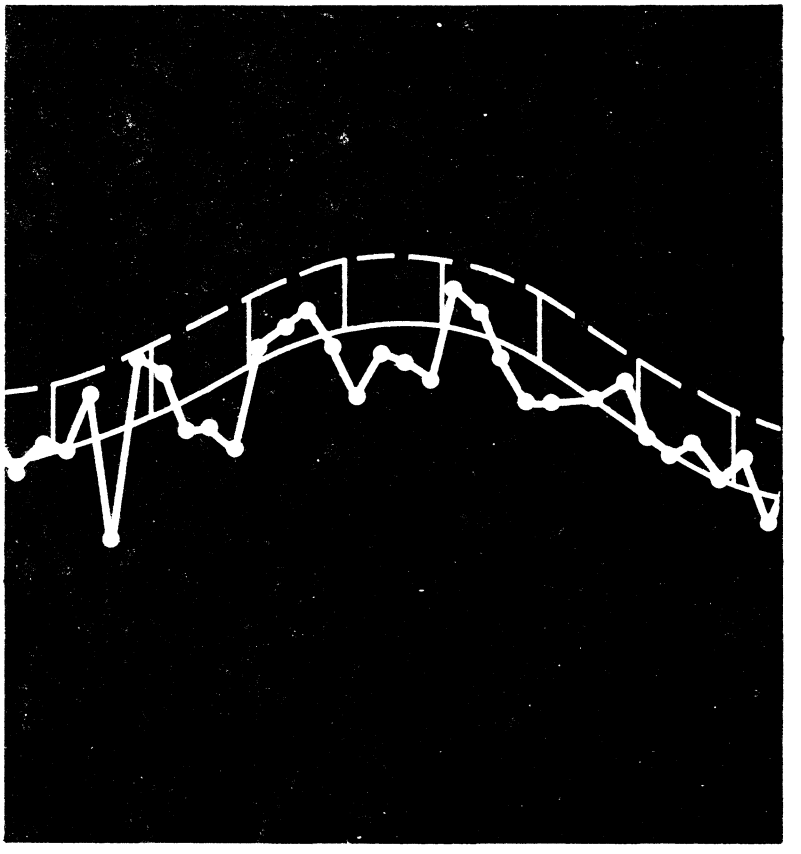
REPORT NO. 94
SUMMARY: JULY 1979 – JUNE 1981
Issued June 1984

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. 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 welcome. Send them to:

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Issued June 1984


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# Influenza Surveillance Report, 1979-1980 and 1980-1981

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## SUMMARY

### 1979-1980 (July 1979-June 1980)

The predominant type of influenza virus isolated in the United States during the 1979-1980 influenza season was influenza B. The virus caused widespread outbreaks in several regions, primarily among school-age children, although outbreaks in older groups were reported. For the first time since 1962, influenza B activity was associated with an excess in reported pneumonia and influenza deaths.

Influenza B Activity - Early warning of an impending influenza B season was provided from isolations of influenza B viruses during July, August, and September from school children in Hawaii. Influenza B outbreaks in the continental United States were first reported in schools in Oregon during the second week of December. In subsequent weeks, 45 states and the District of Columbia reported isolates and 20 states and the District of Columbia reported widespread outbreaks. Peaks in nationwide morbidity and the number of viral isolates were recorded during the week ending February 9, 1980. Deaths from pneumonia and influenza reported by 121 cities were elevated significantly for the 10-week period between January 19 and March 22, 1980. Most influenza B isolates resembled B/Singapore/222/79.

Influenza A (H3N2) Activity - Influenza A(H3N2) isolates were reported from 8 states beginning in late December. The first reported outbreak of influenza A(H3N2) occurred in an Illinois hospital in mid-February. Some influenza A(H3N2) isolates were similar to A/Texas/1/77, a strain used in the 1979-80 vaccine, and others were similar to A/Bangkok/1/79 a strain demonstrating significant antigenic drift from A/Texas/1/77. Influenza A(H3N2) outbreaks and isolates continued to be reported into June.

Influenza A (H1N1) Activity - Influenza A(H1N1) isolates and outbreaks were reported among high school students on the Eastern shore of Maryland during early February. Analysis of A(H1N1) isolates showed them to be similar to A/Brazil/11/78. Sporadic influenza A(H1N1) outbreaks and isolates were reported from the District of Columbia, Delaware, Illinois, Wisconsin, Texas, and Alaska.

Reye's Syndrome - An association between Reye's syndrome and influenza B activity was again noted.

### 1980-1981 (July 1980-June 1981)

The predominant type of influenza circulating in the United States throughout the 1980-81 influenza season was influenza A(H3N2). Early warning was provided by reports of isolates in July and August of 1980. Numerous isolates of influenza A(H1N1) virus were made during the latter two-thirds of the season. This was the second influenza season since 1977 involving

substantial co-circulation of influenza A(H3N2) and A(H1N1) viruses. Influenza A (H3N2) caused widespread outbreaks throughout the country and affected all age groups while influenza A(H1N1) virus activity was quantitatively less and affected primarily children and young adults. During the 1980-1981 influenza season, influenza A(H3N2) activity was associated with excess mortality from pneumonia and/or influenza especially in the >65-year age group.

Influenza B Activity - No reports of influenza B outbreaks were received during the 1980-81 season and only two isolates were reported.

Influenza A(H3N2) Activity - Between July and October small outbreaks of influenza A(H3N2) occurred in Hawaii and Alaska, and sporadic cases were reported from several mid-Western and Western states. The first documented influenza A(H3N2) outbreak in the continental United States was reported in mid-October 1980 in a San Francisco nursing home. During the following weeks 47 states and the District of Columbia reported influenza A(H3N2) isolates and 30 states reported widespread influenza outbreak activity. Excess deaths from pneumonia and/or influenza as reported by 121 cities occurred for a 13-week period beginning December 13 that coincided with a period of maximal reported numbers of influenza A(H3N2) isolates. Influenza A(H3N2) strains isolated were, in general, antigenically intermediate between A/Texas/1/77 and A/Bangkok/1/79 strains.

Influenza A (H1N1) Activity - Serological studies confirmed a limited influenza A (H1N1) outbreak in Puerto Rico in September. Sporadic influenza A(H1N1) activity in continental United States began in mid-December with a report of virus isolation from Washington, D.C. During the following weeks, 40 states reported isolations, but only Georgia and Arizona reported outbreaks due to influenza A(H1N1). The influenza A(H1N1) viruses isolated were similar to the A/England/333/80 or A/India/6263/80 strains.

## SURVEILLANCE METHODS

### Mortality Surveillance

It has been observed repeatedly in the United States that during most epidemics of influenza A the number of deaths recorded as due to pneumonia and influenza (P and I) exceeds expected values for several weeks.[1-4] Therefore, CDC uses reports of P and I deaths attributed to influenza activity as one measure of the extent and impact of influenza activity.

Each week 121 cities in the United States relay mortality data by postcard or telephone to CDC's Consolidated Surveillance and Communications Activity. The number of deaths occurring in these cities is reported separately in each of six age groups for all causes, for influenza, and for pneumonia. A death is attributed to pneumonia if it appeared on Part I(a) of the death certificate as the immediate cause of death or on the lowest used line of Part I as an underlying cause of death. A death is attributed to influenza if the word "influenza" appears anywhere in Part I or Part II of the certificate; if other causes of death are also named, influenza takes precedence. Deaths are not reported to CDC by date of occurrence, but by the date the certificate is filed in the office of vital statistics registrar.

The proportion of all deaths that is attributed to pneumonia and influenza (P and I ratio) is calculated each week and compared to an expected P and I ratio that is generated from all available mortality data using a forecasting

technique called time-series analysis.[2,3] Significant deviations above this expected number are considered in conjunction with morbidity and laboratory data in the determination of epidemic activity.

It should be emphasized that this surveillance method is based on data from 121 urban centers, whose total populations constitute approximately 26% of the U.S. population. The data should be viewed as an index of the national mortality attributable to P and I, not as a representative sample. Nevertheless, these data serve as a readily available indicator of any increases in influenza-related mortality in the United States.

A provisional estimates of the number of excess deaths associated with influenza is calculated on a 10% sample of U.S. deaths reported to the National Center for Health Statistics (NCHS) a few months after the influenza season using time-series analysis. Final estimates are calculated from NCHS statistics that include all U.S. deaths and are usually available 2-3 years following the epidemic period. Prior to 1975, all estimates were generated using a regression model developed by Serfling.[4]

## Morbidity Surveillance

Nationwide surveillance of influenza morbidity for both 1979-80 and 1980-81 consisted of weekly telephonic reports of estimated influenza-like activity from state epidemiologists or their designees. Data were reported according to the following activity categories: none, sporadic (isolated cases or outbreaks), regional (outbreaks occurring in counties with <50 percent of the state's population), and widespread (outbreaks occurring in counties with $\geq$50 percent of the state's population). Epidemiologic and laboratory information on known outbreaks was included, if available.

## Laboratory Reports

During the influenza season, generally from early October through April, postcard reports are received weekly by the WHO Collaborating Center for Influenza (CCI) at CDC from approximately 60 state, county, and city health departments. The reports include the number of specimens tested for isolation and the number of each type or subtype of influenza virus identified for persons born in 1952/3 or later, and for persons born prior to 1952/3. In addition, the CCI receives reports of influenza virus isolates from specimens collected at U.S. Armed.Forces bases throughout the United States and tested at Armed Forces laboratories. The CCI performs detailed antigenic and, where appropriate, genetic analyses of representative influenza viruses submitted by laboratories in the United States and elsewhere.

## International Reports

The epidemiologic behavior of influenza internationally from October 1979-September 1981 and the results of antigenic analysis of viruses received at the WHO Collaborating Center for Influenza, CDC, from various countries are summarized in the text and tables in appendices 1 and 3.

## Epidemic Investigations

CDC receives reports of investigations of selected outbreaks of influenza-like illness performed by state, local, and university health personnel. Besides providing confirmation of influenza virus as the cause of an outbreak, the investigations provide explicit information on the epidemiology of influenza outbreaks by documenting the signs and symptoms of the illness, the outbreak settings, vaccination status, age distributions, underlying illnesses, and the outcomes of influenza illness. When requested, CDC may provide laboratory and personnel suppport in outbreak investigations.

### Quality of Data

All aspects of CDC's influenza surveillance are dependent on voluntary provision of data. Because of the voluntary nature of data collection, the difficulty in quantifying some of the requested data, and the wide diversity among facilities who submit data in resources available for complete surveillance, a quantifiable assessment of the overall quality of the collected data is difficult. During the influenza season mortality, morbidity, and laboratory surveillance data are followed together. In our experience, the national direction and extent of influenza activity are reflected by each surveillance component within a period of a few weeks. Mortality surveillance, because it is quantifiable and, in general, consistently collected, provides reliable data for the comparison of years and the description of trends. Laboratory surveillance alone can specify the exact type of virus and serve to indicate the onset of activity and spread. Morbidity surveillance, while being the least quantifiable or specific, provides a comparable indication of influenza-like activity in a defined region. All surveillance components are important to appreciate influenza activity.

## SURVEILLANCE RESULTS 1979-1980

### Mortality Surveillance

The observed ratio of pneumonia and influenza (P and I) deaths to all deaths in the 121 reporting cities exceeded the epidemic threshold for a 10-week period beginning in January of 1980 (Figure 1). The peak in the P and I ratio occurred during a period of reporting of B/Singapore/79 isolations from collaborating laboratories. In all, an estimated 43,880 excess deaths occurred nationwide during the epidemic based on a 10% sample of mortality data from the NCHS (Table 1). This was the first major outbreak since the 1961-62 influenza season in which excess mortality was almost exclusively associated with an influenza B virus.[5]

### Morbidity Surveillance

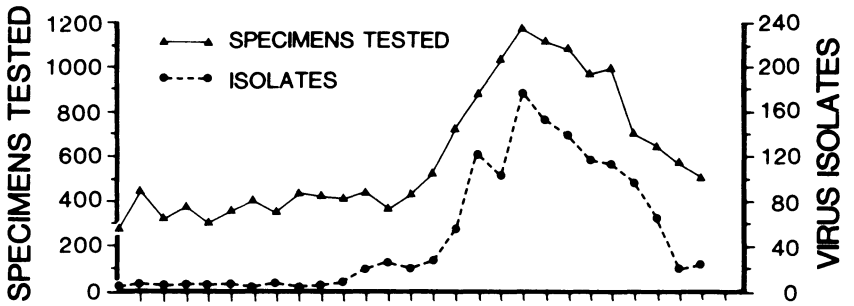
The maximal extent of influenza morbidity of 1979-80 nationwide is shown in Figure 2.

Region I (Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont) - Influenza B virus was first isolated in early February. Widespread outbreaks affecting all age groups, but particularly the age groups under 25, were reported in all Region I states. Connecticut reported up to 70% school absenteeism in its southern part. Influenza A(H3N2) and A(H1N1) strains were not reported from these states.

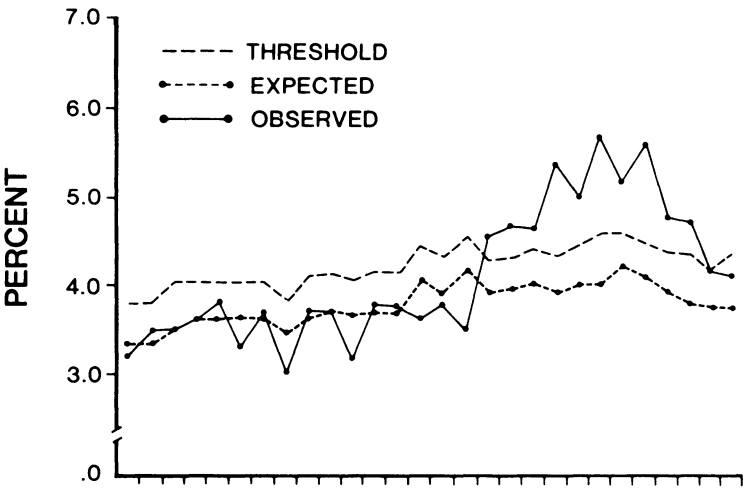
Region II (New Jersey, New York, Puerto Rico, Virgin Islands) - Influenza B isolates were reported from New Jersey and New York starting in December. Both states reported widespread outbreaks at the end of January. Major influenza B outbreaks occurred in nursing home facilities. School absenteeism was 9% above normal in New York City at the peak of the epidemic. New Jersey reported influenza A(H3N2) isolates in mid-February.

## FIGURE 1: INFLUENZA SURVEILLANCE IN THE UNITED STATES, 1979–1980

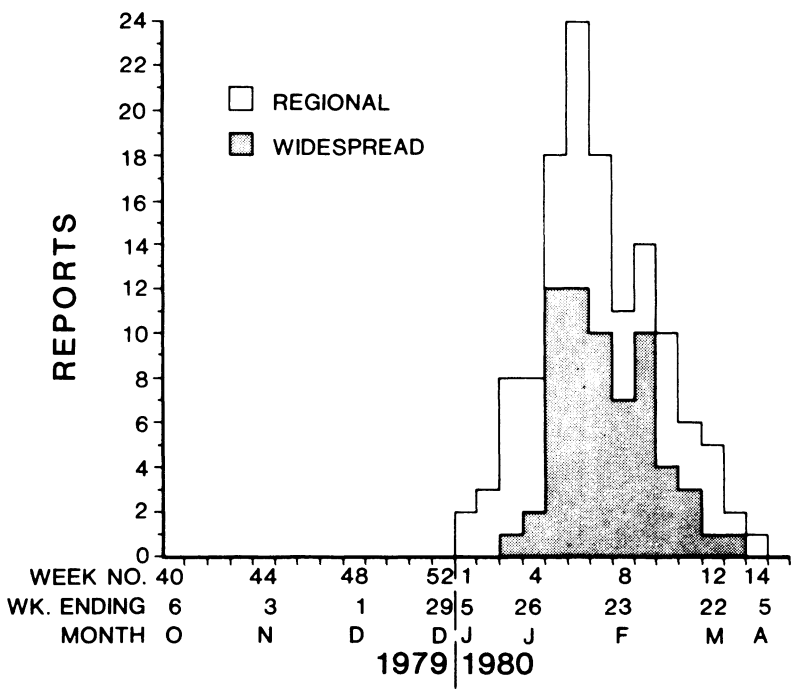
**Laboratory surveillance: isolations of influenza viruses reported by WHO collaborating laboratories**




**Pneumonia and influenza mortality surveillance: ratio of observed and expected deaths attributed to pneumonia and influenza (121 U.S. cities)**




**Morbidity surveillance: reported regional and widespread outbreaks of influenza from reporting areas**



## Table 1. Excess Mortality Due to Pneumonia and Influenza (P and I), U.S., Oct. 1957-Mar. 1981

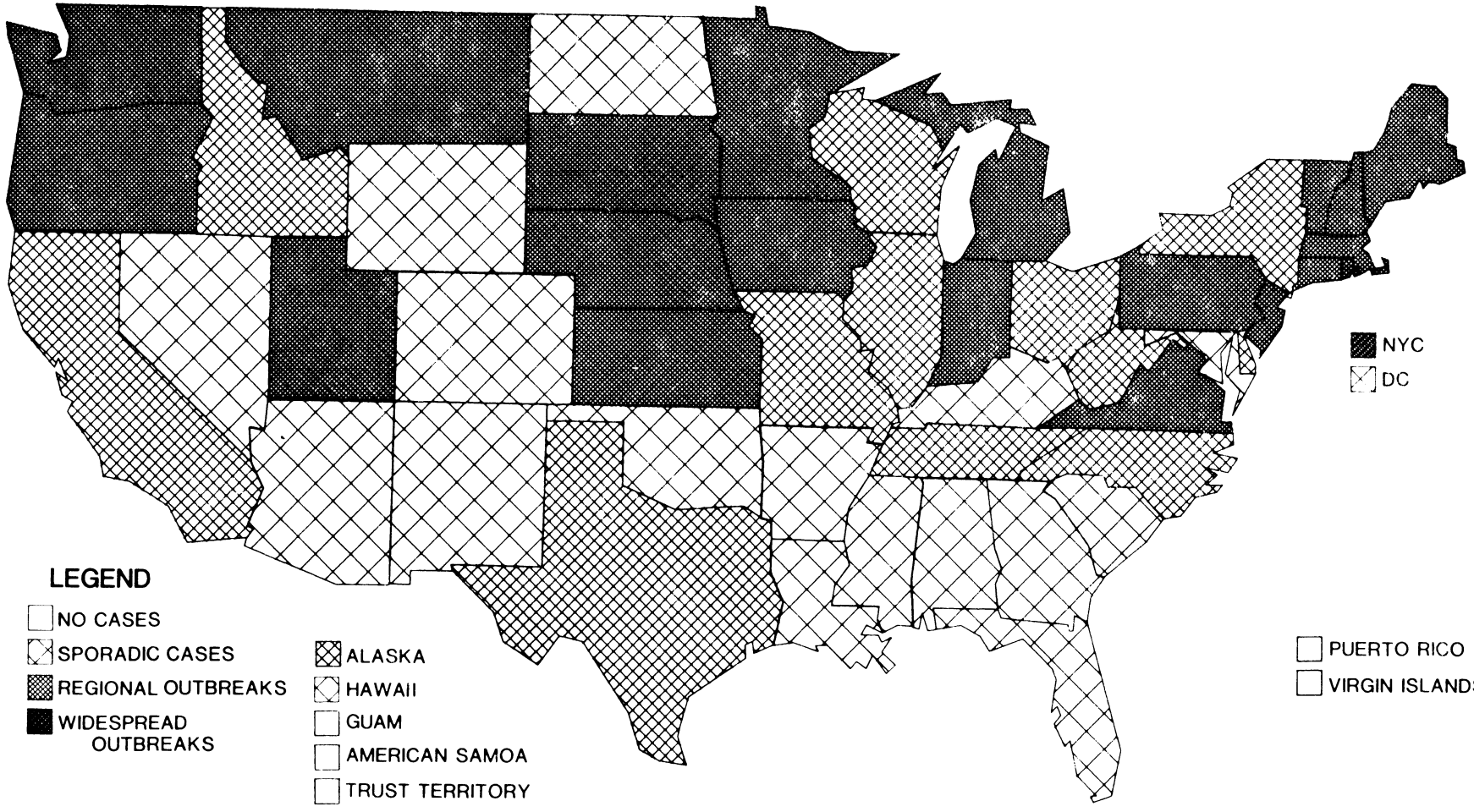
| Period of Excess Mortality* | Population (1,000s) | Estimated Number of Excess Deaths Due to P and I | Rate of Excess P and I Deaths Per 100,000 | Estimated Total Excess Deaths | Rate of Total Excess Deaths Per 100,000 | Type of Influenza |
|---|---|---|---|---|---|---|
| Oct 1957-Mar 1958 | 173,232 | 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 | 6.1 | A/(H2N2) |
| Jan - Feb 1968 | 199,846 | 9,000 | 4.5 | 23,800 | 11.9 | A/(H2N2) |
| Dec 1968-Jan 1969 | 201,911 | 12,000 | 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) |
| Jan - Feb 1975** | 213,121 | 5,638 | 2.6 | 15,244 | 7.2 | A/(H3N2) |
| Feb - Mar 1976 | 214,659 | 10,641 | 5.0 | 26,087 | 12.2 | A/(H3N2) |
| Jan - Feb 1978 | 218,059 | 6,888 | 3.2 | 32,318 | 14.8 | A/(H3N2) |
| Jan - Apr 1980*** | 226,505 | 4,634 | 2.0 | 43,880 | 19.4 | B |
| Dec 1980-Mar 1981*** | 229,304 | 7,787 | 3.4 | 52,209 | 22.8 | A/(H3N2) |

*No excess mortality observed in 1961, 1964, 1967, 1971, 1974 and 1979.

