CENTER FOR DISEASE CONTROL

INFLUENZA SURVEILLANCE

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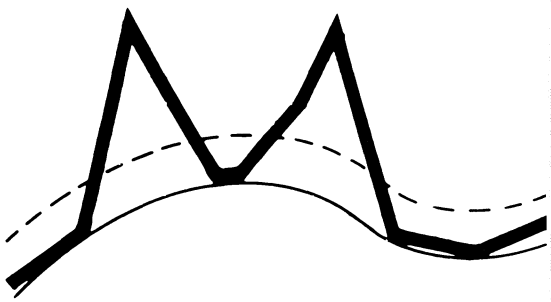

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE

PREFACE

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

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INFLUENZA SURVEILLANCE, 1973-1974 and 1974-1975

I. SUMMARY

A. 1973-1974 (September 1973 through August 1974)

In the 1973-1974 season, epidemics of influenza B occurred throughout central and eastern United States in January and February. Numerous reports of morbidity due to influenza B were received, and deaths due to pneumonia and influenza hovered at the epidemic threshold from January through April. Influenza B strains isolated in the 1973-1974 season were similar to B/Hong Kong/5/72, B/Victoria/98926/70, and strains intermediate between the 2.

In March and April, a localized outbreak of influenza A in the Middle Atlantic states was reported. For 7 weeks pneumonia and influenza mortality exceeded the epidemic threshold for this area. All influenza A isolates were similar to A/Port Chalmers/1/73. Smaller degrees of excess mortality occurred in the West North Central, East North Central, New England, East South Central, and the West South Central states; however, this excess mortality was not conclusively related to influenza.

B. 1974-1975 (September 1974 through August 1975)

From November 1974 through April 1975, influenza reached epidemic proportions in all regions of the United States except the East North Central states. The first confirmed outbreaks were reported in Hawaii in early November. By late December all of the South Atlantic and East South Central states were involved. Subsequent reports indicated that influenza had spread to the West and Northeastern regions of the United States. By March 1975, reports of outbreaks had decreased markedly. Based on excess pneumonia and influenza deaths which occurred in 121 cities, an extrapolation showed that in the entire United States approximately 4,800 such deaths occurred in the 1974-1975 season. The South Atlantic, East South Central, and West North Central states were the areas with the most influenza morbidity and mortality. All virus isolates examined at the World Health Organization (WHO) Collaborating Center for Influenza, Center for Disease Control (CDC), were closely related to A/Port Chalmers/1/73 by the hemagglutination inhibition test.

II. SURVEILLANCE METHODS

A. Mortality

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

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

This procedure allows for a general mean, a standard error of the mean, a slope, and annual and semi-annual cycles in the data. Omission of epidemic data prevents an inflation of the expected level during the influenza season. An "epidemic threshold" is calculated as 1.65 x the standard error of the mean. Charts are prepared which show number of reported deaths, expected deaths, and the epidemic threshold for each area and the entire United States. These charts are scaled to make the distance between the expected and threshold levels constant for every curve which allows visual comparison of influenza activity in different parts of the country (1,2,3).

B. Morbidity

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

Beginning in 1972, to develop more uniform nationwide data, CDC enlisted the cooperation of state and territorial epidemiologists to provide information routinely about: 1) emergency room visits to large community hospitals in major cities within their states and 2) school and industrial absenteeism. Each week during the influenza season, these data are transmitted to the regional offices of the Department of Health, Education, and Welfare and then to CDC. Forty-five states participated in this institutionalized surveillance system in 1973-1974 and 1974-1975 (4).

C. Laboratory Reports

Each week 53 WHO collaborating laboratories in the United States submit preaddressed postcard reports to the WHO Collaborating Center for Influenza (CCI), CDC, on the number of specimens tested, influenzaviruses isolated, and seroconversions detected. In addition, the CCI performs detailed antigenic analysis of representative influenzaviruses which are submitted by laboratories throughout the Americas and elsewhere.

D. International Reports

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

E. Epidemic Investigations

Data received through the surveillance system described above generally reflect influenza activity. However, because events other than influenza epidemics can cause fluctuation in the data, each reported epidemic is confirmed, and if necessary is investigated. Most of the outbreaks described in this report are based on data from several sources.

III. SURVEILLANCE RESULTS, 1973-1974

A. United States

Widespread outbreaks of influenza B occurred from January to March in Central and Eastern United States, followed by several outbreaks of influenza A in March and April in some of the same regions.

