potential recipients or of parents or guardians or by other systems of records judged sufficient to identify those who, after being informed, choose to be vaccinated.

Dosage and Schedule

Only one dose of the bivalent vaccine or the monovalent influenza A vaccine should be needed. Age criteria, proper dosages, and routes of administration will be derived from field study results. Influenza vaccination programs should begin as vaccines become available and should continue through the fall so that the target population can be vaccinated before winter, the season when influenza characteristically occurs.

Side Effects

Influenza vaccines currently produced by manufacturers in the United States are purified by zonal centrifugation and should produce few severe side effects. Before these new purification techniques came into general use in the late 1960s, influenza vaccines fairly commonly caused local and systemic reactions considered objectionable by many recipients. With current influenza vaccines, however, only mild local reactions, such as erythema and tenderness at the injection site, will be relatively common. Systemic reactions, including low-grade fever, chills, malaise, or headache, should occur only infrequently. These conclusions are based on experience with influenza vaccines similar to the ones that will be used this year. Data from field trials with the actual 1976-1977 vaccines will help delineate side effects.

Precautions

Persons with known hypersensitivity to egg protein should not be given influenza vaccine except under the close supervision of a physician.

Concurrent Administration of Influenza and Other Vaccines

It would seem prudent not to administer influenza vaccine along with vaccine containing diphtheria, pertussis, or tetanus antigens since fever is often associated with these antigens, and their simultaneous administration might increase the chance of febrile responses. Furthermore, influenza vaccine should probably not be administered within 14 days after vaccination with the live, attenuated measles virus vaccine since measles vaccine is known to induce fever in 15 percent or more of vaccinees beginning about 6 days after vaccination and lasting several days.

If, in the context of the National Influenza Immunization Program, health agencies plan to provide vaccines other than those against influenza, they should take into account such matters as the risk of coincidental vaccine reactions, the need for informing recipients about all antigens to be given and for documenting vaccine acceptance, and the record-keeping commitments that giving multiple antigens entails.

Every effort should be made during the period of the National Influenza Immunization Program to maintain routine vaccination activities and to conduct whatever programs are needed to prevent and control outbreaks of vaccine-preventable illnesses.

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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

INFLUENZA VACCINE — SUPPLEMENTAL STATEMENT*

INTRODUCTION

This Committee's preliminary statement on influenza vaccine for 1976-77 was published in early June.* In it there was extensive reference to field trials of prototype vaccines to be used in the National Influenza Immunization Program. The trials were conducted to provide a basis for making specific recommendations on vaccine formulation and vaccine dosage for different age groups and for accurately describing the side effects that might be expected to follow vaccination.

Data from these field trials were analyzed at an Influenza Workshop held in Bethesda, Maryland, on June 21, 1976. The Workshop was sponsored by the National Institute of Allergy and Infectious Diseases (National Institutes of Health), the Bureau of Biologics (Food and Drug Administration), the Center for Disease Control, all in the Department of Health, Education, and Welfare, and by the Department of Defense—the same agencies that had sponsored the vaccine studies. The following summary of results, of partial recommendations on swine influenza vaccination for adults, and of related comments and recommendations has been derived from review of field trial data and consideration of other important issues.

SWINE INFLUENZA VACCINE FIELD TRIALS (SPRING 1976)

Field trials of prototype vaccines from the 4 United States influenza vaccine producers involved more than 5,200 adults and children. The trials were designed to evaluate the immunogenicity and reactogenicity of different doses of swine influenza vaccines. Trials were double-blind with placebo controls and used comparable protocols and analytical methods. All serum samples were tested at CDC.

Vaccines in the field trials were monovalent preparations of swine influenza virus (Hsw1N1), bivalent preparations including both swine influenza virus and A/Victoria/75 (H3N2), and monovalent B preparations containing B/Hong Kong/72. All manufacturers used standard procedures to purify, concentrate, and inactivate the virus. Two manufacturers supplied whole-virus vaccines, and 2 provided split-virus (chemically disrupted) vaccines.