**Beginning in 1975, estimates of excess deaths were calculated using time series analysis. Previously regression estimates were used.

***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.

# FIGURE 2: MAXIMUM REPORTED INFLUENZA MORBIDITY, 7/79 - 6/80



Region III (Delaware, D.C., Maryland, Pennsylvania, Virginia, West Virginia) - Influenza B isolates were confirmed in five of the states and the District of Columbia starting in mid-November. Delaware was one of the first states to report influenza B activity. Only Pennsylvania and Virginia reported widespread outbreaks which began in early March. An outbreak of influenza B occurred in March among patients at the Huntington, West Virginia, Veterans Administration Hospital. The outbreak primarily involved persons over the age of 50 years. School absenteeism increased in Maryland, the District of Columbia, and West Virginia. Public schools in one county in West Virginia closed because of an outbreak among students.

Beginning in February, influenza A(H1N1) isolates were reported from Delaware, Maryland, and the District of Columbia. In Maryland influenza A(H1N1) viruses were first isolated from students from the Eastern Shore during an outbreak in early February. Absenteeism reached 26% during the course of the outbreak.

Maryland, Virginia, West Virginia, and the District of Columbia reported influenza A(H3N2) isolates after January.

Region IV (Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, Tennessee) - Influenza B isolates were reported from five states from early February through March. None of the states reported widespread activity, and only North Carolina and Tennessee reported regional outbreaks. Kentucky and North Carolina reported school absenteeism rates of up to 25%. Only Georgia reported influenza A(H3N2) isolates.

Region V (Illinois, Indiana, Michigan, Minnesota, Ohio, Wisconsin) - Influenza B was the predominant virus isolated in all states in this region. Isolations were first reported in early December. Widespread outbreaks were reported in Indiana, Michigan, and Minnesota starting in early February. An increased incidence rate of Reye's syndrome was reported in Ohio and Michigan. A temporal association was observed between influenza B activity and the increased incidence rate of Reye's syndrome (see Section VI). Influenza B illness occurred predominantly in children and young adults. In Ohio increased school absenteeism was reported in 80 of 88 counties. Illinois reported an outbreak of upper respiratory illness in schools with absentee rates as high as 33% in some areas. Wisconsin also reported increased absenteeism in middle schools, and influenza B was isolated. Both Wisconsin and Illinois reported outbreaks of influenza A(H3N2) in hospitals. Illinois and Wisconsin were among the few states that reported influenza A(H1N1) isolates. A hospital-associated outbreak in Wisconsin was the third reported outbreak of influenza A(H1N1) in the country. Illinois reported influenza A (H1N1) isolates from a military installation during late March.

Region VI (Arkansas, Louisiana, New Mexico, Oklahoma, Texas) - All Region VI states reported influenza B isolates. None of the states reported widespread outbreaks, and only Texas noted regional outbreaks. Texas and Arkansas cultured influenza A(H3N2) viruses from sporadic cases and Texas reported isolates of influenza A(H1N1) in mid-February. In Houston, an isolation of swine influenza virus was made from a 6-year-old child who had an influenza-like illness in February shortly after attending a livestock show.

Region VII (Iowa, Kansas, Missouri, Nebraska) - All states in Region VII reported isolates of influenza B between January and March 1980. Three of the states reported widespread outbreaks during this perid. Iowa reported outbreaks of influenza among school children in late January. Iowa also reported deaths in nursing home outbreaks in January.

Region VIII (Colorado, Montana, North Dakota, South Dakota, Utah, Wyoming) - Starting in December, all of these states except Wyoming reported isolates of influenza B. Several Indian reservations in South Dakota experienced outbreaks of influenza-like illness with school absenteeism as high as 33%. Colorado's first reported outbreak of influenza occurred in December among children and staff at National Jewish Hospital in Denver. During February, Utah, South Dakota, and Montana reported widespread outbreaks. Only Colorado reported influenza A(H3N2) strains.

Region IX (American Samoa, Arizona, California, Guam, Hawaii, Nevada, Trust Territory) - Arizona, California, and Hawaii reported influenza B isolates from July 1979 through March 1980. Arizona and California were among the earliest states to report influenza B isolates which were obtained from college students. Hawaii was one of the first areas to report an increase in elementary school absenteeism which began in late July.

California reported regional outbreaks, while Hawaii and Arizona reported sporadic outbreaks. Influenza A(H3N2) virus was first isolated in Arizona and Hawaii in mid-February. An outbreak of influenza A(H3N2) illness occurred among a group of California Shriners and Scottish Rite members who had been on a Mississippi riverboat cruise during the month of March. Outbreaks in California occurred primarily in schools, a few colleges, occupational groups, and skilled nursing homes.

Region X (Alaska, Idaho, Oregon, Washington) - All states in this Region reported influenza B isolates starting in October. Oregon and Washington reported widespread activity, while the remaining two states reported regional and sporadic activity. In Oregon scattered outbreaks of influenza illness occurred in elementary and high school students starting in mid-December. Absenteeism reached 35%. In Washington influenza B outbreaks were reported in a mental hospital and several nursing homes and excess mortality was reported in one nursing home and the mental hospital. Influenza A (H3N2) isolates were reported from Alaska and Washington. Alaska was the only state in the Region that reported influenza A(H1N1) isolates.

## Laboratory Reports (1979-80)

### *Virus Isolation Reports*

Virus surveillance in the United States conducted by WHO Collaborating Laboratories and others in 1979-1980 indicated that 45 states reported isolations of influenza B. Of these, 38 states submitted samples that were confirmed as influenza B strains at the CCI. Influenza A(H3N2) isolates were reported from 9 states and influenza A(H1N1) isolates from 6 states (Table 2). Laboratories in these states reported the testing of 17,881 specimens for respiratory virus isolation and the isolation of 1,359 influenza B viruses, 24 influenza A(H1N1) viruses, and 19 influenza A(H3N2) viruses. Isolation of influenza B viruses peaked in mid-February, 1980. A single isolate of swine influenza virus was reported from a child in Texas. There were no influenza C virus isolations reported during the year.

**Table 2. Influenza Virus Isolates Reported to the WHO Collaborating Laboratories in the U.S., 1979-1980**

| | Influenza A(H3N2) | Influenza A(H1N1) | Influenza B | Influenza C |
|---|---|---|---|---|
| **REGION I** | | | | |
| Connecticut | | | ▒ | |
| Maine | | | ▒ | |
| Massachusetts | | | ▒ | |
| New Hampshire | | | ▒ | |
| Rhode Island | | | ▒ | |
| Vermont | | | ▒ | |
| | | | | |
| **REGION II** | | | | |
| New Jersey | ▒ | | ▒ | |
| New York | | | ▒ | |
| Puerto Rico | | | | |
| Virgin Islands | | | | |
| | | | | |
| **REGION III** | | | | |
| Delaware | | ▒ | ▒ | |
| District of Columbia | | | ▒ | |
| Maryland | ▒ | ▒ | ▒ | |
| Pennsylvania | | | ▒ | |
| Virginia | ▒ | | ▒ | |
| West Virginia | | | ▒ | |
| | | | | |
| **REGION IV** | | | | |
| Alabama | | | | |
| Florida | | | ▒ | |
| Georgia | | | ▒ | |
| Kentucky | | | ▒ | |
| Mississippi | | | ▒ | |
| North Carolina | | | ▒ | |
| South Carolina | | | ▒ | |
| Tennessee | | | | |
| | | | | |
| **REGION V** | | | | |
| Illinois | ▒ | ▒ | ▒ | |
| Indiana | | | ▒ | |
| Michigan | | | ▒ | |
| Minnesota | | | ▒ | |
| Ohio | | ▒ | ▒ | |
| Wisconsin | | | ▒ | |
| **TOTAL** | | | | |

| | Influenza A(H3N2) | Influenza A(H1N1) | Influenza B | Influenza C |
|---|---|---|---|---|
| **REGION VI** | | | | |
| Arkansas | ▒ | | ▒ | |
| Louisiana | | | ▒ | |
| New Mexico | | | ▒ | |
| Oklahoma | | | ▒ | |
| Texas | | ▒ | ▒ | |
| | | | | |
| **REGION VII** | | | | |
| Iowa | | | ▒ | |
| Kansas | | | ▒ | |
| Missouri | | | ▒ | |
| Nebraska | | | ▒ | |
| | | | | |
| **REGION VIII** | | | | |
| Colorado | | | ▒ | |
| Montana | | | ▒ | |
| North Dakota | | | | |
| South Dakota | | | | |
| Utah | | | ▒ | |
| Wyoming | | | | |
| | | | | |
| **REGION IX** | | | | |
| American Samoa | | | | |
| Arizona | ▒ | | ▒ | |
| California | ▒ | | ▒ | |
| Guam | | | | |
| Hawaii | ▒ | | ▒ | |
| Nevada | | | | |
| | | | | |
| **REGION X** | | | | |
| Alaska | ▒ | ▒ | ▒ | |
| Idaho | | | ▒ | |
| Oregon | | | ▒ | |
| Washington | | | ▒ | |
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| **TOTAL** | 9 | 6 | 45 | |

Mortality statistics indicated that the influenza B epidemic was associated with excess mortality in persons over the age of 65. To further analyze the occurrence of influenza B viruses in the elderly compared to younger persons, four participating laboratories were requested to report the age of patients with positive influenza B virus cultures. Analysis of the data confirmed that 11 percent of influenza B virus infections were occurring in patients over the age of 65 years, a proportion comparable to the proportion of the United States population 65 years or older (Table 3). In younger persons, however, the proportion of isolations of influenza B viruses from those less than 25 years old (63%) was disproportionately high taking into account the age composition of the U.S. population.

### *Antigenic Analysis of Influenza Isolates*

Influenza B - From October 5, 1979 through May 1980, 364 influenza B viruses submitted to CDC from the United States were compared with reference strains by hemagglutination inhibition (HI) testing. Analysis revealed that the majority of influenza B viruses exhibited modest antigenic drift away from the B/Hong Kong/5/72 reference strain.

Most isolates were better inhibited by antisera to B/Singapore/222/79 than by B/Hong Kong/5/72. An additional antigenic variant, B/Buenos Aires/37/79, had been identified among isolates from foreign countries and antiserum to this strain was included in the tests of influenza B isolates submitted during the United States epidemics (Table 4). Approximately 50 percent of isolates tested were inhibited equally by antisera to B/Singapore/222/79 and B/Buenos Aires/37/79, although these two reference strains cross-reacted poorly with each other. Further analysis revealed that isolates exhibiting this pattern of broad cross-reactivity were nearly always grown in Maddin-Darby Canine Kidney (MDCK) cells, whereas isolates grown in eggs were well inhibited by B/Singapore/222/79 antiserum, but poorly inhibited by B/Buenos Aires/37/79 antisera. In several instances isolates initially typed as being cross-reactive with the two 1979 strains were repassaged in eggs and then found to be like B/Singapore/222/79. It was concluded that the cross-reactive patterns observed in HI tests for influenza B viruses grown in MDCK cells represented an effect of the host in which the virus was grown.

It was also observed that B viruses isolated in MDCK cells, were often inhibited by normal chicken sera up to titers of 80 or 160. This finding is consistent with previous reports by Meguro and colleagues,[6] who showed that influenza virus grown in MDCK cells may incorporate host antigens that are inhibited by antibodies present in normal chicken sera. Although MDCK cells have been more sensitive than eggs in recent years for the isolation of influenza B strains these observations provide a caution against the widespread adoption of MDCK cells for isolation of influenza viruses in strain surveillance studies to document the type of virus responsible for epidemics or outbreaks.

Influenza A(H3N2) - Influenza A(H3N2) isolates from the United States were primarily found to be cross-reactive with A/Texas/1/77 and A/Bangkok/1/79. Some viruses, e.g., A/Arizona/2/80, were found to have poor reactivity with either of these sera even though antisera to such viruses reacted quite well with A/Texas/1/77 and A/Bangkok/1/79 (Table 5). This indicated a degree of asymmetric cross-reactivity probably enhanced by low avidity of these A/Arizona/2/80-like isolates. A small number of strains tested were also found to be more similar to A/Bangkok/1/79.

**Table 3. Distribution of Specimens Tested for Influenza B Isolates by Age Group during Influenza B Epidemic Periods in Three Areas of the U.S., 1979-1980[1]**

| | Age Group | | | |
|---|---|---|---|---|
| | <25 | 26-64 | >65 | Total |
| Number of specimens tested | 906 | 367 | 156 | 1,429 |
| Number(Percent) of specimens positive | 147(16) | 60(16) | 26(7) | 233(16) |
| Percent of total positives | 63 | 26 | 11 | 100 |
| Percent of total U.S. population | 42 | 42 | 11 | 100 |

[1]Combined results from: Illinois State Department of Health, Dec. 1979-Feb. 1980; Wisconsin State Laboiratory of Hygiene, Dec. 1979-Mar. 1980; Rochester, New York, Jan.-Feb. 1980; and Washington State Department of Health, Dec. 1979-Feb. 1980

**Table 4. Hemagglutination-Inhibition of Influenza B Isolates**

| | Ferret sera | | |
|---|---|---|---|
| Antigens | B/Hong/Kong/ 5/72 | B/Singapore/ 222/79 | B/Buenos Aires/ 37/79 |
| B/Hong Kong/5/72 | 160* | 320 | 15 |
| B/Singapore/222/79 | 40 | 480 | 40 |
| B/Buenos Aires/37/79 | 10 | 40 | 160 |

*All results are the mean of two tests

**Table 5. Hemagglutination-Inhibition Reactions of A/Arizona/2/80(H3N2) Virus**

| | Ferret sera | | | |
|---|---|---|---|---|
| Antigen | A/Texas/ 1/77* | A/Bangkok/ 1/79* | A/Bangkok/ 1/79* | A/Arizona/ 2/80 |
| A/Texas/1/77 | 640 | 80 | 160 | 320 |
| A/Bangkok/1/79 | 160 | 1280 | 320 | 640 |
| A/Bangkok/2/79 | 160 | 80 | 2560 | 160 |
| A/Arizona/2/80 | 160 | 80 | 40 | 320 |

*Serum to recombinant with neuraminidase N7

Influenza A(H1N1) - Influenza A (H1N1) isolates submitted from outbreaks in Maryland and Delaware and from sporadic cases in Houston, Texas, were similar to A/Brazil/11/78 in HI tests.

### *Identification of Recombinant Viruses among Natural Isolates*

Genotypic examination of influenza viruses was carried out to determine the prevalence of recombinant and non-recombinant influenza A (H1N1) viruses in follow up to the demonstration in 1978-1979 that influenza A (H1N1) strains in the United States possessed four genes of influenza A (H3N2) origin. During 1979-1980, recombinant and non-recombinant influenza A (H1N1) viruses circulated (Table 6). In 1980, viruses isolated from outbreaks in Maryland had a non-recombinant genotype, whereas an isolate from one sporadic case in Houston, Texas, had a recombinant influenza A(H1N1) genotype and that from another Houston case had a non-recombinant genotype. These data indicate that displacement of "true" influenza A(H1N1) viruses by recombinant influenza A(H1N1) virus had not yet occurred. The finding also indicates the probable importation of the "true" influenza A (H1N1) viruses in Maryland during 1980 because all tested influenza A(H1N1) isolates in the United States in the preceding winter were recombinant influenza A(H1N1) strains.

### *Prevalence of Serum Antibodies to Influenza Viruses*

Following the detection of the antigenic variants of influenza A(H3N2), A/Bangkok/1/79, and A/Texas/1/77, the prevalence of HI antibodies to these strains was determined in sera of 50 University of Georgia students pre- and post-vaccination with A/Texas/1/77-containing vaccine in a study conducted collaboratively with the Student Health Services. Results indicated that the prevaccination prevalence of serum HI antibodies to A/Bangkok/1/79 was considerably lower than the prevalence of antibody to A/Texas/1/77 at each titer. Similarly, the frequency and magnitude of antibody response to A/Bangkok/1/79 in recipients of A/Texas/1/77 vaccine was somewhat lower than that to the vaccine strain (Table 7).

### *Detection of Heterologous HI Antibody Response to Influenza A (H1N1) Virus in Persons Infected with Influenza B*

During April and May 1979, CDC and the Minnesota State Department of Health investigated an outbreak of influenza B in a Minnesota nursing home. Pre- and post-epidemic sera were studied from a group of ill individuals and a group of well individuals. Results showed that 19 of 20 in the ill group as compared to 6 of 19 in the well group developed antibodies to influenza B using either the complement-fixation or HI test. Surprisingly, the analysis indicated that 6 of the persons who showed an HI and CF antibody response to influenza B also exhibited a significant (fourfold or greater) antibody response in HI tests with the influenza A(H1N1) viruses, A/USSR/90/77 or A/Brazil/11/78.

Surveillance for influenza during the time of this outbreak did not reveal the presence of influenza A(H1N1) anywhere in the United States; only influenza B strains were being isolated. Analysis suggested that a heterotypic antibody response to influenza A(H1N1) virus was occurring in persons infected with influenza B and that this response could be detected by HI. To further evaluate this possibility, a group of sera from individuals was titrated by a neutralization test to determine levels of antibody to influenza B and influenza A(H1N1) in their pre- and post-outbreak specimens.