1. Influenza B. The first isolates of B/Hong Kong/5/72 were obtained early in December from 2 siblings in California. By early January, isolated cases of influenza B were reported in Minnesota, Missouri, Illinois, and Oregon. In January and February, outbreaks of influenza B were reported in the following areas: South Atlantic (Georgia, Florida), East North Central (Wisconsin, Michigan, Illinois), West North Central (Minnesota, Iowa, Missouri, Nebraska, Kansas), Middle Atlantic (New York, Pennsylvania, New Jersey), West South Central (Arkansas, Louisiana, Oklahoma, Texas), and Mountain (Arizona, New Mexico). School absenteeism was the most consistently elevated parameter.

Absenteeism in outbreaks ranged from 5% to 80%, with most reports ranging from 20% to 30%. Epidemics peaked in late February and early March, and no new outbreaks of influenza B were reported after April 1. The central areas of the United States were most heavily affected. Isolates similar to B/Hong Kong/5/72, B/Victoria/98926/70, and intermediate strains confirmed the presence of influenza B in 30 states by March 1.

2. Influenza A. Six states (Kansas, Illinois, North Carolina, Oregon, Tennessee, and Texas) had reported isolated cases of influenza A by early January 1974. Beginning in March, outbreaks were confirmed in Ohio, New York, and Virginia. Middle Atlantic states (New York, New Jersey, Pennsylvania) reported communitywide outbreaks in late March and April.

3. Mortality. Figure 1 gives the following mortality data for the 121 reporting cities, 1972-1975: pneumonia-influenza deaths (all ages) and deaths from all causes (by age groups). Figure 2 shows pneumonia-influenza deaths for all reporting cities 1972-1975 and for the individual geographic areas 1973-1974. In the first 8 weeks of 1974 during the reported influenza B epidemics, excess mortality was noted only in the West North Central states, and it occurred there in the 2nd through the 4th weeks of 1974, before the morbidity peak in these states. After the 8th week, the Middle Atlantic states had the most excess pneumonia and influenza mortality associated with influenza A. The West North Central, New England, East South Central, Pacific, and West South Central states had fewer excess pneumonia and influenza deaths, but an association with influenza A was not so clear as in the Middle Atlantic states. Nationwide mortality due to pneumonia and influenza surpassed the epidemic threshold between the 13th and 20th weeks of 1974. Approximately 550 deaths in excess of the number that would have been expected in a nonepidemic year occurred in the 70 million people in 121 cities represented by these figures. In comparison with other epidemic seasons, the 1973-1974 season was unusually mild in terms of mortality.