Preliminary analysis of field trial data provides the following general conclusions:

1. Approximately 90% of the vaccinees 25 years of age or older responded well to even the lowest adult dose (200 CCA units) of monovalent swine influenza vaccines; whole-virus and split-virus vaccines induced comparable antibody responses. Vaccine side effects, principally low-grade fever, malaise, and myalgia, among the adult volunteers were most frequent with the highest test dose (800 CCA units) of whole-virus vaccines. Only about 2% of adults receiving 200 CCA unit vaccines had any such effects, a rate essentially equivalent to that following injection of placebo material.

2. Children 3-10 years old had less favorable immune responses to the swine influenza vaccines than did adults. Although whole-virus vaccines were considerably more effective inducers of antibody in this age group than were split-virus vaccines, the whole-virus antigens were also more reactogenic, even at the lowest childhood doses used (50 and 100 CCA units). Additional field trials with children and adolescents will be needed to measure the immunogenicity and reactogenicity of other doses of vaccine and the benefit of second doses.

3. Young adults ages 18-24 had less favorable antibody responses to the swine influenza vaccines than did older adults. Like younger children, their best responses were to whole-virus vaccines, particularly to the most potent ones tested (800 CCA units). However, persons in this age group experienced considerably fewer side effects to the more potent vaccines than did young children.

4. Bivalent A vaccines containing both swine influenza virus and A/Victoria/75 virus, either whole or split, at 200 CCA or 400 CCA units of each component antigen, were about equally immunogenic in persons 25 years of age or older. They were less effective in younger persons. Side effects from these vaccines were similar in adults to those from monovalent swine influenza vaccines.

5. Monovalent B/Hong Kong/72 vaccines containing 500 CCA units of antigen produced good antibody responses in nearly all adult vaccinees tested. The antigen induced few side effects of its own, and, when given simultaneously with bivalent A vaccine, did not appear appreciably to enhance reactogenicity.

6. Vaccines administered by needle/syringe and by jet injector produced comparable rates of seroconversion and levels of antibody response.

INFLUENZA VACCINE RECOMMENDATIONS

General Comments

Results of the recent field trials provide clear evidence that adults of approximately 25 years of age or older can safely and effectively be immunized against A/New Jersey influenza with a single dose of vaccine. Furthermore, the trials indicate that younger adults and children as young as 3 years old can also be safely immunized but that additional data will be needed before specifying the precise vaccine potency and optimal schedule for them. Although data from additional field studies will be needed to substantiate and complete recommendations for the young adult and childhood age groups, plans for vaccinating all age groups of the population should continue.

Studies underway now and others soon to begin should be completed by mid-to-late-September in time for vaccination programs to proceed.

The current recommendations address the population above secondary school age, namely that 18 years of age and older. Although within this adult group, those 18-24 years old are immunologically distinctive from those 25 years of age and older, as a result of having had less experience with various naturally occurring influenza viruses, all

*Supplemental to *Influenza Vaccine — Preliminary Statement*, published in the MMWR (25)21:165-171, June 4, 1976.

persons in this age group can be given the same potency vaccine. If additional vaccine trials in the 18- to 24-year-old group indicate that sufficient benefit will be derived from a second dose of vaccine, it will be recommended. Furthermore, since whole-virus vaccine produces better antibody responses in the 18- to 24-year-old group, plans should be made to utilize this vaccine for this group.

Swine Influenza Vaccine Formulations

For those 18 years of age and older, influenza vaccines, both monovalent A and bivalent A, will contain 200 CCA units of A/New Jersey/76 (swine influenza virus). The bivalent A vaccine will also contain 200 CCA units of the A/Victoria/75 antigen. A single dose of either vaccine should result in antibody responses against swine influenza generally considered protective in at least 85-90% of vaccinees of approximately age 25 or more. Persons 18-24 years of age will probably not respond as well to the swine influenza antigen, but at least 85% of those receiving whole-virus vaccine should develop demonstrable antibodies.

Side effects from these vaccines, including 1-2 days of generally low-grade fever, malaise, and myalgia, should occur in less than 2-3% of vaccinees 18 years of age or older.

High-Risk Persons 18 Years of Age and Older

Bivalent A Vaccine: *One* dose of *bivalent A* influenza vaccine containing 200 CCA units of A/New Jersey/76 (swine influenza virus) and 200 CCA units of A/Victoria/75 should be given. (As noted, if additional field trials show sufficient benefit from a second dose for persons 18-24 years old, it will be recommended.)