**Table 6. Influenza A(H1N1) Viruses Identified at WHO Influenza Center, Atlanta, by RNA-RNA Hybridization or Oligonucleotide Mapping as Recombinant* or Non-recombinant Strains**

| Non-recombinant | Recombinant |
|---|---|
| July 1978-June 1979 | July 1978-June 1979 |
| A/Kumamoto/103/78** | A/California/10/78*** |
| A/Dundee/1611/78** | A/California/45/78** |
| A/Shanghai/2/79** | A/Kitakyushu/4/79*** |
| A/India/2/79*** | A/Texas/23/79** |
| | A/Philippines/2/79*** |
| | A/Finland/6/79**** |
| | A/Plzen/7/79*** |
| | A/Hanover/11/79**** |
| | A/Munich/1/79*** |
| | A/USSR/46/79*** |
| | A/USSR/50/79** |
| | A/Tokyo/501/79** |
| July 1979-June 1980 | July 1979-June 1980 |
| A/Victoria/90/79*** | A/Taiwan/3/79*** |
| A/Jamaica/2/79** | A/Kumamota/35/79** |
| A/Victoria/91/79*** | A/Sao Paulo/2/79** |
| A/Victoria/94/79*** | A/Texas/1/80*** |
| A/Maryland/1/80*** | |
| A/Maryland/2/80*** | |
| A/Texas/3/80*** | |

*Recombinant strains possess polymerase and NP gene of H3N2 origin
**HA variant
****HA similar to A/USSR/90/77
***HA similar to A/Brazil/11/78

**Table 7. Antibody Prevelance and Response to 7-ug Dose of A/Texas/1/77-like Vaccine in 50 Students, Nov.-Dec. 1979 University of Georgia, Athens**

| | | Cumulative percentage with HI titer | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Antigen | Serum | ≥10 | ≥20 | ≥40 | ≥80 | ≥160 | GMT* | >4xrise No. (%) |
| A/Texas/1/77 | prevac. | 78 | 28 | 6 | 2 | - | 11.0 | |
| | postvac. | 100 | 100 | 100 | 88 | 80 | 291.0 | 49(98) |
| A/Bangkok/1/79 | prevac. | 68 | 6 | - | - | - | 8.4 | |
| | postvac. | 100 | 76 | 66 | 38 | 20 | 44.0 | 34(68) |

*Geometric mean titer

The data confirmed the occurrence of influenza B infections by demonstrating rises in neutralizing antibody titers to this virus type. However, no rises in neutralizing antibodies to influenza A(H1N1) were detected. The reason for the heterotypic HI response is not known.

## International Reports

The epidemiolgic behavior of influenza internationally from October 1979-September 1980 and the results of antigenic analysis of viruses received at the WHO Collaborating Center for Influenza, CDC, from various countries are summarized in the text and tables of appendix I.

## Epidemic Investigations

Long Island, New York - In late January, 1980, the Bureau of Preventable Diseases, New York City Department of Health, was notified of an outbreak of influenza-like illness in residents of a geriatric long-term care facility on Long Island; the 527-bed, skilled care-nursing facility is contiguous to an acute-care teaching hospital and is the site of a geriatric medicine residency program. The outbreak occurred concurrently with an outbreak of influenza B in the surrounding community. The mean age of residents was 83 years (range 56-103) and 82 percent of residents were female. Patients resided in single or double occupancy rooms in 12 wards with 42-52 patients assigned to each ward.

The outbreak occurred from January 1 through March 10, 1980. A case was defined as a resident having onset of illness during the outbreak period characterized by documented respiratory tract symptoms or signs in association with a temperature of $\geq 38^{\circ}C$ ($\geq 100^{\circ}F$) and/or laboratory confirmation of influenza B virus infection. Records were reviewed on 556 of the 570 patients who were present for some period during the outbreak. Cases of influenza-like illness occurred in 152 (27.3 percent) of the residents; symptoms were documented in all but one patient, who was asymptomatic but culture positive. A bimodal epidemic curve indicated that the numbers of cases peaked during January 18-22 again and on February 9. Attack rates varied among wards, ranging from 6.4 to 58.1 percent, and differed significantly by sex (males, 36.6 percent versus females, 25.3 percent) but not by age. Influenza B virus was isolated from specimens obtained from 12 of the ill residents.

Vaccine efficacy was studied among 441 residents who had been admitted to the facility before October 1, 1979, and for whom vaccination status was known. Influenza-like illness occurred between January 1 and March 10 in 47 of 183 vaccinated patients (26 percent) versus 85 of 258 (33 percent) unvaccinated patients, indicating a clinical vaccine efficacy of 21 percent. No significant differences were noted between vaccinated and unvaccinated cases for apparent duration of illness, mean recorded temperature, or incidence rate of complications. Pneumonia occurred in 8 vaccinated cases (17 percent) and 9 unvaccinated individuals (11 percent); 3 of the vaccinated cases (6 percent) versus 7 of the unvaccinated cases (8 percent) died of causes attributed to influenza.

Reported by: J. Prior, L. Lyon, M.D., New York City Department of Health, F. Silverstone, M.D., New Hyde Park, New York; J. McPhee, Viral Laboratory, Nassau County Medical Center; WHO Collaborating Center for Influenza, CID,; Immunization Division, CPS, CDC

Erie County, New York - In late February 1980, the Bureau of Disease Control, New York State Department of Health, was notified of an outbreak of acute respiratory disease in an 82-bed skilled nursing facility in Erie County. The outbreak period was December 15, 1979 - February 23, 1980. For the purposes of the investigation, a case of influenza-like illness was considered to be an individual with oral temperature of $\geq 38^{\circ}C$ ($\geq 100.4^{\circ}F$) plus at least one of the following: cough, congestion, or documented "viral syndrome" which lasted greater than 24 hours. Among 98 residents present during the outbreak, 52 cases (53 percent) of influenza-like illness were identified; 14 resident cases died (case-fatality ratio = 27 percent). On March 6, 1980, serum specimens were obtained from residents who had not been ill and from residents who were convalescent. Comparison of geometric mean titers between the groups revealed a significant difference in GMT for influenza B, but not for influenza A/Brazil (H1N1), influenza A/Texas (H3N2), mycoplasma, or adenovirus. Because only 8 residents had received vaccine, vaccine efficacy could not be evaluated.

Reported by: R. Stricof, M.P.H., R. Rothenberg, M.D., State Epidemiologist, State Department of Health, New York; WHO Collaborating Center for Influenza, CID; Immunization Division, CPS, CDC

Ohio - During the period January 28, 1980-February 8, 1980 an outbreak of influenza-like illness occurred in a high school and a middle school in a rural area of Madison County, Ohio. Five hundred forty-seven students were enrolled in the high school (grades 9-12) and 380 students in the middle school (grades 8-12). Absenteeism attributed to the illness exceeded 25 percent in both schools at the peak of the outbreak. A case of influenza-like illness was defined as cough and/or headache plus at least two of the following: sore throat, coryza, fever, myalgia or conjunctivitis. Influenza B virus was isolated from nasopharyngeal or throat swabs from 13 students. Fourfold antibody titer changes in HI antibody to influenza B were found in an additional five students.

A questionnaire survey of 88 students with illnesses that met the case definition revealed an estimated attack rate in household contacts $\leq$ 18 years old of 44 percent (71 of 160) and in those > 18 years old of 29 percent (51 of 176) for an overall household attack rate of 36 percent (121 of 333). There was no significant difference in attack rates by household size.

Reported by: K. Wilson, R.N., M. Jackson, R.N., Madison County Health Department; T. Halpin, M.D., State Epidemiologist, K. Sullivan, Ohio State Department of Health; Field Services Division, EPO; Immunization Division, CPS, CDC

## SURVEILLANCE RESULTS, 1980-1981

### Mortality Surveillance

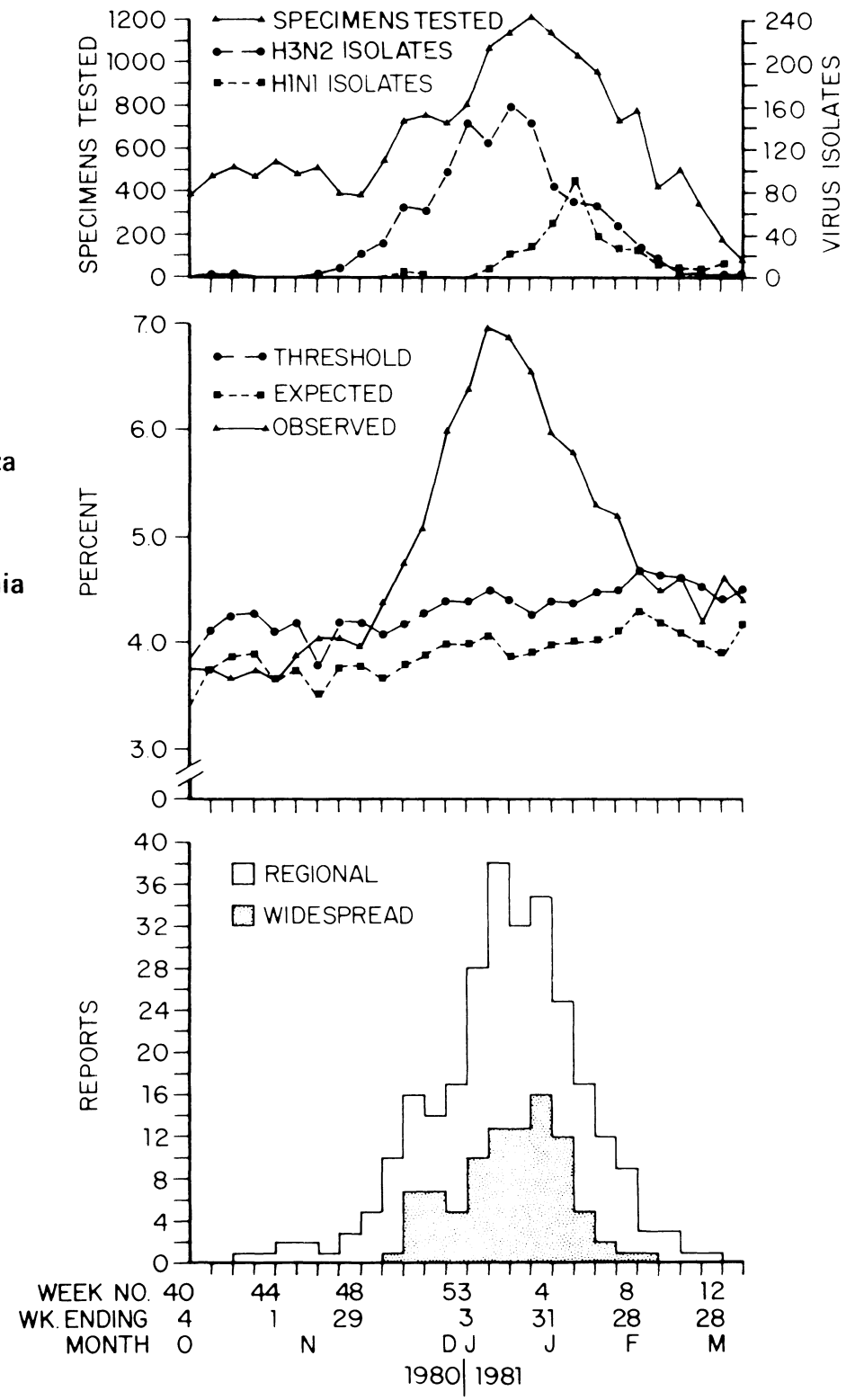
The observed ratio of pneumonia and influenza deaths to all deaths in the 121 reporting cities exceeded the epidemic threshold for a 13-week period beginning December 13, 1980 (Figure 3). The P and I ratio peak coincided with the period of peak reporting of influenza A(H3N2) isolations from collaborating laboratories. In all, a provisional estimate of 52,200 excess

## FIGURE 3: INFLUENZA SURVEILLANCE IN THE UNITED STATES, 1980–1981

Laboratory surveillance: isolations of influenza viruses reported by WHO collaborating laboratories

Pneumonia and influenza mortality surveillance: ratio of observed and expected deaths attributed to pneumonia and influenza (121 U.S. cities)

Morbidity surveillance: reported regional and widespread outbreaks of influenza from reporting areas



deaths occurred nationwide during the epidemic (Table 1), the largest number of deaths associated with an influenza epidemic in the United States since the 1957-1958 influenza season. The number of deaths may have been due in part to the extended duration of the epidemic, the longest epidemic period since the 1968-1969 influenza season.

## Morbidity Surveillance

The maximum extent of influenza morbidity for 1980-81 nationwide is shown in Figure 4.

Region I (Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont) - All of the states in Region I except New Hampshire reported isolations of influenza A (H3N2), and all states except Rhode Island reported influenza A (H1N1) virus isolates. Beginning the latter part of December, New Hampshire, Maine, Massachusetts and Rhode Island reported widespread influenza-like disease activity. In Massachusetts virus isolates were reported in nursing home patients, college students, hospital staff, school-age children, and adults. Concurrent with isolation of the virus school absenteeism increased.

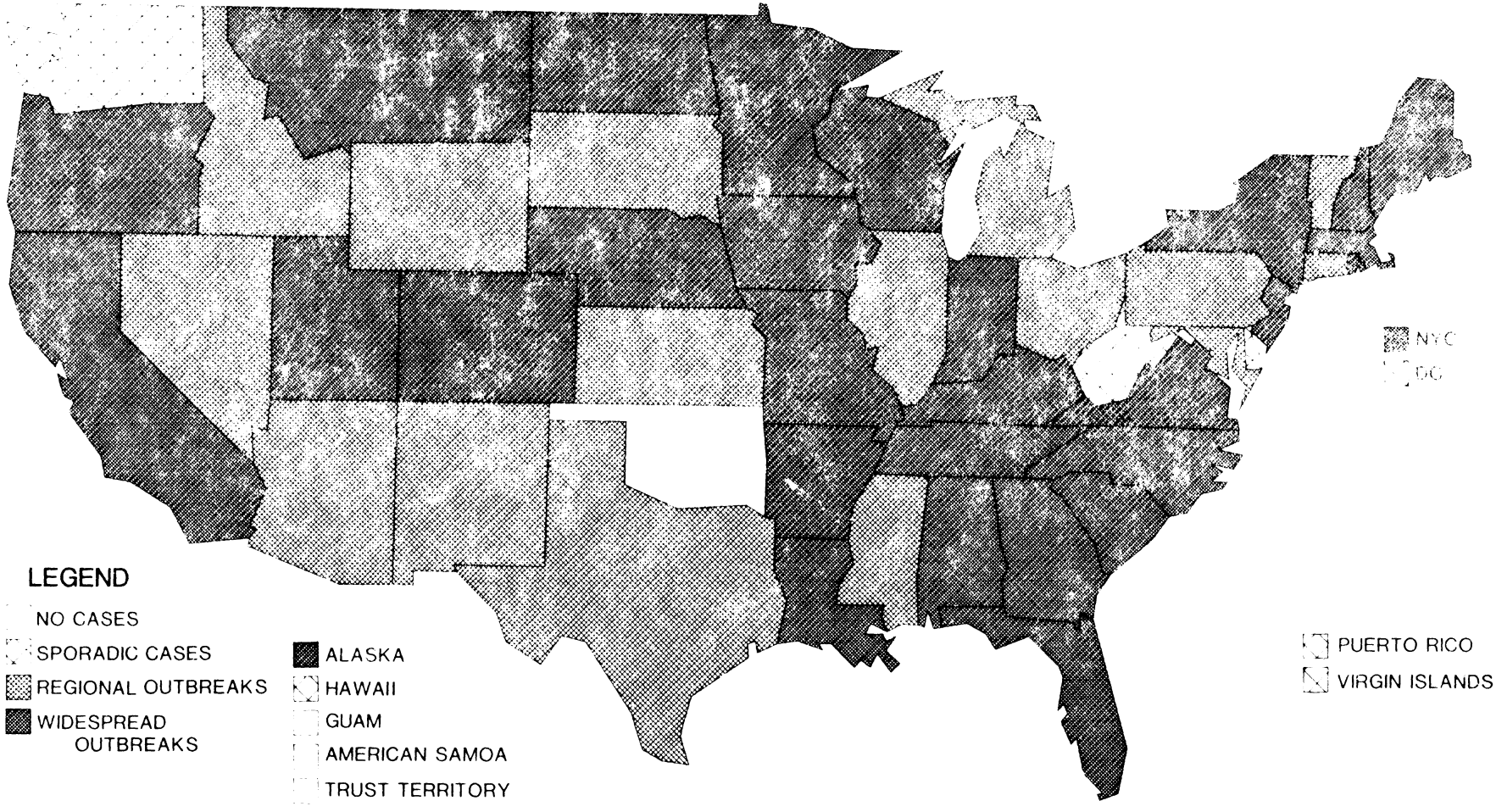
Region II (New Jersey, New York, Puerto Rico, Virgin Islands) - All of the reporting areas, except the Virgin Islands, reported influenza A (H3N2) and A (H1N1) virus strains starting in September. Only New York reported an influenza B isolate. Beginning in mid-December, New Jersey and New York reported widespread activity associated with influenza A (H3N2) infections.

Region III (Delaware, D.C., Maryland, Pennsylvania, Virginia, West Virginia) - All of these states reported both influenza A (H3N2) and A (H1N1) isolates beginning in mid-December. Only Virginia reported widespread activity, which began in mid-January. The remaining states reported regional and sporadic outbreaks between October 1980 and March 1981. An outbreak of influenza A(H3N2) illness occurred in a Pennsylvania geriatric center in December. In mid-March, an outbreak of influenza A(H3N2) illness occurred in Maryland in an institution for the mentally retarded and in nursing homes; West Virginia reported an outbreak in a hospital.

Region IV (Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, Tennessee) - Influenza A (H3N2) isolates were confirmed in seven of the states beginning in December. Influenza A(H1N1) isolates were reported from six of the states beginning in mid-January. Only Georgia reported an influenza B isolate. In late December an outbreak of influenza-like illness associated with influenza A (H3N2) virus occurred in a Veterans Administration Hospital in Alabama. All of the states except Mississippi reported widespread influenza activity starting in January. Influenza A (H1N1) virus isolates were reported from a mid-January outbreak of respiratory illness in an elementary school in Georgia.

Region V (Illinois, Indiana, Michigan, Minnesota, Ohio, Wisconsin) - Influenza A(H3N2) strains were isolated by all of the states in Region V after early December. Influenza A(H1N1) isolates were reported from all of the states beginning in January. Minnesota, Indiana, and Wisconsin reported widespread influenza activity beginning in mid-January. During November and December, an outbreak of influenza A(H3N2) illness occurred among the patients and staff of two psychiatric wards in a Chicago hospital.

# FIGURE 4: MAXIMUM REPORTED INFLUENZA MORBIDITY, 7/80 - 6/81



Region VI (Arkansas, Louisiana, New Mexico, Oklahoma, Texas) - All Region VI states reported influenza A (H3N2) isolates starting in November. Only New Mexico did not report the isolation of an influenza A (H1N1) strain. Arkansas and Louisiana reported widespread influenza-like outbreak activity in mid-January. The remaining states except Oklahoma reported regional or sporadic outbreaks between November and the end of March.

Region VII (Iowa, Kansas, Missouri, Nebraska) - Influenza A (H3N2) virus isolates were reported from all of the states starting in January. Widespread disease activity was reported by all of the states except Kansas. Only Missouri and Nebraska reported influenza A (H1N1) strains which were isolated in February and March. Several elementary schools in Iowa were closed with absenteeism of greater than 25 percent. A simultaneous outbreak of influenza A (H3N2) and staphylococcal food-poisoning occurred in a nursing home in Iowa during January.

Region VIII (Colorado, Montana, North Dakota, South Dakota, Utah, Wyoming) - Colorado reported an influenza A (H3N2) isolate in November. Beginning in January, all of the other states, except Wyoming, reported influenza A (H3N2) isolates. All states but South Dakota and Wyoming reported widespread influenza activity from mid-December through the beginning of February. Colorado, South Dakota, and Utah reported influenza A (H1N1) strains in January. An outbreak of influenza A (H1N1) illness was reported among inmates at a Federal correctional institute in Colorado in December.

Region IX (American Samoa, Arizona, California, Guam, Hawaii, Nevada, Trust Territory) - Influenza A(H3N2) isolates were reported from all of the states. Arizona, California, and Nevada reported isolates of influenza A (H1N1) viruses during February. In July 1980 a Tucson, Arizona, nursing home experienced a laboratory confirmed outbreak of influenza A(H3N2) illness. Hawaii reported several outbreaks of influenza A (H3N2) beginning in late August. In October an outbreak of influenza A (H3N2) illness occurred among residents and staff in a San Francisco nursing home.