Fig. 1 MORTALITY IN 121 UNITED STATES CITIES

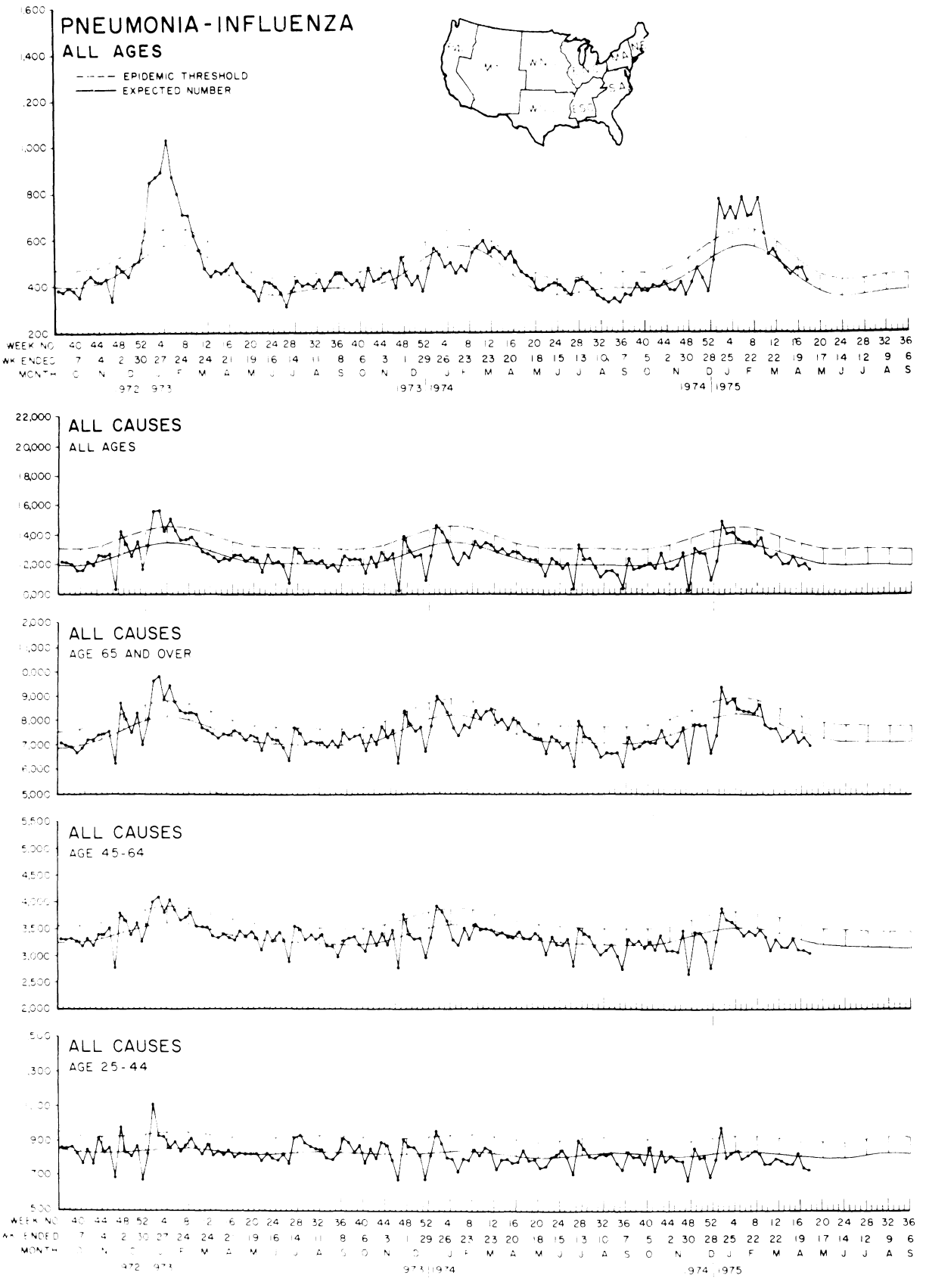
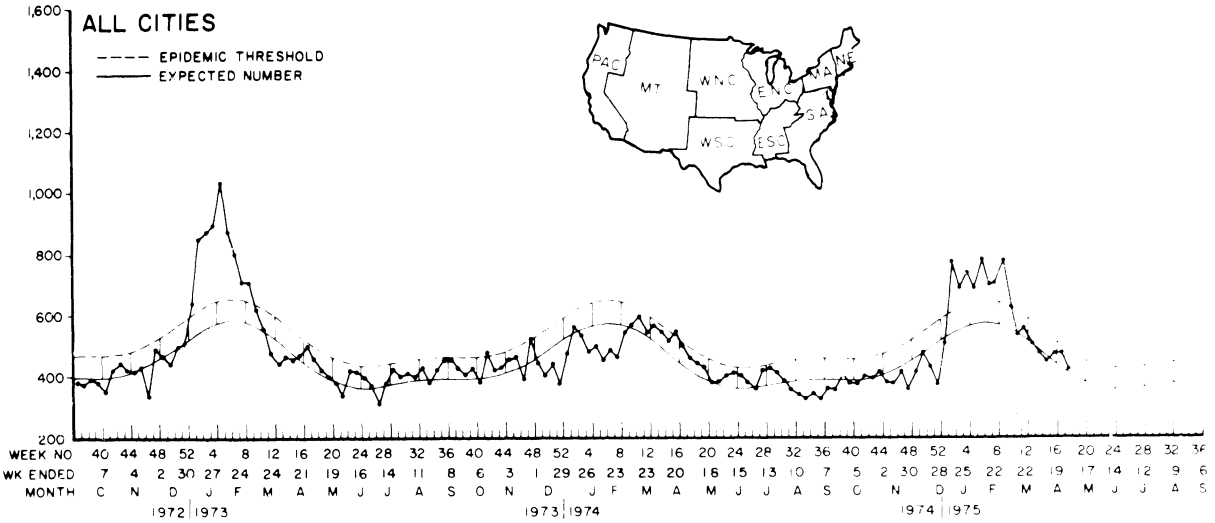
