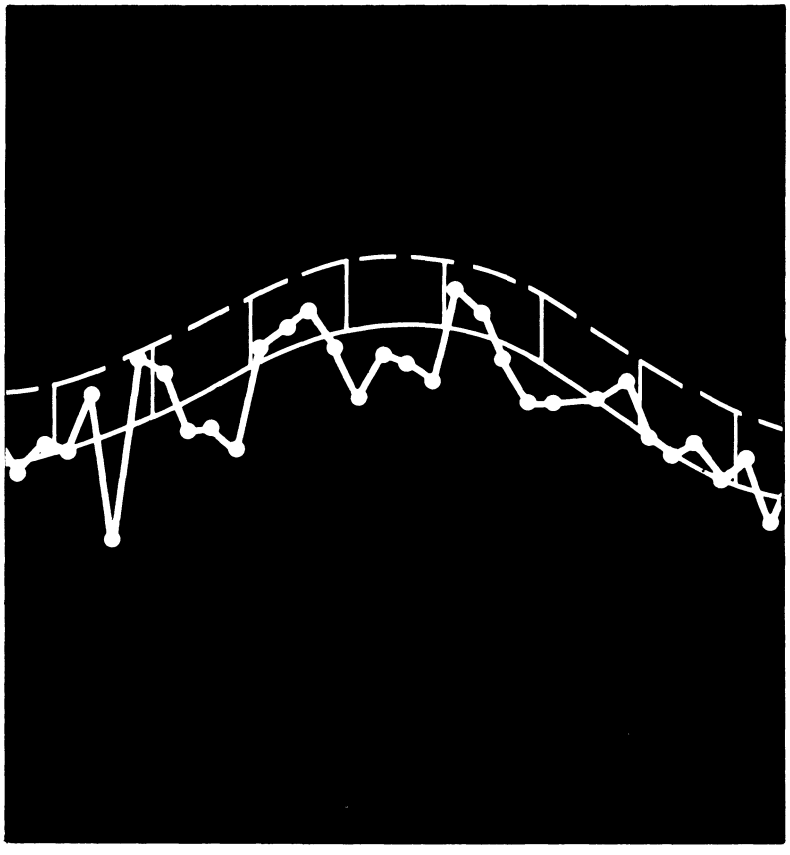
REPORT NO. 92
SUMMARY: SEPTEMBER 1976–JUNE 1977
Issued January 1981

CENTERS FOR DISEASE CONTROL

INFLUENZA

SURVEILLANCE



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES • Public Health Service

PREFACE

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:

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Issued January 1981

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In addition to the above, the following persons were involved in the planning, implementation, and evaluation of the National Influenza Immunization Program. Their positions during the 1976-77 influenza season were as follows: David J. Sencer, M.D., Director, Center for Disease Control; J. Donald Millar, M.D., Director, Bureau of State Services; Walter R. Dowdle, Ph.D., Director, Virology Division, Bureau of Laboratories; John A. Bryan, M.D., Director, Viral Diseases Division, Bureau of Epidemiology (BE); Michael A. W. Hattwick, M.D., Chief, Respiratory and Special Pathogens Branch, BE; Robert B. Craven, M.D., Philip J. Gratteer, D.D.S., Henry F. Retailliau, M.D., and Richard J. O'Brien, M.D., EIS Officers, Respiratory and Special Pathogens Branch, BE; and Dennis J. Bregman, M.S., Chief, Statistical Services and Evaluation Branch, Viral Diseases Division, BE.

CONTENTS

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I. SUMMARY

The 1976-77 influenza season (September 1976 through June 1977) was a mild one characterized primarily by type B influenza infections (1-4). Mortality from influenza and pneumonia never exceeded the epidemic threshold in the United States that year (5). The season was remarkable, however, because of several events.

a. In February 1976 an outbreak of confirmed swine influenza-like virus-A/New Jersey/8/76 (HswlNl) occurred at Fort Dix, New Jersey, and an unprecedented effort was launched to immunize the United States population against a potential pandemic strain of influenza (6-15). This National Influenza Immunization Program (NIIP) was the single largest short-term public health measure ever undertaken. Two hundred million doses of vaccine were produced, and by the time a moratorium was initiated in December, over 48 million people had been vaccinated (16).

b. For the first time in the history of Centers for Disease Control* (CDC) influenza surveillance activities, all 50 states and all United States territories participated in an active surveillance program with over 4,000 separate reporting sources (17).

c. A system for monitoring adverse reactions detected an association between influenza vaccination and Guillain-Barré syndrome (18-23).

d. From January 1 through March 31, 1977, during an epidemic of influenza B, 220 cases of Reye syndrome were reported. This was the largest case total reported since the influenza B epidemic of 1973-74 when 379 cases were reported (24-28).

A. HswlNl Influenza Virus Activity (September 1976-June 1977)

Intensive surveillance was maintained for swine influenza-like virus infections for 10 months. Six sporadic cases were detected (29-37), 3 of which were documented cases of A/New Jersey-like virus transmitted from swine to man. One of the 6 cases probably reflected person-to-person spread from someone whose illness was related to sick swine. The other 2 cases were diagnosed by seroconversion and no source of infection was found, although both occurred in pork-producing areas. Three of the cases occurred in Wisconsin, and 1 case each was detected in Missouri, Minnesota, and South Carolina.

B. H3N2 Influenza Virus Activity (September 1976-June 1977)

The first influenza A outbreak in 1976-77 occurred on Guam in September and was due to A/Victoria/3/75 (38). Widespread illness was documented in both the military and civilian populations of the island. With the exception of an outbreak among the unvaccinated residents of a Florida nursing home, other A/Victoria activity occurred in sporadic cases from January through March in 14 states, mainly in the southeast and southwest (2).

In March 1977 an influenza A isolate from a San Antonio, Texas, resident who had been ill in December 1976 was sent to CDC and characterized as an H3N2 variant distinct from A/Victoria/75 and more closely resembling A/England/864/75. This virus, designated A/Texas/1/77, was representative of isolates recovered in February from influenza outbreaks among air force personnel in San Antonio, Texas, and Denver, Colorado (5, 39-40). Isolates resembling this virus were also obtained from sporadic cases in Alaska, Hawaii, Virginia, Oregon, California, Washington, and Arizona (41-42).

C. Influenza B (September 1976-June 1977)

Viruses resembling B/Hong Kong/5/72 were the predominant B strains isolated in the 1976-77 season. The first B outbreak reported to CDC involved students at Vanderbilt University in Nashville in mid-January (35,36,43). In subsequent weeks, outbreaks occurred primarily in schoolchildren in most states except for those in the northern part of the western region.† The states in the southern region were the most widely affected.

*Formerly Center for Disease Control

†Geographic areas of the United States referred to in this report consist of 4 regions and 9 divisions, as listed below. The states in each division are shown on the map in Figure 21.

Northeast Region		North Central Region	
Divisions:	New England	Divisions:	East North Central
	Middle Atlantic		West North Central
South Region		West Region	
Divisions:	South Atlantic	Divisions:	Mountain
	East South Central		Pacific
	West South Central		

D. Reye Syndrome (January-April 1977)

A total of 220 suspected cases of Reye syndrome were reported to CDC during the period of influenza B activity. This is the largest case total since the 1973-74 outbreak when 379 cases were documented. The majority of areas reporting cases also reported concurrent influenza B activity (29 of 33). Reye syndrome was reported from all areas of the continental United States except the northern part of the West Region. The Northeast Region and the South Atlantic Division (South Region) reported the greatest activity.

E. Guillain-Barré Syndrome

Two clusters of Guillain-Barré syndrome (GBS) following influenza vaccination were reported to CDC from Minnesota (4 cases) and Alabama (3 cases) between November 10 and December 2, 1976. An epidemiologic investigation was then begun in 4 states (Alabama, New Jersey, Minnesota, and Colorado) to identify all cases of the syndrome with onset after September 30, 1976. Case-finding techniques included surveys of neurologists and reviews of hospital records. By December 15, preliminary results from the 4 states showed a markedly elevated incidence of GBS among vaccinees compared with nonvaccinees. Based on these preliminary findings, the National Influenza Immunization Program was suspended on December 16 until a more complete investigation could be made.

In the expanded investigation phase, all state health departments in the United States, District of Columbia, and Puerto Rico were requested by CDC to contact as many practicing neurologists as possible to identify cases in at least the period October 1, 1976-January 31, 1977. Through March 1978, 50 states, Puerto Rico, and the District of Columbia had reported a total of 1,098 cases from October through January. Five hundred thirty-two cases occurred in patients who had received an A/New Jersey influenza vaccination before their onset of GBS. Based on the observed differences in attack rate between the vaccinated and unvaccinated populations, the attributable risk of GBS in adult vaccinees was estimated at just under 1 case per 100,000 vaccinations (18-23). The case-fatality rate in adults of 5.9% was essentially the same in vaccinees as in nonvaccinees.

F. Other Reported Adverse Reactions During NIIP

CDC coordinated nationwide surveillance of illnesses following influenza vaccination as part of the effort to immunize the nation against influenza A/New Jersey/8/76. All state health departments were asked to report any illnesses requiring medical attention that had occurred in persons who had recently been vaccinated. By January 1, 1978, a total of 4,733 reports were received--including 223 fatalities and the 1,830 cases in military personnel--from the total of 48,101,019 persons vaccinated. As indicated above, a separate active surveillance system for all cases of GBS regardless of vaccination history was established after 2 clusters of cases in recent vaccinees had been reported. Other reported illnesses, including fatal ones, did not exceed levels expected for the general population. No serious illnesses detected through the surveillance system, other than GBS and rare cases of anaphylaxis, were clearly associated with influenza vaccination (44).

II. SURVEILLANCE METHODS

A. Mortality

Deaths are reported to CDC each week by the vital statistics offices of 121 United States cities. These reports are published weekly 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 these 121 reporting cities. The city reports contain a count of death certificates filed in these cities the previous week. A death is attributed to pneumonia if pneumonia is entered on line 1 or 3 in Part I of the certificate. Influenza takes precedence over any other conditions on the certificate and can appear anywhere in Part I or Part II. It should be understood that the reported number of certificates being filed with vital statistics offices may include deaths that occurred 2 or more weeks before the filing. For example, the number of delayed certificates usually increases in holiday seasons, resulting in a decrease in the number of deaths reported to CDC for these periods. An increase in reported deaths will follow when the delayed reports are eventually received in the vital statistics offices and the information is forwarded to CDC. Influenza epidemics are thought to be associated with statistically significant rises above expected mortality from all causes and in mortality due to pneumonia and influenza 2 to 4 weeks after widespread clinical illness is noted. The reported number of deaths due to pneumonia and influenza provides statistical evidence describing the extent and severity of epidemic influenza in large geographic regions. The expected number of

deaths is based on fitting weekly mortality reports for the previous 5 years (omitting epidemic weeks) to the following equation by a least squares Fourier Regression Model:

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

The equation contains terms for a linear trend over time and seasonal variation. Omission of the epidemic observations of previous years prevents an artifactual inflation of the expected level during the influenza season. The epidemic threshold is calculated by multiplying the standard error of the residual by 1.65 and adding the product to the expected number. Two successive weeks of reported deaths that exceed the threshold indicate an event of epidemiological interest. Based on the equations, graphs are prepared for publication which show the number of reported deaths, expected deaths, and the epidemic threshold by week (45-47).

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) admissions and emergency room visits because of pneumonia and influenza to large community hospitals in major cities within their states, 2) school and industrial absenteeism, and 3) visits to sentinel physicians. Each week during the influenza season, written summaries of these data were sent to CDC and entered into a computer program for analysis. Since denominator information such as school enrollment, total emergency room visits, etc., was supplied for most of these surveillance sources, mean rates may be calculated by the computer. From these rates, significant deviations from the mean may also be calculated, thereby freeing surveillance personnel to concentrate on probable outbreak areas. In 1976-77, all 50 states and the District of Columbia participated in this institutional surveillance system, reporting data from over 4,000 reporting sources.

Twenty-five states included influenza on their list of reportable diseases. These data were also used by CDC for influenza morbidity surveillance.

Since weekly reports were sometimes delayed in reaching the computer-based reporting system, a weekly telephonic report of the state epidemiologist's assessment of influenza activity was obtained by regional offices of the Department of Health and Human Services.* These 10 offices in turn compiled the assessments and phoned them to CDC. In this way, influenza activity could be detected and acted upon in a timely fashion (17,48).

C. National Health Interview Survey Data

In 1976-77 the Center for Disease Control and the National Center for Health Statistics through an interagency agreement modified the section on influenza in the National Health Interview Survey (NHIS) and provided rapid processing of these data. Each week a probability sample of households representing the civilian noninstitutionalized population of the United States was interviewed by trained personnel of the United States Bureau of the Census. Interviewing was done continuously in a weekly sample of about 800 households. For purposes of a rapid reporting system on "flu" (influenza), a supplemental set of questions was added to the end of the regular NHIS beginning the last week of September 1976. The data collected included incidence of reported flu-like illness in the NHIS as well as the average number of persons in bed each day because of flu-like illnesses.

Special tabulation and processing procedures were used for the purpose of rapid reporting. Each week the statistics for the week immediately preceding were adjusted for late receipts.

In this survey the following definitions were used: Flu-like illness--Condition reported as either "flu," "influenza," or "grippe" with onset 2 weeks before the interview week and involving medical attention or restricted activity during that 2-week period. A day of restricted activity--Day in which a person reduces his/her usual activities for the entire day because of flu-like illness. Bed day--Day in which a person stays in bed all or most of the day

*Formerly Department of Health, Education, and Welfare

because of a flu-like illness within the 2 weeks before the interview week regardless of onset date. All or most of the day--More than half of the daylight hours. All hospital days for inpatients are considered to be bed days even if the patient was not actually in bed at the hospital. Average number of persons in bed each day--The total number of bed days in a given week associated with flu-like illness divided by 7.

A single estimation procedure was used to estimate the weekly incidences of flu-like illness and the total number of bed days due to flu-like illness. The weekly estimates were computed by combining the data collected over a 2-week period. During each interview week respondents were asked questions pertaining to acute illnesses for the past 2 weeks. Thus for any 2 consecutive interview weeks, the 2 respective 2-week recall periods overlapped for 1 week. Estimates for this overlapping week were obtained by averaging the weekly incidences associated with the 2 weeks of interviewing. The weekly averages for each week of interviewing were ratio estimates that had been inflated to the United States totals using U.S. Bureau of the Census current population estimate. The primary purpose of this adjustment was to account for the week-to-week variation in sample size.

Approximate sampling errors were calculated for the statistics each week. In addition, sampling errors were calculated for the weekly estimates of flu-like illness and bed days for the entire 1975-1976 flu season (September-March). The estimates vary; the relative standard error (a standard error divided by the estimate) for cases of flu-like illness is about 15%, and the relative standard error for the average number of persons in bed each day and the total number of bed days due to flu-like illness is about 20%. All the estimates of relative standard errors will be slightly higher for smaller numbers and slightly lower for larger numbers.

The standard error is primarily a measure of sampling variability. As in any survey, the results were also subject to nonsampling errors, such as errors due to processing and nonresponse. To the extent possible, these types of errors were kept to a minimum by methods built into the survey. The overall response rate for the survey generally exceeded 95% (49).

D. Laboratory Reports

Each of 58 World Health Organization (WHO) Collaborating Laboratories in the United States is requested to submit preaddressed postcard reports to the WHO Collaborating Center for Influenza, Atlanta, on the number of specimens tested, influenza viruses isolated, and serum antibody rises detected. In addition, the WHO Collaborating Center performs detailed antigenic analysis of the representative influenza viruses submitted by laboratories throughout the Americas and elsewhere.

E. International Reports

The WHO Weekly Epidemiologic 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, 1976-77

A. Morbidity Surveillance

This year for the second 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. The 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 item 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 end of the B/Hong Kong epidemic in March 1977, state epidemiologists were asked to evaluate these data, and in many 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. As expected, however, the system also detected other causes of illness and absenteeism (e.g., measles outbreaks).

A total of 4,358 separate reporting sources were utilized during the 1976-77 season. Table 1 shows the number of reporting sources by type of institution. Table 2 shows the number of reporting sources by type of data reported and the percentage of the total these represent. Figures 1 through 4 show influenza surveillance sources by state. Figure 1 shows the number of schools and industries monitored by various states; Figure 2 shows the number of hospitals and sentinel physicians by state; Figure 3 demonstrates states with county-based reporting systems and reflects the number of these counties which reported influenza data; and Figure 4 shows which states have virus surveillance programs.

Table 1
Number of Reporting Sources in Influenza Surveillance System,
By Type of Institution, 1976-77

	Number	Percent
Industries	360	8
Schools	1,202	28
Hospitals/Clinics	570	13
Sentinel Physicians	260	6
State Flu Morbidity Rep (Counties)	1,603	37
Laboratories	81	2
Mortality (Cities)	124	3
Virus Surveillance Stations	157	4
TOTAL	4,358	

Table 2
Number of Reporting Sources,
By Type of Data, 1976-77

	Number	Percent
Number of people absent	684	14
Number of people-days absent	411	8
Number of people absent with flu	313	6
Number of people-days absent with flu	44	1
Number of visits for flu	602	12
Number of flu visits-1 day	55	1
Number of flu & pneumonia admissions	137	3
Pneumonia deaths	124	2
Influenza deaths	124	2
A/Victoria isolates	81	2
A/New Jersey isolates	81	2
B isolates	81	2
A seroconversions	81	2
B seroconversions	81	2
Total visits-week	128	3
Total visits-1 day	0	0
Number of cultures taken	157	3
Extent of activity	54	1
Number of influenza cases	1,593	32