Region X (Alaska, Idaho, Oregon, Washington) - All of the states reported influenza A (H3N2) isolates. Idaho was the only state that did not report the isolation of influenza A (H1N1). Alaska and Oregon reported widespread activity which began at the end of December. The remaining states reported sporadic and regional outbreaks from October, 1980 through March, 1981.

## Laboratory Reports

### *Virus Isolation Reports*

Virus surveillance in the United States conducted by WHO Collaborating Laboratories and others in 1980-81 resulted in the documentation of influenza A (H3N2) infections in 50 states and territories, of influenza A (H1N1) infections in 41 reporting areas, and of influenza B infections in two areas (Table 8).

These laboratories reported the testing of 18,952 specimens for respiratory virus isolation and the isolation of 1,266 influenza A (H3N2) viruses, 387 influenza A (H1N1) viruses, and two influenza B viruses. A single influenza C isolate was recovered from a specimen from Mississippi. No isolates of swine influenza-like virus were reported from man.

**Table 8. Influenza Virus Isolates Reported to the WHO Collaborating Laboratories in the U.S., 1980-1981**

| | Influenza A(H3N2) | Influenza A(H1N1) | Influenza B | Influenza C |
|---|---|---|---|---|
| **REGION I** | | | | |
| Connecticut | ▒ | ▒ | | |
| Maine | ▒ | ▒ | | |
| Massachusetts | ▒ | ▒ | | |
| New Hampshire | | ▒ | | |
| Rhode Island | ▒ | | | |
| Vermont | ▒ | ▒ | | |
| **REGION II** | | | | |
| New Jersey | ▒ | ▒ | | |
| New York | ▒ | ▒ | ▒ | |
| Puerto Rico | ▒ | ▒ | | |
| Virgin Islands | | | | |
| **REGION III** | | | | |
| Delaware | ▒ | ▒ | | |
| District of Columbia | ▒ | ▒ | | |
| Maryland | ▒ | ▒ | | |
| Pennsylvania | ▒ | ▒ | | |
| Virginia | ▒ | ▒ | | |
| West Virginia | ▒ | ▒ | | |
| **REGION IV** | | | | |
| Alabama | ▒ | | | |
| Florida | ▒ | ▒ | | |
| Georgia | ▒ | ▒ | ▒ | |
| Kentucky | | | | |
| Mississippi | ▒ | ▒ | | ▒ |
| North Carolina | ▒ | ▒ | | |
| South Carolina | ▒ | ▒ | | |
| Tennessee | ▒ | ▒ | | |
| **REGION V** | | | | |
| Illinois | ▒ | ▒ | | |
| Indiana | ▒ | ▒ | | |
| Michigan | ▒ | ▒ | | |
| Minnesota | ▒ | ▒ | | |
| Ohio | ▒ | ▒ | | |
| Wisconsin | ▒ | ▒ | | |
| **TOTAL** | | | | |

| | Influenza A(H3N2) | Influenza A(H1N1) | Influenza B | Influenza C |
|---|---|---|---|---|
| **REGION VI** | | | | |
| Arkansas | ▒ | ▒ | | |
| Louisiana | ▒ | ▒ | | |
| New Mexico | ▒ | | | |
| Oklahoma | ▒ | ▒ | | |
| Texas | ▒ | ▒ | | |
| **REGION VII** | | | | |
| Iowa | ▒ | | | |
| Kansas | ▒ | | | |
| Missouri | ▒ | ▒ | | |
| Nebraska | ▒ | ▒ | | |
| **REGION VIII** | | | | |
| Colorado | ▒ | ▒ | | |
| Montana | ▒ | | | |
| North Dakota | ▒ | | | |
| South Dakota | ▒ | ▒ | | |
| Utah | ▒ | ▒ | | |
| Wyoming | | | | |
| **REGION IX** | | | | |
| American Samoa | | | | |
| Arizona | ▒ | ▒ | | |
| California | ▒ | ▒ | | |
| Guam | ▒ | | | |
| Hawaii | ▒ | | | |
| Nevada | ▒ | ▒ | | |
| **REGION X** | | | | |
| Alaska | ▒ | ▒ | | |
| Idaho | ▒ | | | |
| Oregon | ▒ | ▒ | | |
| Washington | ▒ | ▒ | | |
| **TOTAL** | 50 | 41 | 2 | 1 |

Measurable nationwide influenza A(H3N2) activity began in late November 1980. However, laboratory-confirmed sporadic cases and/or outbreaks of influenza A (H3N2) were reported in July an August of 1980, an unusual occurrence. Influenza A (H3N2) viruses were isolated earlier, for a longer period of time, (Figure 3), and in greater total numbers than influenza A (H1N1) viruses. The number of influenza A (H3N2) virus isolations peaked during mid-January 1981. Influenza A (H1N1) virus isolations peaked in early February 1981. Influenza A (H3N2) and A (H1N1) were found to be circulating simultaneously.

Participating laboratories reported, where known, the ages of patients with positive influenza virus cultures as $\leq$28 or >28 years of age which provided, specifically, an indication of the spread of influenza A (H1N1) infection into the older age group. Approximately 90 percent of all influenza A (H1N1) viruses obtained were from persons $\leq$28 years of age (Table 9). For reported influenza A (H3N2) isolates the number of cases above 28 years of age was similar to the number of cases $\leq$28 years of age.

**Table 9. Distribution by Type and Age Group of Influenza Virus Isolates, Reported by Collaborating Laboratories in the U.S., Oct. 3, 1980-Feb. 20, 1981**

| | No. (%) of laboratory reports for persons of known age | | |
|---|---|---|---|
| | $\leq$28 yrs. | $\geq$28 yrs. | Total of known age |
| Specimens tested | 6,202(72) | 2,366(28) | 8,568(100) |
| Influenza A (H3N2) isolates | 516(57) | 389(43) | 905(100) |
| Influenza A (H1N1) isolates | 161(89) | 19(11) | 180(100) |

### *Antigenic Analysis of Isolates Submitted*

Influenza A (H3N2) - From October 1, 1980 through June of 1981, 377 isolates of influenza A(H3N2) strains were submitted to CDC from the United States for reference antigenic analysis. As in the 1979-1980 influenza season, influenza A (H3N2) viruses were found to be antigenically heterogeneous. Viruses similar to previously described strains, i.e., A/Texas/1/77, A/Bangkok/1/79, and A/Arizona/2/80 continued to circulate. Viruses antigenically intermediate between A/Texas/1/77 and A/Bangkok/1/79 had the highest prevalence. A/Oregon/4/80 was selected as a reference strain for these 1980-81 intermediate viruses.

Among influenza viruses submitted from the Far East, a new influenza A (H3N2) variant, A/Shanghai/31/80, was detected. A/Shanghai/31/80 appeared to be derived from A/Bangkok/1/79 as shown by the HI reactions of A/Shanghai-like sera, and was inhibited less by antiserum to A/Texas/1/77 than other contemporary influenza A(H3N2) strains (Table 10).

**Table 10. Hemagglutination-Inhibition (HI) Reactions of A/Shanghai/31/80(H3N2) Variants**

| | Ferret sera | | | | |
|---|---|---|---|---|---|
| Antigens | A/Texas 1/77 | A/Oregon 4/80 | A/Bangkok 1/79 | A/Arizona 2/80 | A/Shanghai 31/80 |
| A/Texas/1/77 | 2560 | 640 | 160 | 320 | 160 |
| A/Oregon/4/80 | 1280 | 640 | 640 | 320 | 160 |
| A/Bangkok/1/79 | 640 | 640 | 1280 | 640 | 1280 |
| A/Arizona/2/80 | 640 | 320 | 160 | 320 | 160 |
| A/Shanghai/31/80 | 160 | 160 | 320 | 160 | 1280 |

Representative influenza A (H3N2) viruses throughout the year were compared by neuraminidase inhibition and did not exhibit major antigenic drift in their neuraminidase antigen from the preceding A/Texas/1/77 or A/Bangkok/1/79 reference strains.

Influenza A (H1N1) - Influenza A (H1N1) isolates from the United States were found to be antigenically heterogenous. The predominant influenza A (H1N1) strains in the United States in 1980-81 were considered to be slight variants from A/Brazil/11/78 and generally resembled A/England/333/80 or A/India/6238/80. Most of the isolates were well inhibited by antiserum to A/Brazil/11/78. Approximately 10 percent were inhibited 4- to 8-fold less by A/Brazil/11/78 serum than was the reference strain. Reciprocal hemagglutination inhibition tests showed that even strains well inhibited by A/Brazil/11/78 antiserum (e.g., A/England/333/80) were somewhat different from A/Brazil/11/78 in that they were better inhibited by antiserum to the more distinct variants isolated in 1980, such as A/India/6263/80 (Table 11). Similar strains were prevalent in many countries throughout 1981. A/Brazil/11/78-like strains ceased to circulate.

**Table 11. Hemagglutination-Inhibition (HI) Reactions of Influenza A (H1N1) Variants* from 1980**

| | Ferret sera | | | |
|---|---|---|---|---|
| Antigen | A/USSR/ 92/77 | A/Brazil/ 11/78 | A/England/ 33/80 | A/India 6263/80 |
| A/USSR/90/77 | 320 | 320 | 640 | 40 |
| A/Brazil/11/78 | 80 | 640 | 640 | 40 |
| A/England/333/80 | 80 | 320 | 1280 | 160 |
| A/India/6263/80 | 20 | 80 | 160 | 160 |

### *Antibody Prevalence Studies*

HI Antibody Levels Pre- and Post-immunization with the 1980-81 Trivalent Influenza Vaccine - Prior to the 1980-81 influenza season, 102 volunteers consisting of 30 high-risk children, 25 college students, and 47 elderly persons were enrolled in vaccine studies in Hackensack, New Jersey, Ann Arbor, Michigan and Rochester, New York, by Drs. P. Gross, Hackensack Hospital, N.J., A. Monto, University of Michigan, Ann Arbor, and G. Douglas, Rochester Medical School. Sera were collected prior to the administration of a single dose of the 1980-81 influenza vaccine comprising 7 ug each of A/Bangkok/1/79, A/Brazil/11/78 and B/Singapore/222/79 antigens. Prior to vaccination, 61 percent of subjects possessed HI antibody titers of 40 or greater when tested with A/Texas/1/77 or A/Bangkok/1/79. After a single dose of the trivalent vaccine 93 to 95 percent of recipients were shown to have antibody titers of at least 40. Fifty percent of recipients experienced a four-fold antibody rise. Geometric mean titers (GMT) of 40-50 before vaccination rose to 140-175 after vaccination (Table 12).

**Table 12. Antibody Prevalence and Response to a Single Dose of Trivalent Vaccine* in 102 Volunteers† 1980-81**

| | | Cumulative % with HI titer | | | | | |
|---|---|---|---|---|---|---|---|
| Virus strain | Serum | ≥20 | ≥40 | ≥80 | 160 | % with ≥4 rise+ | GMT** |
| A/Texas/1/77 | Pre-vac | 85 | 61 | 36 | 22 | - | 50 |
| | Post-vac | 99 | 93 | 77 | 56 | 50 | 175 |
| A/Bangkok/1/79 | Pre-vac | 88 | 60 | 30 | 13 | - | 39 |
| | Post-vac | 99 | 95 | 71 | 52 | 51 | 140 |
| B/Singapore/222/70 | Pre-vac | 44 | 25 | 11 | 2 | - | 14 |
| | Post-vac | 81 | 66 | 47 | 0 | 26 | 51 |

*Trivalent vaccine composed of 7 ug A/Bangkok/1/79(H3N2), 7 ug A/Brazil/11/78(H1N1), and 7ug B/Singapore/222/79.

+102 volunteers comprised 30 high-risk pediatric subjects, 25 college students and 47 elderly subjects enrolled in vaccine studies. All sera were tested over two days at the CDC, with approximately equal numbers of sera from each group in each day's test.

**Assuming a titer of 5 for values <10.

For influenza B the prevalence of antibody to B/Singapore/222/79 at a level of 40 or greater was 25 percent prior to receipt of vaccine and 60 percent after vaccination, with 51 percent of the recipients exhibiting a four-fold or greater antibody rise (Table 12).

Since influenza A(H1N1) viruses predominantly infect young persons, antibody prevalence data for influenza A(H1N1) viruses were collected only from the 25 University of Michigan students. The students received two doses of the vaccine as recommended for this age group in the absence of knowledge of prior vaccination or infection with influenza A(H1N1) viruses.

Prevaccination prevalences of antibodies at a titer of ≥40 ranged from 0 percent for the newer HI variant, A/India/6263/80, to 8 percent for A/Brazil/11/78 (Table 13). A single dose of vaccine elicited an antibody titer of 40 or greater to both strains in at least 60 percent of the students. The effect of the second dose of vaccine was very small with the overall prevalence of an antibody titer of 40 or greater to A/India/80 increasing to 64 percent and to A/Brazil/78 increasing to 72 percent. GMT following one dose of vaccine increased from a prevaccination level of approximately 7-8 to a post vaccination level of 47-51. There was no siginificant rise in GMT following the second dose of vaccine.

These studies indicated that the 1980-81 trivalent vaccine, used according to ACIP recommendations, produced antibody titer responses of 40 or greater* to influenza A(H3N2), A(H1N1), and B influenza viruses representative of viruses in circulation during the 1980-81 influenza season in at least two-thirds of the vaccinees.

**Table 13. Antibody Response to Influenza A (H1N1) Variants After One or Two Doses of Inactivated Vaccine Containing 7 ug of A/Brazil/11/78 Hemagglutinin in 25 College Students (<27 Years), 1980-81***

| | | Cumulative % with titer | | | | | |
|---|---|---|---|---|---|---|---|
| Virus strain | Serum | ≥20 | ≥40 | ≥80 | ≥160 | % with ≥4-fold rise | GMT |
| A/Brazil/11/78 | Pre-vac | 12 | 8 | 4 | 0 | - | 7.6 |
| | Post-vac[1] | 68 | 64 | 60 | 44 | 64 | 51 |
| | Post-vac[2] | 72 | 72 | 56 | 44 | 68 | 62 |
| A/India/6263/80 | Pre-vac | 12 | 0 | 0 | 0 | - | 6.6 |
| | Post-vac | 68 | 60 | 56 | 40 | 64 | 47 |
| | Post-boost | 68 | 64 | 56 | 40 | 68 | 56 |

*University of Michigan, Ann Arbor, interval between doses was one month; sera collected two weeks after each dose.

Prevalences of Antibodies to Influenza A(H1N1) Variants, A/England/333/80 and A/India/6263/80 - Sera collected from 95 persons of various ages from Atlanta, Georgia, prior to the 1980-81 influenza season were tested for antibodies to the new influenza A(H1N1) variants, A/England/333/80 and A/India/6263/80 (Table 14). The prevalence of antibodies to the variant, A/India/6263/80, in persons 27 years of age or younger (persons who could have been infected with an influenza A(H1N1) virus only between 1977 and 1980) was slightly lower than the prevalence of A/Brazil/11/78 antibodies. In contrast, in older age groups, including persons presumed to have been infected with influenza A(H1N1) viruses circulating prior to 1957, there was a higher prevalence of antibodies to the A/India/80 variant than to the A/Brazil/78. This was surprising in that tests comparing the A/India/6263/80 isolate with much earlier influenza A(H1N1) reference strains did not indicate prior circulation of A/India/6263/80-like strains.

*An antibody titer of ≥40 is the level at which significant protection against influenza disease is considered to be demonstrated.

Table 14. Prevalence of Antibodies to A(H1N1) Variants A/England/333/80 and A/India/6263/80, Atlanta, Ga. 1980-81

| Age (years) | No. Tested | Titers ≥10 | |
|---|---|---|---|
| | | A/Brazil/11/78 | A/India/6263/80 |
| | | %(No.) | |
| 1 - 27 | 41 | 51 (11) | 39 (9) |
| 28 - 65 | 29 | 66 (12) | 90 (17) |
| ≥65 | 25 | 44 (8) | 68 (12) |

### *Identification of Recombinant Viruses among Natural Isolates*

A representative selection of isolates was examined by oligonucleotide mapping of virion RNA to further monitor the long-term survival and spread of viruses with recombinant genomes derived partially from influenza A (H1N1) and A(H3N2) viruses. Results showed that during 1980-81 "true" influenza A(H1N1) viruses deriving all genes from non-recombinant influenza A(H1N1) precursor viruses were prevalent. This included viruses antigenically characterized as similar to influenza viruses A/England/333/80 or A/India/6263/80, the predominant influenza A(H1N1) viruses from outbreaks during the period. A small number of viruses with recombinant genomes were identified. Most were identified prior to September 1980 and had hemagglutinins related to those of A/Brazil/78. These recombinant viruses are assumed to have evolved from the previously prevalent recombinant strains with A/Brazil-like hemagglutinin and four or five genes of influenza A(H3N2) origin. However, several viruses from Taiwan were identified that had low-avidity A/England/333/80-like hemagglutinins. Oligonucleotide mapping indicated that those influenza viruses contained recombinant genomes with some influenza A(H3N2) segments. These viruses may have resulted from an additional recombination event between low-avidity A/England/333/80-like virus and influenza A(H3N2) viruses which were circulating simultaneously or, alternatively, by independent evolution from A/Brazil/79 precursors which underwent antigenic variation paralleling that found in the A/England/333/80 group.

Oligonucleotide mapping of influenza A(H3N2) viruses showed a very high degree of similarity among viruses from 1979, 1980, and 1981. Although these viruses exhibited approximately seven to ten spot differences by oligonucleotide mapping from the preceding A/Texas/77-like viruses, the degree of similarity was sufficiently large that they are not believed to be recombinant viruses containing influenza A(H1N1) gene segments. Oligonucleotide mapping, alone, does not exclude the possibility that one or two of the smallest RNA segments might have been derived from influenza A(H3N2) viruses. However, RNA hybridizaton studies eliminated this possibility for several isolates tested from 1979-1980.

## International Report

The epidemiologic behavior of influenza internationally from October 1980-September 1981 and the results of antigenic analyses of viruses received at the WHO Collaborating Center for Influenza, CDC, from various countries are summarized in the text and tables of appendix III.

## Epidemic Investigations

Frederick, Maryland - During the period December 12-26, 1980 an outbreak of influenza-like illness occurred at a nursing home, resident population 162. Ninety-five (58.6 percent) of these residents had received the 1980-81 influenza vaccine in early November. A case was defined as having a temperature $\geq$37.8°C ($\geq$100°F), cough, or chest congestion. Thirty-four (30 percent) of the residents became ill. Two specimens from throat swabs were positive for an influenza A (H3N2) virus. The clinical attack rate in the vaccinated persons was 22.1 percent and in the unvaccinated was 23.6 percent for an estimated vaccine efficacy of 6.5 percent (95% confidence limits, 0 to 49.7). Six deaths occurred, four in vaccinated and two in unvaccinated residents.

Reported by: J. Horman, DVM, Frederick County Health Department; E. Israel, M.D., State Epidemiologist, Maryland State Department of Health and Mental Hygiene; WHO Collaborating Center for Influenza, CID; Immunization Division, CPS, CDC

Alabama - During the period January 1-10, 1981, an outbreak of influenza-like illness occurred in a Veterans Administration Medical Center. The outbreak was confined mostly to an 82-bed intermediate care facility (ICF) housing 78 residents. Fifty-nine (76 percent) of these residents had received the 1980-81 influenza vaccine during the first week of November 1980. A case was defined as having a temperature $\geq$37.8°C ($\geq$100°F) and at least two of the following symptoms: cough, malaise, or coryza. Twenty-three of 40 (58 percent) ambulatory or wheelchair-bound patients in the north side of the ICF became ill and 6 of 38 (16 percent) bedridden patients on the south side of the ICF became ill. One patient died of an arrythmia following clinical improvement.