Monovalent B Vaccine: *One* dose of *monovalent B* influenza vaccine containing 500 CCA units of B/Hong Kong/72 should be given. This vaccine will be available only through commercial sources. It can be given at the same time as the bivalent A vaccine or at another time. If given concurrently, slightly enhanced side effects might be observed. In vaccinating an adult who has previously experienced significant side effects from influenza vaccines, it would be prudent to give the 2 vaccines separately, preferably with the bivalent A vaccine's being given a few days or a week or more before the monovalent B vaccine.

General Population 18 Years of Age or Older

Monovalent A Vaccine: *One* dose of *monovalent A* influenza vaccine containing 200 CCA units of A/New Jersey/76 (swine influenza virus) should be given. (As noted, if additional field trials show sufficient benefit from a second dose for persons 18-24 years old, it will be recommended.)

General Population 17 Years of Age or Younger

Monovalent A Vaccine: Recommendations will be made based on results of studies now underway.

Precautions

Before being vaccinated, persons known to be hypersensitive to egg protein should be given a skin test or other allergy-evaluating test using the swine influenza vaccine as the antigen. Persons with adverse reactions to such testing should not be vaccinated.

Persons with acute febrile illnesses should not be vaccinated until they have recovered.

SIDE EFFECTS AND REACTIONS, GENERAL ASPECTS

Side effects of influenza vaccine are generally inconsequential and occur at low frequency. Severe reactions are uncommon, and truly disabling effects appear to be exceedingly rare. Three types of responses to influenza vaccines have been described:

1. Fever, malaise, myalgia, and other systemic symptoms of toxicity occurring 6-12 hours after vaccination and persisting 1-2 days. These responses to influenza vaccine are usually attributed to characteristics of the influenza virus itself (even though it is inactivated in available vaccines) and represent the bulk of the side effects of influenza vaccination. Such effects occur most frequently in children and in others who have had no previous experience with influenza viruses comparable to the vaccine antigen(s).

2. Immediate, presumably allergic, responses, such as flare and wheal or various respiratory expressions of hypersensitivity. These reactions are exceedingly uncommon but can occur after influenza vaccination. They probably derive from exquisite sensitivity to some vaccine component, most likely to residual egg protein. Although current influenza vaccines contain only a minute quantity of egg protein, they do, on rare occasions, provoke hypersensitivity reactions.

3. Neurologic disorders, including such central nervous system conditions as encephalopathy, with at least temporal association with influenza vaccination. A survey of the medical literature since the early 1950s revealed only about a dozen such reports. Almost all persons affected were adults, and the described clinical reactions began as soon as a few hours and as late as 2 weeks after vaccination. Full recovery was almost always reported.

Three fatalities have been reported in temporal association with influenza vaccination. However, in 2 instances, the patients displayed clinical characteristics and had antecedents which strongly suggested causes other than influenza vaccine, and the third was equally compatible with another viral disease.

In summary, influenza vaccine has only rarely, if ever, been associated with severe adverse reactions or permanent disability. Although vaccination relatively frequently causes transient redness and tenderness at the injection site and sometimes causes such systemic reactions as low-grade fever, malaise, and myalgia for 1-2 days, influenza vaccine is considered to be very safe and is quite suitable for widescale, community use.

PREGNANCY

Elevated rates of maternal and fetal mortality and of congenital anomalies and other fetal effects resulting from influenza infection during pregnancy have been widely discussed. Numerous reports during the 1918-19 influenza pandemic and a limited number of small but better controlled studies in 1957-58, when the Asian influenza pandemic occurred, suggest that influenza can result in increased maternal deaths and fetal wastage. However, a number of prospective studies in the past decade or more have failed to corroborate this association. Although there are no persuasive data to document that pregnancy is a risk-factor with influenza, the effect of swine influenza in pregnancy cannot be forecast with assurance.

Physicians generally avoid prescribing unnecessary drugs and biologics for pregnant women, especially in the first trimester; however,there are no data specifically to contraindicate vaccination with the available killed virus vaccine in pregnancy. Women who are pregnant should be considered as having essentially the same balance of benefits and risks regarding influenza vaccination and influenza as the general population.