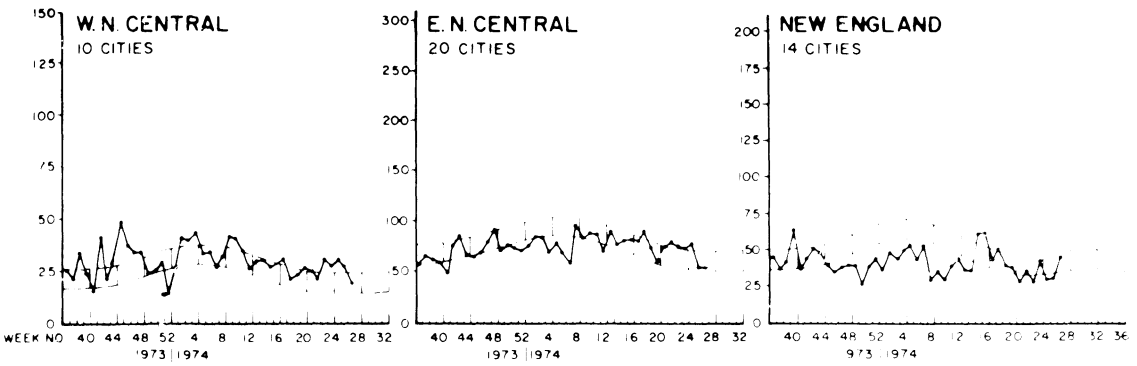
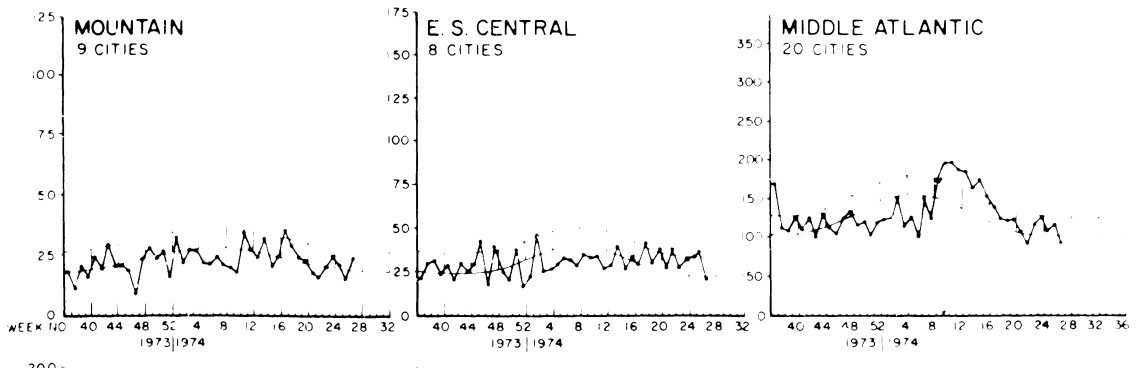
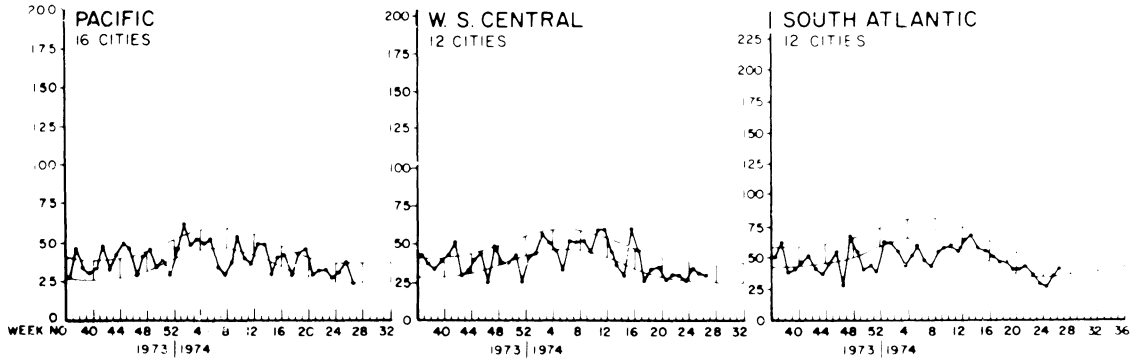