Throat and nasopharyngeal specimens were obtained from seven ICF patients late in their illness and no isolates were recovered. However, viral isolates cross reactive with A/Texas/1/77 were obtained from 3 of 12 specimens from sporadic cases in other areas of the hospital. Of 77 acute and convalescent paired serum specimens from ICF residents, 12 (16 percent) yielded a $\geq$ fourfold rise in titer against A/Bangkok/1/79 and A/Texas/1/77. Sixteen symptomatic residents did not show serological evidence of influenza A infection.

The clinical attack rate among all vaccinated ICF patients was 33.9 percent compared to 47.4 percent for unvaccinated patients, providing a vaccine efficacy estimate of 28.4 percent (95 percent confidence limits, 0 to 64.4 percent).

Reported by: Jung Chwe, R.N., B. Roisum, M.D., Chief of Staff, Tuscaloosa VA Medical Center; J. McCall, E. K. Aycock, M.D, Assistant State Health Officer; T. Chester, M.D., Acting State Epidemiologist; Alabama State Department of Health; WHO Collaborating Laboratory, CID; Field Services Division, EPO; Immunization Division, CPS, CDC

New Jersey - During the period December 3-22, 1980, an outbreak of influenza-like illness occurred in a nursing home in New Jersey. Vaccine status and illness information were known for 184 persons who had been residents in the nursing home since November 25. Ninety (49 percent) of these residents had received influenza vaccine on November 25. A case was defined as having a temperature $\geq$37.8°C ($\geq$100°F) plus at least one respiratory symptom: cough, coryza, congestion, or "cold symptoms."

Clinical illness occurred in 48 (26 percent) of the 184 residents. Influenza A virus was isolated from two of 11 ill residents. Twelve of 15 paired sera from cases were shown to have evidence of a current infection with influenza.

Thirty-one (33 percent) of the 94 unimmunized residents had illness compared with 17 (19 percent) for the 90 immunized residents. The vaccine efficacy was calculated to be 43 percent (95 percent confidence limits, 0-66 percent). Four of the ill residents died; a case-fatality ratio of 8 percent. Two fatal cases were in unimmunized residents and two in immunized residents.

Reported by: J. Prusakowski, R.N., W. Parkin, DVM, State Epidemiologist, New Jersey Department of Health; Field Services Div., EPO, CDC

Georgia - Between December 12, 1980-January 21, 1981, an outbreak of influenza-like illness occurred in a nursing home in Atlanta. The total resident population was 120 and 36 residents had received influenza vaccine in the fall of 1980. A case of influenza was defined as a nursing home resident who had illness consisting of a rectal temperature $\geq$37.8°C ($\geq$100°F) and/or development of a cough during the outbreak period.

Clinical illness occurred in 30 (25 percent) of the 120 residents. Thirteen persons were hospitalized and twelve had evidence of pneumonia. Nine of the hospitalized residents died, eight of whom had clinical pneumonia. The case-fatality ratio was 30 percent. Influenza A/Bangkok/79-like virus was isolated from five of eight acutely ill persons. Diagnostic (fourfold) titer rises of CF antibody occurred in 11 of 13 ill residents; serologic testing was negative for other pathogens. Twenty-four (28.6 percent) of the 84 unimmunized residents had cases compared with 6 (16.7 percent) of the 36 immunized residents. Vaccine efficacy was calculated to be 41.6 percent (95 percent confidence limits, 0-72.2 percent). All nine fatal cases were in unimmunized residents.

Reported by: S. Smith, BSN, Smyrna, GA; M. Chaney, T. Munroe, MS, Virology Laboratory, R.K. Sikes, DVM, State Epidemiologist, Georgia Department of Human Resources; Field Services Division, EPO, CDC

Arizona - Between March 24 and April 15, 1981, an outbreak of influenza-like illness occurred at a nursing home in Tucson. The resident population was 57; 47 (82 percent) of these had received influenza vaccine. Illness was characterized by temperature $\geq$38°C ($\geq$100°F) or greater plus two or more flu-like symptoms.

Twenty-four of the residents became ill. Four of the ill residents died, two with pneumonia and two with cardiac problems. Influenza A (H1N1) was reported to have been isolated from 7 patients. The attack rate in vaccinees was 34 percent and in unvaccinated persons was 80 percent resulting in an estimated vaccine efficacy of 57.5 percent (95 percent confidence limits, 0 - 79.86).

This outbreak was unusual in that influenza A(H1N1) was reported to have caused severe illness in an elderly population. Isolates sent to the CDC for confirmation were lost in the mails making exact etiologic confirmation of the outbreak inpossible.

Reported by: L. Minnich, M.S., G. Ray, M.D., Dept. of Pathology, Arizona Health Sciences Center, R. Worrell, R.N., Pima County Health Deprtment; K. Starko, M.D., Arizona State Department of Health Services

## INFLUENZA VACCINE EFFICACY

The protective effect of influenza vaccination against influenza disease was estimated by calculating vaccine efficacy rates.

Estimated vaccine efficacy rates (VE) are determined as follows:

$$VE(\%) = \frac{\text{Attack Rate (Unvaccinated)} - \text{Attack Rate (Vaccinated)}}{\text{Attack Rate (Unvaccinated)}} \times 100$$

The estimated vaccine efficacy rate reflects the effect of events preceding exposure to natural influenza virus including the degree of similarity between the vaccine antigen(s) and the circulating strains(s) and variations in antibody response of individuals to vaccination because of age and previous exposure to both natural and vaccine antigens.

Vaccine efficacy has frequently been determined in retrospective cohort studies of suspected influenza outbreaks. Methodological problems associated with such studies include:

(a) difficulties in establishing a case definition of influenza disease often because of incomplete records;
(b) laboratory confirmation in few of the cases because of a lack of, or delays in collection of, appropriate specimens for confirmation of causal agent;
(c) biases in use of influenza vaccine, including age or underlying illness;
(d) unequal exposure in vaccinated and unvaccinated persons; and
(e) relatively small numbers of people involved in the outbreak.

Many of these problems can be overcome by prospective studies. However, as the occurrence of influenza in any population cannot be predicted, the chances of choosing appropriate populations in advance are small unless very large studies are undertaken. In addition, for ethical reasons a control population of high risk persons could not be designed into a study.

For studies calculating clinical vaccine efficacy rates the wide variations in case definitions and methods of data collection do not permit reliable comparison of rates. Past studies have shown rates ranging from 20-90 percent[7-8] with most in the 50-80 percent range.[9-13] The investigations summarized in this report suggest vaccine efficacy of 21 percent against influenza B in 1979-80 (one report) and 6.5-57.5 percent against influenza A(H3N2) in 1980-81 (5 reports). Other approaches to evaluating vaccine efficacy have compared hospitalization bronchopneumonia or mortality rates in vaccinated and unvaccinated groups.[9, 14] Although the criteria are more accurately definable, the number of events necessary for a reliable study generally requires a sizeable study population.

## REYE'S SYNDROME

### 1979-1980 Season

Between December 2, 1979-November 30, 1980, 548 cases of Reye's syndrome (RS) were reported to CDC, the largest number of cases reported to CDC in one season. As in the 1973-74 and 1976-77 influenza seasons of extensive influenza B activity, RS cases were temporally associated with influenza B isolates and outbreaks in the United States.[15, 16] Eighty-three percent of the RS cases occurred between the weeks ending December 1, 1979 and April 18, 1980. Both influenza B isolates and RS cases peaked the week ending February 8 (Figure 5).[17]

Two case-control studies conducted in 1980 in Ohio and Michigan suggested a relationship between Reye's syndrome and salicylates (i.e., aspirin) taken during an associated antecedent illness.[18, 19] The frequency of usage of salicylates and acetaminophen was found to be significantly different in cases and controls. Salicylates, including those contained in various compounds, were the only medications taken significantly more frequently in cases than controls. Medications containing acetaminophen were taken more frequently by controls. The results of the studies suggest that during certain viral illnesses the use of salicylates before the onset of vomiting may be a risk factor in the pathogenesis of RS.

### 1980-1981 Season

Between December 1, 1980 and July 30, 1981, 189 cases of RS were reported to CDC. The number of RS cases peaked at the time influenza A(H3N2) and A(H1N1) isolates peaked in the United States as reported by WHO collaborating laboratories (figure 6). However, clusters of RS cases were not reported in association with local outbreaks of influenza A. The 1980-1981 seasonal pattern of RS is similar to the previous influenza A(H3N2) and A(H1N1) season in 1977-1978 during which RS cases occurred at approximately one-half the rate seen in influenza B years.

## GUILLAIN-BARRÉ SYNDROME (1979-80 and 1980-81)

In 1978, CDC established a surveillance system to detect cases of Guillain-Barré Syndrome (GBS) through a group of American Academy of Neurology physicians estimated to comprise approximately 40 percent of the neurologists in private practice and in academic centers in the United States. Surveillance was intensified from September through March of each year in order to determine whether an increased risk of GBS exists among recipients of each year's influenza vaccines.

Figure 7 shows the monthly distribution of 528 vacccinated and unvaccinated cases of GBS with onset between September 1979 and March 1980 and of 459 cases with onset between September 1980 and March 1981. An association was not found between influenza vaccination and the development of GBS in the subsequent 8 weeks for either of the periods.[21]

FIGURE 5

REPORTED REYE SYNDROME CASES, BY WEEK OF ONSET OF PRODROME, AND INFLUENZA B ISOLATES, BY WEEK OF REPORT, UNITED STATES, NOVEMBER 30, 1979-APRIL 25, 1980

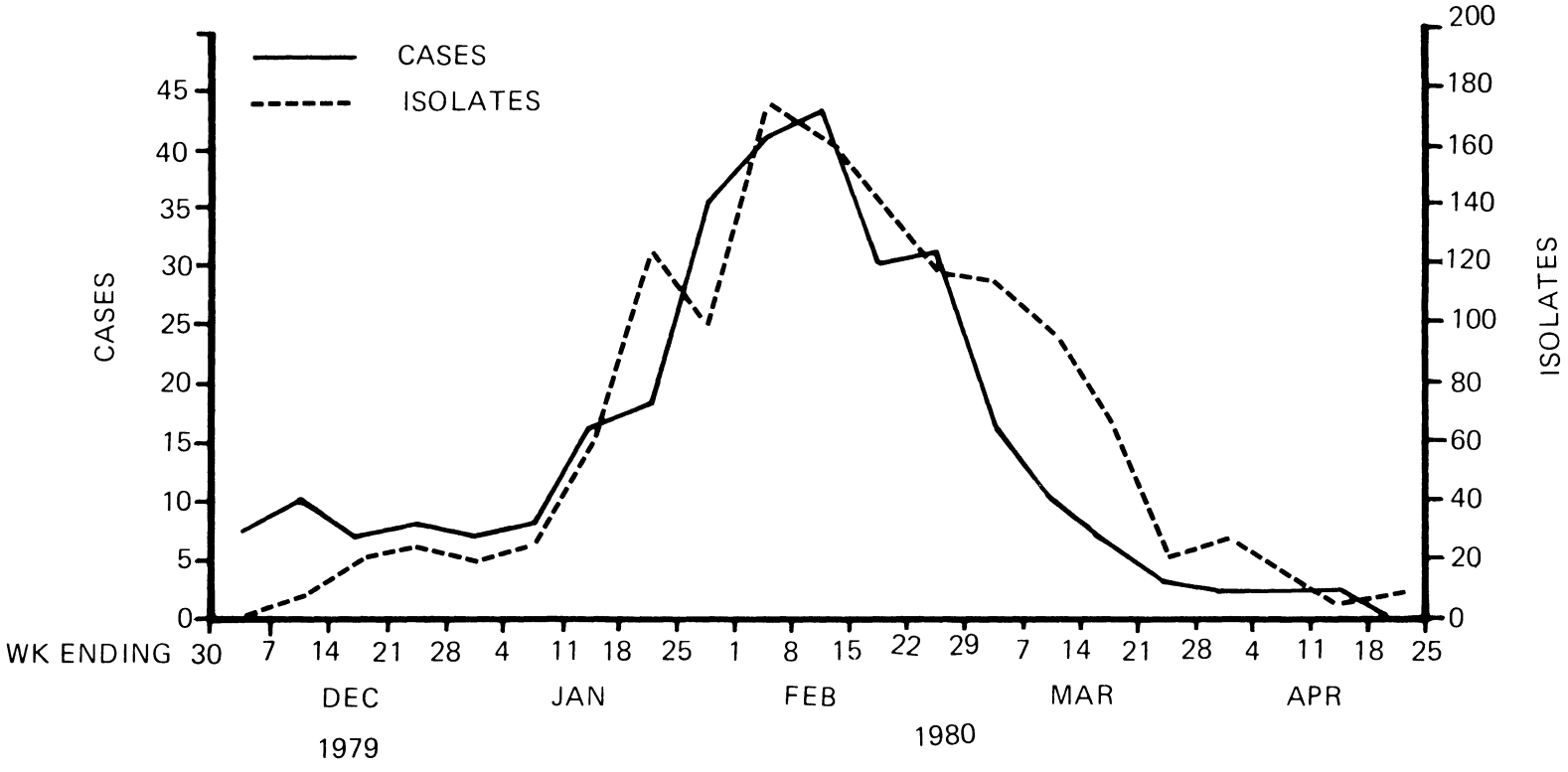



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Figure 6

REPORTED REYE SYNDROME CASES, BY WEEK OF ONSET OF PRODROME, AND INFLUENZA A($H_3N_2$) AND A($H_1N_1$) ISOLATES, BY WEEK OF REPORT, UNITED STATES, DECEMBER 5, 1980–APRIL 3, 1981

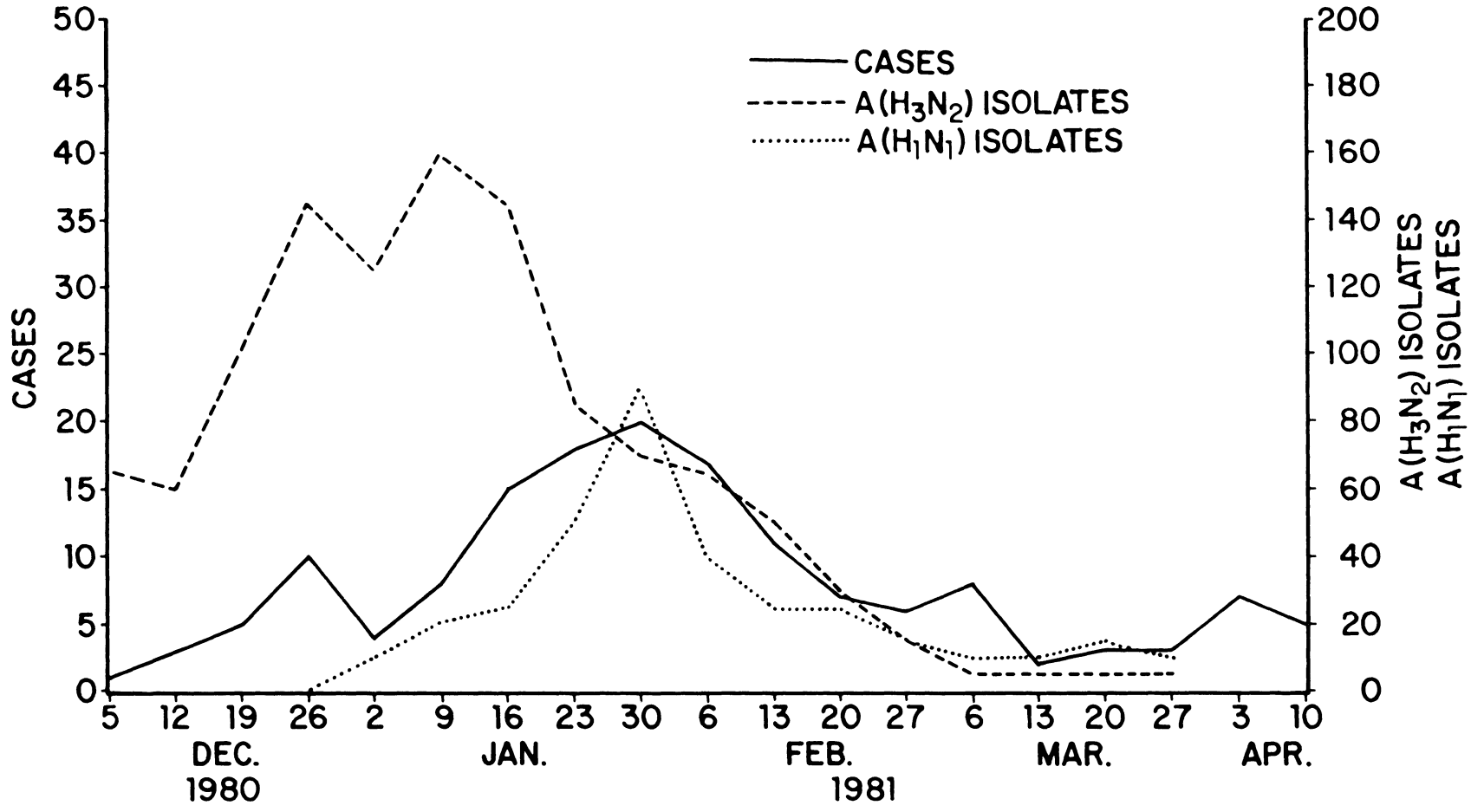
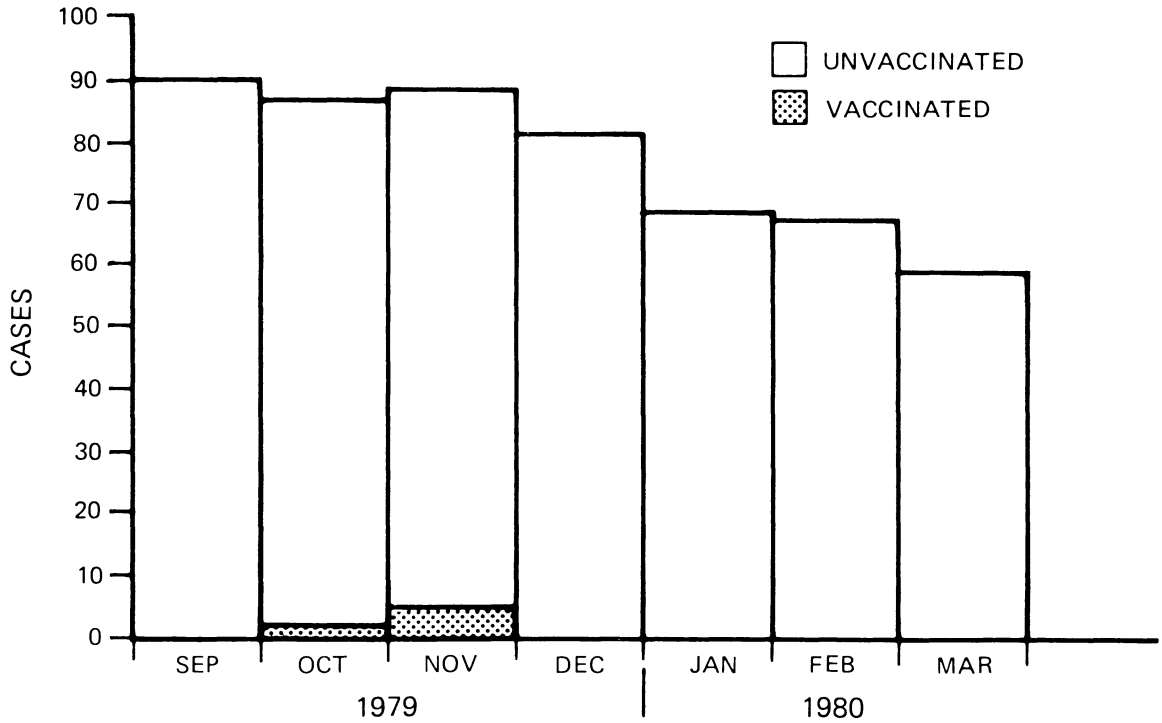
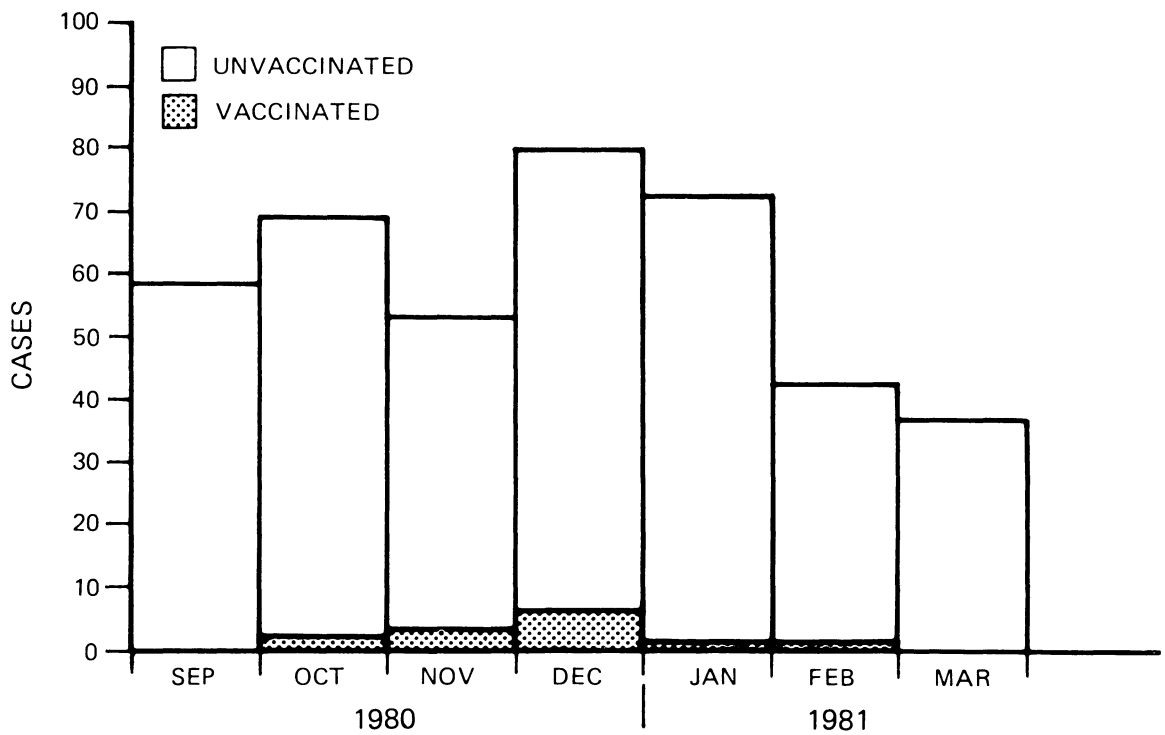