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RECOMMENDATIONS OF THE COMMITTEE ON INFECTIOUS DISEASES OF THE AMERICAN ACADEMY OF PEDIATRICS

IMMUNIZATION OF CHILDREN AT HIGH RISK FROM INFLUENZA INFECTION*

Children considered to be at high risk of serious illness if infected with influenza viruses include those with: 1) chronic bronchopulmonary disease, such as asthma and cystic fibrosis; 2) heart disease; 3) chronic renal disease; 4) diabetes and other chronic metabolic diseases; 5) chronic neuromuscular disorders; and 6) malignancies and immunodeficient states. It is recommended that these high-risk children be immunized against influenza.

The following recommendations are based on data from continuing clinical trials to evaluate the potency and safety of influenza vaccines in children 3 and over. The trials are not yet completed but do provide sufficient information at the present time from which to formulate recommendations for immunizing children 3 years and over and adolescents at high risk from influenza.

Bivalent A Vaccine

Dose: Children and adolescents ages 3-18 years should receive 2 intramuscular injections (0.5 ml each) of split-virus ("subvirion," "split product") vaccine containing 200 CCA units each of A/New Jersey/76 and A/Victoria/75 antigens separated by at least 4 weeks. *Split-virus vaccine is recommended* because the field trials showed that whole-virus vaccines produced substantially more side effects. Two doses of split-virus bivalent A vaccine should induce a good antibody response in most children and adolescents 3-18 years of age. A single dose of split-virus vaccine would be far less satisfactory. Therefore, it is important that parents of children at high risk be informed of the inadequacy of a single dose and be urged to see that their children receive a second dose.

Data are not yet available from the current field trials to derive recommendations for immunizing children less than 3 years of age. The Committee, therefore, recommends that current studies be extended to include immunization of infants and young children. It is hoped that the continuing field trials of influenza vaccines will provide data on which to base vaccine recommendations for normal children.

Side effects: In the clinical trials of split-virus vaccines conducted this year, side effects were mild and infrequent; low-grade fever (less than 101°) occurred in approximately 2% of vaccinated children. The symptoms reported were local reactions, fever, headache, malaise, and abdominal pain which usually occurred 6-12 hours after vaccination and rarely lasted more than 24 hours. The incidence of these symptoms was not significantly different from that observed in recipients of the placebo preparation. There were no seizures.

Monovalent B Vaccine

Over the past several years, limited clinical trials of vaccine containing the B/Hong Kong/72 antigen have been conducted in children. Since no new data are available, dosage recommendations will remain unchanged. Physicians should refer to individual manufacturers' package circulars for the recommended dosage of monovalent B vaccine. These instructions call for administering a fraction of the adult dosage to children 10 years of age or less. Because of the risk of increasing the frequency of side effects, it is desirable to avoid administering the monovalent B and bivalent A vaccines at the same time.

Precautions

Whole-virus bivalent A vaccine should not be used in place of the split-virus vaccine. If whole-virus vaccine were used, side effects would be greatly accentuated.

Other vaccines should not be given at the same time as influenza vaccine because side effects would be difficult to classify and interpret.

Children highly sensitive to egg protein should not be given influenza vaccine except under close supervision of a physician. They should be skin tested or otherwise evaluated and should not be vaccinated if a severe reaction occurs.

Vaccination of children with acute febrile illnesses should be postponed.

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*The Committee on Infectious Diseases of the American Academy of Pediatrics developed these recommendations on request from the Public Health Service's National Influenza Immunization Program. The Committee reviewed all available data from the current series of influenza vaccine field trials in children and adolescents and directs its advice both to private physicians and to the health agencies which may be providing vaccine to high-risk children.

RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

INFLUENZA VACCINE—SECOND SUPPLEMENTAL STATEMENT

INTRODUCTION

Several issues of importance in the National Influenza Immunization Program regarding vaccination recommendations remain to be addressed: (1) immunization of normal infants, children, and adolescents up to age 18 years old, (2) the pending options for recommending a booster for young adults 18-24 years old who already have been given 1 dose, (3) immunization of children less than 3 years old at high risk of severe influenza, and (4) monovalent influenza B vaccine dosage in high-risk children.