Fig. 2 PNEUMONIA-INFLUENZA DEATHS IN 121 UNITED STATES CITIES



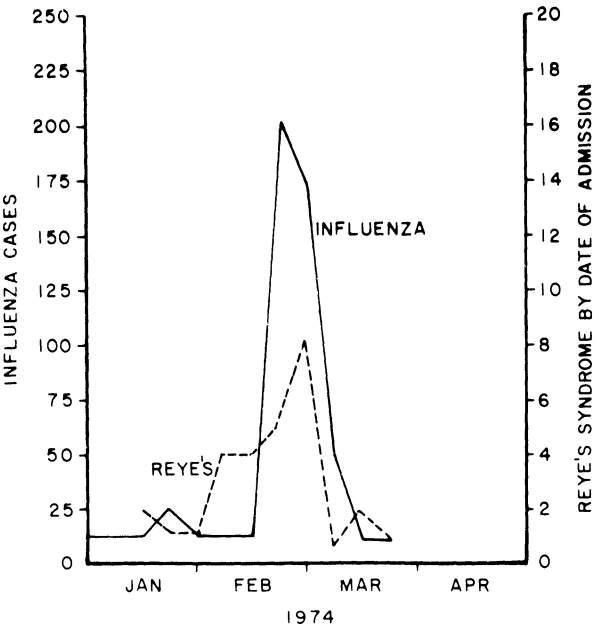






4. Reye's Syndrome. Reye's syndrome, an acute noninflammatory encephalopathy combined with fatty metamorphosis of the liver, has been associated with several antecedent viral illnesses, including influenza B. From December 15, 1973, through June 30, 1974, 379 cases of Reye's syndrome were reported to CDC; 316 (83%) occurred in February and March 1974. Many cases of Reye's syndrome appeared to be temporally and geographically associated with influenza B (Figure 3), while others occurred in a sporadic fashion and were unrelated to influenza B. Of the 379 cases, 178 (47%) were in males and 201 (53%) in females. Case fatality rate was 42%. Patients ranged in age from 3 months to 28 years, with a median age of 11; 37% of cases occurred in children 11-14 years (5). Further studies of epidemiologic factors as well as evaluation of clinical data are continuing at CDC.

Fig. 3 INFLUENZA SURVEILLANCE AND REYE'S SYNDROME, HAMILTON COUNTY, OHIO

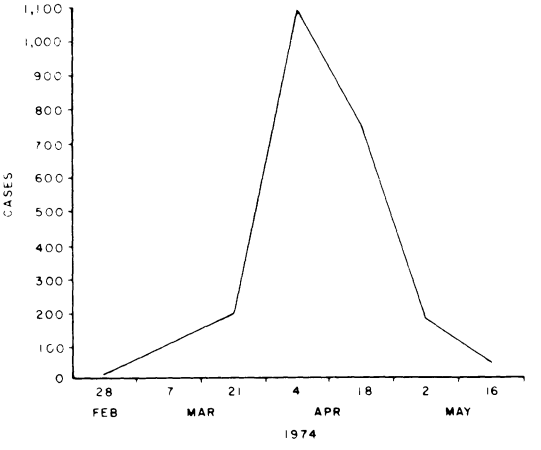


5. Regional Summaries. The following summaries of influenza activity by U.S. census divisions represent a composite of information received from the several surveillance programs.

a. New England: Connecticut and Rhode Island indicated that physicians were seeing an increased number of patients with an influenza-like illness in April and May. Overall, mortality was low and the epidemic of upper respiratory illness was mild.

b. Middle Atlantic: Surveillance in Rochester, New York, indicated that an increase in school absenteeism in February and March was associated with influenza B. In March, April, and May, a well-documented outbreak of influenza A occurred. By May, a total of 2,150 upper respiratory infections had been reported by local physicians (Figure 4). Eighty-eight isolates of influenza A and no isolates of influenza B were obtained (6).

Fig. 4 UPPER RESPIRATORY TRACT INFECTIONS, ROCHESTER, NEW YORK, FEBRUARY - MAY 1974*

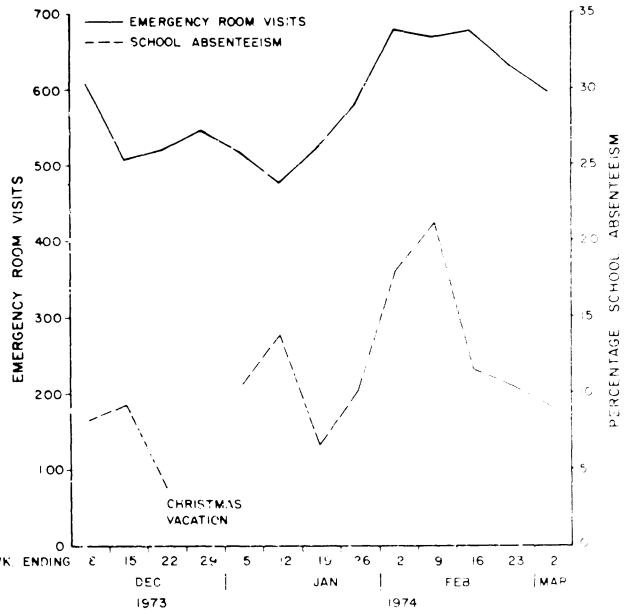


*DATA SUPPLIED BY CAROLYN B. HALL, M.D., DEPARTMENTS OF MEDICINE AND PEDIATRICS, UNIVERSITY OF ROCHESTER SCHOOL OF MEDICINE AND DENTISTRY