FIGURE 7

GUILLAIN-BARRÉ SYNDROME
REPORTED CASES BY MONTH OF ONSET OF NEUROLOGIC SYMPTOMS,
UNITED STATES, 1979–1980 AND 1980–1981



## ADVERSE EVENTS FOLLOWING INFLUENZA VACCINATION

The Immunization Division maintains a passive surveillance system of events occurring in vaccine recipients within 30 days following DTP, Td, polio, measles, mumps, rubella and influenza vaccine administration. The system primarily covers vaccine administered in the public sector. Report forms describing the event and the outcome are completed at the state level and forwarded to CDC where the event or events are classified according to ICDA codes and entered into a computerized registry along with age, sex, date of immunization, date of onset of event, and vaccine lot identification.

Presently, except in instances of severe illness or death following immunization, no systematic attempt is made to follow up reports to ascertain if there was a causal relation between receipt of the vaccine and occurrence of the reported event. Because of the passive nature of information collection, the reports received probably represent only a small portion of the actual number of events following vaccination. Finally, the more severe events and those closely following vaccine administraton are most likely to be reported.

The present system does provide the only available systematically recorded information on events following immunization. The data obtained serve to indicate the types of events occurring and potentially can identify vaccine lots with unusual numbers of adverse events following use.

It must be emphasized that this system collects data on events temporally associated with vaccine administration. To epidemiologically prove causation requires establishing that in a defined population the rate of a given illness following immunization is significantly higher than the background rate of that illness.

Reports received at CDC of adverse events following administration of influenza vaccine for the influenza seasons of 1979-80 and 1980-81 combined are summarized in Table 15. Data are presented only for the age group 20 years or older which receives nearly all of the influenza vaccine yearly. During the 1979-80 influenza season 18.3 million net doses of trivalent whole virus vaccine composed of A/Brazil/78, A/Texas/77 and B/Hong Kong/72 were distributed, of which 1.6 million doses were administered through the public sector. In the 1980-81 influenza season 12.4 million net doses of trivalent virus vaccine composed of A/Brazil/78, A/Bangkok/79 and B/Hong Kong/72 were distributed, of which 0.9 million were distributed through the public sector. While most influenza vaccine was administered by the private medical sector, most reports of events following influenza vaccination were received from the public sector providers.

**Table 15. Adverse Events Reported Within 30 Days Following Influenza Vaccine (6/79-6/81)**

| | 6/79 - 5/80 | 6/80 - 5/81 |
|---|---|---|
| Local reactions | 26 | 17 |
| Fever only | 25 | 26 |
| Rash | 7 | 5 |
| Allergic reactions | 7 | 8 |
| Convulsions | 0 | 0 |
| Encephalopathy | 0 | 0 |
| Guillian-Barre | 3 | 0 |
| Paralysis (nonGBS) | 2 | 3 |
| Other neurologic | 10 | 4 |
| Deaths | 3 | 3 |

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# APPENDICES

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## INFLUENZA IN THE WORLD
### October 1979-September 1980

Three influenza viruses circulated in the 1979-1980 influenza season: influenza A virus of H3N2 and H1N1 subtypes and influenza B viruses. Co-circulation of two or even all three was not infrequently reported. In general in most countries there was however only one virus type or subtype associated with sporadic cases or outbreaks at any one time: influenza A (H3N2) viruses in Europe and the Southern Hemisphere, influenza B viruses in North America and Scotland and influenza A (H1N1) viruses in the Middle East. A mixed pattern of influenza A (H3N2) and B viruses was seen in Europe (Greece) and of influenza A (H3N2) and A (H1N1) viruses in the Far East (Japan).

**Antigenic Drift in Influenza A (H3N2) and Influenza B Viruses**

Among the influenza A viruses of the H3N2 subtype, strains showing some antigenic drift from the previous variant A/Texas/1/77 (H3N2) appeared and two strains isolated in Thailand during an outbreak in August-September 1979 were chosen as reference strains: A/Bangkok/1/79 (H3N2) and A/Bangkok/2/79 (H3N2). Of the two, A/Bangkok/1/79 (H3N2) became the more prevalent and was isolated in most countries where influenza A (H3N2) viruses were found. As the influenza season progressed in the Northern Hemisphere, other minor variants of influenza A (H3N2) viruses appeared, strains which reacted equally well with sera prepared against both A/Texas/1/77 (H3N2)-like and A/Bangkok/1/79 (H3N2)-like strains. Strains of the older variant A/Texas/1/77 (H3N2) were also found and it was not clear that one had completely replaced the other at any one time.

Among the influenza B viruses there also appeared strains showing some antigenic drift from the previously prevalent variant, the B/Hong Kong/5/72. Such drifting strains had already been isolated during the previous season, e.g. B/Johannesburg/9/75, B/Hannover/13/78, all of which showed some antigenic relationship with a strain B/Singapore/222/79 which had been isolated during 1979 and was chosen as a reference strain for these newer variants. Most of the strains isolated during the 1979-1980 season were similar to this new variant; the older variant B/Hong Kong/5/72 was very infrequently isolated.

Among the influenza A viruses of the H1N1 subtype, the two variants A/Brazil/11/78 (H1N1) and A/USSR/90/77 (H1N1), continued to circulate in a few countries.

**The Impact of the Influenza Viruses**

*Influenza A (H3N2) Viruses*

Regardless of the variant, i.e. whether similar to A/Texas/1/77 (H3N2), to A/Bangkok/1/79 (H3N2), to A/Bangkok/2/79 (H3N2), or if reacting equally well with sera prepared against several of these variants, the disease was rarely of severe nature. The virus was isolated from cases in all age groups, but in some countries more cases were among children than among adults while in others most cases were in adults.

*Influenza A (H1N1) Viruses*

As in previous seasons this virus caused outbreaks among young adults and school children. A few isolates were however from adult cases.

*Influenza B Viruses*

This virus caused disease mainly among children leading to school closures due to high absenteeism rates in Canada and the United States of America. In the USA the virus also affected the higher age groups, and during the peak of the wave excess mortality was seen during two months, involving at its peak also the age groups of 45 years and older.

**The Spread of Influenza and the Influenza Viruses in the Northern Hemisphere**

*Europe*

The influenza season in Europe was heralded by outbreaks in the USSR in November-December 1979. In January 1980, several other Eastern European countries such as Bulgaria, Czechoslovakia, Finland, the German Democratic Republic and Romania experienced increasing influenza activity which peaked in February in general. In the same month, influenza began to spread in Greece, Hungary, Italy and Scotland. In March a second wave hit Czechoslovakia and Greece while in England the season had just begun. In the United Kingdom the influenza season lingered on with outbreaks occurring in April and May and cases were seen even in June. Localized outbreaks were also reported from Hungary and Spain in May-June 1980.

Other European countries reported little influenza activity, in general limited to sporadic cases or localized outbreaks.

The influenza viruses isolated in most European countries were mainly influenza A viruses of the H3N2 subtype. In the early outbreaks in Eastern Europe the A/Texas/1/77 (H3N2) variant dominated while strains more closely related to A/Bangkok/1/79 (H3N2) became more prevalent in Eastern European countries affected later. The outbreaks occurring at the end of the season, i.e. in England and Wales, were associated with influenza strains reacting equally well with sera prepared against A/Texas/1/77 (H3N2)-like and A/Bangkok/1/79 (H3N2)-like strains.

Also in countries with low influenza activity, the newer variants of influenza A (H3N2) viruses, especially A/Bangkok/1/79 (H3N2)-like strains, were prevalent.

The influenza A (H3N2) viruses were isolated from cases in all age groups and were in general associated with mild or moderately severe illness. A few countries such as Bulgaria and Hungary reported most cases in children while in Romania adult cases predominated. In England and Wales outbreaks were seen among school children but most were among the elderly living in nursing homes or other institutions. Although the older age groups were affected there was little excess mortality from respiratory diseases during the season.

Strains of influenza A (H1N1) virus caused the late outbreaks in Hungary and Spain. In both countries the strains were similar to A/Brazil/11/78 (H1N1). All age groups were affected in Spain while in Hungary the outbreaks were limited to communities of young adults and children. One outbreak of influenza A (H1N1) was also reported to occur in a paediatric ward in Poland. The strains isolated from this outbreak were similar to A/USSR/90/77 (H1N1). Influenza A viruses of the H1N1 subtype were otherwise only sporadically found in Europe. Some cases occurring in Norway were unusual in that they were adults.

Influenza B viruses dominated the influenza season in Greece and Scotland. Most strains were similar to B/Singapore/222/79. In Scotland most isolates were from children in the early part of the outbreak; more and more adult cases occurred in the later part of the season. This shift to older age groups was reflected in a sharp but narrow peak in the mortality from respiratory disease in April. The second wave of influenza in Czechoslovakia was associated with the spread of influenza B/Singapore/222/79-like strains affecting mainly children. In Greece, both influenza A and B viruses were isolated in the second wave. Many of the influenza B viruses were isolated from adult cases with rather severe disease. It should be noted that several European countries had experienced outbreaks of influenza B in the 1978-1979 influenza season.

*Asia*

The first reports on influenza activity were from Southern Japan in September-October 1979. The epidemic developed slowly to involve the whole country by January 1980, peaked in February and was over by April. In the northern provinces of China, an increased influenza activity was noted in November 1979 and, by the end of that year and the beginning of 1980, the outbreak was widespread in the northern provinces. Later in the year, in May-July, the southern provinces were affected.

From other parts of the continent, outbreaks were reported in northern Pakistan in December 1979 through January 1980, in Western India in March and in July through September 1980, and in Malaysia in April through May 1980. Sporadic cases and localized outbreaks were also reported in Hong Kong, the Republic of Korea, Philippines, Singapore and Thailand.

The influenza viruses were influenza A of the H3N2 and H1N1 subtypes and influenza B viruses. Influenza A (H3N2) viruses caused the two outbreaks in China; most strains in the first wave were similar to A/Bangkok/1/79 (H3N2), while those in the second wave reacted equally well with sera prepared against A/Texas/1/77 (H3N2)-like and A/Bangkok/1/79 (H3N2)-like strains. About one-third of the influenza viruses isolated in Japan were influenza A of the H3N2 subtype, a return of the subtype after an absence during the 1978-1979 influenza season. The strains were reported as similar to A/Texas/1/77 (H3N2) and were mainly isolated from preschool children and adults.

Strains of influenza A (H3N2) virus were also isolated in the outbreaks in India and Malaysia (together with influenza A viruses of the H1N1 subtype) and from sporadic cases in Hong Kong, Indonesia, Philippines, the Republic of Korea, Singapore and Thailand. Most strains were A/Bangkok/1/79 (H3N2)-like or reacted equally well with sera prepared against A/Texas/1/77 (H3N2)-like and A/Bangkok/1/79 (H3N2)-like strains. A few isolates of A/Bangkok/2/79 (H3N2)-like strains were reported and the variant A/Texas/1/77 (H3N2) was still circulating in Thailand in August 1980.

Influenza A viruses of the H1N1 subtype caused most of the cases of influenza in Japan. The strains which were mainly isolated from school children were similar to A/Brazil/11/78 (H1N1). Such strains were also isolated during the outbreak in Pakistan and sporadically in China during the two outbreaks and in Mongolia. Strains similar to A/USSR/90/77 (H1N1) were isolated from cases during the two outbreaks in Western India and from sporadic cases in Hong Kong, Iran and Singapore.

Influenza B viruses were isolated from preschool children and adults in the end of the influenza season in Japan, from cases in family outbreaks and other localized outbreaks in Israel in February-March 1980 but were otherwise infrequently found in Asia. The strains isolated in Israel, and from sporadic cases in Indonesia, were similar to B/Singapore/222/79 except for a few which reacted mostly with sera prepared against B/Hong Kong/5/72-like strains.

*Americas*

In North America, the influenza activity was first reported from the Western parts of the United States in November-December 1979. From January 1980 onwards the influenza wave spread and involved, during its peak in the end of February, 13 States with widespread influenza activity. In February a few provinces in Canada began to report influenza activity.

Influenza B viruses dominated in both countries; most strains were of the B/Singapore/222/79-variant. Most outbreaks were reported among school children forcing many schools to close due to high absenteeism. In the United States most of the laboratory-confirmed influenza cases were adults, and the peak of the influenza wave was associated with a marked increase in mortality from respiratory diseases; during the highest peak excess mortality was seen also in the age groups of 45 years and older.

The influenza A viruses were rarely isolated during the actual influenza season in the United States and in Canada not at all. In July 1980, influenza A viruses of the H3N2 subtype caused one outbreak among the elderly in a nursing home in Arizona, USA, and in August-September in Hawaii. In both instances the isolated strains reacted equally well with sera prepared against A/Texas/1/77 (H3N2)-like and A/Bangkok/1/79 (H3N2)-like strains. Similar strains or strains more closely related to A/Bangkok/1/79 (H3N2) were also isolated from sporadic cases or outbreaks further south on the American continent: Ecuador in June, Panama in June-August, French Guiana in July and Colombia in September.

Influenza A viruses of H1N1 subtype were isolated sporadically during the outbreaks in the United States, but were also detected in an outbreak affecting young people in Puerto Rico in September 1980. The strains isolated during the latter outbreak were similar to A/Brazil/11/78 (H1N1). Influenza A (H1N1) virus was also isolated sporadically in Ecuador.

*Africa*

From the northern part of the continent, reports were received from Egypt on outbreaks affecting all age groups lasting from December 1979 through March 1980 with a peak in January. Strains of influenza A viruses of the H1N1 subtype similar to A/Brazil/11/78 (H1N1) were isolated but other respiratory viruses were also implicated in the outbreak. In Senegal, strains of influenza B viruses, similar to B/Singapore/222/79, were isolated from sporadic cases occurring in October-November 1979 and in February-March 1980.

**The Spread of Influenza and Influenza Viruses in the Southern Hemisphere**

In the *Americas* outbreaks were first reported from the northern provinces of Chile in the end of April 1980. The disease spread rapidly causing high morbidity rates but with little impact on the mortality. In June most parts of the country were affected. In May-June, localized outbreaks were reported among the general population in Cordoba, Argentina. The disease which affected all age groups was mild; a marked increase in school and industrial absenteeism was nevertheless seen during the second half of June 1980. In Brazil, sporadic cases were detected in Rio de Janeiro and São Paulo in May-June 1980.

Apart from one strain of influenza A virus of the H1N1 subtype similar to A/Brazil/11/78 (H1N1) isolated from a case in Santiago, Chile, all strains were influenza A of the H3N2 subtype. All recent variants were represented among these isolates, as well as the older A/Texas/1/77 (H3N2)-like variant.

In *Africa* outbreaks were reported in South Africa beginning in June in Johannesburg. The outbreak spread during July to other cities and was over in Mid-August. The outbreak was characterized as rather severe and the absenteeism in Johannesburg reached 10%, among the adult working population. All strains isolated were influenza A virus of the H3N2 subtype. Most reacted equally well with sera prepared against A/Texas/1/77 (H3N2)-like and A/Bangkok/1/79 (H3N2)-like strains but strains more closely related to A/Bangkok/1/79 (H3N2), or to A/Bangkok/2/79 (H3N2), or to A/Texas/1/77 (H3N2) were also isolated. In Madagascar, where influenza A (H1N1) had dominated in the previous season, a strain of influenza A (H3N2) virus was isolated in January 1980. The strain was similar to A/Texas/1/77 (H3N2).

In *Australia* the influenza activity was limited to sporadic cases or localized outbreaks. The influenza A of the H1N1 subtype which had dominated in the previous seasons was isolated once in the beginning of 1980. The influenza A (H1N1) viruses were replaced by the A (H3N2) subtype which had not been found during two seasons. Most strains were A/Bangkok/1/79 (H3N2)-like. Strains of influenza B viruses were also isolated, especially during August 1980. All strains were characterized as similar to B/Singapore/222/79.

In *New Zealand* the influenza activity became more widespread. Influenza-like illness was first reported in May-June 1980, the first influenza virus, a strain of influenza A (H3N2), was isolated in July. During this month and August, the influenza activity became widespread causing outbreaks among the elderly in geriatric homes and other institutions. The disease was quite severe among these but also in children (below five years of age). There were even two fatal cases in infants with pneumonia and positive influenza A (H3N2) virus isolations. The isolated strains were similar to A/Bangkok/1/79 (H3N2) or reacted equally well with sera prepared against A/Texas/1/77 (H3N2)-like and A/Bangkok/1/79 (H3N2)-like strains. Concurrently with influenza viruses, parainfluenza viruses types 2 and 3 caused disease.

**Conclusions**

The overall impression of the 1979-1980 influenza season with few exceptions was mild. The antigenic drift among the influenza A viruses of H3N2 subtype created several new minor variants, of which none really dominated over the others or even completely replaced the previous variant A/Texas/1/77 (H3N2).

The disease associated with the new variants did not show any significant differences, nor did the age groups affected. Strains of influenza A (H3N2) viruses dominated the influenza season in most of the Asian and European countries reporting outbreaks or sporadic cases, and it was almost exclusively the virus causing the outbreaks during the influenza season in the Southern Hemisphere.