The following discussion of these issues derives from the results of clinical field trials of current influenza vaccines which have been carried out during the spring, summer, and early fall of 1976 and from past experience with influenza vaccines.

SUMMARY OF VACCINE FIELD TRIALS

Field trials of swine influenza vaccines in children, adolescents, and young adults have now been essentially completed. Data on immunogenicity and reactogenicity of both whole-virus and split-virus vaccines given to approximately 3,300 persons 6 months through 23 years of age were reviewed on October 22, 1976, by scientists who conducted or supervised the trials and by representatives of the various immunization recommending groups in the country including the Advisory Committee on Immunization Practices (ACIP). Since that workshop meeting, additional discussions and evaluations have occurred in preparation for this statement.

The conclusions drawn from the field trials indicate the clear possibility for safely and effectively immunizing infants as young as 6 months of age, children, adolescents, and young adults against influenza. In essence, this would generally require giving 2 doses of *split-virus* vaccine in doses selected to minimize side effects – especially important at the younger ages where side effects are particularly common. The whole-virus vaccines, while quite immunogenic, were much more frequently associated with transient fever and systemic side effects and were not felt to be an alternative to the split-virus vaccines for childhood immunization at the present time.

However, the split-virus vaccines particularly suited to infant and childhood immunization are not and will not be available in sufficient supply in 1976 for timely protection of *all* normal children and adolescents less than 18 years of age against swine influenza – that is, prior to the 1976-77 influenza season – and priority should be given to older adults.

While the inability to recommend and implement a program of systematic immunization of children and adolescents less than 18 years of age will be disappointing to some, the field trials have provided a greatly expanded body of scientific data on influenza immunization. They clearly will influence future influenza vaccine formulations and recommendations on vaccine use in children. Furthermore, although influenza can be very common in children and adolescents, the number of severe and fatal illnesses in these groups is characteristically very small.

In brief summary, field trials of monovalent swine influenza vaccine containing A/New Jersey/76 and a bivalent vaccine containing both swine influenza and A/Victoria/75 viruses demonstrated:

(1) Split-virus influenza vaccines resulted in considerably fewer febrile and systemic side effects than whole-virus vaccines, especially in children.

(2) In the young age groups tested (6-36 months, 3-5 years, and 6-10 years) small, fractional doses of whole-virus vaccines induced fever (usually low grade and of less than 24-hours duration) in 10-50% of recipients, depending on age.

(3) Both whole-virus and split-virus vaccines, adjusted in dose to minimize side effects, required 2 doses at 4-week or greater intervals generally to induce seroconversion rates with final HI antibody titers of $\geq$ 1:20 in more than 85-90% of vaccinees and HI antibody titers of $\geq$ 1:40 in more than 80% of vaccinees.

(4) The 2 available split-virus vaccines were essentially equivalent in potency. Both of the split-virus vaccines required considerably more antigen than either of the whole-virus vaccines to produce comparable rates of seroconversion and levels of antibody.

(5) Now-completed trials of bivalent vaccine containing both A/New Jersey/76 (swine influenza virus) and A/Victoria/75 in children and adolescents extended but did not alter the already available data which formed the basis of recent recommendations for immunizing high-risk younger age groups.*

(6) Young adults 18-24 years old were regularly benefited by a second dose of either whole-virus or split-virus vaccine 4 weeks or more after the first dose. Seroconversion rates following 2 doses of monovalent swine influenza vaccine generally at HI antibody titers of $\geq$ 1:20 occurred in more than 90% of vaccinees and at HI antibody titers of $\geq$ 1:40 in more than 80% of vaccinees. (Single dose seroconversion rates were quite variable depending on whether whole-virus or split-virus vaccines were administered but generally involved production of HI antibody titers of $\geq$ 1:20 in somewhat more than 50% of vaccinees and of HI antibody titers of $\geq$ 1:40 in more than 40% of recipients.)

*Recommendations of the Committee on Infectious Diseases of the American Academy of Pediatrics: Immunization of Children at High Risk from Influenza Infection. MMWR 25 (36):285, September 17, 1976.

GENERAL RECOMMENDATIONS

Monovalent A/New Jersey/76 Vaccine

Normal infants and children less than 3 years old: No recommendaton.