Pneumonia and influenza deaths rose above the epidemic threshold in late February and reached a peak in late March. A similar pattern was noted for New York City, in which the number of deaths due to pneumonia and influenza rose above the upper tolerance zone in the week ending March 8, 1974, accompanying a sharp increase in the number of influenza A virus isolations. Increased mortality also occurred in several New Jersey and Pennsylvania cities.

c. East North Central: Sharp epidemics of influenza B occurred in all 5 states from January through March 1974, with peak activity in February In Illinois (Figure 5) and Michigan, peaks in school absenteeism occurred in mid- to late February, resulting in 20% to 30% peak absenteeism and closure of many schools. In Michigan, 41 cases of Reye's syndrome were reported in the first 3 months of 1974. Strong temporal association with influenza B was noted. A similar association was observed in Ohio, where many influenza B virus isolates were obtained. Sporadic influenza A viruses were isolated in April in much smaller numbers.

Fig. 5 EMERGENCY ROOM VISITS AND SCHOOL ABSENTEEISM, SPRINGFIELD, ILLINOIS, DECEMBER 1973 - MARCH 1974



d. West North Central: All states reported increased school absenteeism which peaked in February and March. Many influenza B viruses were isolated in this same period. Absenteeism generally was less marked than in the East North Central states, generally ranging from 20% to 30%. Industrial absenteeism and emergency room visits did not increase significantly during the epidemic.

e. South Atlantic and East South Central: All states reported increases in influenza-like illness in February and March. Almost all isolates and seroconversions indicated influenza B infection. Reye's syndrome was reported in Maryland, North Carolina, and Georgia.

f. Pacific and Mountain States: Influenza activity occurred in February, March, and April. Mortality did not increase. Many influenza B viruses and sporadic influenza A viruses were isolated.

B. International Influenza Surveillance

Countries in nontropical areas of the northern hemisphere reported a pattern of influenza activity similar to that observed in the United States. Israel, Japan, Norway, Spain, Sweden, the United Kingdom, and the United States reported a wave of influenza B infections in December, January, and February 1974, followed by influenza A infections in March and April. Influenza activity ranged from sporadic localized cases to epidemic levels. No increase in mortality was detected with influenza B epidemics, although occasionally increases in death rates were associated with influenza A epidemics. In the southern hemisphere and tropical areas, influenza A virus was associated with sporadic outbreaks. Excerpts of the WER influenza summary for 1973-1974 appear in Table 1.

TABLE 1

INFLUENZA IN THE WORLD: October 1973 – September 1974*

Country	Approximate Date of [a]			Geographic Location / Epidemiological Data / Remarks	Attack Rate	Virus
	Start	Peak	End			
AFRICA						
South Africa	Early June	20 June	July	Widespread epidemic in the Transvaal "highveld", especially in cities in the industrial complex around Johannesburg and Pretoria, affecting 20-40% of the population.	High	A/Port Chalmers/1/73 A/Puerto Rico/1/74 (one strain) B "intermediate" (very rare) B/Hong Kong/5/72 (very rare)
NORTH AMERICA						
Canada	February		May	Waves of influenza-like illness, with school outbreaks in particular, were reported in Ontario (viruses A and B), in Nova Scotia (virus A), in Manitoba (viruses A and B; six influenza A viruses and 30 non-influenza viruses were isolated in 36 influenza-like cases examined in a hospital in Winnipeg), and on Vancouver Island (virus B). Several isolations of virus A in Saskatchewan, and of virus B in Quebec (including one from a case of Reye's syndrome).	Low	B "intermediate" B/Hong Kong/5/72 B/Victoria/98926/70 A
SOUTH AMERICA						
Argentina	Mid-June		July	Sporadic cases and localized outbreaks in Buenos Aires.	Low	A
Brazil			Mid-July	Epidemic in the general population of Rio de Janeiro.		A/Port Chalmers/1/73
Chile	End/May	17-23 June	Mid-July	Epidemic which affected all age groups in the general population of Santiago.	Moderate	A
Uruguay	March		April	Small wave of mild respiratory disease.	Low to Moderate	B/Hong Kong/5/72
ASIA						
Hong Kong	Mid-Jan.	End Feb.	March	Sporadic cases were reported from mid-January, and then a widespread epidemic developed as from the week ended 16 February. Disease clinically mild.	Moderate	A/Port Chalmers/1/73
Israel	End Nov.		January	Sporadic cases in the central part of the country and Tel Aviv, and, during January, local outbreaks in agricultural settlements in the north. Disease of moderate clinical severity, affecting mostly children and young adults.	Low to moderate	B "intermediate"
	Mid-March			Sporadic cases in the central part of the country, and a local outbreak in a settlement in the south where the disease was of moderate severity and affected mostly children and young adults.	Low to moderate	A
Japan	End Sept. 1973		End Dec. 1973	Nationwide epidemic associated with virus B.	Moderate	B/Hong Kong/5/72
	January		Early March	Small epidemic wave associated with virus A throughout the country. A few strains isolated during the previous autumn were already virus A strains.	Low	A/Port Chalmers/1/73 A/Hannover/61/73 (few)