The influenza A viruses of the H1N1 subtype caused widespread outbreaks in Japan, Egypt and Pakistan but was otherwise found in localized outbreaks or sporadic cases. Most cases were in school children or young adults but some isolates from higher age groups were also reported.

Among the influenza B viruses an antigenic drift occurred and the new variant, B/Singapore/222/79, almost completely replaced the old variant B/Hong Kong/5/72. The new variant caused widespread disease in North America where the influenza A viruses were rarely found during the regular influenza season. In Europe, the influenza B/Singapore/222/79-like viruses dominated in Scotland (in contrast to England where almost all cases were associated with influenza A viruses of the H3N2 subtype), and in Greece where it co-circulated with influenza A (H3N2) viruses. Influenza B viruses also caused second influenza waves in Czechoslovakia and Japan. Most cases were in children but the older age groups were not always spared and rather severe disease or excess mortality from respiratory diseases were associated with influenza B virus infection in adults in Greece, Scotland and the United States.

APPENDIX I-B

Distribution of Influenza Viruses Tested at WHO Collaborating Center for Influenza, CDC, October 1979-September 1980 by Country and Type

| | | H3N2 | H1N1 | B | OTHER |
|---|---|---|---|---|---|
| **NORTH AMERICA** | | | | | |
| United States | | 42 | 7 | 364 | 1* |
| Canada | | 1 | | 39 | |
| | Sub-total | 43 | 7 | 403 | 1 |
| **SOUTH AMERICA** | | | | | |
| Argentina | | 15 | | 7 | |
| Brazil | | 17 | 4 | 2 | |
| Chile | | 18 | 1 | | |
| Columbia | | 1 | | | |
| Peru | | | | 6 | |
| French Guyana | | 1 | | | |
| | Sub-total | 52 | 5 | 15 | |
| **CARIBBEAN** | | | | | |
| Canal Zone | | 13 | | | |
| Jamaica | | | 1 | | |
| | Sub-total | 13 | 1 | | |
| **EUROPE** | | | | | |
| Czechoslovakia | | 4 | | | |
| Finland | | 1 | 1 | | |
| France | | 1 | | 5 | |
| Greece | | 1 | | | |
| USSR | | 2 | 2 | | |
| United Kingdom | | 2 | | | |
| | Sub-total | 11 | 3 | 5 | |
| **PACIFIC AND FAR EAST** | | | | | |
| Australia | | 3 | 5 | 1 | |
| Africa | | 17 | | | |
| India | | 7 | 3 | | |
| Indonesia | | 16 | | 17 | |
| Japan | | | 1 | | |
| Peoples Republic of China | | 6 | | | |
| Philippines | | 2 | | | |
| Singapore | | 3 | 2 | | |
| Taiwan | | 5 | | 10 | |
| Thailand | | 24 | 1 | 4 | |
| | Sub-total | 83 | 12 | 32 | |
| | TOTAL | 202 | 28 | 455 | 1 |

*A/New Jersey/76/like

APPENDIX I-C

Distributing Influenza Viruses Tested at WHO
Collaborating Center for Influenza, CDC, October 1979 – September 1980
by Geographic Source and Antigenic Specificity

| | INFLUENZA A (H1N1) | | | | INFLUENZA A (H3N2) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | A/USSR/90/77 | A/Brazil/11/78 | Other | TOTAL | A/Texas/1/77 | A/Bangkok/1/79 | Cross-reactive | A/Bangkok/2/79 | Other | TOTAL |
| North America | 0 | 7 | 1 | 8 | 10 | 6 | 22 | | 3 | 41 |
| South America | 3 | 1 | 1 | 5 | 4 | 9 | 31 | 5 | | 49 |
| Caribbean | | | 1 | 1 | 1 | 3 | 9 | | | 13 |
| Europe | 2 | | 1 | 3 | 1 | 3 | 5 | 1 | | 10 |
| Pacific and Asia (including India) | | 6 | 6 | 12 | 16 | 18 | 31 | 6 | 12 | 83 |
| TOTAL | 5 | 14 | 10 | 29 | 32 | 39 | 98 | 12 | 15 | 196 |
| PERCENTAGE | (17) | (48) | (34) | (100) | (16) | (20) | (50) | (6) | (8) | (100) |

Total Viruses Tested = 225

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# INFLUENZA IN THE WORLD

## OCTOBER 1980 – SEPTEMBER 1981

The epidemiological behaviour of influenza has been of particular interest since 1977 when viruses of the influenza A subtype H1N1 made their reappearance. They had been circulating throughout the world up to 1975 and then disappeared when the H2N2 virus became pandemic. In 1968 the H2N2 viruses gave way to those of the H3N2 subtype.

When the H1N1 virus did reappear, its impact fell almost entirely on those in the population who had been born since 1957 and had no immunity to these antigens. The H3N2 virus however did not disappear with the appearance of another subtype but continued to circulate not only in the older age groups but concurrently with the H1N1 virus in the younger age groups. The overall result has been a series of influenza seasons with only a mild impact on the world population even though seasonal outbreaks have occurred more or less regularly in the appropriate seasons in most countries.

The 1980-1981 influenza season was in general mild, except in the USA and Canada where severe epidemics of influenza A (H3N2) caused considerable mortality. (See *Fig. 1*). Some activity due to influenza B viruses was reported. As in the previous three years there were occasions during the 1980-1981 season when influenza A viruses of both the H1N1 and H3N2 subtype circulated at the same time but most often those of one subtype were responsible for the main influenza activity while those of the other were only observed sporadically or appeared in another part of the season.

The most severe outreaks were reported in North America and were associated with influenza A (H3N2) viruses. Influenza due to this subtype was also reported fron South and Central America, large parts of Western Europe, some African, and several Asian countries.

The influenza A viruses of the H1N1 subtype predominated in a few, mainly Eastern European, countries They also caused some late outbreaks in Asia and in Central America and they were responsible for most of the influenza activity in Australia. They were isolated all over the world, but almost always from younger persons (below 30 years of age) and were rarely reported in association with severe illness.

Influenza B viruses which had been the main cause of influenza in North America in the 1979-1980 season were virtually absent from the entire continent during the 1980-1981 season. Three countries in Eastern Europe reported influenza B viruses as the main cause of outbreaks and many other countries in the world had localized outbreaks or sporadic cases.

Nearly 3 000 strains of influenza viruses isolated in the National Influenza Centres in the period October 1980-September 1981 were studied in the WHO Collaborating Centres for Reference and Research on Influenza in Atlanta and London. Influenza A viruses of the H3N2 subtype accounted for the major part (68%), those of the H1N1 subtype for 28% and only a small part were influenza B viruses. Most of the H3N2 viruses reacted with sera prepared against A/Texas/1/77 (H3N2) or A/Bangkok/1/79 (H3N2), or equally well with both.

About 800 H1N1 strains were investigated: 70% of these were of the A/England/333/80 (H1N1) variant, 13% were closer to A/India/6263 (H1N1), 9% were similar to A/Brazil/11/78 (H1N1) and a very few were A/USSR/90/77 (H1N1)-like. The latter variant was only isolated in a few European countries whereas the Brazil-like variant was also submitted from countries in Asia and Oceania.

Almost all influenza B viruses investigated in the WHO Collaborating Centres were similar to B/Singapore/222/79 but a few of the older variants, more closely related to B/Hong Kong/5/72, were also found.

### Europe

The influenza season in Europe showed great variations. There were explosive outbreaks among young people in some countries while others reported a steady spread over a wider age range in the general population. Outbreaks among the elderly were noted in nursing homes and other geriatric institutions. The impact of influenza was unusually mild in some countries whereas others experienced a more severe season than during 1979-1980. Some countries were almost exclusively affected by influenza A (H1N1) and others by A (H3N2) viruses. Some had both subtypes in sequence or concurrently and then there were others which had mainly influenza B.

The influenza season began early with the first outbreak being reported in November 1980 from Hungary and the United Kingom. All influenza activity in Hungary and most of the activity in the United Kingdom at that time were associated with influenza A (H1N1) viruses which spread among young persons, especially those living in closed communities like boarding schools or military camps. This early wave soon reached a peak and was practically over by the end of December.

A second wave of influenza activity built up during December 1980 and January 1981. It was mainly associated with influenza A (H3N2) viruses in Western Europe and with influenza A (H1N1) or influenza B viruses in Eastern Europe.

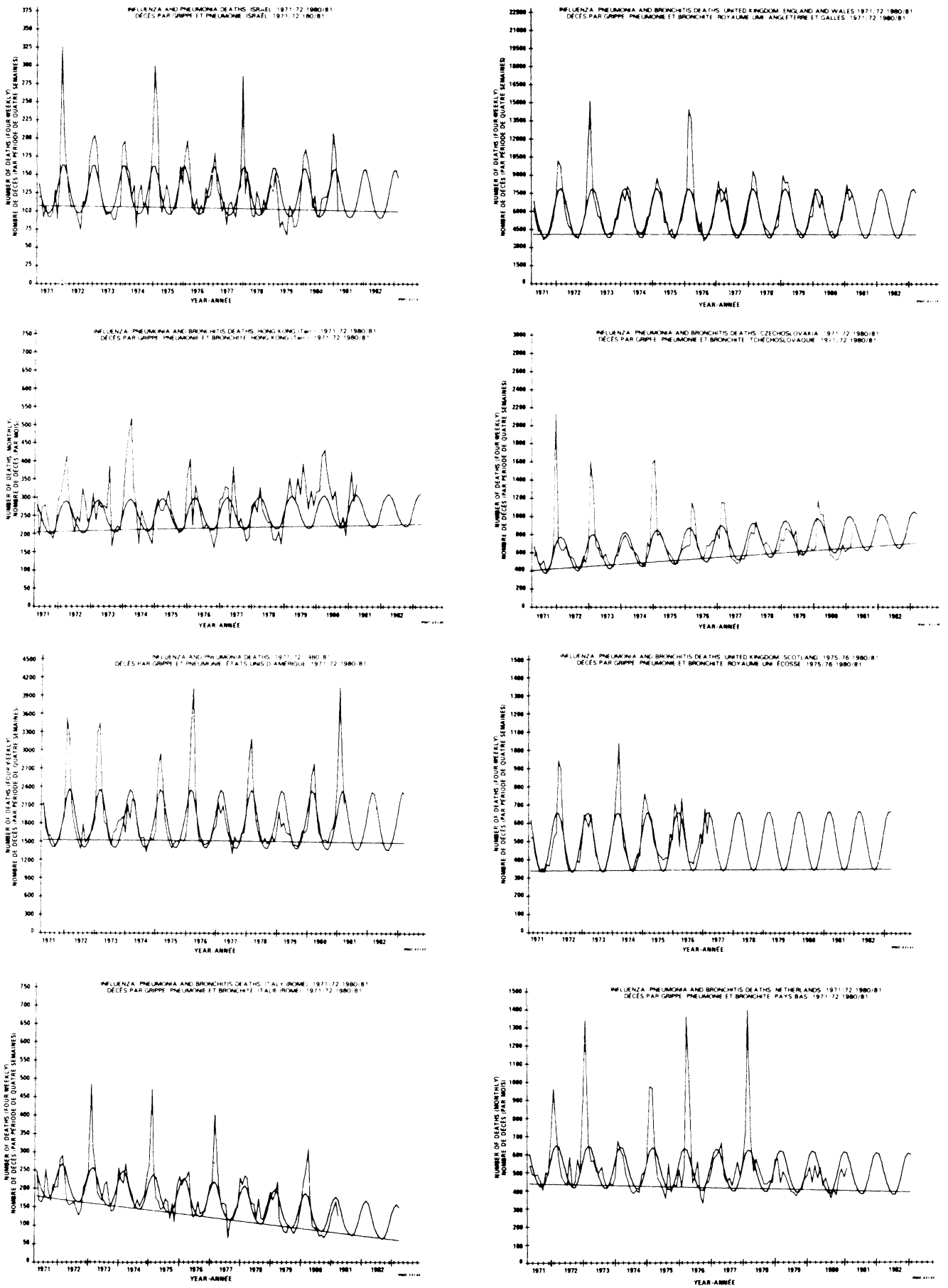
*Influenza A (H3N2)* viruses predominated throughout the season in some countries (Denmark, Norway, Sweden, Ireland, France, Belgium, Albania, Greece, Italy, Spain). In the Netherlands and Switzerland the A (H3N2) and A (H1N1) subtypes were reported over the same period with equal frequency. The H3N2 subtype succeeded H1N1 in the United Kingdom and preceded it in the Federal Republic of Germany.

Among the strains of influenza A (H3N2) viruses investigated further by the WHO Collaborating Centres for Reference and Research on Influenza, there was a preponderance of those reacting equally well with sera prepared against A/Texas/1/77-like and A/Bangkok/1/79-like strains. Of the 324 strains investigated from laboratories in the United kingdom, 306 had this reaction pattern, 12 were A/Texas/1/77-like, four were closer to A/Bangkok/1/79 and two were similar to A/Bangkok/2/79. Among the strains submitted from other European countries there was a less marked predominance of the cross-reacting strains over the more distinct A/Bangkok/1/79 or A/Texas/1/77 variants. The A/Bangkok/2/79 variant was only sporadically found.

After the first wave of *influenza A (H1N1)* in Hungary and in the United Kingdom, outbreaks associated with viruses of this subtype were reported in Finland, Bulgaria, Czechoslovakia and Yugoslavia. In all four countries this remained the predominating influenza virus during the season. As the season progressed they became increasingly frequent in parts of the Federal Republic of Germany and in Switzerland. Localized outbreaks or sporadic cases due to influenza A (H1N1) viruses were also reported elsewhere (France, German Democratic

*Fig. 1*

**Excess Mortality from Acute Respiratory Diseases***




*See/Voir: Use of excess mortality from respiratory diseases in the study of influenza. *Bulletin of the World Health Organization*, *49* pp. 219-233 (1973).

Republic, Ireland, Italy, Netherlands, Sweden). Viruses of the H1N1 subtype caused outbreaks and isolated cases in Romania in May-June 1981. Most of the strains submitted by the National Influenza Centres in Europe to the WHO Collaborating Centres for Reference and Research were similar to A/England/333/80 but there were also strains which were more closely related to A/Brazil/11/78, to A/USSR/90/77 or to the other new variant A/India/6263/80.

**Asia**

Few countries in Asia reported widespread activity in the 1980-1981 influenza season. The outbreaks were associated mainly with influenza A viruses of the H1N1 and H3N2 subtypes. Influenza B was detected in sporadic cases and a few localized outbreaks.

Outbreaks associated with *influenza A (H1N1)* viruses were reported in Israel, Malaysia, Singapore and China; the first from Israel and China were in December 1980. The outbreak in Israel initially affected mainly children and young adults but soon spread to older age groups and was accompanied by some excess mortality in January 1981 (see *Fig. 1*). By that time some influenza A (H3N2) viruses were also implicated. The outbreaks in Malaysia and Singapore occurred in March through June 1981. In Malaysia they were reported mainly among young adults. A second wave of influenza A (H1N1) occurred in several of the southern and one of the northern provinces of China in June-August 1981.

In many other Asian countries, reports of A (H1N1) activity were very limited. In Japan however where the overall influenza activity was low, viruses of this subtype were still the most frequently isolated. In Hong Kong, A (H1N1) reappeared in July after an absence of a year and soon became the most frequently isolated influenza virus although never associated with more than sporadic illness. Influenza A (H1N1) viruses were further isolated in India, Thailand and Mongolia along with viruses of the H3N2 subtype and influenza B viruses. Over half the strains submitted from National Influenza Centres in Asia to the WHO Collaborating Centres for Reference and Reserch on Influenza were characterized as A/England/333/80. Some strains, mostly from the outbreak in Israel, were more closely related to A/Brazil/11/78. A few of the investigated strains were A/India/6263/80-like.

Outbreaks of *influenza A(H3N2)* were reported in Iran, Pakistan and the Republic of Korea. The outbreaks in Iran and Pakistan began in December 1980 and the one in Pakistan which spread in the northern parts of the country in January 1981 had declined by the end of February. All age groups were affected in Pakistan. The outbreak in the Republic of Korea affected mainly children below 15 years of age; it began in February and lasted through March 1981.

Localized outbreaks associated with influenza A (H3N2) viruses were reported in western India in November 1980 and again in July 1981 and among schoolchildren in Japan in January 1981. Influenza A (H3N2) viruses were isolated during the latter part of the H1N1 outbreak in Israel, as well as in Indonesia, China, Hong Kong and Mongolia. Among the viruses investigated in the WHO Collaborating Centres for Reference and Research on Influenza the A/Bangkok/1/79-like and the A/Texas/1/77-like variants were the most frequent.

*Influenza B* viruses did not cause any widespread illness but a few localized outbreaks were reported: in Japan in December 1980 and in India in February-March 1981. Strains of influenza B viruses were also isolated in Indonesia, Singapore, Hong Kong and China. All strains further investigated were very closely related to the variant which has been prevalent since 1979, i.e. B/Singapore/222/79.

**America**

In 1980-1981 the influenza season in North America was one of the most severe experienced in the last ten years but was very mild in South America. The influenza A (H3N2) viruses predominated throughout the continent but a few outbreaks associated with influenza A (H1N1) viruses were reported.

The North American season began in October 1980 with outbreaks of *influenza A (H3N2)* in nursing homes and similar institutions for the elderly in California (USA) and in November in Manitoba (Canada). The general population was soon affected, often with severe illness. Excess mortality from respiratory illness was noted in the USA from mid-December through to January 1981, and in Canada from mid-January of that year. The main influenza wave peaked in early February.

In South America a mild but widespread outbreak of influenza A (H3N2) occurred in Chile in August-October 1981. Localized outbreaks were reported from Argentina in May-June 1981. Sporadic cases occurred in Mexico in October 1980 and in Brazil during February-September 1981. In general, the influenza A (H3N2) viruses isolated in America in the 1980-1981 season reacted equally well with sera prepared against A/Bangkok/1/79-like and A/Texas/1/77-like strains.

*Influenza A (H1N1)* viruses became increasingly frequent as the season progressed in North Amercia, although they were rarely reported in association with outbreaks. In South America two localized H1N1 outbreaks were reported in French Guyana in July 1981 and viruses of this subtype were also isolated in Guyaquil (Ecuador) in February-March and in Brazil in June-July 1981. The most prevalent H1N1 variant was A/England/333/80 but A/India/6263/80 was identified to some extent.

*Influenza B* viruses were infrequently isolated during the 1980-1981 season in America. They caused a late wave of influenza among school children in many parts of Canada in March 1981; a few strains were also isolated in Brazil.

**Africa**

The more widespread influenza activity reported from African countries in 1980-1981 was associated with *influenza A (H3N2)* viruses while H1N1 and influenza B viruses were detected only sporadically. From the northern part of the continent, Egypt reported outbreaks in the general population affecting all age groups in January-February 1981. Influenza A (H3N2) virus was also confirmed in Algeria.

Further south, one outbreak of influenza A (H3N2) was reported in Madagascar in April-June 1981 and another, which lasted for five weeks, in the Cape Province (South Africa), in June. During the latter outbreak there were some severely ill cases, many of whom were young children requiring hospital care.

The *influenza A (H3N2)* viruses investigated in the WHO Collaborating Centres for Reference and Research on Influenza were similar to the variants isolated elsewhere in the world, i.e. A/Bangkok/1/79, A/Texas/1/77 and strains reacting equally well with sera prepared against both variants. A few A/Bangkok/2/79-like strains were also found.

The *influenza A (H1N1)* activity was sporadic. A few strains were isolated in Senegal in February and March 1981, in Johannesburg and the Cape Province (South Africa), and also in Madagascar in August of that year. The strains isolated in Senegal and Johannesburg were similar to A/England/333/80 while those from Madagascar and the Cape province were more closely related to A/India/626/80.

Apart from some *influenza B* diagnosed in immunofluorescence tests during the early part of the outbreak in Egypt there were no signs of influenza B activity in Africa in the 1980-1981 season. One influenza C virus strain identified as *C/Taylor/1233/47* was isolated in Johannesburg (South Africa).