Fig. 1 INFLUENZA SURVEILLANCE SOURCES: SCHOOLS AND INDUSTRIES, 1976-1977

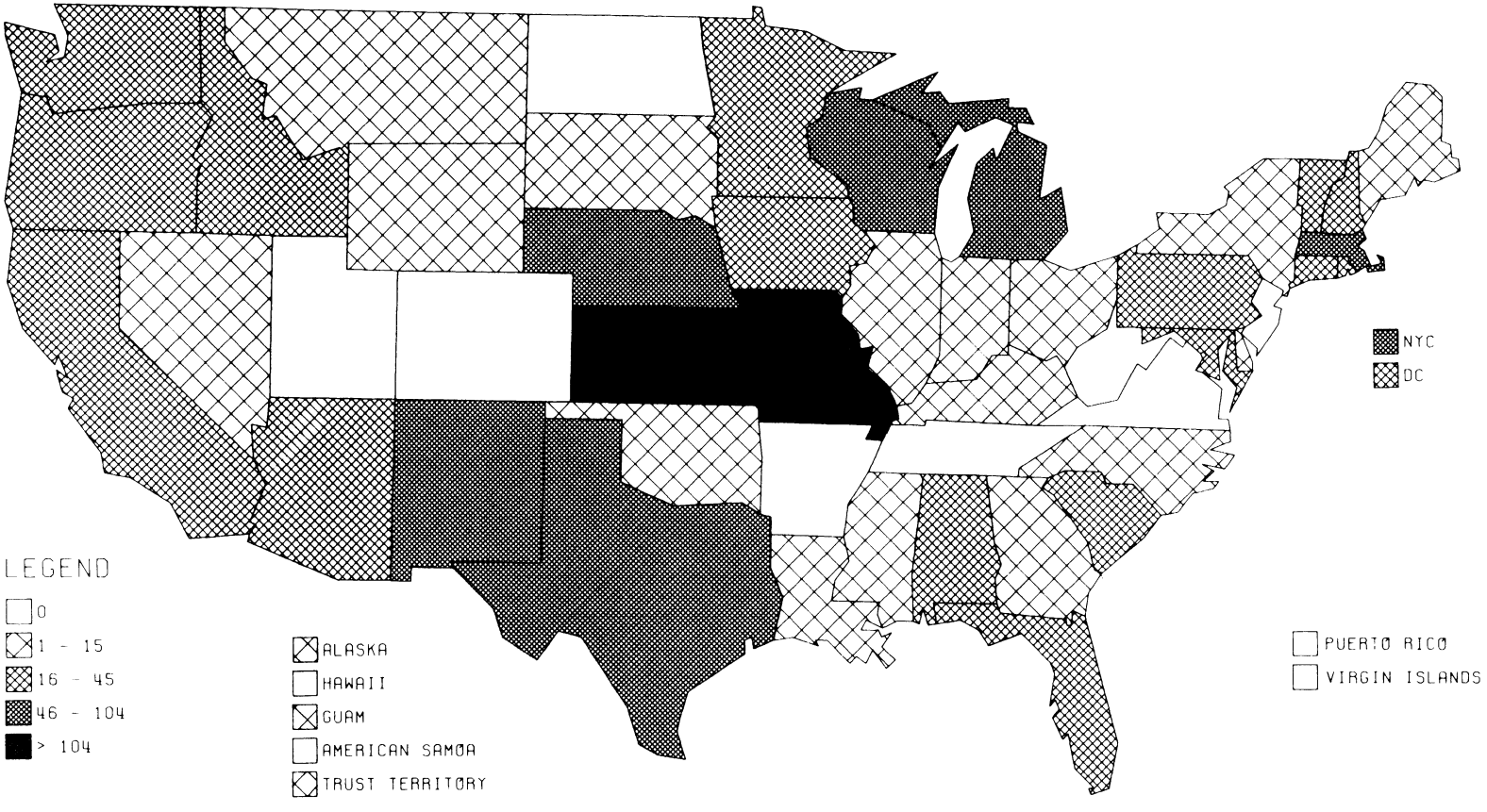


Fig. 2 INFLUENZA SURVEILLANCE SOURCES: HOSPITALS AND SENTINEL PHYSICIANS, 1976-1977

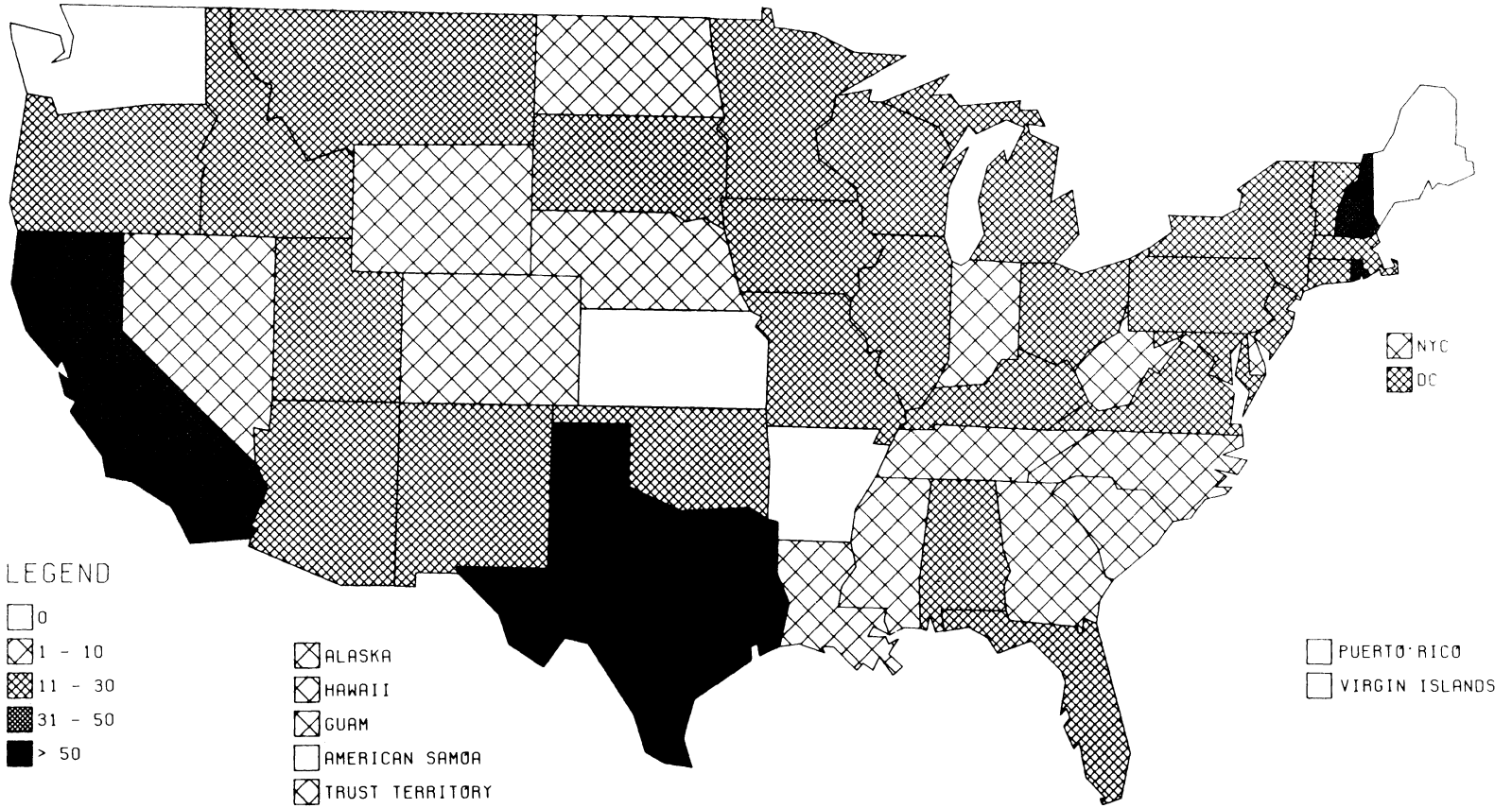


Fig. 3 INFLUENZA SURVEILLANCE SOURCES: COUNTY-BASED REPORTING SYSTEMS, 1976-1977

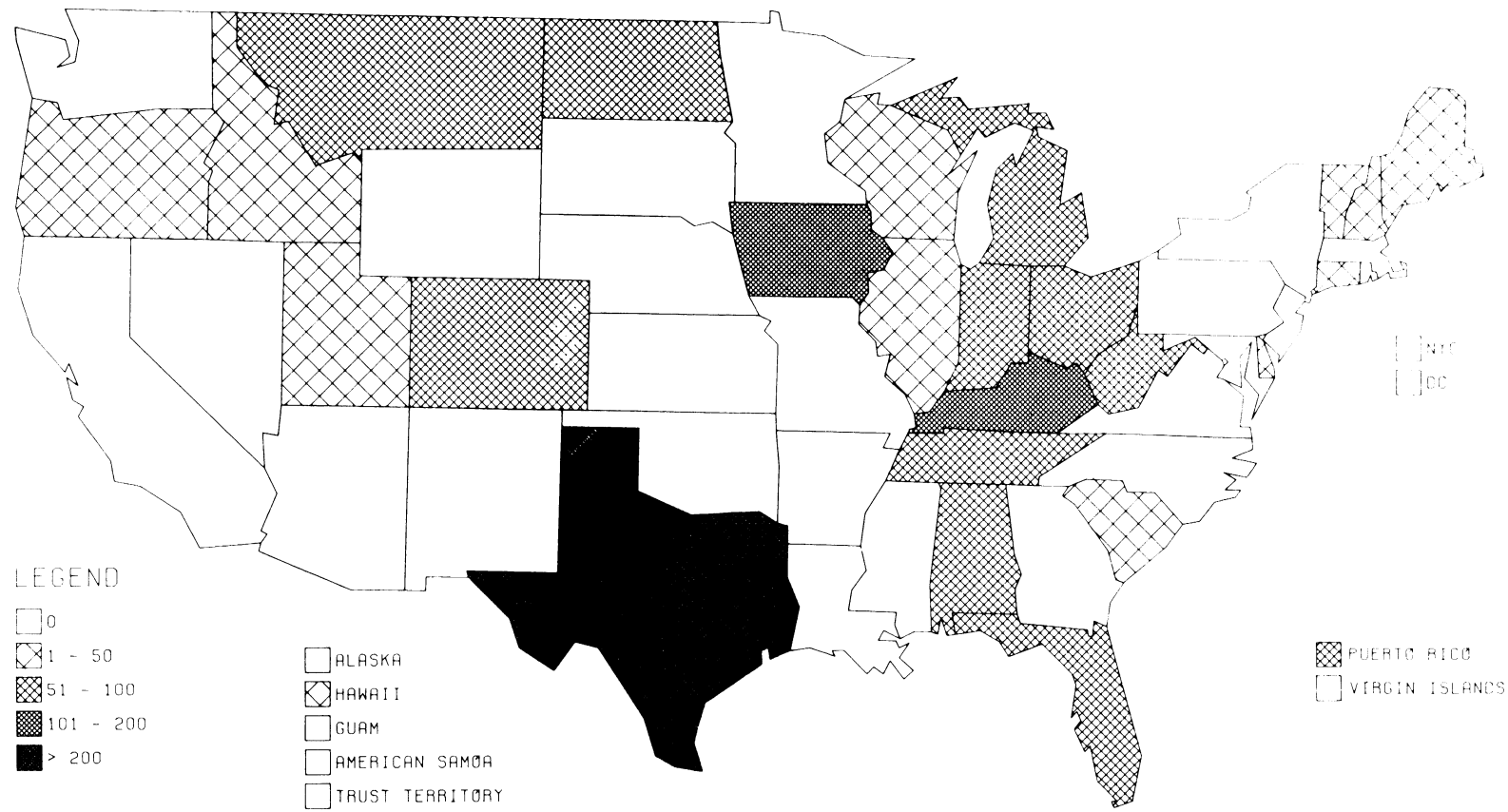
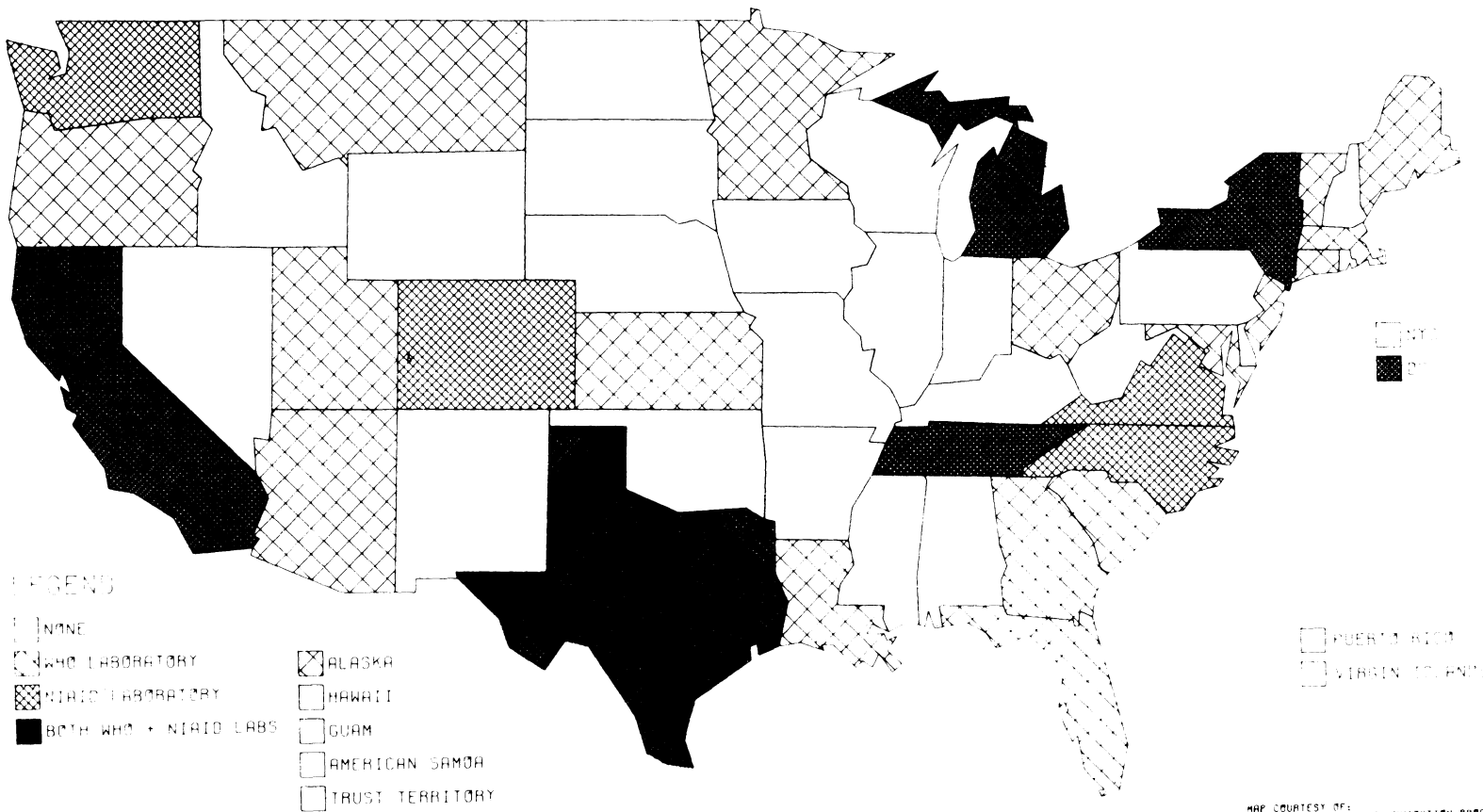


Fig. 4 VIRUS SURVEILLANCE PROGRAMS, 1976-1977



MAP COURTESY OF:
NATIONAL INFLUENZA IMMUNIZATION PROGRAM:
SURVEILLANCE AND ASSESSMENT CENTER, CDC

Figure 5 demonstrates the isolates of influenza virus reported to the WHO Collaborating Center for Influenza for the period July 2, 1976, through June 24, 1977. Figures 6-11 demonstrate reported isolates by various periods from July 1976 through June 1977, and show the early and predominant influenza B activity as it occurred in the country--with the late scattered reports of Influenza A (H3N2) isolates in the latter part of the season. Figures 12-17 demonstrate the state epidemiologists' assessments of influenza activity by state for selected weeks from December 26, 1976, through April 16, 1977.

Figure 18 shows the weekly estimates of flu-like illnesses in the United States obtained from the National Center for Health Statistics of the National Health Interview Survey compared with similar data obtained for 1975-76. Figure 19 shows the weekly estimates of the average number of persons in bed each day because of flu-like illness in the United States also compared with the 1975-76 influenza data. The decrease in number of flu-like illnesses as well as average number of persons in bed each day when compared with the A/Victoria epidemic of 1975-76 is readily apparent in these figures.

The majority of influenza activity in the United States occurred in the South Atlantic and East South Central portions of the country (Figures 12-17). Combined data on viral surveillance in these areas are presented in Figure 20, along with the NCHS Health Interview Survey data for the same areas. It is apparent that a good correlation exists between the 2 systems for detecting influenza activity in the United States (50).

B. Mortality Surveillance

Figure 21 shows pneumonia- and influenza-associated deaths reported from 121 cities in the United States for the entire country from 1974-77 and for the 9 geographic divisions from 1976-1977. For the country, such mortality remained below the epidemic threshold for the entire 1976-77 influenza season. By geographic divisions, only the South Atlantic had a pneumonia and influenza death rate that exceeded the epidemic threshold, and that occurred in a 3-week period in March 1977 (5). Table 3 lists excess mortality due to pneumonia and influenza and total excess deaths from October 1957-April 1976. For the nation, no excess deaths due to pneumonia and influenza occurred during the 1976-77 influenza season. Figure 22 shows a comparison of pneumonia- and influenza-associated deaths with 1) total deaths for all causes for all ages and 2) deaths from all causes by age groups. No excess mortality from all causes appeared during the 1976-77 influenza season.

C. Summaries by Geographic Areas

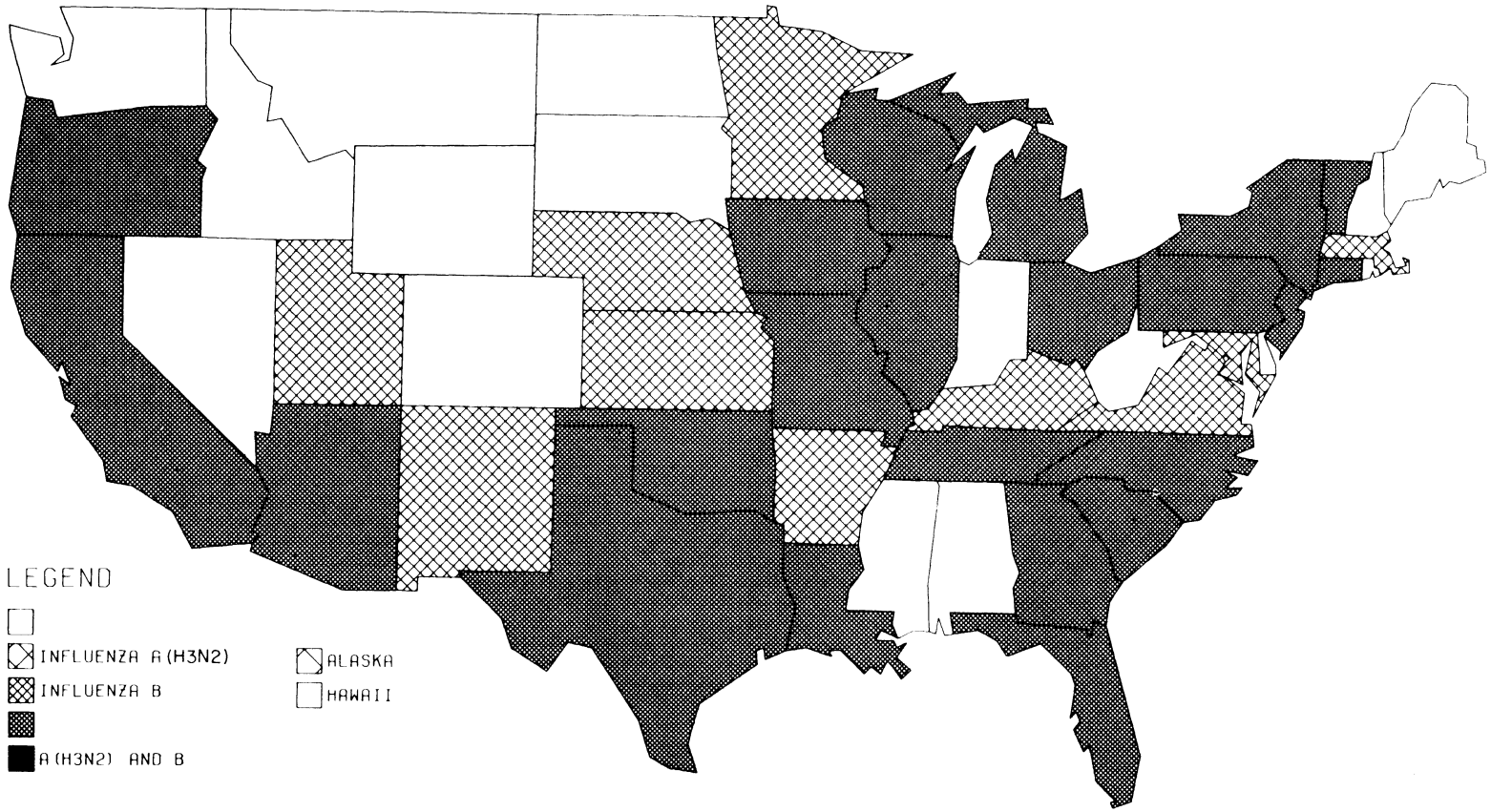
Figures 12 through 17 reflect the extent of reported influenza activity in the states by selected 2-week periods within the peak period December 26-April 16, 1977.

1. New England Division. This region had a very mild influenza season. School outbreaks occurred in late January in both Connecticut and Vermont. B/Hong Kong influenza outbreaks occurred in Maine in late February, with activity continuing into March.

2. Middle Atlantic Division. The influenza season in this division began with B/Hong Kong in early December in Reading, Pennsylvania, with more generalized outbreaks occurring in Pennsylvania by mid-January. An outbreak of A/Victoria influenza which occurred in Pittsburgh, Pennsylvania, was traced to a group of physicians and their families who had taken a ski vacation in Vail, Colorado, from March 17-27, 1977. Of 62 persons who took this trip, 30 reported influenza-like illness subsequent to their return to Pittsburgh. A/Victoria/3/75 virus was isolated from 4 of the ill persons (51). A school outbreak involving 30% of 450 students occurred in late April in Pennsylvania. Specimens were obtained from 10 students, and 9 were found to be positive for A/Victoria/76. New York reported school outbreaks due to B/Hong Kong in Orange County by mid-January. Sporadic B/Hong Kong cases continued to occur in New York through early February. New Jersey reported sporadic cases of B/Hong Kong occurring in late January. In mid-April an A/Victoria outbreak involved elderly unvaccinated domiciliary patients in Yonkers, New York, resulting in 3 deaths; autopsy lung specimens from 2 of the 3 subjects yielded A/Victoria isolates (52).