TABLE 1

INFLUENZA IN THE WORLD: October 1973 – September 1974 (cont'd.)*

Country	Approximate Date of (a)			Geographical Location / Epidemiological Data / Remarks	Attack Rate	Virus
	Start	Peak	End			
EUROPE						
Bulgaria	Early Dec.	Mid-Jan.	Mid-March	Epidemic which affected Sofia and 22 districts; outbreaks mostly in schools and among groups of adolescents (where attack rates up to 90% were reported); 110,000 cases were notified between 5 December and 12 March.	Low to moderate	B/Hong Kong/5/72 B "intermediate" A/England/42/72 (very rare)
Czechoslovakia	Early Dec.	5th/6th weeks 1974	February	Small epidemic in the Czech regions affecting all age groups.	Low to moderate	B/Hong Kong/5/72 B "intermediate" B/Victoria/98926/70 (few)
France	End Jan.		Mid-May	In all regions, sporadic cases and localized outbreaks associated either with virus A or virus B.	Low	A/Port Chalmers/1/73
German Democratic Republic	Mid-Jan.		April	Localized outbreaks and numerous sporadic cases associated either with virus A or virus B in all regions.	Low to moderate	A/Port Chalmers/1/73
Federal Republic of Germany	Mid-Dec.	Early Feb.	End	A marked increase associated with viruses A and B, affecting all age groups, was observed as from mid-January; virus B became predominant in February, causing mild diseases with outbreaks mostly in schools and kindergartens.	Low to moderate	A/Port Chalmers/1&63 A/Hannover/61/73 B/Victoria/98926/70 B/Hong Kong/5/72 B "intermediate"
Sweden	Mid-Nov.	3rd week December	Mid-Feb.	Small influenza wave which spread throughout the country.	Low to moderate	B "intermediate"
United Kingdom	September 1973		November 1973	In England and Wales, school outbreaks and sporadic cases associated with viruses A and B.	Low	B "intermediate" B/Hong Kong/5/72 B/Victoria/98926/70 (one only) A/England/42/72
	End Nov.	Mid-Feb.	May	Epidemic associated with virus B throughout England and Wales, which started in November with school outbreaks.	Moderate	B "intermediate" B/Hong Kong/5/72 (less)
	March	Early April	End May	Increase in the incidence of virus A infection throughout England and Wales, affecting all age groups, at the time the epidemic associated with virus B was declining.	Low	A/Port Chalmers/1/73
USSR	Early Jan.	February	March	Increase in the incidence of influenza-like illness in most regions, but not to an epidemic level.	Low	A/England/42/72 A/Port Chalmers/1/73
OCEANIA						
Australia	Early May	Mid-July	Mid-Sept.		Low to moderate	A/Port Chalmers/1/73
New Zealand	Early July		September	Sporadic cases in the regions of Wellington, Auckland and Dunedin, and regional outbreak in July in the region of Hawke Bay (eastern part of North Island).	Low	A/Port Chalmers/1/73

*World Epidemiological Record 50(4):32-41, 1975

(a) The year is only mentioned in these columns when the month falls outside the period shown in the heading.

C. Laboratory Results

1. Influenza Laboratory Surveillance in the United States. For 26 weeks from November 3, 1973, through April 27, 1974, up to 43 WHO collaborating laboratories in the United States submitted weekly summaries of the number of influenza virus isolations and serodiagnoses. In this period 6,841 specimens were tested, 159 A and 506 B viruses were isolated, and 619 B and 183 A serodiagnoses by hemagglutination inhibition (HI) or complement fixation (CF) were reported. Seven weeks after the peak of reported influenza B virus isolations, a peak of seroconversions occurred. A peak of influenza A isolations occurred in mid-April, 2 months after the influenza B peaks in mid-February (Table 2).