**Oceania**

The influenza activity was in general mild and limited in Australia to sporadic cases. In New Zealand moderate activity was reported from some areas. One frank outbreak of *influenza A (H1N1)* flared up in Fiji in January-February 1981 after the hurricane "Arthur" had hit the area. Influenza A (H1N1) viruses also dominated the influenza season in Australia and some strains were reported in New Zealand. Almost all strains investigated in the WHO Collaborating Centres for Reference and Research on Influenza were similar to A/England/333/80, only two were more closely related to A/India/6263/80.

Some *influenza A (H3N2)* viruses were isolated in Australia and New Zealand. Those tested in the Collaborating Centres reacted with sera prepared against A/Bangkok/1/79 or A/Texas/1/77, or with both.

*Influenza B* viruses became increasingly frequent towards the end of the season both in both Australia and New Zealand. All strains tested were found similar to B/Singapore/222/79.

APPENDIX II-B

Distribution of Influenza Viruses Tested ad WHO Collaborating Cnter for Influenza, CDC, October 1980 - 1981 by Country and Type

| Source | | H3N2 | H1N1 | B |
|---|---|---|---|---|
| **NORTH AMERICA** | | | | |
| United States | | 143 | 364 | 1 |
| Canada | | 8 | 3 | 0 |
| Mexico | | 0 | 9 | 0 |
| | Sub-total | 151 | 376 | |
| **SOUTH AMERICA** | | | | |
| Brazil | | 0 | 15 | 0 |
| Chile | | 0 | 3 | 0 |
| Ecuador | | 1 | 3 | 0 |
| Guyana | | 3 | 8 | 0 |
| | Sub-Total | 4 | 29 | 0 |
| **CARIBBEAN** | | | | |
| Trinidad | | 1 | 2 | 0 |
| | Sub-total | 1 | 2 | 0 |
| **EUROPE** | | | | |
| Czechoslovakia | | 13 | 0 | 2 |
| Finland | | 7 | 0 | 0 |
| France | | 1 | 0 | 0 |
| Germany (Dem.) | | 0 | 0 | 2 |
| Germany (Fed) | | 1 | 1 | 0 |
| Hungary | | 3 | 1 | 0 |
| Israel | | 2 | 0 | 0 |
| United Kingdom | | 9 | 0 | 0 |
| USSR | | 2 | 0 | 2 |
| | Sub-total | 38 | 2 | 6 |
| **PACIFIC AND FAR EAST** | | | | |
| Australia | | 6 | 3 | 0 |
| China (PCR) | | 3 | 5 | 1 |
| Fiji | | 1 | 0 | 0 |
| India | | 7 | 6 | 4 |
| Indonesia | | 0 | 6 | 7 |
| Japan | | 23 | 5 | 2 |
| Philippines | | 1 | 0 | 1 |
| Singapore | | 10 | 0 | 3 |
| Taiwan (ROC) | | 13 | 11 | 7 |
| Thailand | | 7 | 10 | 2 |
| | Sub-total | 71 | 46 | 27 |
| | TOTAL | 265 | 455 | 34 |

Overall Total = 754

## Distributing Influenza Viruses Tested at WHO Collaborating Center for Influenza, CDC, October 1980 - September 1981 by Geographic Source and Antigenic Specificity

| Source | A/England/333/80 | A/India/6263/80 | Other | TOTAL | A/Texas/1/77 | Intermediate | A/Bangkok/1/79 | A/Bangkok/2/79 | A/Shanghai/31/80 | Other | TOTAL | B/Singapore/222/79 | Other | TOTAL |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | INFLUENZA A (H1N1) | | | | INFLUENZA A (H3N2) | | | | | | | Influenza B | | |
| North America | 119 | 32 | 0 | 151 | 9 | 274 | 54 | 11 | 0 | 28 | 376 | 1 | 0 | 1 |
| South America | 3 | 0 | 1 | 4 | 1 | 22 | 5 | 1 | 0 | 0 | 29 | 0 | 0 | 0 |
| Caribbean | 1 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| Europe | 27 | 6 | 5 | 38 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 6 | 0 | 6 |
| Pacific and Asia (including India) | 58 | 5 | 8 | 71 | 12 | 16 | 4 | 2 | 6 | 6 | 46 | 26 | 1 | 27 |
| TOTAL | 208 | 43 | 14 | 265 | 23 | 313 | 65 | 14 | 6 | 34 | 455 | 33 | 1 | 34 |
| (PERCENTAGE) | (78) | (16) | (5) | (100) | (5) | (69) | (14) | (3) | (1) | (7) | (100) | (97) | (3) | (100) |

Total Viruses Tested = 754

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PUBLIC HEALTH SERVICE

from MORBIDITY AND MORTALITY WEEKLY REPORT, May 25, 1979, Vol. 28, No. 22, pp. 231-232, 237-239

*Recommendation of the Public Health Service*
*Advisory Committee on Immunization Practices*

# Influenza Vaccine

## INTRODUCTION

Influenza virus infections occur every year in the United States, but they vary greatly in incidence and geographic distribution. Infections may be asymptomatic, or they may produce a spectrum of manifestations, ranging from mild upper respiratory infection to pneumonia and death. Influenza viruses A and B are responsible for only a portion of all respiratory disease. However, they are unique in their ability to cause periodic widespread outbreaks of febrile respiratory disease in both adults and children. Influenza epidemics are frequently associated with deaths in excess of the number normally expected. During the period from 1968 to 1979, more than 150,000 excess deaths are estimated to have occurred during epidemics of influenza A in the United States.

Efforts to prevent or control influenza in the United States have been aimed at protecting those at greatest risk of serious illness or death. Observations during influenza epidemics have indicated that influenza-related deaths occur primarily among chronically ill adults and children and in older persons, especially those over age 65. Therefore, annual vaccination is recommended for these "high-risk" individuals.

Influenza A viruses can be classified into subtypes on the basis of 2 antigens: hemagglutinin (H) and neuraminidase (N). Four subtypes of hemagglutinin (HO-H3) and 2 subtypes of neuraminidase (N1, N2) are recognized among viruses causing widespread disease among humans. Immunity to these antigens reduces the likelihood of infection and reduces the severity of disease in infected persons. However, there may be sufficient antigenic variation within the same subtype over time (antigenic drift) that infection or immunization with 1 strain may not induce immunity to distantly related strains. As a consequence, the antigenic composition of the most current strains is considered in selecting the virus strain(s) to be included in the vaccine.

The predominant influenza strain in the United States during 1978-79 was A/Brazil/78—a variant of the H1N1 prototype A/USSR/77. This strain caused outbreaks in schools, colleges, and military bases, as had been the case with the prototype strain. People over 25 years of age generally were not affected, presumably because of previous infection with antigenically related strains that had circulated throughout the world in the early 1950s. Strains of the subtype H3N2 were not isolated in the United States, but other countries reported the isolation of both H1N1 and H3N2 strains. Since it is uncertain which strain will predominate in the future, continued circulation of strains related to A/Texas/77 (H3N2) and A/Brazil/78 (H1N1) must be anticipated.

Outbreaks caused by influenza B viruses occur less frequently than influenza A epidemics, but influenza B infection can also cause serious illness or death. Influenza B viruses have shown much more antigenic stability than influenza A viruses. Strains of influenza B that were isolated in 1978 and 1979 in the United States and elsewhere resembled the B/Hong Kong/5/72 virus.

## INFLUENZA VIRUS VACCINE FOR 1979-80

Influenza vaccine for 1979-80* will consist of inactivated trivalent preparations of antigens representative of influenza viruses expected to be prevalent: A/Brazil/78 (H1N1), A/Texas/77 (H3N2), and B/Hong Kong/72. The formulation will contain 7 micrograms of hemagglutinin of each antigen in each 0.5 ml dose. Persons 27 years and older will require only 1 dose. Because of lack of previous contact with H1N1 strains, persons less than 27 who did not receive at least 1 dose of the 1978-79 trivalent vaccine will require 2 doses of the 1979-80 vaccine. Those who received the 1978-79 vaccine will require only

*Official name: Influenza Virus Vaccine, Trivalent.

1 dose. The vaccine will be available as whole virion (whole-virus) and subviron (split-virus) preparations. Based on past data, split-virus vaccines have been associated with somewhat fewer side effects than whole-virus vaccines in children. Thus, only split-virus vaccines are recommended for persons less than 13 years of age. The vaccines prepared for the 1978-79 respiratory disease season contained A/USSR/77 as the H1N1 component. Because of the antigenic similarities between the A/USSR/77 and the A/Brazil/78 strains, the stocks of vaccine remaining from last year may be used, until the expiration date, according to the instructions on the package insert.

## VACCINE USAGE

### General Recommendations

Annual vaccination is strongly recommended for all individuals at increased risk of adverse consequences from infections of the lower respiratory tract. Conditions predisposing to such risk include (1) acquired or congential heart disease associated with altered circulatory dynamics, actual or potential (for example, mitral stenosis, congestive heart failure, or pulmonary vascular overload); (2) any chronic disorder with compromised pulmonary function, such as chronic obstructive pulmonary disease, bronchiectasis, tuberculosis, severe asthma, cystic fibrosis, neuromuscular and orthopedic disorders with impaired ventilation, and residual pulmonary dysplasia following the neonatal respiratory distress syndrome; (3) chronic renal disease with azotemia or the nephrotic syndrome; (4) diabetes mellitus and other metabolic diseases with increased susceptibility to infection; (5) chronic, severe anemia, such as sickle cell disease; and (6) conditions which compromise the immune mechanism, including certain malignancies and immunosuppressive therapy.

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

In considering vaccination of persons who provide essential community services or who may be at increased risk of exposure, such as medical care personnel, the inherent benefits, risks, and cost of vaccination should be taken into account.

Table 1 summarizes vaccine and dosage recommendations by age group for 1979-80.

**TABLE 1. Influenza vaccine* dosage, by age, 1979-80**

| Age group | Product | Dosage (ml) | Number of doses |
|---|---|---|---|
| 27 years and older | whole virion (whole virus) or subvirion (split virus) | 0.5 | 1 |
| 13-26 years | whole virion (whole virus) or subvirion (split virus) | 0.5 | 2** |
| 3-12 years | subvirion (split virus) | 0.5 | 2** |
| 6-35 months*** | subvirion (split virus) | 0.25 | 2** |

* Contains 7 μg each of A/Brazil/78, A/Texas/77, B/Hong Kong/72 hemagglutinin antigens in each 0.5 ml.

** 4 weeks or more between doses; both doses essential for good protection, unless the individual received at least 1 dose of 1978-79 vaccine.

*** Based on limited data. Since the likelihood of febrile convulsions is greater in this age group, special care should be taken in weighing relative risks and benefits.

### Use in Pregnancy

Although the issue has been much discussed, only in the pandemics of 1918-19 and 1957-58 has strong evidence appeared relating influenza infections with increased maternal mortality. Although several studies have reported an increased risk of congenital malformations and childhood leukemia among children born to women who had influenza infection during pregnancy, other studies have not shown an increased risk; the issue is not settled.

Physicians prudently limit prescription of drugs and biologics for pregnant women. However, no evidence has been presented to suggest that influenza vaccination of pregnant women poses any special maternal or fetal risk. Furthermore, because influenza vaccine is an inactivated viral preparation, it does not share the theoretical risks that impel caution in the use of live virus vaccines. Taking the above uncertainites into account, physicians should evaluate pregnant women for influenza immunization according to the same criteria applied to other persons. (See VACCINE USAGE—General Recommendations.)

## SIDE EFFECTS AND ADVERSE REACTIONS

Recent influenza virus vaccines have been associated with few side effects. Local reactions, consisting of redness and induration at the site of injection lasting 1 or 2 days, have been observed in less than one-third of vaccinees. Three types of systemic reactions to influenza vaccines have been described.

1. Fever, malaise, myalgia, and other systemic symptoms of toxicity, although infrequent, occur more often in children and others who have had no experience with influenza viruses containing the vaccine antigen(s). These reactions, which begin 6-12 hours after vaccination and persist 1-2 days, are usually attributed to the influenza virus itself (even though it is inactivated) and constitute most of the side effects of influenza vaccination.

2. Immediate—presumably allergic—responses, such as flare and wheal or various respiratory expressions of hypersensitivity occur extremely rarely after influenza vaccination. They probably derive from sensitivity to some vaccine component, most likely residual egg protein. Although current influenza vaccines contain only a small quantity of egg protein, on rare occasions they can provoke hypersensitivity reactions. Individuals with anaphylactic hypersensitivity to eggs should not be given influenza vaccine. This would include persons who, upon ingestion of eggs, develop swelling of the lips or tongue or who experience acute respiratory distress or collapse.

3. Guillain-Barré syndrome (GBS) is an uncommon illness characterized by ascending paralysis which is usually self-limited and reversible. Though most persons with GBS recover without residual weakness, approximately 5% of cases are fatal. Before 1976, no association of GBS with influenza vaccination was recognized. That year, however, GBS appeared in excess frequency among persons who had received the A/New Jersey/76 influenza vaccine. For the 10 weeks following vaccination the excess risk was found to be approximately 10 cases of GBS for every million persons vaccinated—an incidence 5-6 times higher than that in unvaccinated persons. Younger persons (under 25 years) had a lower relative risk than others and also had a lower case-fatality rate. Preliminary analysis of data from GBS surveillance during the 1978-79 influenza season suggests that, in contrast to the 1976 situation, the risk of GBS in recipients of the 1978-79 vaccine was not significantly higher than that in non-vaccinees. Nonetheless, persons who receive influenza vaccine should be made aware of this possible risk as compared with the risk of influenza and its complications.

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APPENDIX III-B

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PUBLIC HEALTH SERVICE

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*Recommendation of the Public Health Service*
*Immunization Practices Advisory Committee*

## Influenza Vaccine 1980-81

*This annual revision of influenza vaccine recommendations updates information on influenza activity in the United States during 1979-80 and provides information on the vaccine to be available for the 1980-81 influenza season.*

### INTRODUCTION

Influenza virus infections occur every year in the United States, but they vary greatly in incidence and geographic distribution. Infections may be asymptomatic, or they may produce a spectrum of manifestations, ranging from mild upper respiratory infection to pneumonia and death. Influenza viruses A and B are responsible for only a portion of all respiratory disease. However, they are unique in their ability to cause periodic widespread outbreaks of febrile respiratory disease in both adults and children. Influenza epidemics are frequently associated with deaths in excess of the number normally expected. During the period from 1968 to 1980, more than 150,000 excess deaths are estimated to have occurred during epidemics of influenza in the United States.

Efforts to prevent or control influenza in the United States have been aimed at protecting those at greatest risk of serious illness or death. Observations during influenza epidemics have indicated that influenza-related deaths occur primarily among chronically ill adults and children and in older persons, especially those over age 65. Therefore, annual vaccination is recommended for these "high-risk" individua'

Influenza A viruses can be classified into subtypes on the basis of 2 antigens: hemagglutinin (H) and neuraminidase (N). Four subtypes of hemagglutinin (H0-H3) and 2 subtypes of neuraminidase (N1,N2) are recognized among viruses causing widespread disease among humans. Immunity to these antigens reduces the likelihood of infection and reduces the severity of diseases in infected persons. However, there may be sufficient antigenic variation (antigenic drift) within the same subtype over time that infection or immunization with 1 strain may not induce immunity to distantly related strains. Although influenza B viruses have shown much more antigenic stability than influenza A viruses, antigenic variation does occur and was noted in the 1979-80 influenza season. As a consequence, the antigenic composition of the most current strains is considered in selecting the virus strain(s) to be included in the vaccine.

The predominant strain of influenza virus in the United States during 1979-80 was B/Singapore/79, a variant of the prototype B/Hong Kong/72. Most reported influenza B outbreaks involved children and young adults, but outbreaks also occurred in older populations. Excess mortality due to pneumonia and influenza was noted in association with influenza B activity in 1979-80, confirming that infections with this virus can cause serious illness and death.

Isolates of influenza A virus of the H3N2 subtype, similar to A/Texas/77 and A/Bangkok/79, were obtained from sporadic cases of febrile respiratory disease. A/Bangkok/79 strains show significant antigenic drift from A/Texas/77. Influenza A/Brazil/78 (H1N1)-like viruses caused outbreaks of illness among young people.

### INFLUENZA VIRUS VACCINE FOR 1980-81

Influenza vaccine for 1980-81* will consist of inactivated trivalent preparations of antigens representative of influenza viruses expected to be prevalent: A/Brazil/78 (H1N1), A/Bangkok/79(H3N2), and B/Singapore/79. The formulation will contain 7 micrograms of hemagglutinin of each antigen in each 0.5 ml dose. Persons 28 years and older will require only 1 dose. Because of lack of previous contact with H1N1 strains, persons less than 28 years of age who did not receive at least 1 dose of the 1978-79 or 1979-80 trivalent vaccine will require 2 doses of the 1980-81 vaccine. Those who received the 1978-79 or 1979-80 vaccine will require only 1 dose. The vaccine will be available as

whole virion (whole-virus) and subvirion (split-virus) preparations. Based on past data, split-virus vaccines have been associated with somewhat fewer side effects than whole-virus vaccines in children. Thus, only split-virus vaccines are recommended for persons less than 13 years of age.

## VACCINE USAGE

### General Recommendations

Annual vaccination is strongly recommended for all individuals at increased risk of adverse consequences from infections of the lower respiratory tract. Conditions predisposing to such risk include (1) acquired or congenital heart disease associated with altered circulatory dynamics, actual or potential (for example, mitral stenosis, congestive heart failure, or pulmonary vascular overload); (2) any chronic disorder with compromised pulmonary function, such as chronic obstructive pulmonary disease, bronchiectasis, tuberculosis, severe asthma, cystic fibrosis, neuromuscular and orthopedic disorders with impaired ventilation, and residual pulmonary dysplasia following the neonatal respiratory distress syndrome; (3) chronic renal disease with azotemia or the nephrotic syndrome; (4) diabetes mellitus and other metabolic diseases with increased susceptibility to infection; (5) chronic, severe anemia, such as sickle cell disease; and (6) conditions which compromise the immune mechanism, including certain maligancies and immunosuppressive therapy.

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Table 1 summarizes vaccine and dosage recommendations by age group for 1980-81.

**TABLE 1. Influenza vaccine* dosage, by age, 1980-81**

| Age group | Product | Dosage (ml) | Number of doses |
|---|---|---|---|
| 28 years and older | whole virion (whole virus) or subvirion (split virus) | 0.5 | 1 |
| 13-27 years | whole virion (whole virus) or subvirion (split virus) | 0.5 | 2† |
| 3-12 years | subvirion (split virus) | 0.5 | 2† |
| 6-35 months‡ | subvirion (split virus) | 0.25 | 2† |

* Contains 7 μg each of A/Brazil/78 hemagglutinin antigens in each 0.5 ml.

† 4 weeks or more between doses; both doses essential for good protection, unless the individual received at least 1 dose of 1978-79 or 1979-80 vaccine. In latter instance, 1 dose is sufficient.

‡ Based on limited data. Since the likelihood of febrile convulsions is greater in this age group, special care should be taken in weighing relative risks and benefits.

### Use in Pregnancy

Only in the pandemics of 1918-19 and 1957-58 has strong evidence appeared relating influenza infections to increased maternal mortality. Although several studies have reported an increased risk of congenital malformations and childhood leukemia among children born to women who had influenza infection during pregnancy, other studies have not shown an increased risk; the issue is not settled.

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*Official Name: Influenza Virus Vaccine, Trivalent.

## SIDE EFFECTS AND ADVERSE REACTIONS

Recent influenza virus vaccines have been associated with few side effects. Local reactions, consisting of redness and induration at the site of injection lasting 1 or 2 days, have been observed in less than one-third of vaccinees. Three types of systemic reactions to influenza vaccines have been described:

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