3. South Atlantic. The South Atlantic was the only geographic division to suffer excess mortality due to pneumonia and influenza during the 1976-77 influenza season. A/Victoria activity began early in the season in this division; the first reported isolate was from a child who had a sporadic case of influenza and was hospitalized at the District of Columbia Children's Hospital in mid-November. Sporadic isolates of B/Hong Kong from children were obtained in early

Fig. 5 STATES REPORTING ISOLATES OF INFLUENZA VIRUS, WEEKS ENDING JULY 2, 1976 - JUNE 24, 1977



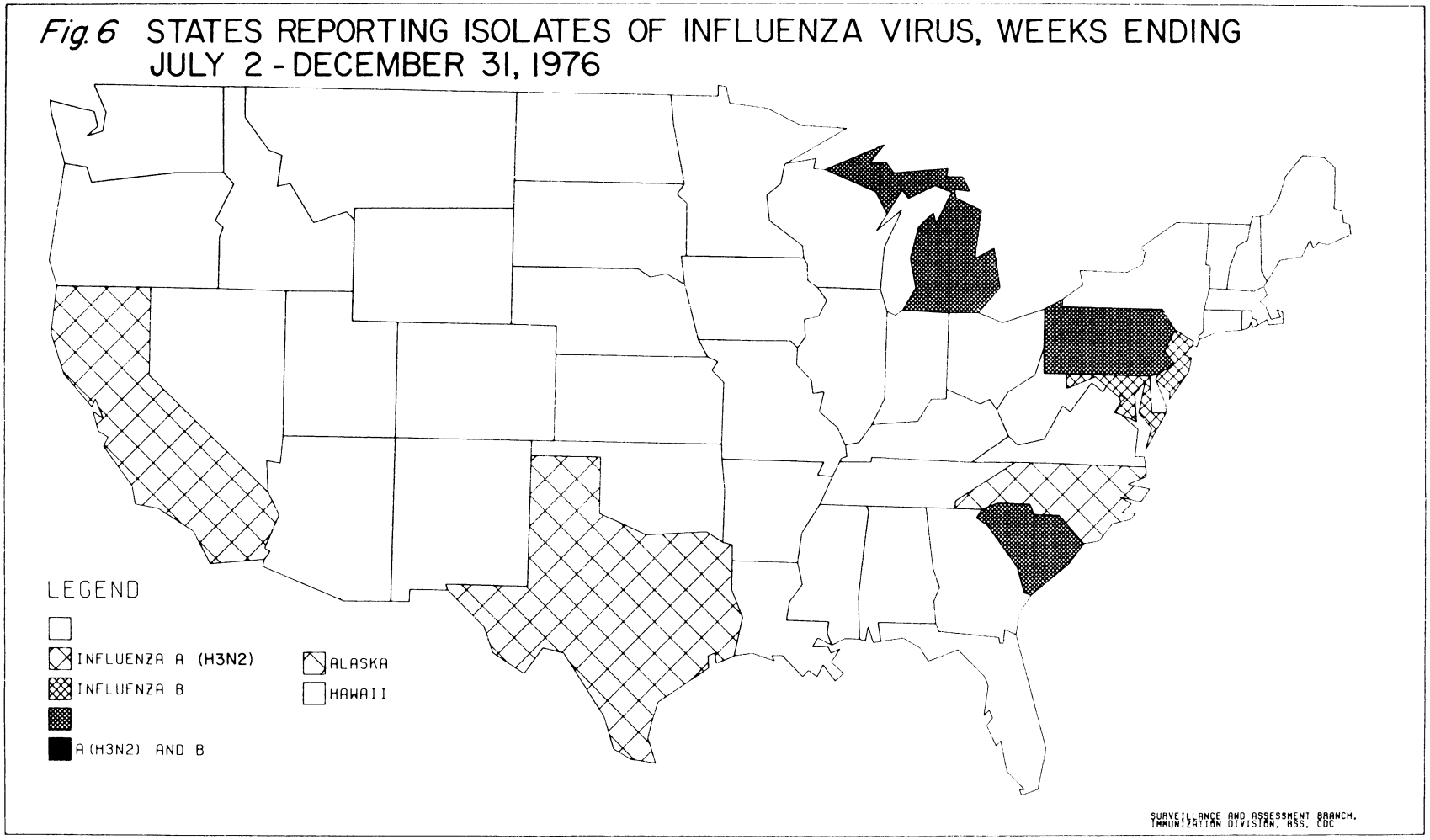


Fig. 6 STATES REPORTING ISOLATES OF INFLUENZA VIRUS, WEEKS ENDING JULY 2 - DECEMBER 31, 1976
LEGEND
INFLUENZA A (H3N2)
INFLUENZA B
A (H3N2) AND B
ALASKA
HAWAII
SURVEILLANCE AND ASSESSMENT BRANCH, IMMUNIZATION DIVISION, BSS, CDC

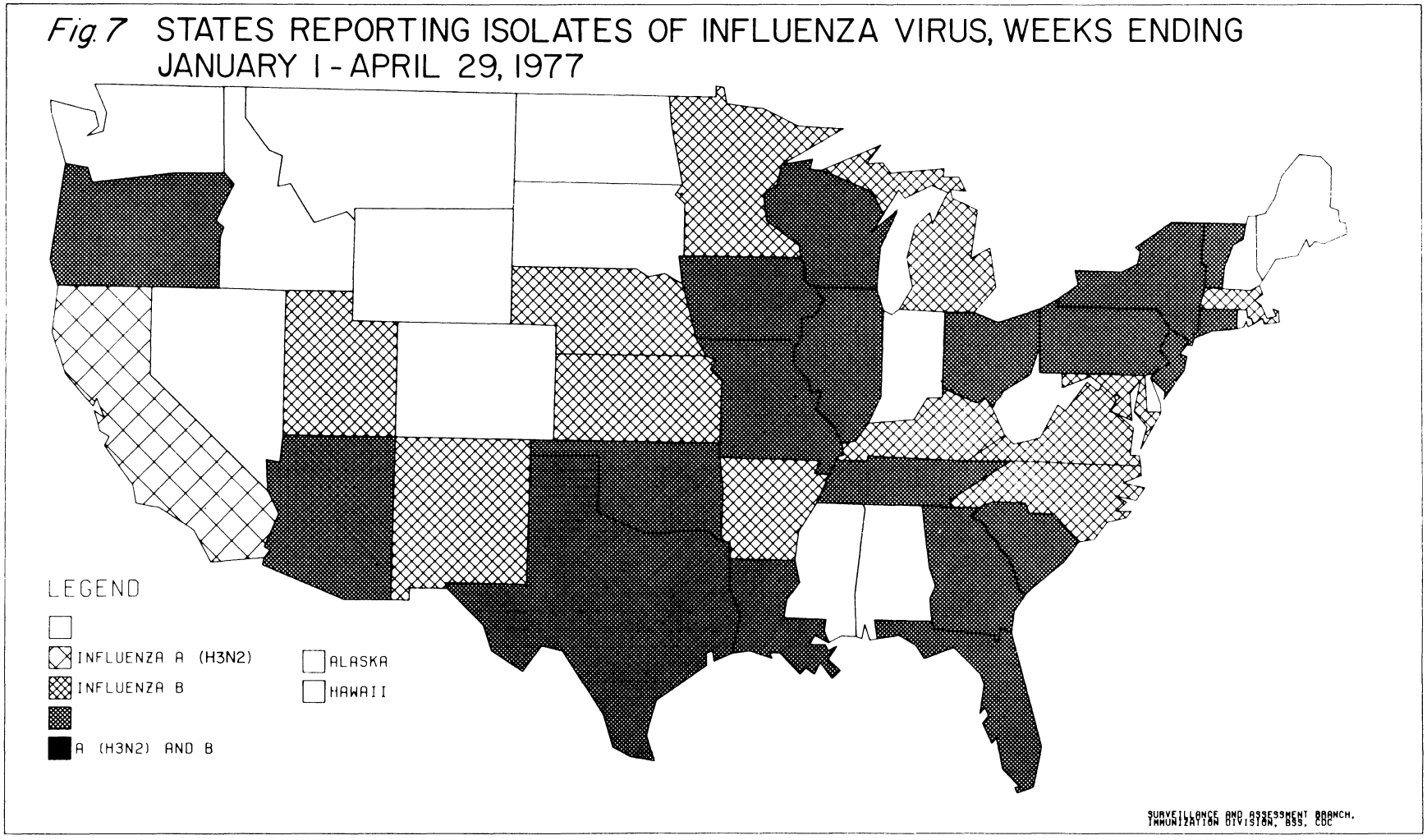


Fig. 7 STATES REPORTING ISOLATES OF INFLUENZA VIRUS, WEEKS ENDING JANUARY 1 - APRIL 29, 1977
LEGEND
INFLUENZA A (H3N2)
INFLUENZA B
A (H3N2) AND B
ALASKA
HAWAII
SURVEILLANCE AND ASSESSMENT BRANCH, IMMUNIZATION DIVISION, BSS, CDC