Normal children and adolescents 3-17 years old: No recommendation for systematic, communitywide programs. To the extent vaccine is available, 2 doses of *split-virus* monovalent A vaccine containing 200 CCA units of A/New Jersey/76 (swine influenza virus) separated by at least 4 weeks.

Normal young adults 18-24 years old: A second dose of either whole-virus or split-virus monovalent A influenza vaccine containing 200 CCA units of A/New Jersey/76 (swine influenza virus) at least 4 weeks after the first dose. With regard to any side effects associated with this dose, available data suggest that the already very low rate of side effects from influenza vaccine might be even lower with the second dose.

Bivalent A/New Jersey/76 (Swine Influenza Virus) and A/Victoria/75 Vaccine

High-risk children 6-36 months old: The American Academy of Pediatrics Committee on Infectious Diseases has reviewed the limited data which are available and recommends 2 intramuscular injections of the *split-virus* bivalent A influenza vaccine separated by at least 4 weeks. For these infants and young children a dose of 0.25 ml should be used. This volume represents 50% of the dose used in older children and adults and contains 100 CCA units each of A/New Jersey/76 (swine influenza virus) and A/Victoria/75.

High-risk children and adolescents 3-17 years old: See previous recommendation of the American Academy of Pediatrics Committee on Infectious Diseases, "Immunization of Children at High Risk from Influenza Infection," September 1976.

High-risk young adults 18-24 years old: A second dose of either whole-virus or split-virus bivalent A influenza vaccine containing 200 CCA units of A/New Jersey/76 (swine influenza virus) and 200 CCA units of A/Victoria/75 at least 4 weeks after the first dose.

Monovalent B/Hong Kong/72 Vaccine for High-Risk Children and Adolescents

Recommended dosages of influenza A vaccines for children have been derived in large part from the current field trials in relevant age groups and from clinical experience and judgment. Studies of influenza B vaccines have been much less extensive. In the absence of new data on which to base dosages of the monovalent B vaccine containing 500 CCA units of B/Hong Kong/72 generally recommended for children at risk of serious or fatal influenza, it is reasonable to employ dosage concepts used in past years. This has been for fractional doses of vaccine according to age group, derived, in part, empirically. It is represented in package literature for the monovalent B/Hong Kong influenza vaccine for use in 1976. A single dose of this vaccine is believed to be sufficient for high-risk children because of their likely prior natural exposures to related influenza B strains. The following single-dose schedules of monovalent B/Hong Kong influenza vaccine are recommended:

Infants and children less than 3 years old: No recommendation.

Children 3-5 years old: 0.05 ml to 0.1 ml (this volume represents 10-20% of the adult dose and contains 50-100 CCA units of antigen). (A second dose of the same volume 2 weeks or more later has sometimes been recommended to add to the initial antigenic stimulus.)

Children 6-9 years old: 0.25 ml (this volume represents 50% of the adult dose and contains 250 CCA units of antigen).

Children 10-17 years old: 0.5 ml (this volume is the same as that recommended for adults and contains 500 CCA units of antigen).

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STATE EPIDEMIOLOGISTS

Key to all disease surveillance activities are those in each state who serve as State Epidemiologists. Responsible for the collection, interpretation, and transmission of data and epidemiologic information from their individual states, the State Epidemiologists perform a most vital role. Their contributions to this report are gratefully acknowledged.

Alabama	Frederick S Wolf, MD
Alaska	John Starr, MD
Arizona	Jon M Counts, DrPH, Acting
Arkansas	Paul C White, Jr, MD
California	James Chin, MD
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Oregon	John A Googins, MD
Pennsylvania	William E Parkin, DVM
Puerto Rico	Henry Negron, MD
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South Carolina	Richard L Parker, DVM
South Dakota	James D Corning, BA, Acting
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Texas	Charles R Webb, Jr, MD
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Vermont	William N Watson, MD, Acting
Virginia	Grayson B Miller, Jr, MD
Washington	Jack Allard, PhD
West Virginia	William L Cooke, MD
Wisconsin	H Grant Skinner, MD
Wyoming	Herman S Parish, MD

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
CENTER FOR DISEASE CONTROL
ATLANTA, GEORGIA 30333

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