Fig. 8 STATES REPORTING ISOLATES OF INFLUENZA VIRUS, WEEKS ENDING FEBRUARY 7-28, 1977

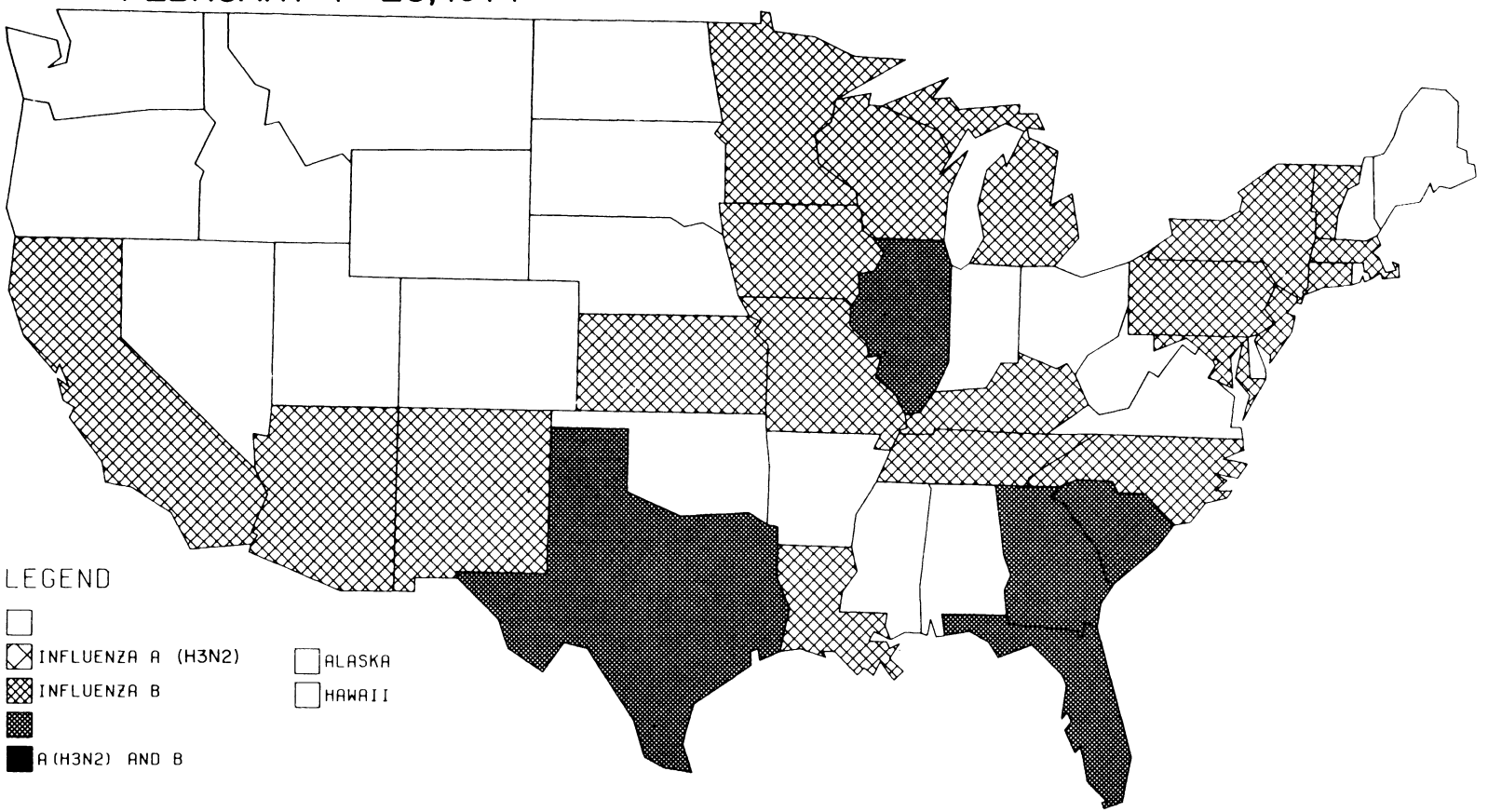


Fig. 9 STATES REPORTING ISOLATES OF INFLUENZA VIRUS, WEEKS ENDING MARCH 4 - 25, 1977

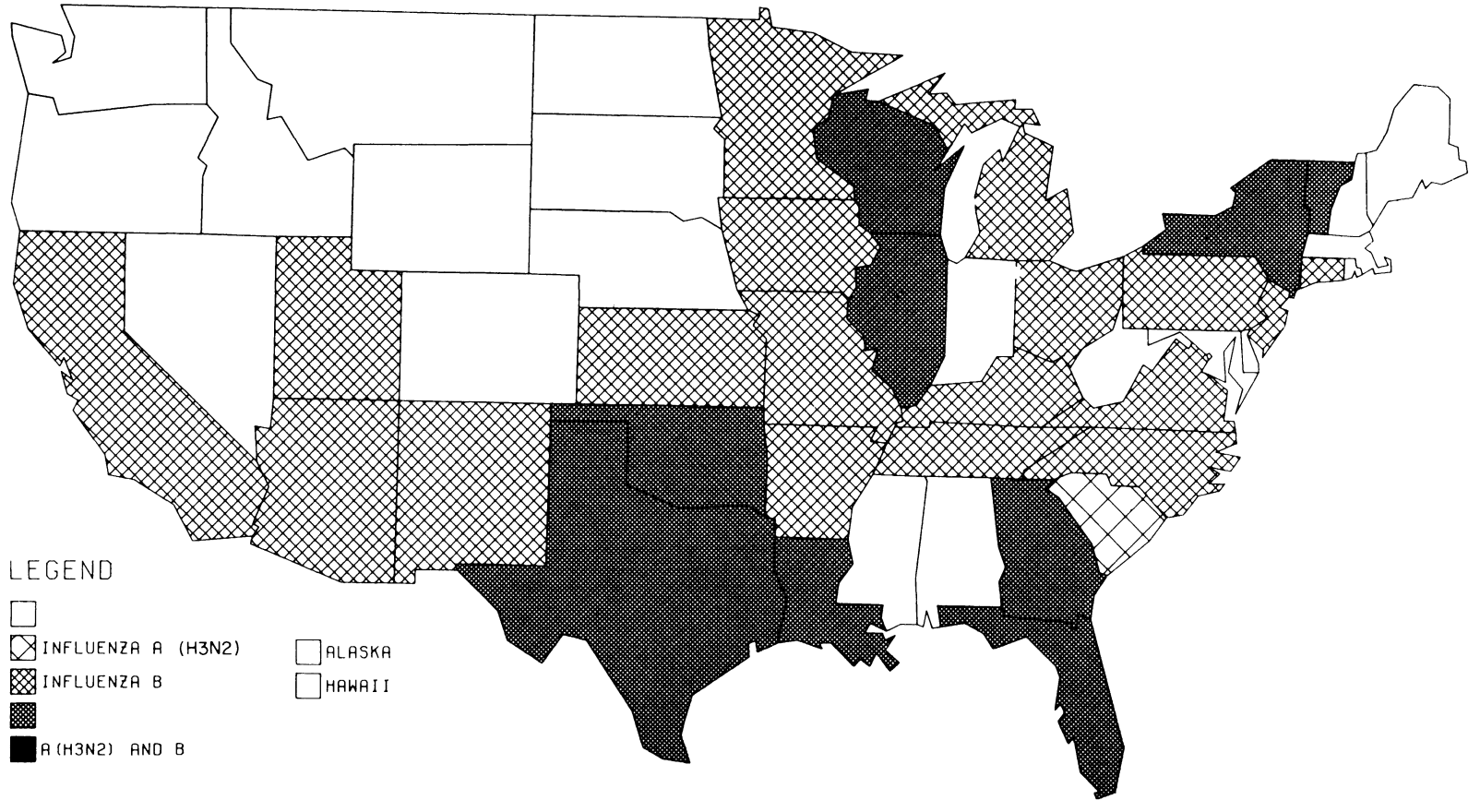


Fig. 10 STATES REPORTING ISOLATES OF INFLUENZA VIRUS, WEEKS ENDING APRIL 1-29, 1977

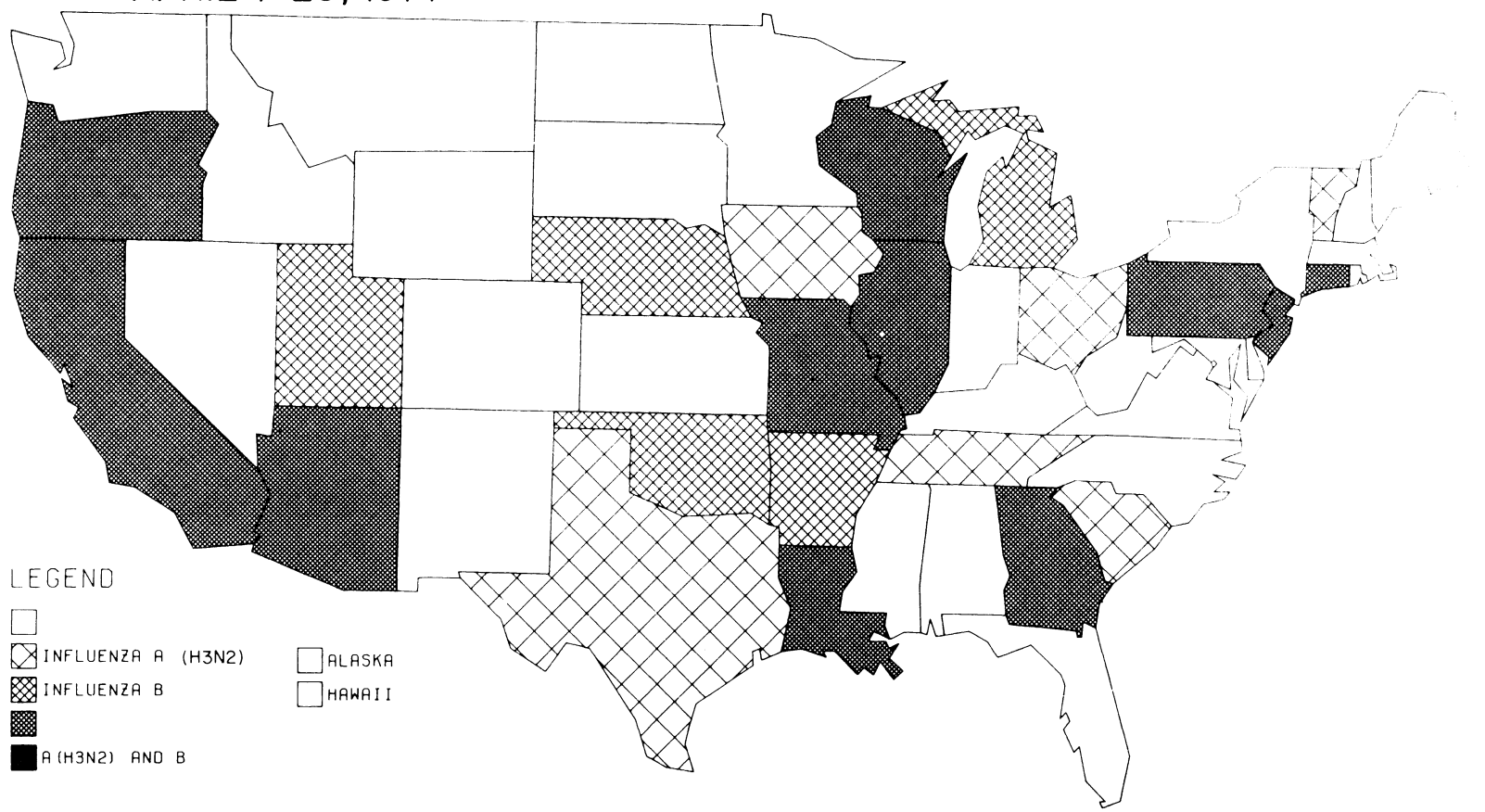


Fig. 11 STATES REPORTING ISOLATES OF INFLUENZA VIRUS, WEEKS ENDING MAY 6, - JUNE 24, 1977

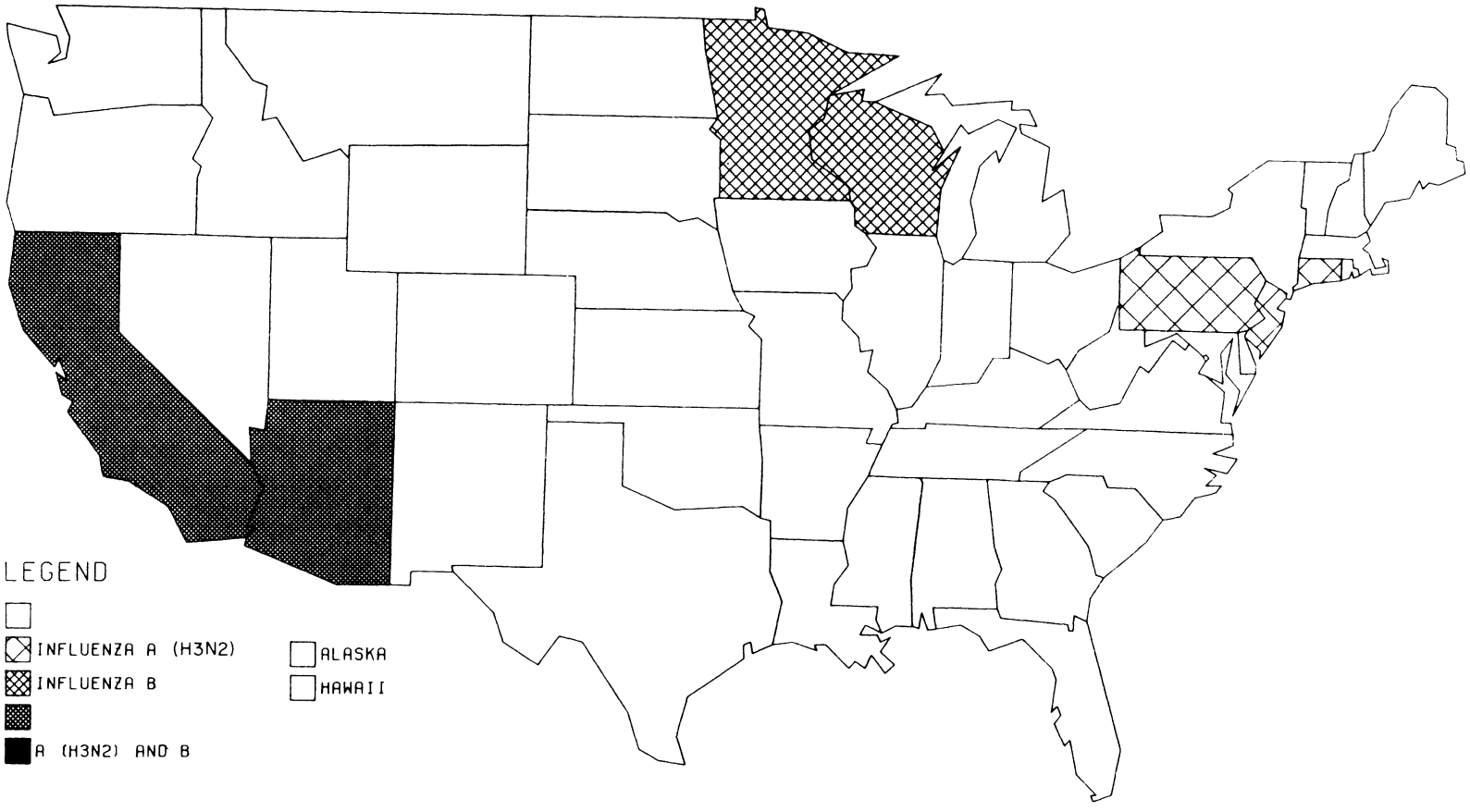


Fig. 12 INFLUENZA-LIKE ACTIVITY, DECEMBER 26, 1976 - JANUARY 15, 1977

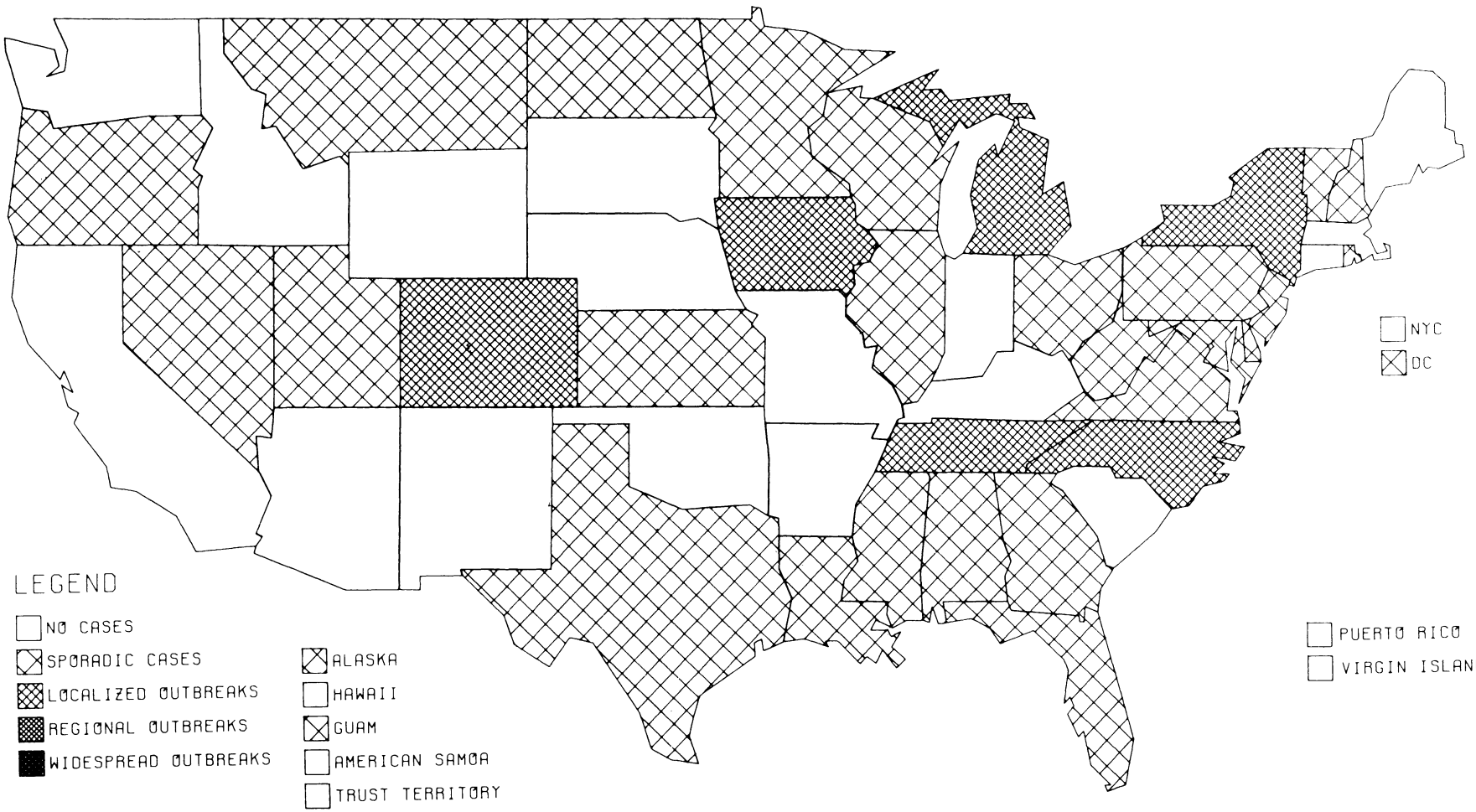


Fig. 13 INFLUENZA-LIKE ACTIVITY, JANUARY 16 - FEBRUARY 5, 1977

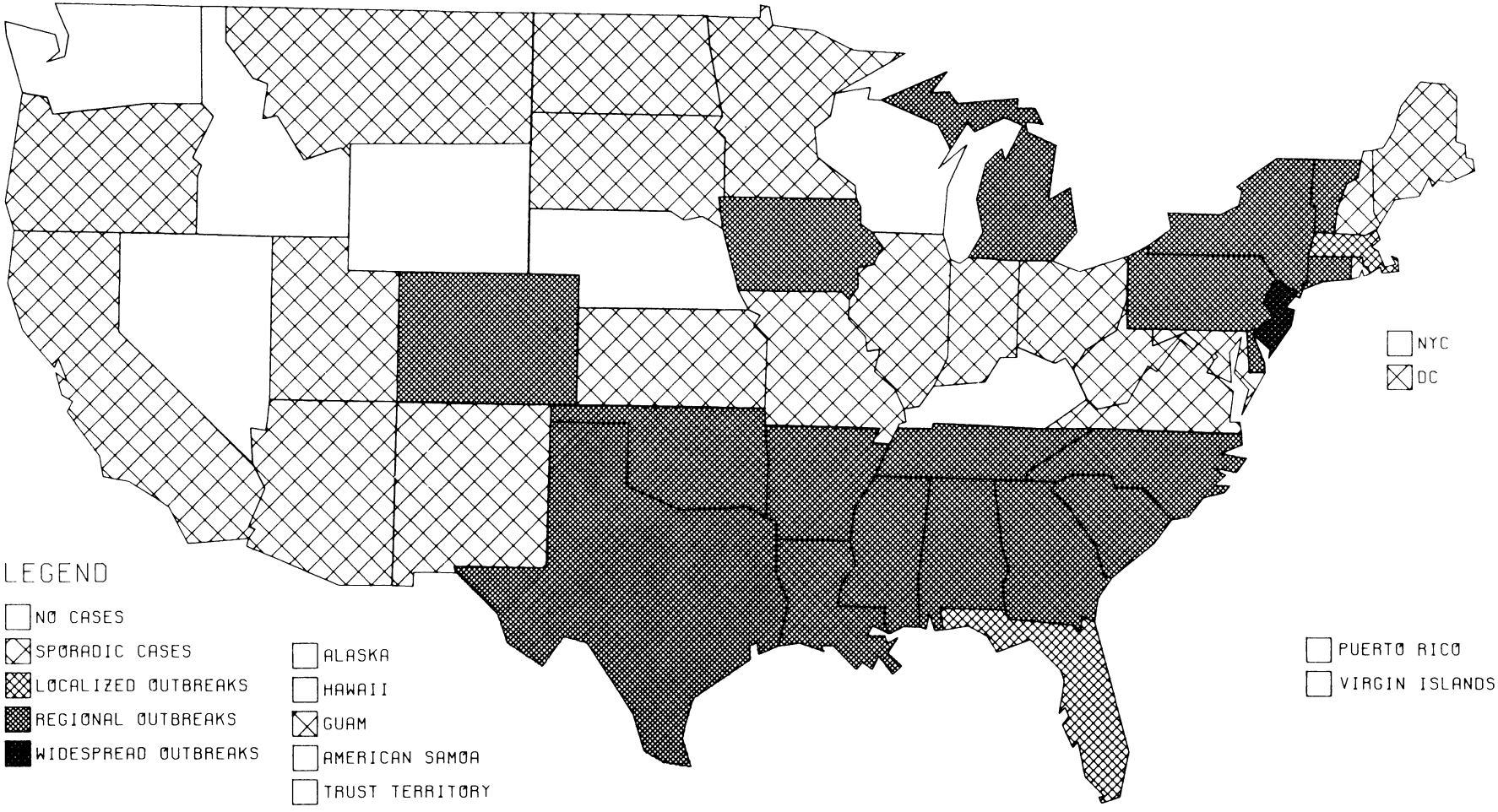


Fig. 14 INFLUENZA-LIKE ACTIVITY, FEBRUARY 6 - 26, 1977

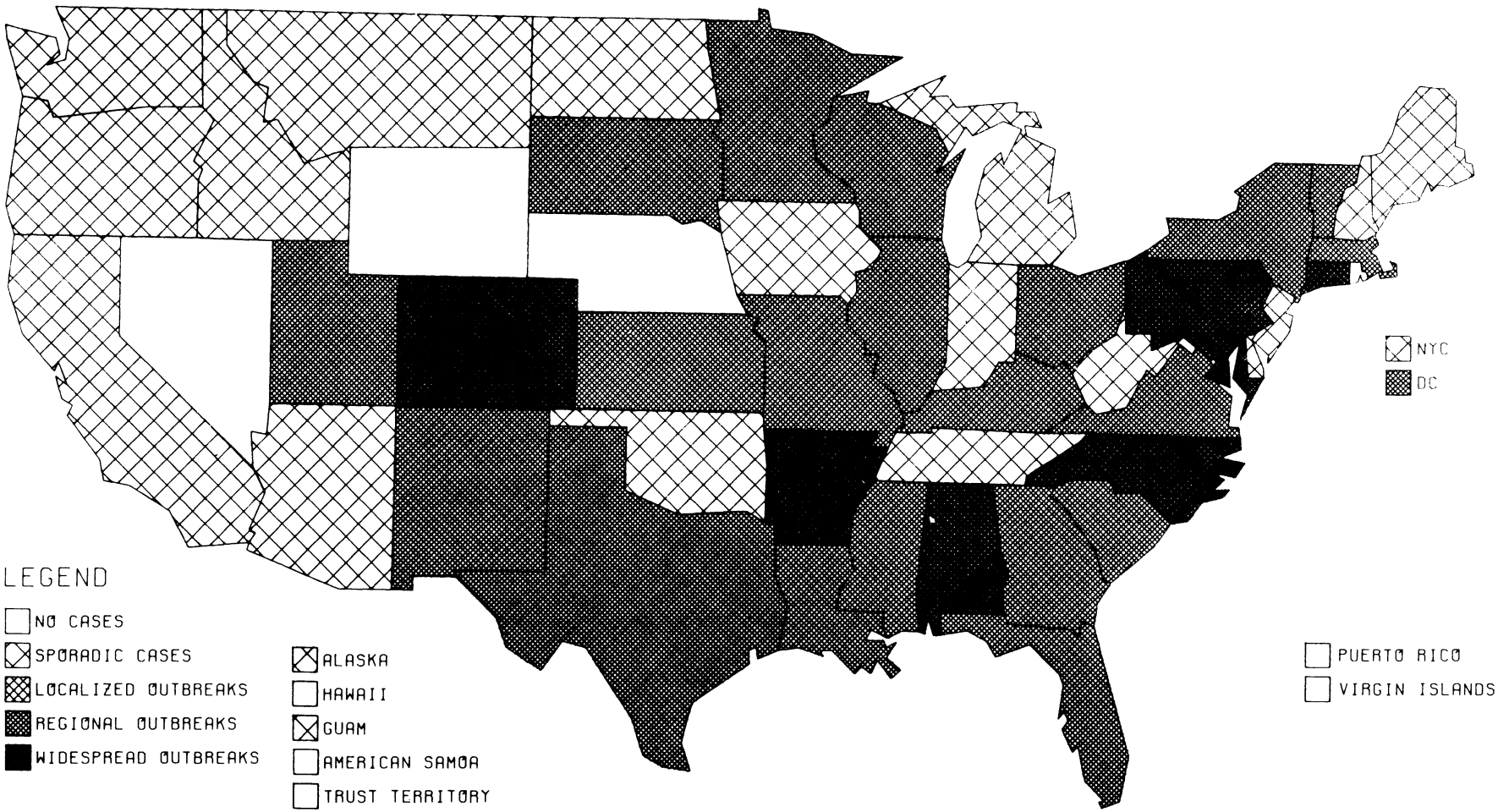


Fig. 15 INFLUENZA-LIKE ACTIVITY, FEBRUARY 27 - MARCH 19, 1977

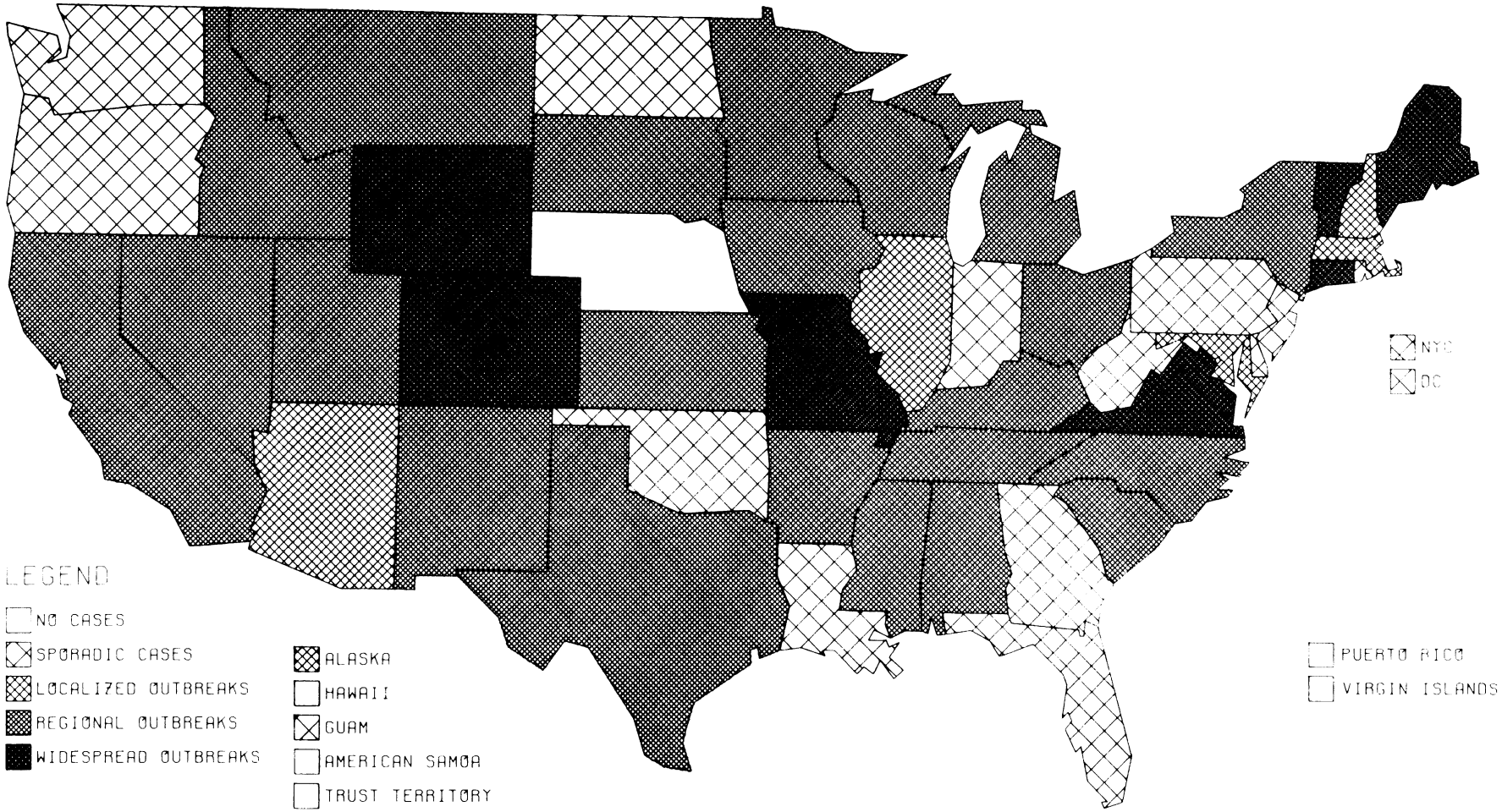


Fig. 16 INFLUENZA-LIKE ACTIVITY, MARCH 20 - APRIL 9, 1977

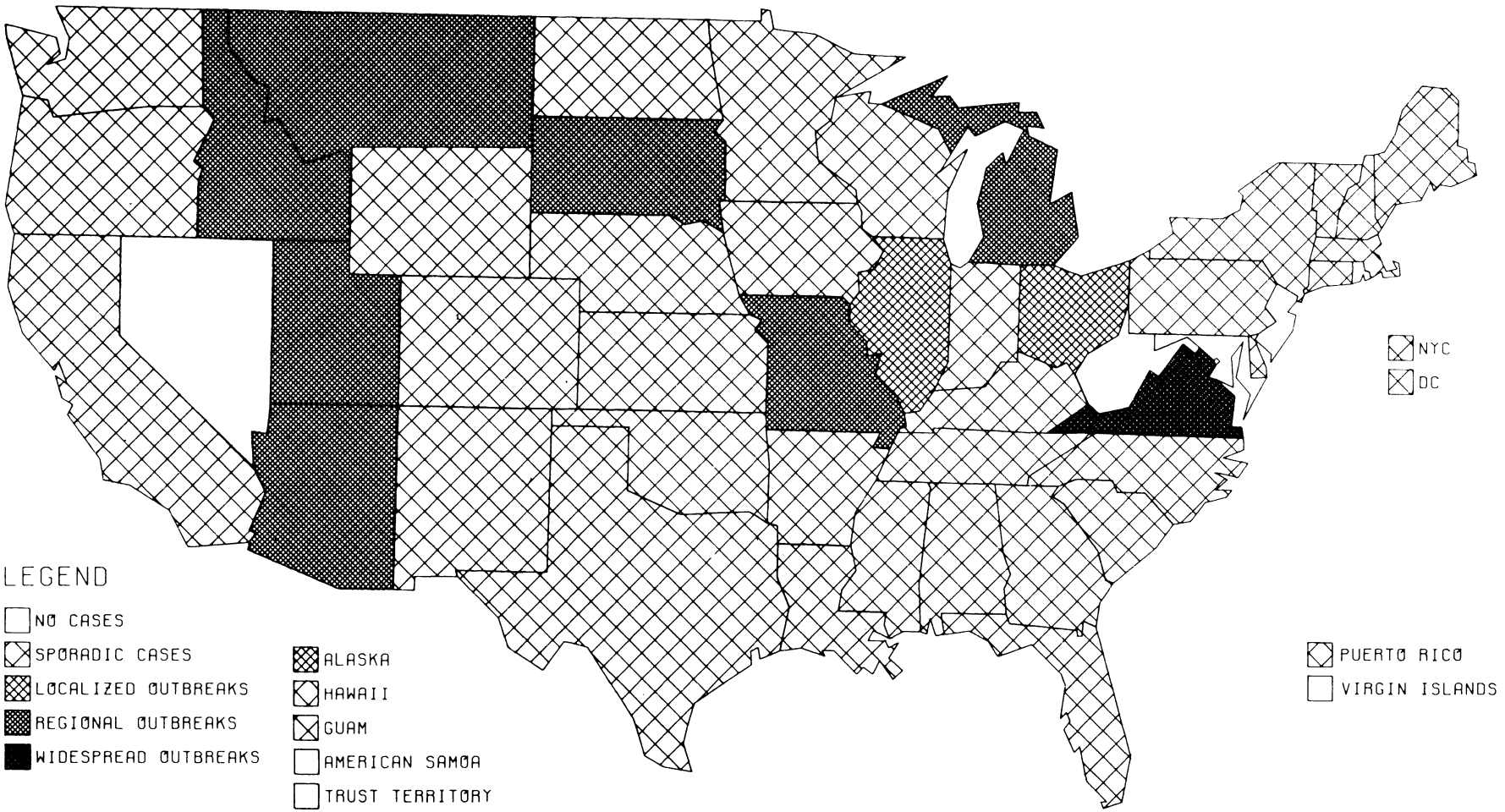


Fig. 17 INFLUENZA-LIKE ACTIVITY, APRIL 10-16, 1977

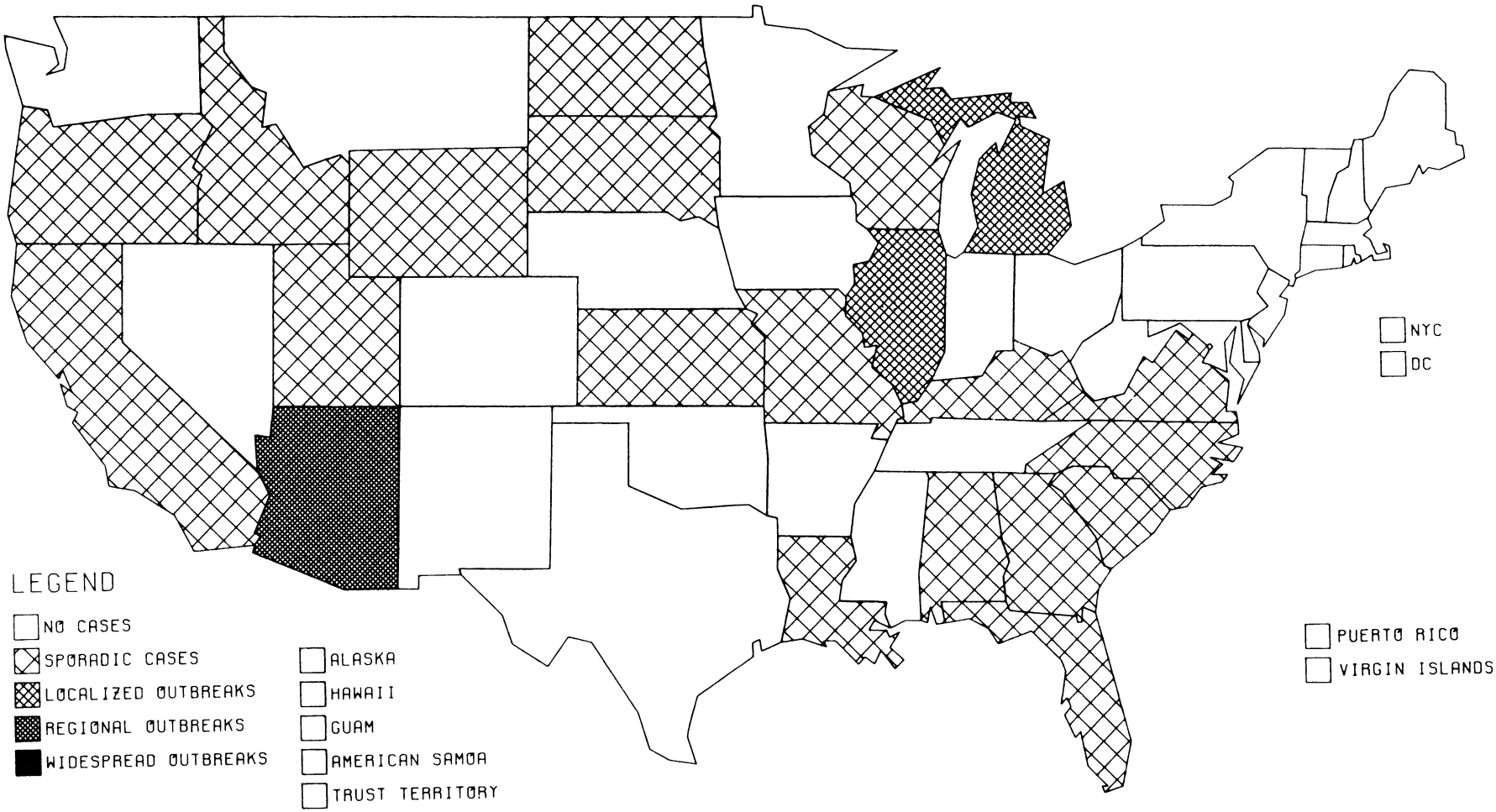


FIG. 18 ESTIMATED* NUMBER OF FLU-LIKE ILLNESSES, BY WEEK, UNITED STATES, JULY 1975-APRIL 1976 AND JULY 1976-APRIL 1977

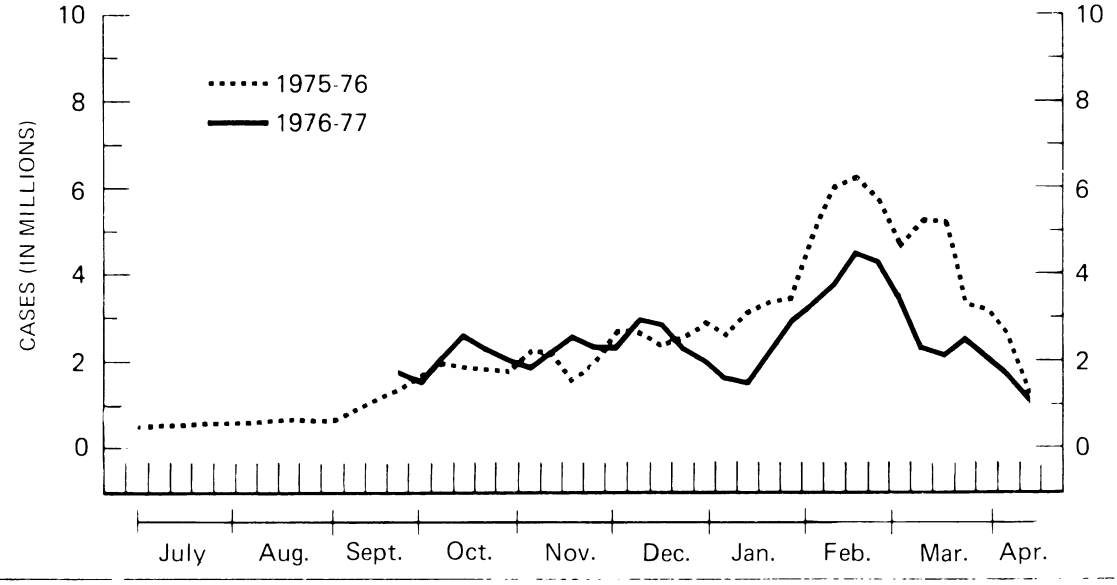
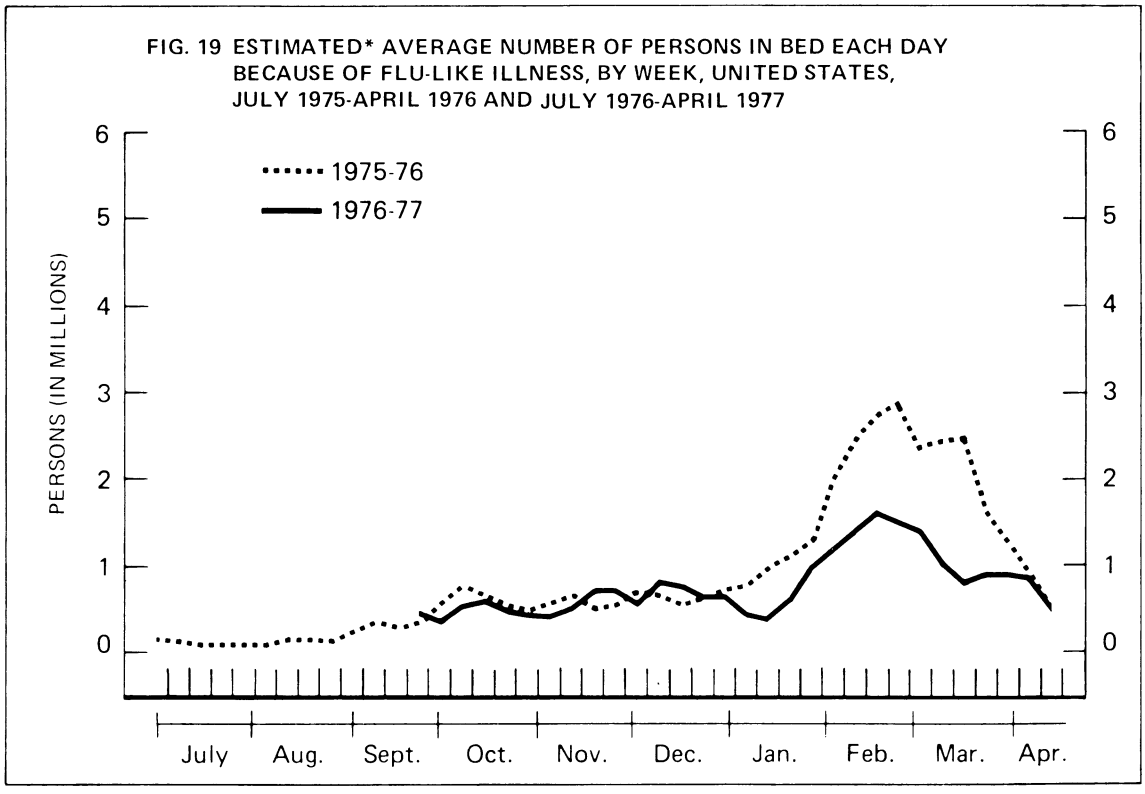


FIG. 19 ESTIMATED* AVERAGE NUMBER OF PERSONS IN BED EACH DAY BECAUSE OF FLU-LIKE ILLNESS, BY WEEK, UNITED STATES, JULY 1975-APRIL 1976 AND JULY 1976-APRIL 1977



*Data from The National Center for Health Statistics

Fig. 20 COMPARISON OF CDC INFLUENZA SURVEILLANCE DATA WITH NCHS HEALTH INTERVIEW SURVEY DATA FOR SOUTH ATLANTIC AND EAST SOUTH CENTRAL DIVISIONS, 1976-1977

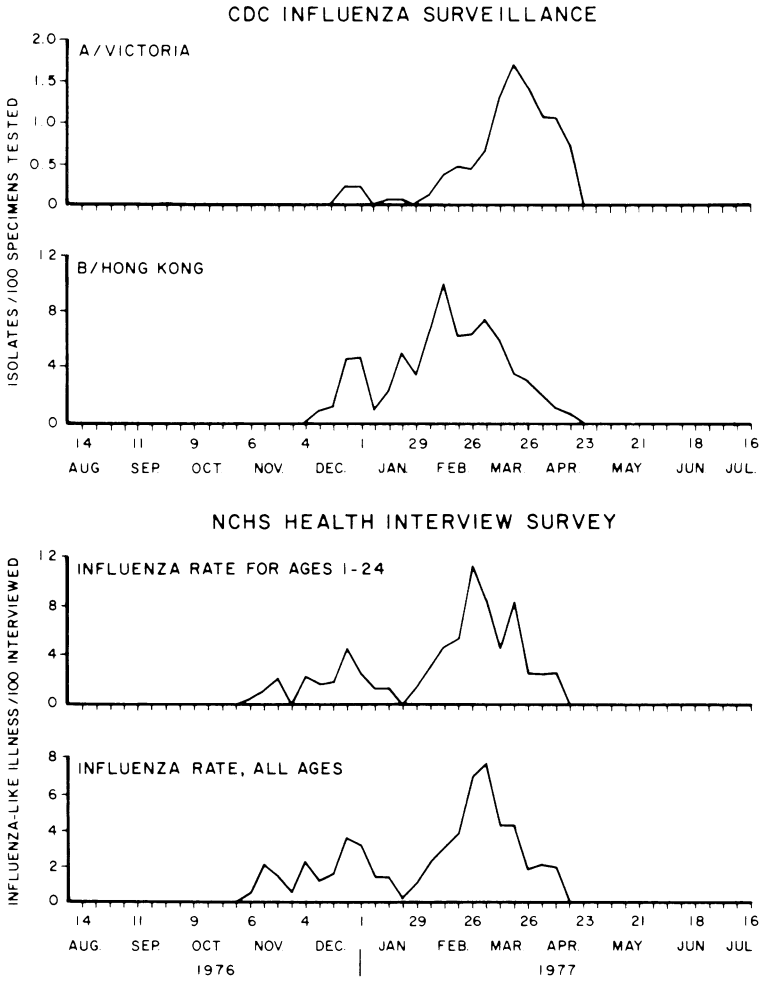


Fig. 21 PNEUMONIA-INFLUENZA DEATHS IN 121 UNITED STATES CITIES

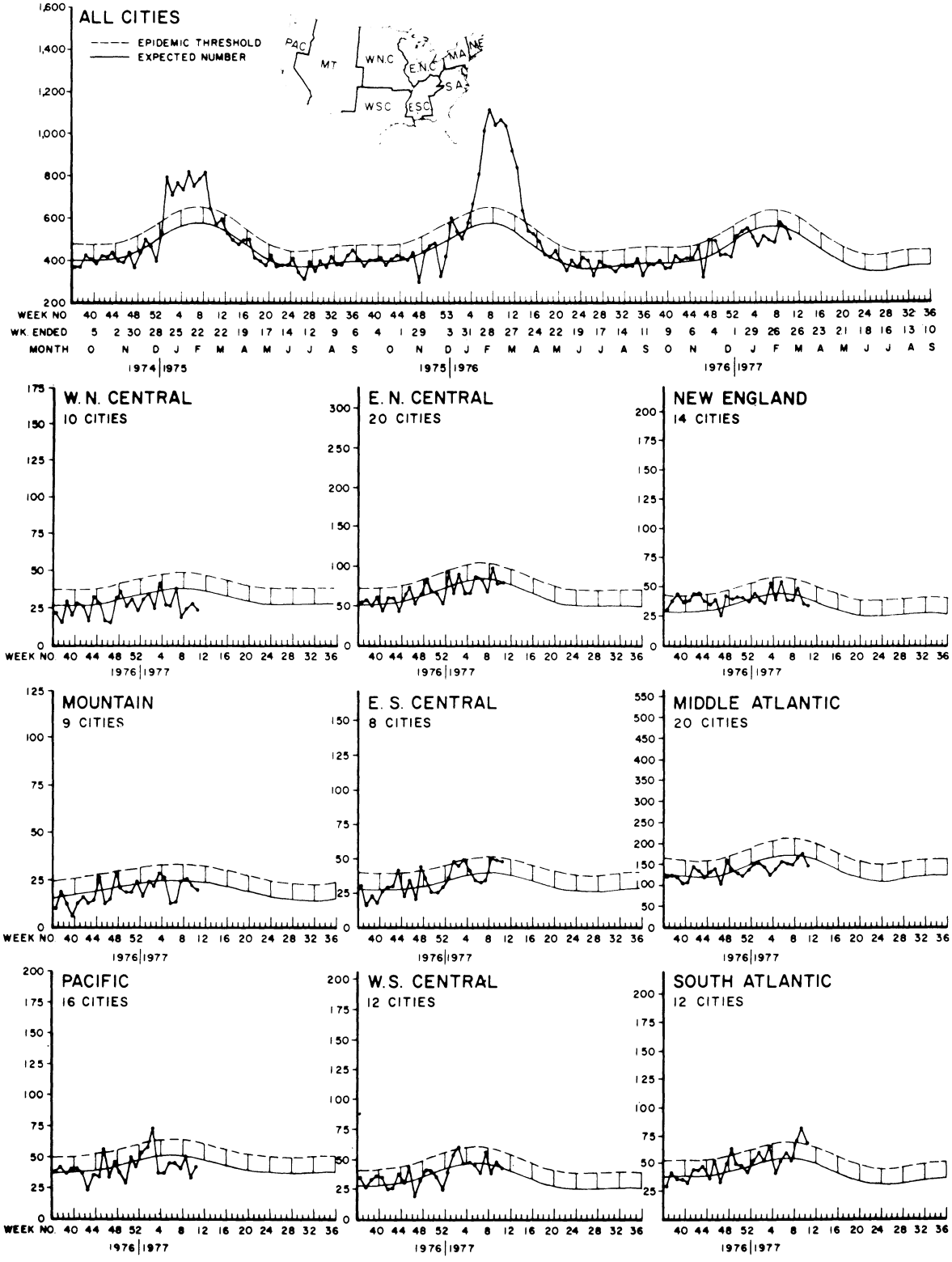


Fig. 22 MORTALITY IN 121 UNITED STATES CITIES

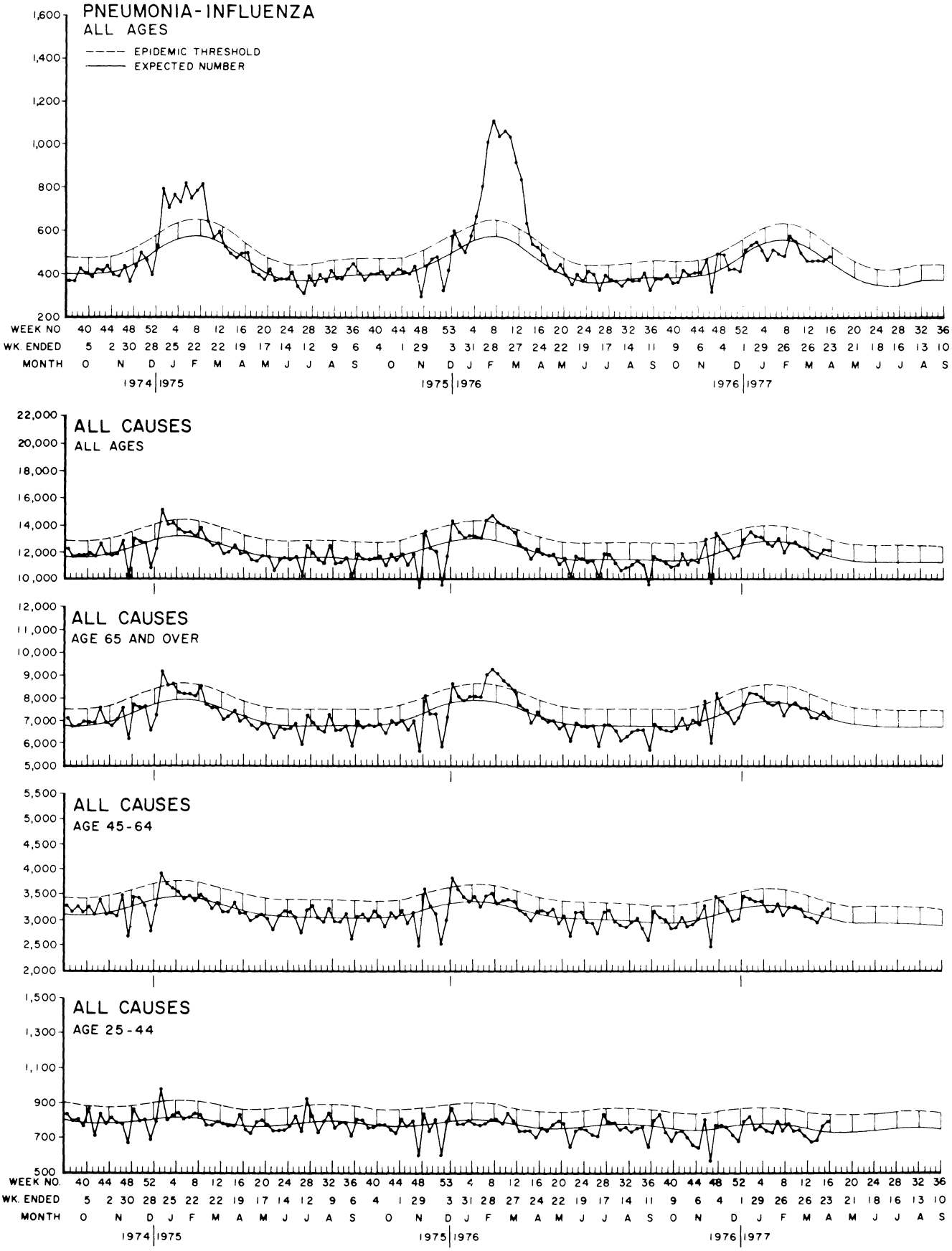


Table 3
Excess Mortality Due to Pneumonia and Influenza (P and I),
United States, October 1957-April 1976

Period of Excess Mortality*	Population (1,000s)	Estimated Number of Excess Deaths Due To P and I	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/(H2N2)
Mar - Apr 1959	176,420	1,400	0.8	7,900	4.5	A/(H2N2)
Jan - Mar 1960	179,323	12,700	7.1	38,000	21.2	A/(H2N2)
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/(H2N2)
Feb - Mar 1965	193,818	2,900	1.5	14,900	7.7	A/(H2N2)
Feb - Apr 1966	195,875	3,700	1.9	15,900	8.1	A/(H2N2)
Jan - Feb 1968	199,846	9,000	4.5	23,800	11.9	A/(H2N2)
Dec 1968-Jan 1969	201,921	12,700	6.3	33,800	16.7	A/(H3N2)
Jan - Feb 1970	203,736	3,500	1.7	17,200	8.5	A/(H3N2)
Jan - Feb 1972	208,232	5,600	2.7	24,600	11.8	A/(H3N2)
Jan - Feb 1973	209,851	3,680	1.8	8,997	4.3	A/(H3N2)
Feb - Apr 1976†	213,000	10,002	4.7	32,517	15.3	A/(H3N2)

*No excess mortality observed in 1961, 1964, 1967, 1971, 1974, 1975.
†Based on a 10% sample of mortality data from the National Center for Health Statistics. The mortality data for the earlier periods are based on final NCHS data.

December in North Carolina. The first A/Victoria activity in North Carolina began with sporadic cases in early January. By mid-January influenza B school outbreaks were widespread throughout North Carolina. In late December and early January sporadic B/Hong Kong cases were being noted in Georgia. By late January sporadic B activity was occurring in Maryland. Also in late January an outbreak caused by A/Victoria occurred in a Dade County, Florida, nursing home (2). This outbreak is described in more detail in Section IV,A3. Delaware and South Carolina experienced B/Hong Kong outbreaks in schoolchildren in late January. Sporadic A/Victoria activity began in late January and lasted through February in Georgia, North Carolina, and South Carolina. An outbreak of influenza illness due to A/Victoria occurred in mid-February among university students at Seneca, South Carolina. Throughout the month of February several school outbreaks due to B/Hong Kong were noted in DeKalb County, Georgia. The first B isolate in Florida came from a schoolgirl in Orlando in early February. School outbreaks due to A/Victoria occurred in Miami the last 2 weeks of February.

4. East South Central. With the exception of an outbreak of A/Victoria influenza involving schoolchildren and a college in Tuscaloosa, Alabama, in mid-February (4), all reported influenza in this division was due to B/Hong Kong. The first reported sporadic cases of B/Hong Kong occurred in schoolchildren in Tennessee in December. A large outbreak of B/Hong Kong influenza occurred at Vanderbilt University in Nashville and is described in greater detail in Section IV,D1 (35,36,43). In early February an outbreak of B/Hong Kong illness involving children and teenagers was detected in Newell, Alabama. By late February outbreaks of B/Hong Kong were occurring in schoolchildren in Kentucky.

5. East North Central. Two of 3 documented instances of transmission of A/New Jersey influenza from swine to man occurred in Wisconsin in the 1976-77 influenza season (1,31-36). The first case occurred in a farm worker in Brodhead, Wisconsin, amd the date of onset was November 26. The second case occurred in a 13-year-old boy who cared for the family pigs in Ixonia, Wisconsin. These cases are reported in more detail in Section IV,B2 and 3. In addition, Wisconsin reported the occurrence of sporadic B/Hong Kong activity beginning in mid-February, and by mid-March the state was also finding A/Victoria isolates. In mid-January, B outbreaks were occurring in Wayne County, Michigan, schools. By early February, B isolates had been obtained from hospitalized children in Illinois. College students in Evanston, Illinois, experienced 2 waves of influenza during the season. The first, a small outbreak due to B/Hong Kong influenza, occurred in mid-February; the second was due to A/Victoria and occurred in early April. The first influenza noted involved students returning from spring vacation skiing trips to Colorado. In late February both Indiana and Michigan reported

outbreaks of B/Hong Kong in nursing homes (40). Sporadic B isolates were obtained in early March in Ohio. A/Victoria outbreaks occurred in several Litchfield, Illinois, schools in March. Indiana obtained sporadic isolates of A/Victoria in late March.

6. West North Central. A possible case of A/New Jersey influenza, diagnosed serologically, occurred in a 32-year-old telephone lineman in Concordia, Missouri, who had onset of illness on October 10 (29,30). No source of his infection or spread of infection to his family or other members of the community was documented. (See Section IV,B1.) Missouri also reported sporadic B isolates occurring in February and sporadic A/Victoria isolates in mid-April. The final documented case of transmission of A/New Jersey influenza from swine to man occurred in Litchfield, Minnesota, in early January. The person concerned was an employee of a swine farm. (See Section IV,B4.) Minnesota also reported a B outbreak in Rochester in late January. Widespread school outbreaks due to B/Hong Kong influenza occurred in late January in Iowa. Kansas reported widespread school outbreaks due to B/Hong Kong the latter half of February. Sporadic isolates of A/Victoria were obtained in late March from North Dakota.

7. West South Central. Texas was the center of much influenza activity in the 1976-77 influenza season. In early December sporadic B isolates were first obtained from children. Sporadic A/Victoria isolates were obtained in Houston, Texas, and Bexar County, Texas, in February. From February 6 through 16, a mixed outbreak of B/Hong Kong and H3N2 influenza identified as A/Victoria affected air force recruits at Lackland Air Force Base in San Antonio (40). This outbreak was the presumed source of a subsequent outbreak that occurred at Lowry Air Force Base in Denver, Colorado (39). On March 17 isolates from both the Lowry and Lackland outbreaks as well as an isolate from a San Antonio civilian were found by CDC to be different from A/Victoria, and this virus was named A/Texas/1/77 (41). In early January Louisiana reported outbreaks of influenza B/Hong Kong in elementary schoolchildren in the western central part of the state (1,53). In early February B/Hong Kong outbreaks occurred in schoolchildren in Oklahoma. An outbreak of A/Victoria influenza occurred primarily in college students in Norman, Oklahoma, in mid-February. Arkansas reported widespread school outbreaks due to B/Hong Kong in February. Sporadic A/Victoria isolates were obtained in late February in Arkansas.

8. Mountain. The first report in this division was of school outbreaks of B/Hong Kong in Grand County, Colorado. By early February one-third of the counties in Colorado were reporting school outbreaks due to B/Hong Kong. Beginning on February 10, 1977, an outbreak of influenza initially attributed to the A/Victoria strain began at Lowry Air Force Base in Denver. Subsequent analysis of these strains revealed that they were related to the A/Texas/1/77 type (39,41). In late February Idaho and Utah reported widespread influenza outbreaks due to B/Hong Kong in schoolchildren. New Mexico reported A/Victoria isolates from middle to late February. Sporadic B isolates were obtained in late February from Arizona. Sharp outbreaks of influenza-like illness caused the closing of schools in Lincoln and Clark counties in Nevada in February. Arizona obtained sporadic A/Victoria isolates in late March and, in late April, also isolated sporadic A/Texas influenza viruses. A school outbreak due to A/Victoria occurred in a Tucson junior high school with a 25% attack rate.

9. Pacific. The first reported case in this division was in Albany, California, where an isolate of A/Victoria was obtained from a patient returning from a trip to the Orient who had onset of illness on October 11, 1976. (See Section IV,A2.) By late November local outbreaks of A/Victoria influenza were noted in Anchorage, Alaska. In late March an outbreak of A/Texas influenza occurred among airline passengers in Alaska (54). This outbreak is described in more detail in Section IV,C2. In mid-December a mixed outbreak due to A/Victoria and B/Hong Kong occurred at the San Diego Naval Regional Medical Center. By early February sporadic B isolates were being obtained in California. Sporadic A/Victoria isolates were obtained in California in early March. An epidemic due to B/Hong Kong involving 50% of the residents of a youth training camp in San Bernadino County, California, was reported in March. Sporadic isolates of A/Victoria were obtained in Washington from late February through early March. California obtained sporadic A/Texas isolates in late April. Sporadic A/Texas isolates were also obtained in Hawaii in late March. In late April A/Texas isolates were obtained from an outbreak at the Job Corps Training Center in Portland, Oregon. A/Victoria isolates were obtained from an outbreak among university students in Corvallis, Oregon.

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

1. Virus Surveillance. All WHO collaborating laboratories were alerted to the need for early detection of any swine influenza infections that might occur in 1976 prior to the winter. Thus, from September 1976 until the beginning of influenza activity, about 300 to 500 specimens were processed for virus isolation each week. From September 1976 through June 1977, a total of 24,772 specimens were reported to have been tested in WHO collaborating laboratories, and of these specimens 664 yielded influenza B strains compared with 279 influenza A (H3N2) strains, with nearly all isolates recovered between February and April (Figure 23). The peak of influenza B activity was from the end of February through March, whereas influenza A (H3N2) isolations in the United States were more frequent from March through April. (A cluster of influenza A (H3N2) isolates also was recovered in October 1976 from an outbreak in Guam.) Three isolates of swine influenza-like virus were also reported in December and January. (See Section IV,D3.) In addition to virus isolation, the WHO collaborating laboratories also tested 16,296 paired sera by hemagglutination inhibition (HI) and/or complement fixation (CF) test. Diagnostic antibody titer rises ($\geq$4-fold) were found for influenza A in 598 (4%) and for influenza B in 1,463 (9%) of these serum pairs.

2. Antigenic Analysis of Influenza A (H3N2) Viruses. From July 1, 1976, through September 30, 1977, a total of 663 influenza virus isolates were studied, comprising 452 influenza A strains and 211 influenza B strains. Influenza A (H3N2) viruses received from within the United States during the initial period of scattered outbreaks across the country were all identified in HI tests as resembling A/Victoria/3/75. A virus isolate (A/Texas/1/77) received from Texas in March (recovered from a specimen collected in December 1976), however, was found to be representative of other isolates from outbreaks among air force personnel in Texas and Colorado, and subsequently in many of the western states. When the A/Texas/1/77 strain was initially received, it was poorly reactive with antisera to all earlier reference viruses except a variant A/Victoria/112/76, which also was poorly inhibited by antisera to A/Victoria/3/75. After laboratory adaptation, however, A/Texas/1/77 virus was found to be reactive with the variant A/England/864/75 (described in CDC Influenza Surveillance Report No 91), and this relationship was confirmed by reciprocal HI tests (Table 4). Among all other influenza A (H3N2) viruses tested, only 3 isolates, recovered in Manila in August 1976, were found to resemble A/Victoria/112/76 and the similarly isolated A/Victoria/113/76 virus in reciprocal HI tests with ferret sera, whereas about 40% of all H3N2 strains from the United States resembled A/Texas/1/77. A further unusual variant, which was identified in small numbers, cross-reacted equally with A/Victoria/3/75 and A/Texas/1/77. This variant was A/Wisconsin/3/77, isolated in March, but analysis of strains submitted later indicated that A/Wisconsin/3/77-like strains were present in Brazil during the A/Victoria/3/75-like epidemics of April to May 1976, and in San Diego, California, during January 1977. HI reactions of A/Wisconsin/3/77 are shown in Table 5. Influenza A (H3N2) strains submitted from elsewhere in the Western Hemisphere and the Pacific and Far East resembled predominantly either A/Victoria/3/75 or A/Texas/1/77, with the exception of the above-mentioned A/Victoria/112 and 113/76 variants (isolated in July in Melbourne) and the 3 similar viruses from the Philippines. Only a small number of viruses were received from Europe. These were mainly similar to A/Victoria/3/75, although 2 viruses similar to a single unusual variant A/Allegheny County/29/76 isolated during the winter of 1975-76 were received from England and Italy (Table 5). A small number of representative A/Victoria/3/75-like and A/Texas/1/77-like strains, as well as the viruses with variant HAs, were examined in neuraminidase inhibition (NI) tests without detecting any trends toward significant antigenic drift in their N2 neuraminidase.

A novel finding was the co-circulation of the 2 H3N2 variants A/Texas/1/77 and A/Victoria/3/75 within single communities, without either strain becoming predominant. This was documented for the student population of Berkeley, California, and for the suburban populations of Seattle, Washington, by a collaborative study with laboratories in these locations (Table 6).

3. Antigenic Analysis of Influenza A (HswlNl) Viruses. All 3 swine influenza-like viruses isolated from humans in December 1976 and January 1977 were antigenically similar to A/New Jersey/76. One virus from Wisconsin (A/Wisconsin/263/76) was shown to contain 2 antigenically distinguishable subpopulations, similar to those found in the A/New Jersey/76 isolate. A virus (A/swine/Wisconsin/49/76) isolated from a pig on the farm where A/Wisconsin/263/76 was recovered from a farmhand also had this property (55). In contrast to the report from the New Jersey

Fig. 23 LABORATORY SURVEILLANCE FOR INFLUENZA INFECTIONS
Dec. 1976 through May 1977

Virus Isolations by WHO Collaborating Laboratories (including military sources) in the U.S.

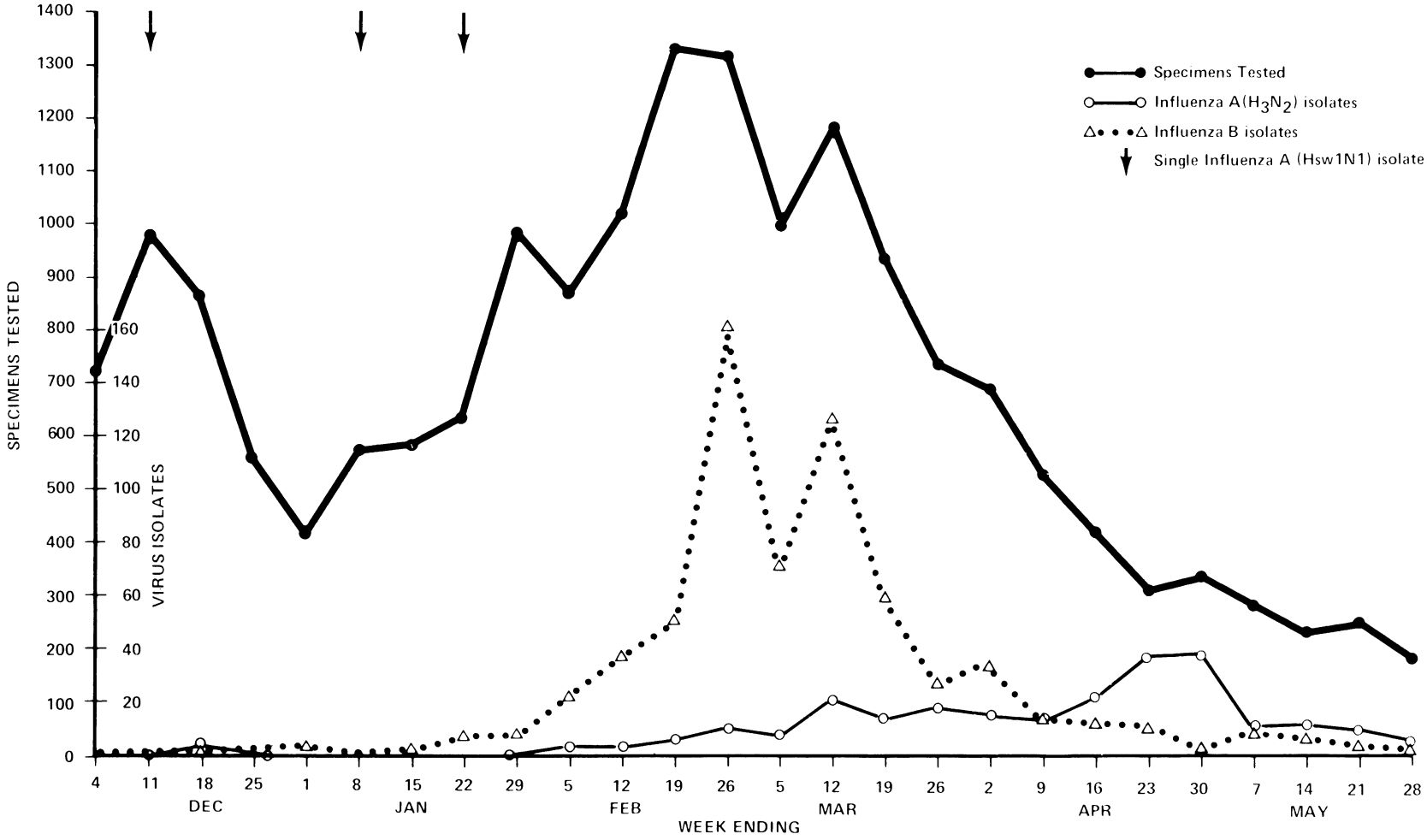


Table 4
Variability in Hemagglutination-inhibition Reactions of A/Texas/1/77-like Viruses Isolated in 1976-77

Antigen	Ferret Sera: A/Victoria/3/75*	A/Victoria/112/76	A/England/864/75*	A/Jamaica/1/76	A/Texas/1/77
A/Victoria/3/75	1280	320	80	80	80
A/Victoria/112/76	80	640	160	80	80
A/England/864/75	160	640	2560	640	2560
A/Jamaica/1/76	80	160	320	1280	640
A/Texas/1/77 (E4)	40	320	160	640	640
A/Texas/1/77 (E8)	80	320	1280	640	2560
A/Baylor, Houston/9/77	80	640	1280	640	2560
A/Lackland AFB/8/77	160	1280	2560	640	1280
A/Lackland AFB/11/77	40	320	320	160	640
A/Lowry AFB/9/77	40	320	640	160	320
A/Alaska/1/77	160	1280	1280	640	1280
A/Alaska/6/77†	80	640	640	320	1280

*Serum to recombinant containing an irrelevant neuraminidase (Neq1)
†Isolated from a passenger on the airplane delayed in Homer, Alaska

State Health Laboratory that A/New Jersey/76 viruses could not be isolated in monkey kidney (MK) cells, at least 2 of the new swine influenza viruses isolated from man could be recovered in MK cells, as reported from Wisconsin and Minnesota. Cell cultures used in these cases, however, were derived from rhesus monkeys, rather than the cynomolgus monkeys which were the source of cells employed in New Jersey during the time of the Fort Dix outbreak.

4. Antigenic Analysis of Influenza B Isolates. The reactivity of influenza B isolates with reference antisera was found in many cases to vary according to the passage history of the virus in different host systems. Commonly, viruses isolated in MK tissue culture cells had a low avidity, compared with reference influenza B strains, when tested with chicken or ferret sera. After passage in eggs the reactivity of some isolates often increased to the point where they could not clearly be distinguished from B/Hong Kong/5/72. In other instances, however, tissue culture isolates failed to grow in eggs, or were poorly inhibited by antisera to B/Hong Kong/5/72 even after repeated passage in eggs. Occasionally viruses isolated in eggs (e.g., B/Vermont/4/77) also failed to react well with B/Hong Kong/5/72 serum. A clue as to the possible explanation for this variability between isolates emerged from studies of the virus B/Arkansas/1/77, which was present in muscle tissue obtained at an autopsy. An isolate made in MK cells (clone 1) sent to CDC was grown in eggs and found to closely resemble B/Hong Kong/5/72 (Table 7), although virus reisolated in eggs from the muscle tissue at CDC by egg inoculation (clone 2) was poorly inhibited by B/Hong Kong/5/72 serum. This suggests that at least 2 antigenically distinguishable subpopulations of influenza B isolates were present in the same tissue, and may explain the variations between other influenza B isolates that were observed during the season. To assist in the identification of influenza B isolates that were poorly reactive with the standard B/Hong Kong/5/72 serum, CDC prepared a new reagent by hyperimmunization of roosters with the B/Hong Kong/5/72 reference strain. The birds were

Table 5
Hemagglutination-inhibition Reactions of A/Allegheny County/29/76-like and A/Wisconsin/3/77-like Variants

Antigen	Ferret Sera: A/Hong Kong/8/68*	A/Port Chalmers/1/73*	A/Mayo Clinic/4/75	A/Tokyo/1/75*	A/Victoria/3/75*	A/Philippines/18019/76	A/Wisconsin/3/77	A/Texas/1/77*	A/Tokyo/1/77	A/Brazil/31/76	A/Allegheny County/29/76	A/England/932/77
A/Hong Kong/8/68	640	160	80	80	320	160	160	320	40	320	640	640
A/Port Chalmers/1/73	80	1280	160	80	160	80	160	160	40	80	160	160
A/Mayo Clinic/4/75	80	80	640	40	80	80	80	160	20	40	80	40
A/Tokyo/1/75	80	160	40	640	640	160	320	160	160	320	160	80
A/Victoria/3/75	80	160	320	80	1280	320	1280	320	80	1280	640	640
A/Philippines/18019/76†	80	160	80	80	320	2560	640	320	160	640	320	320
A/Wisconsin/3/77	80	320	40	80	640	320	2560	1280	640	1280	640	640
A/Texas/1/77	160	160	80	80	160	320	1280	2560	1280	160	320	80
A/England/321/77	320	160	320	160	640	640	640	1280	320	320	640	160
A/Tokyo/1/77	40	40	20	40	80	80	320	640	640	80	80	20
A/Brazil/31/76	40	80	20	40	640	320	640	80	40	640	320	320
A/Allegheny County/29/76	80	160	80	80	320	320	160	80	40	1280	1280	640
A/England/932/77	80	160	80	40	160	320	160	80	40	320	640	640

*Serum to recombinant containing neuraminidase Neq1
†Similar to A/Victoria/112/76

Table 6
Isolations of A/Victoria/3/75-like and A/Texas/1/77-like Influenza A Viruses in Berkeley and Seattle, March-June 1977

Month of Specimen Collection	Berkeley: No. of Specimens Resembling* A/Victoria/3/75	Berkeley: No. of Specimens Resembling* A/Texas/1/77	Seattle: No. of Specimens Resembling* A/Victoria/3/75	Seattle: No. of Specimens Resembling* A/Texas/1/77
March	0	1	0	1
April	5	10	3	7
May	6	6	8	6
June	2	1	6	1
Total	13	18	17	15

*Determined by hemagglutination-inhibition testing with postinfection ferret sera

intravenously inoculated on days 1 and 21 with allantoic fluid containing B/Hong Kong/5/72 (boosted with a similar inoculum after 21 days) and bled at day 28. Sera obtained in this way were reactive with all influenza B isolates during the year.

Table 7
Antigenic Heterogeneity in Influenza B Viruses, 1976-77

Antigen	Hemagglutination-inhibition Reactions with Ferret Serum*					
	B/Hong Kong/5/72	B/University North Carolina/3/77	B/Washington DC/6/77	B/Taiwan/2/76	B/Arkansas/1/77 (clone 2)	B/Vermont/4/77
B/Hong Kong/5/72	160	40	40	40	40	20
B/University North Carolina/3/77	160	160	160	80	80	40
B/Arkansas/1/77 (clone 1)†	160	80	80	40	40	40
B/Washington DC/6/77	320	320	640	320	320	160
B/Taiwan/2/76	80	160	640	320	320	160
B/Arkansas/1/77 (clone 2)§	20	160	640	320	320	160
B/Vermont/4/77	40	80	640	640	320	160

*Serum treated with heat, trypsin, and periodate to inactivate nonspecific inhibitors
†Isolated by inoculation of muscle cell suspension in MK cells
§Isolated by inoculation of muscle cell suspension in eggs

An additional type of variability observed with influenza B viruses during the season was their reactivity with normal serum inhibitors in ferret sera. Although in most instances viruses were not reactive with non-antibody inhibitors in periodate-treated ferret sera, occasional isolates were observed to resemble pre-1967 influenza B isolates in having an enhanced inhibition by serum components in ferret sera that were treated with periodate (HI titers of up to 1,000 were seen in these cases). Use of the trypsin-heat-periodate combined treatment, however, satisfactorily inactivated such nonspecific inhibitors in ferret sera.

5. Evaluation of Antibody Persistence 1 Year After Influenza A/New Jersey/76(Hsw1N1) Vaccination. Volunteers aged 25-67 years received 1 dose of monovalent A/New Jersey/76 vaccine (200, 400, or 800 chick cellagglutination [CCA] units) in May 1976 in Atlanta; sera obtained from 438 individuals before vaccination and at 3, 32, and 52 weeks after vaccination were examined for HI antibody to vaccine virus. The HI antibody titers were higher at all intervals in the sera of individuals 52 to 67 years of age compared with the 25- to 51-year-old group; in sera from this latter group the HI titers were also slightly higher at all intervals among those receiving the higher CCA dose vaccines. However, the rate of decline was similar in all groups and the levels reached at 1 year were proportionate to the maximum 3-week postvaccination titers. In recipients of the 200 CCA vaccine, the prevalence of HI antibody titers $\geq$40 to A/New Jersey/76 virus before and at 3, 32, and 52 weeks after vaccination was, for the 25- to 51-year-old group, 2%, 95%, 78%, and 73%; for the 52- to 67-year age group, the corresponding figures were 65%, 100%, 97%, and 97%.

Neuraminidase inhibiting (NI) antibody, produced after A/swine/76/37 (Hsw1N1) vaccination but not after A/New Jersey/76 vaccination, appeared more frequently and declined more rapidly in

those without than in those with prevaccination NI antibody. Among those with prevaccination NI antibody, the rate of NI antibody decline at 1 year was comparable with the decline of HI antibody in the population with prevaccination HI antibody (56).

IV. SUMMARIES OF EPIDEMIC INVESTIGATIONS AND SPECIAL STUDIES

A. A/Victoria Influenza

1. Guam. Surveillance of influenza in Guam during 1976 and 1977 included the monitoring of school absenteeism as well as outpatient visits to Guam Memorial Hospital. The Guam Department of Health Laboratories also provided serologic diagnostic services for influenza. The influenza outbreak at Guam was first suggested by a 2-fold increase in a number of influenza cases diagnosed at Guam Memorial Hospital outpatient clinic for the week ending September 18. For the inclusive period September 19 through September 21, a 4-fold increase in reported cases was noted.

Interviews were conducted with all patients at Guam Memorial Hospital Outpatient Clinic who had diagnosed cases of influenza. They were queried about illness in other household members, neighbors, and fellow workers. Based on this information the estimated attack rate during this outbreak was 25%. Throat swabs were obtained from 18 nonrandomly selected patients with the onset of an influenza-like syndrome within 48 hours of reporting to the outpatient clinic. Sixteen of 18 throat swabs were positive for A/Victoria/75. Illness was documented in both the civilian and military population of Guam. Four fatalities were attributed to the acute outbreak, 2 of which occurred in elderly residents. A 27-year-old woman with rheumatic heart disease died in this period after a typical influenza illness, and a 31-year-old man with a history of seizure disorder also died. His case was later proven to be A/Victoria influenza by isolation of the virus from an autopsy specimen (38).

Reported by David J. Oblon, M.D., EIS Officer, and Ned Wiebenga, M.D., State Epidemiologist, Hawaii Department of Health, and Robert Haddock, M.D., Territorial Epidemiologist, Guam, Trust Territory of the Pacific.

2. Albany, California. On September 24, 1976, a 68-year-old resident of Albany, California, and her husband left the United States for a tour which took them to Tokyo, Taiwan, and Hong Kong. The patient first became ill on October 11, the day on which she returned from Hong Kong. On October 13 she became ill with a temperature of 103F, myalgia, cough, and sore throat. A throat swab taken on October 13 subsequently grew A/Victoria/75-like virus, and acute- and convalescent-phase blood specimens revealed a rising titer of CF antibody to influenza A from 1:8 to 1:32. The patient's husband also became ill with fever, myalgias, sore throat, and cough beginning on October 15. There was no evidence of further spread of illness into the community of Albany. This represents an example of importation of influenza from foreign travel in the Orient.

Reported by Brian M. Boni, M.D., Medical Epidemiologist, Infectious Disease Section, and James Chin, M.D., State Epidemiologist, California Department of Health.

3. Dade County, Florida. In late January 1977 the first documented outbreak of A/Victoria influenza in the United States occurred in a nursing home in Miami Beach, Florida. The resident population of this nursing home numbered 176, and 40 of these residents had received bivalent A/New Jersey-A/Victoria vaccine before the onset of this outbreak. Illness was characterized by fever and cough of 3 to 4 days' duration. Fifty-six (32%) of the 176 residents became ill. The index patient had onset of symptoms on January 18, 1977, with other onsets occurring between January 21 and 24, 1977. Nine of these 56 patients required hospitalization. Three deaths subsequently occurred, 1 of which was felt to be flu-related. The attack rate in vaccinees was 8% (3/40) in this population (2), while the attack rate in nonvaccinees was 40% (54/136). The efficacy of the bivalent vaccine containing A/Victoria antigen was calculated to be 83% in this population.

Reported by Robert Lumish, M.D., EIS Officer, Dade County, Florida, and E. Michael Yeller, M.D., Acting State Epidemiologist, Florida State Department of Health and Rehabilitative Services.

B. A/New Jersey Influenza

1. Concordia, Missouri. On November 19, 1976, the Missouri State Division of Health reported to CDC a serodiagnosis of A/New Jersey/76-like influenza infection in a 32-year-old telephone lineman with onset of illness on October 10. Symptoms included low-grade fever, myalgia, nasal congestion, and a dry cough. The influenza A/New Jersey/8/76 HI antibody titer on serum obtained on October 20 was less than 1:10, while sera obtained on November 13 and 23 and on December 2 had titers of 1:80, 1:80, and 1:40, respectively. No change in the A/Victoria/3/75 or B/Hong Kong/5/72 titers occurred. The patient had no known direct contact with swine, but influenza infections of swine were reported in the state. Investigation of household, business, and social contacts revealed no clinical, serological, or virological evidence of other influenza illnesses. There was no significant increase in school or industrial absenteeism (29,30).

Reported by John E. Jacobson, M.D., EIS Officer located in Missouri; H. Denny Donnell, M.D., State Epidemiologist, Missouri State Department of Social Services, Division of Health, and the Surveillance and Assessment Center, Bureau of State Services, CDC.

2. Brodhead, Wisconsin. On December 3, B. C. Easterday, D.V.M., University of Wisconsin, informed CDC that he had isolated a virus similar to A/New Jersey from throat washings taken on November 27 from a 23-year-old man in rural southern Wisconsin. The patient, who worked on a pig and dairy farm, had onset of illness on November 24. Symptoms included temperature ≥103F, chills, myalgia, cough, and 1 episode of vomiting. Sera taken on November 29, December 5, and December 8 exhibited A/New Jersey/8/76 HI titers of <1:5, 1:10, and 1:20, respectively. Investigation of household and other contacts did not indicate spread of infection, and no increased school or industrial absenteeism was observed. Ongoing swine surveillance conducted by the University of Wisconsin demonstrated influenza infections in swine in this area, and influenza viruses were obtained from 6 swine on the farm where this patient worked at the time of his illness (31,32).

Reported by H. Grant Skinner, M.D., State Epidemiologist, Wisconsin State Department of Health; B. C. Easterday, D.V.M., Department of Veterinary Sciences, University of Wisconsin; Ronaldean Pawlisch, D.V.M., Brodhead, Wisconsin; and the Surveillance and Assessment Center, Bureau of State Services, CDC.

3. Ixonia, Wisconsin. On December 20 an A/New Jersey-like virus was isolated by CDC from a specimen obtained by the Wisconsin Department of Health and Social Services from a 13-year-old boy in Ixonia, Jefferson County, Wisconsin. The patient's illness, characterized by fever to 102F, headache, and myalgia, began December 8. Serum specimens taken on December 12 and December 21 showed an A/New Jersey/8/76 antibody titer rise from <1:10 to 1:20. One influenza virus isolate was obtained from a sick pig on the farm where the patient worked. Investigation of household, school, and social contacts revealed several persons with influenza-like illnesses. Serologic tests detected rises of HI and NI antibody to A/New Jersey/76 in a 14-year-old classmate who had no swine contact. HI antibody at titers ≥1:20 was present in a single serum from 4 of 99 classmates. These 4 children had illness and contact with the index patient, and 1 lived on a pig farm. Surveillance of schools, institutions, and doctors' offices showed no evidence of increased respiratory illness in the community (33-36).

Reported by H. Grant Skinner, M.D., State Epidemiologist, Wisconsin State Department of Health; B. C. Easterday, D.V.M., Department of Veterinary Sciences, University of Wisconsin; and the Surveillance and Assessment Center, Bureau of State Services, CDC.

4. Litchfield, Minnesota. On January 11, 1977, the Minnesota State Department of Health reported an isolate of A/New Jersey-like virus from a 27-year-old farm worker from Litchfield, Minnesota. The man had been in contact with ill swine before the onset of his illness, which was characterized by fever, chills, myalgia, cough, and headache.

Viral specimens obtained from the pigs did not grow virus at the University of Minnesota. Serologic studies demonstrated a 4-fold rise in titers of HI antibody to A/New Jersey/76 virus in 4 of 6 pigs tested. Throat and nasal specimens from 6 persons ill with influenza symptoms, but not contacts of the index patient, were negative. Investigation of household and face-to-face contacts of the patient revealed 1 man with an initial titer of 1:40 to A/New Jersey virus, but later sera were not available for testing. The wife and teenage son and daughter of the owner of the index herd had HI titers to A/New Jersey of 1:20, 1:10, and 1:20, respectively, which remained stable at 3 weeks.

School, institutional, and physician surveillance showed no evidence of widespread illness in the community.

Reported by John Andrews, M.D. Acting State Epidemiologist, Minnesota State Department of Health; Richard E. Shope, Jr. D.V.M., College of Veterinary Medicine, University of Minnesota; and the Surveillance and Assessment Center, Bureau of State Services, CDC.

5. South Carolina. On April 25, 1977, the South Carolina Department of Health and Environmental Control reported to CDC the diagnosis of A/New Jersey/76-like influenza infection in a pregnant 17-year-old girl with an onset of respiratory illness on March 26 (the onset date might have been even earlier). She was hospitalized with "viral pneumonia" on March 30, and she died on April 12 with severe pneumonia. No virus was isolated in the state laboratory or at CDC from lung specimens obtained on autopsy, although Pseudomonas sp. was grown from the lung. Sera obtained on March 18 and April 1 were tested at CDC: HI titers to A/New Jersey/76 increased from $\leq$1:10 to 1:80, and NI antibody rose from $\leq$1:3 to 1:55, while titers of CF antibody to influenza A rose from $\leq$1:8 to 1:512. Antibody to A/Victoria/3/75 virus was absent in both specimens by HI and NI testing, and B/Hong Kong/5/72 antibody did not rise. These results were similar to the findings reported by the South Carolina State Department of Health Laboratory.

Although the patient resided in an active pork-producing area, she had no known contact with swine, and sera obtained from 18 family members and close contacts demonstrated no unusual HI antibody to A/New Jersey/76. Also, there was no evidence of clinical influenza in these contacts. Both influenza A/Victoria/3/75 and B/Hong Kong/5/72 viruses were isolated in the community this year, but no unusual morbidity or mortality was reported (37).

Reported by Richard L. Parker, D.V.M., State Epidemiologist, South Carolina Department of Health and Environmental Control.

C. A/Texas Influenza

1. San Antonio, Texas. The first A/Texas isolate in the United States was obtained from a 28-year-old white medical equipment salesman who had onset of illness on December 2, 1976. His illness was characterized by fever, cough, myalgia, and malaise. This man's primary business accounts were military hospitals in the San Antonio area. During the last week of November and the first week of December 1976 he had visited Wilford Hall Hospital, located on Lackland Air Force Base in San Antonio, where he visited nearly all clinics from the ninth floor of the hospital to the basement; he also visited the Lackland Air Force Recruit Dispensary.

Lackland Air Force Base is a major recruit center for the Air Force. Approximately 10,000 recruits are on the base at any given time. Beginning the week of February 7, a slight increase in upper respiratory tract infections was noted. In the week beginning February 14, URI illness rates increased dramatically. An estimated 600-700 cases of influenza occurred among the 10,000 recruits. Thirty isolates of A/Texas/1/77 influenza were obtained from this outbreak. Due to suspension of the National Influenza Immunization Program on December 22, none of these recruits had been immunized with the military trivalent vaccine preparation. The illness in general was characterized as mild and more typical of a B than of an A influenza outbreak (40,42).

Reported by Col. George D. Lathrop, Chief, Epidemiology Section, Brooke Air Force Base, San Antonio, Texas; Charles R. Webb, Jr. Acting State Epidemiologist, Texas State Department of Health Resources; and Surveillance and Assessment Branch, Bureau of State Services, CDC.

2. Alaska. On March 14, 1977, an internal Alaska Airlines flight developed engine trouble on take-off and was forced to return to Homer, Alaska. The plane sat on the runway for approximately 4 hours without its usual ventilation system in operation. An investigation begun on March 16 into the cause of illness among several passengers revealed that an influenza-like illness developed in 35 of 49 persons on this flight. Five of them were hospitalized. The ill passengers described the acute onset of a febrile illness consisting of fever, cough, myalgia, and headache, with an average incubation time of 33-1/2 hours following the airflight. Distribution of symptoms among primary cases were: 91% fever, 94% cough, 91% chills, 91% malaise, 74% sore throat, 57% myalgia, 24% diarrhea, 17% vomiting, and 8% nausea. Epidemiologic investigation indicated that the index case occurred in a 21-year-old woman who was well when she boarded the plane in Homer, but she became ill during the delay at the airport. Her symptoms included sudden fever, myalgia, cough, and chills. She had visited friends in Clam Gulch, Homer, Anchorage, and Seattle. Several of the friends she had visited before the flight subsequently became ill.

Throat swab specimens from 35 ill passengers later produced 11 A/Texas/1/77-like isolates. An additional isolate was obtained from a secondary contact of the persons who had primary cases on the airplane. Influenza-like illness occurred in 6 of 35 secondary contacts studied.

Several other outbreaks of influenza-like illness occurred in scattered areas across Alaska; however, since transportation is difficult at that time of the year, not all of these could be investigated and shown to be caused by A/Texas influenza. A short outbreak of illness was reported on Kodiak Island in both civilian and active duty coast guard personnel stationed at the base at Kodiak. Between March 30 and April 6, 1977, approximately 500 of 3,000 workers on the Alaska pipeline had a flu-like illness. The symptoms included headache, muscle pains, fever to 103 and 104F, some nausea, and malaise. Approximately 30 workers per day were confined to bed.

Beginning the second week of March 1977 and continuing to the end of March 1977, an outbreak of febrile upper respiratory illness was reported by the United States Public Health Service Hospital in Kotzebue, Alaska. Symptoms included high fever, muscle pains, cough, headache, and, in a few cases, nausea and vomiting. A small Air Force base in Kotzebue had reported sporadic cases of influenza-like illness between March 25 and April 4. Although throat swab specimens taken from acutely ill air force personnel did not yield an influenza virus, the medical epidemiologist who collected the specimens subsequently had an influenza syndrome, and a culture from him grew an A/Texas/1/77-like virus. Symptoms in the epidemiologist developed while he was returning to Fairbanks after having spent 5 days in the Kotzebue area.

A single A/Victoria and 4 A/Texas-like isolates were obtained from specimens collected in Kodiak. B/Hong Kong and A/Texas isolates were obtained from the Anchorage area. One isolate of A/Texas/1/77 was obtained from an ill woman in Fairbanks. Twenty-two of 26 paired sera from passengers on the airplane that was stalled in Homer, and their secondary contacts, exhibited a 4-fold antibody rise to A/Texas/1/77 (54).

Reported by John Middaugh, M.D., Acting State Epidemiologist, Alaska State Department of Health and Social Services; Thomas R. Bender, M.D., Director, Harold S. Margolis, M.D., and Michael R. Moser, M.D., Alaska Investigations Division, Bureau of Epidemiology, CDC; and Surveillance and Assessment Center, Bureau of State Services, CDC.

D. B/Hong Kong Influenza

1. Nashville, Tennessee. During the week of January 9 through 17, 1977, visits to the Vanderbilt Student Health Center for influenza-like illness increased from 4- to 6-fold. Between January 10 and February 5, influenza B/Hong Kong was isolated from 75 students who visited the health center. A random sample of 196 students were questioned by telephone in the first week of February concerning recent flu-like illness. Fifty-nine (30%) reported symptoms consistent with influenza. Of the 59 ill persons, 22 (37%) saw a doctor during their illness. The median length of illness was 6 days with a range of 2 to 22. On-campus residents were found to be at significantly higher risk of having flu-like illness than off-campus students. Of 102 household contacts, 48 (47%) had had a similar illness. There was no evidence of spread of influenza B to the surrounding community until the first week in February (35,36,43).

Reported by R. Campbell MacIntyre, M.D., EIS Officer, and Alan Hinman, M.D., State Epidemiologist, Tennessee State Department of Health.

2. Louisiana. An outbreak of influenza-like illness which occurred in January and early February in 2 rural northeastern parishes of Louisiana were studied in depth. The overall attack rate of influenza-like illness was 30.2%, with the highest attack rate of 55.6% occurring in the 6- to 10-year-old group; the attack rate declined gradually with advancing age. The outbreak was started the first week in January and lasted 6 weeks, with the peak incidence occurring the week of January 28. Fever was present in 95.5% of the cases, malaise in 88.7%, cough in 86.3%, headache in 81.8%, rhinitis in 76.4% of the cases, and myalgia in 64.5%. Six isolates of influenza B virus were recovered from ill patients cultured on January 17 (36,53,54).

Reported by Charles Caraway, D.V.M., and Gregory Storch, M.D., EIS Officer, Louisiana State Health and Human Resources Administration, and Surveillance and Assessment Center, Bureau of State Services, CDC.

E. Adverse Reaction Investigation

1. A Cluster of 3 Deaths in Pittsburgh, Pennsylvania. On October 11, 1976, 3 of 1,242 individuals vaccinated with the same lot of bivalent A/New Jersey, A/Victoria influenza vaccine in the same clinic in Pittsburgh died within 1 to 6 hours of vaccination. Because of this cluster of deaths, a field investigation was conducted on October 12 and 13, 1976. Unopened and opened vials of influenza vaccine of the same lots used at the clinic were forwarded to the Bureau of Biologics for analysis. A survey of persons who had been vaccinated at the involved clinic on October 11 was conducted. A 10% random sample was drawn from consent forms of recipients of the 3 lots of vaccine used at the clinic. Each survey participant was asked whether or not he or she had experienced reactions to the vaccination. The Public Health Clinic was visited, consent forms and incident logs examined, and 11 clinic personnel were interviewed to determine the procedures that had been followed there and the sequence of events that had occurred on October 11. Hospital emergency room logs in the clinic area were examined in an effort to locate sudden deaths possibly related to vaccination. All influenza immunization clinic directors in the counties immediately surrounding Pittsburgh were contacted to determine if any adverse reactions had occurred and to determine use of various vaccines by lot.

The sequence of events on October 11 was as follows: The clinic opened at 9:30 a.m. A line had already formed and recipients reported a 10- to 30-minute wait. No rain fell on this date, and the low temperature was 43F, the high 60F, and the average 52F. One thousand two hundred and forty-two people received 1 of 2 bivalent vaccine lots produced by the same manufacturer (1,000 doses from Lot A and 242 doses from Lot B). Vaccine was administered in a 0.5cc dose via 25 gauge 5/8 disposable needle and syringe. The clinic remained in operation until 3:30 p.m., when there was no longer any demand for vaccination.

Incident logs kept by the clinic nurses showed that 3 medical emergencies occurred in the clinic on October 11.

a. Case 1. The first of these emergencies occurred at 10:15 a.m. when a pallor developed in a 64-year-old woman who complained of feeling dizzy. An emergency rescue vehicle was summoned and arrived approximately 10 minutes later. The patient, however, refused to be taken to the hospital. She was driven home at 11:00 a.m. When contacted on October 13 by the field investigators, she was in apparently good health.

b. Case 2. At 10:55 a.m. a 77-year-old woman with previously diagnosed arteriosclerosis stated that she felt weak seconds after receiving her vaccination. The clinic nurse reported that she was pale, cyanotic, and had difficulty breathing. She was seated in a chair in the waiting area, and oxygen was administered. An emergency rescue vehicle was summoned and arrived in 10 minutes. The woman was taken to a local hospital where she was found to have acute pulmonary edema. In spite of aggressive therapy she suffered a cardiac arrest and was pronounced dead at 12:10 p.m. The cause of death was listed as arteriosclerotic cardiovascular disease and coronary artery insufficiency. These findings were later confirmed by autopsy.

c. Case 3. At 11:10 a.m. an 83-year-old woman with a history of angina was vaccinated. Following vaccination, she was seated in the waiting area approximately 6 feet from the woman described above in Case 2. As she observed the nurses and medical rescue team working with the patient, she, too, reportedly felt faint. She was helped to a cot, and a nurse gave her oxygen and a blanket. The emergency team was called for a third time. The patient was taken to another hospital where she was given oxygen and had an electrocardiogram performed, the results of which were within normal limits. She was discharged from the hospital at 2:15 p.m. She was contacted on October 13 and was in good health.

Two other patients who were vaccinated, apparently uneventfully, in the clinic that morning died later that day. (See d and e below.)

d. Case 4. A 71-year-old man with a history of arteriosclerotic cardiovascular disease was vaccinated at 11:15 a.m. His wife was also vaccinated, and both left the clinic at 11:30 a.m. to shop in a nearby supermarket. While shopping he complained of pain in both arms. The couple went home, and he immediately went to rest in an upstairs bedroom. At approximately 12:45 p.m. he was found apparently dead and was pronounced dead at 1:30 p.m. by his family physician. Following an autopsy, the cause of death was listed as acute myocardial infarction with thrombosis of the right coronary artery and severe arteriosclerotic vascular disease.

e. Case 5. A 73-year-old woman with a history of heart disease and emphysema was vaccinated at 11:25 a.m. As she arrived at the clinic accompanied by her son-in-law, an emergency vehicle pulled up on the sidewalk and 2 medical personnel went inside the clinic. While the woman stood in line, the emergency medical personnel came from behind the screen pushing a stretcher with a patient (See Case 3). The vaccination line was broken, and the potential vaccinees stepped aside to allow passage of the stretcher. The woman and the son-in-law were vaccinated in the clinic at 12:15 p.m. She was driven home, where she ate lunch and then retired to her room to watch television. She was found dead at 6:30 p.m. An autopsy revealed an acute myocardial infarction. All of these patients received vaccine from Lot A.

Eighty-three patients receiving Lot A and 50 patients receiving Lot B were contacted by telephone on October 12. Each recipient was asked whether he or she had had a reaction following vaccination, whether the reaction required bedrest or a physician visit, and how he or she would describe the reaction. Reactions reported by these patients were well within the limits reported in the national studies that found 1%-3% of recipients with minor reactions.

In other immunization clinics in western Pennsylvania between October 8 and 11, 5,750 doses of Lot A were administered in West Moreland County State Health Department clinics and 8,450 doses of the same lot were administered in Washington County clinics. No adverse reactions were reported to health authorities in either of these counties.

Empty and full vials of both lots used at the clinic on October 11 were examined by the Bureau of Biologics, Food and Drug Administration. All safety and sterility tests were repeated at the Bureau of Biologics, and no irregularities were found in the vaccine tested.

Examination of nearby hospital emergency room logs on October 11 revealed no additional cases of vaccine-associated reactions. No patients other than those mentioned above received emergency treatment at local hospitals following vaccination.

Before the National Influenza Immunization Program was initiated, statistical summaries of major medical events were prepared at the Center for Disease Control. In anticipation of the occurrence of common major medical events such as stroke and myocardial infarction only temporally related to vaccination, the expected number of deaths per 24-hour period for stroke and myocardial infarction was computed for each age group by using National Center for Health Statistics mortality data. Based on vital statistics data for the State of Pennsylvania, the same rates were calculated for that state. In 65 Pennsylvania counties a total of 77,000 doses of Lot A were administered to persons $\geq$65 years old on October 11. Four deaths--including the 3 in Pittsburgh--occurred within 24 hours in recipients of Lot A, for a rate of 5/100,000 per 24 hours. The expected death rate for this age group per day calculated from Pennsylvania's 1973 Natality and Mortality Statistics was 17/100,000; thus, no excess mortality occurred in vaccinees in this age group who received Lot A. Clinic procedures were performed according to the guidelines prescribed by the National Influenza Immunization Program. No irregularities were noted in the conduct of this clinic or in the technique for administering the vaccine.

Since the probability that 3 persons vaccinated in the same hour at the same clinic would subsequently die is low, it was postulated that the deaths of 1 or more of these 3 persons may have been related to stress involved in observing the medical emergency procedures described above. Interviews with next of kin in Cases 4 and 5 revealed that the persons concerned were in the clinic and had watched as at least 2 persons were taken out on stretchers (38).

Reported by William Parkin, D.V.M., Acting State Epidemiologist, Pennsylvania State Department of Health; Frank Clark, D.V.M., and Eleanor Sheiff, R.N., Allegheny County Department of Health; and Surveillance and Assessment Center, Bureau of State Services, CDC.

F. Vaccine Antigenicity Study

1. Immunologic Response of Immunosuppressed Children to Influenza Vaccine. To determine the response to influenza vaccine in immunosuppressed children, the University of Texas Health Science Center at San Antonio conducted a study on 46 patients. The patients, ranging in age from 3 to 18 years, were on standard cancer chemotherapy regimens. Patients with absolute neutrophil counts of less than 1,000/mm or absolute lymphocyte counts of less than 100/mm were excluded.

Two doses of bivalent A/New Jersey/76 and A/Victoria/75 or control saline were administered intramuscularly 4 weeks apart. Both split and whole antigens were used. Children received vaccine in doses ranging from 25 CCA to 400 CCA units.

Serum samples obtained at the time of the second injection and again 2 weeks later were tested by standard hemagglutination inhibition against A/New Jersey/76. Systemic and local reactions were monitored over a 48-hour period.

Antibody titers and reaction indices were compared with those of normal healthy children who received similar amounts of monovalent A/New Jersey/76 vaccine. No significant differences in antibody titers were found between normal children and the immunosuppressed group. Minor local and systemic reactions were similar for both groups; neither group had serious side effects (36,57).

Reported by P.A. Brunell, M.D., Chairman, Department of Pediatrics, University of Texas, San Antonio.

V. WORLDWIDE SURVEILLANCE

Influenza outbreaks worldwide during 1976-1977 generally paralleled the U.S. experience with the exception of the appearance in the U.S. of HswlN1 virus and of A/Texas strains in outbreaks. The reduction of susceptibles by the worldwide A/Victoria epidemics of 1975-1976 probably diminished the extent of H3N2 activity in 1976-1977 (14).

On the African continent, only Senegal and South Africa reported significant activity. In Asia, Japan reported widespread B/Hong Kong activity while A/Victoria outbreaks were common in Pakistan and Singapore. For the South Pacific, epidemics of A/Victoria occurred in Australia, New Zealand, and Guam. Europe experienced mostly sporadic activity with the exception of widespread activity due to A/Victoria in Hungary and Italy and due to both A/Victoria and B/Hong Kong in the Netherlands, the United Kingdom, the USSR, and Yugoslavia. From the Middle East, Israel reported widespread illness in young adults due to A/Victoria.

In North America, Canada reported an epidemic due to A/Victoria in March and April 1977 as well as countrywide outbreaks of B/Hong Kong during the same period. Martinique was the only country in the Caribbean to report significant influenza A outbreaks. For South America, the only reported epidemic was due to A/Victoria, and it occurred in Chile.

VI. METHOD FOR DIAGNOSING INFLUENZA OUTBREAKS

Two principal procedures are available to diagnose infection by influenza virus: 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 often believes that all febrile upper respiratory disease is the "flu," laboratory confirmation of influenza is important to document the true cause of "influenza-like" illness. Facilities for such diagnosis are available in almost every state and large city. Only when a virus has been isolated during an outbreak can the strain 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 can be easier to demonstrate a diagnostic rise in antibody than to isolate a virus from a single infected person because often only about one-third of respiratory specimens yield virus, whereas 50-80% of paired sera usually exhibit a significant rise in antibody titers.

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 (58-59).

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 an 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 through 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 usually shed before the onset of clinical illness and continues to be shed for 3 to 5 days after symptoms begin (60). Thus an individual with influenza may be infectious to others for a period of 5 to 7 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 (61). Because of viral shedding before illness, asymptomatic infection, and high transmissibility in closed populations, the measures commonly employed to limit nosocomial spread of other infectious diseases generally have not proven efficacious when applied to influenza. 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 may seem 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, 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 (62), 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 (63-66), and its value in preventing nosocomial influenza has been suggested (65). 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.

Considerations 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 (65). 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 are probably of limited value in preventing the introduction and spread of influenza in the hospital. Patients with confirmed or suspected influenza may be isolated or segregated in 1 area of the hospital if they are within 5 days of the onset of clinical illness. Patients with suspected acute influenza requiring admission should be admitted to the same area. Patients who are more than 5 days from the onset of their symptoms need not be segregated. Patients with uncomplicated influenza and no other illness requiring urgent hospitalization should not be admitted. Other elective admissions to hospitals need not be restricted.

During an influenza outbreak, hospital staff members should leave work as soon as they have the first sign of respiratory illness or other indication of influenza (fever, myalgia, malaise, or headache) and not return until they are recovered. Consideration should be given to having high-risk patient areas staffed by personnel who have either recovered from influenza, been adequately vaccinated, or who are on amantadine prophylaxis.

Restriction of healthy visitors is unlikely to significantly affect nosocomial transmission during influenza outbreaks. Persons with acute respiratory ilness should be asked not to visit the hospital.

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ERRATUM

The following change should be made in the Center for Disease Control Influenza Surveillance Report No. 91, 1975-1976, issued July 1977:

On page 1, paragraph IB, line 2, "8 WHO Collaborating Laboratories" should read "58 WHO Collaborating Laboratories."

RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

INFLUENZA VACCINE

INTRODUCTION

Influenza occurs in the United States every year, but with great variation in incidence and geographic distribution. It periodically becomes epidemic when the antigens of prevalent influenza viruses have changed enough for a significant proportion of the pupulation to become susceptible. More epidemics are caused by influenza A viruses than by influenza B viruses, and influenza A epidemics are notable for causing mortality in excess of what is normally expected. Furthermore, only influenza A viruses undergo major antigen changes that result in pandemics (worldwide epidemics).

An example of the sudden appearances of antigenically distinctive influenza A viruses occurred in February 1976, when A/New Jersey/76 (swine) influenza virus was identified as the cause of a focal epidemic at Fort Dix, New Jersey. Recognition of the potential of this new virus for supplanting prevalent strains of influenza A, the threat of subsequent pandemic spread, and the Federal porgram to provide specific swine influenza vaccines in 1976 are well known. The fact that A/New Jersey/76 virus did not spread beyond Fort Dix makes it unlikely that this virus constitutes a risk in 1977-78. Nevertheless, because swine influenza viruses continue to exist in swine in the United States and to cause occasional human cases, primarily in those with agricultural exposures, the swine influenza vaccines remaining from 1976 have been stockpiled in the event of future need.

Thousands of persons have died of influenza in epidemics in the United States in the past 20 years. In the 1957-58 influenza season, when a new influenza A virus (Asian strain) appeared, nearly 70,000 deaths were attributed to it in this country alone. In 1968-69, 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 have involved most of the country, 10,000 to 20,000 excess deaths resulted.

Efforts to prevent or control influenza in the United States usually have been aimed at protecting those at the greatest risk of becoming seriously ill or dying. Repeated observations during influenza epidemics have indicated that deaths occur primarily among chronically ill adults and children and in older persons, especially those over age 65. These "high-risk" persons should be vaccinated annually regradless of the amount of influenza in their geographic areas.

In interpandemic periods, vaccinating the entire population has not been considered to be a reasonable public health objective for several reasons: the limited duration of protection from influenza vaccines, the relatively low attack rates of influenza in community outbreaks, and the usual lack of serious complications of disease in healthy people.

INFLUENZA VIRUS VACCINE FOR 1977-78

The Bureau of Biologics, Food and Drug Administration, reviews influenza vaccine formulation regularly and recommends reformulation with contemporary antigens when indicated. Bivalent influenza vaccine for 1977-78 will contain inactivated influenza A and B viruses representative of currently prevalent strains. Each adult dose of vaccine will contain 400 chick cell agglutinating (CCA) units of antigen or its equivalent in the following proportion: 200 CCA units of influenza A virus comparable to the prototype A/Victoria/3/75 (H3N2) and 200 CCA units of B/Hong Kong/5/72 influenza virus.

The 1977-78 vaccine will be available in "split-virus" and "whole-virus" preparations. Split-virus vaccines, which contain antigens produced by chemically disrupting the influenza virus, have been associated with somewhat fewer side effects than whole-virus vaccines, particularly in children. However, the split-virus vaccines appear to be somewhat less effective in eliciting antibodies when given as a single dose to persons who have not been "primed" by exposure to related viruses in nature or through vaccination.

The characteristic side effects and immunogenicity of split-virus and whole-virus influenza vaccines are important in understanding dosage recommendations for various age groups. Adults and older children, most of whom have had experience with influenza antigens related to A/Victoria/3/75 or B/Hong Kong/5/72 either by infection or through vaccination, can be expected to have a good antibody response to a single dose of the 1977-78 bivalent influenza vaccine. Children less than 6 years of age, some of whom have not encountered the currently prevalent viruses, will need 2 doses of vaccine given 4 or more weeks apart in order to achieve satisfactory antibody responses. These children will not be adequately protected unless the second dose is given. Furthermore, because children and adolescents tend to experience somewhat more side effects from influenza vaccine than adults, *only* split-virus vaccines should be given to persons less than 18 years of age.

VACCINE USAGE

General Recommendations

Annual vaccination is strongly recommended for adults and children of all ages who have such chronic conditions

as: 1) heart disease of any etiology, particularly with mitral stenosis or cardiac insufficiency, 2) chronic bronchopulmonary diseases, such as chronic bronchitis, bronchiectasis, tuberculosis, emphysema, and cystic fibrosis, 3) chronic renal disease, and 4) diabetes mellitus and other chronic metabolic disorders.

Vaccination is also recommended for older persons, particularly those over age 65 years, because excess mortality in influenza outbreaks occurs in this age group.

Vaccination may also be considered for persons who provide essential community services and may be at increased risk of exposure. Vaccination of such persons and of patients not specified in the high-risk groups should be made on an individual basis giving consideration to the inherent benefits, risks, and costs.

The following table summarizes vaccine and dosage recommendations by age group for 1977-78. These recommendations are derived from observations made during the field trails of influenza vaccines conducted in 1976. Because information from the immunization of infants and young children is limited, the dosages recommended for them are conservative.

INFLUENZA VACCINE DOSAGE BY AGE, 1977-78

Age	Product Type	Dose Volume (ml)	Total CCA Units*	Number of Doses
18 years and older	Whole-virus or Split-virus	0.5	400	1
6-17 years	Split-virus	0.5	400	1
3-5 years	Split-virus	0.25	200	2**
6-35 months	Split-virus	0.15	120	2**

*Representing equal amounts of A/Victoria/75 and B/Hong Kong/72.
**4 weeks or more between doses; both doses essential for good protection.

SIDE EFFECTS AND ADVERSE REACTIONS

Side effects of influenza vaccine occur infrequently. Three types of responses to influenza vaccines have been described:

1. Fever, malaise, myalgia, and other systemic symptoms of toxicity starting 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) and constitute most of the side effects of influenza vaccination. Such effects occur most frequently in children and others who have had no 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 residual egg protein. Although current influenza vaccines contain only a minute quantity of egg protein, they can, on rare occasions, provoke hypersensitivity reactions. Individuals with known or suspected hypersensitivity to eggs should be given influenza vaccine only under the care and close observation of a physician.
3. Guillain-Barre syndrome, usually a self-limited paralysis, is observed within 8 weeks after influenza vaccination in approximately 10 of every million persons vaccinated. It also occurs, but less frequently, in unvaccinated persons. Prior to the intensive surveillance of influenza vaccine that occurred during the swine influenza vaccination program in 1976, serious adverse reactions, such as this syndrome, to influenza vaccines had been virtually unrecognized. While the risk is not high, persons who receive influenza vaccine should be aware of it and should recognize that 5-10% of persons with the Guillain-Barre syndrome have residual weakness to some degree and approximately 5% of them die.

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 from the 1918-19 influenza pandemic and a few small but better controlled studies in 1957-58, when the Asian influenza pandemic occurred, suggested that influenza can cause increased maternal and fetal deaths. However, a number of more recent, prospective studies have failed to corroborate those findings. Thus, although there are no persuasive data to document that pregnancy is a risk-factor with influenza, the effect of influenza in pregnancy cannot be forecast with assurance. Physicians generally avoid perscribing unnecessary drugs and biologics for pregnant women, especially in the first trimester; however, there are no data that specifically contraindicate influenza vaccination in pregnancy.

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