Table 2

Influenza Laboratory Surveillance for the United States
November 1973 - April 1974

Week Ending	No. of Laboratories Participating	Viral Isolation			Paired Sera		
		No. Tested	No. Isolates		No. Tested	No. Positive	
			A*	B**		A*	B**
11/3/73	5	23	0	0	40	0	0
11/10/73	17	106	0	0	161	0	0
11/17/73	19	67	0	0	160	1	0
11/24/73	21	128	1	0	149	0	1
12/1/73	23	115	0	0	224	2	1
12/8/73	20	113	0	0	173	1	1
12/15/73	23	131	0	0	215	2	0
12/22/73	20	128	0	0	173	1	0
12/29/73	21	100	0	0	96	0	2
1/5/74	23	89	0	0	168	0	0
1/12/74	28	158	0	0	220	2	1
1/19/74	23	147	0	0	253	0	2
1/26/74	26	180	2	11	211	1	1
2/2/74	32	426	0	18	292	3	1
2/9/74	34	424	1	81	235	0	9
2/16/74	36	550	1	77	302	2	46
2/23/74	36	580	6	71	305	2	60
3/2/74	36	604	7	75	304	14	66
3/9/74	43	604	11	62	391	8	46
3/16/74	38	472	18	26	379	6	86
3/23/74	34	494	17	23	369	10	50
3/30/74	32	407	19	28	458	25	100
4/6/74	22	243	27	11	352	16	36
4/13/74	26	246	29	11	363	19	53
4/20/74	18	149	12	8	242	42	35
4/27/74	16	157	8	4	300	28	22
TOTAL		6,841	159	506	6,532	185	619

* Influenza Type A
** Influenza Type B

In the 1973-1974 influenza season, diagnostic serology at CDC was routinely performed by HI tests using A/Hong Kong/8/68(H3N2), A/England/42/72(H3N2), and B/Hong Kong/5/72 antigens and by CF tests using influenza A and B nucleoprotein (NP) antigens. A total of 58 diagnostic (>4-fold) rises to influenza B were obtained by

HI and/or CF tests (Table 3). The CF test detected 90% of the total number of diagnostic rises and therefore was the most sensitive single test. Of the 58 diagnostic rises, 72% were detected by the HI test with B/Victoria and 64% with B/Hong Kong. The CF test detected 12 diagnostic rises to type B that were missed by the HI test. HI tests detected only 6 diagnostic rises which were missed by the CF test.

Table 3

Results of Influenza B Hemagglutination Inhibition (HI) and Complement Fixation (CF) Tests on Acute and Convalescent Sera, 1973-1974

Serologic Test Demonstrating >Fourfold Antibody Titer Rise	Patients	
	No.	%
HI* and/or CF**	58	100
CF	52	90
HI	46	79
CF (HI negative)	12	21
HI (CF negative)	6	10

* B/Victoria/98926/70 and/or B/Hong Kong/5/72
**Influenza B ribonucleoprotein

2. Geographical Distribution and Antigenic Analysis of Isolates. From July 1973 to June 1974, the WHO Collaborating Center for Influenza, CDC, examined 154 influenza A and 243 influenza B strains which were sent from numerous laboratories in the United States and other countries (Table 4). The 1973-1974 A strains formed a homogeneous group of strains closely related to A/England/42/72 and A/Port Chalmers/1/73 (Table 5).

Table 4

Influenza A and B Isolates Examined
July 1973-June 1974

Geographic Origin	No. of Strains	
North America	A	B
AK		2
AZ	1	6
AR		2
CA	1	2
CO	9	9
CT	4	
GA	3	36
IL	4	4
IA	2	4
KS		4
KY		4
LA	3	2
MA	1	
MD	14	4
MI	1	2
MN	2	18
MO		2
NC	7	25
NH		1
NJ	7	3
NY	15	9
OH	3	21
OK		3
OR		2
PA	5	11
RI	3	
TN		2
TX	1	16
UT	1	
VA	8	3
WA	1	4
WI	6	14
Ontario	2	1
British Columbia		1
Saskatchewan	3	
TOTAL	107	217

Geographic Origin	No. of Strains	
Caribbean	A	B
Puerto Rico	25	
Trinidad	3	7
Western Pacific		
Hawaii	4	11
Okinawa	2	
Taiwan	9	1
Japan	2	4
South America		
Argentina		3
Brazil	2	
TOTAL	47	26

Table 5

Hemagglutination Inhibition Test Results with 1973-1974 Influenza A Viruses

Virus Strains	Antisera			
	A/HK/8/68(H3)*	A/Eng/72(H3)**	A/PC/1/73	A/PR/2/74
A/Hong Kong/8/68	160***	320	160	160
A/England/42/72	80	640	1280	160
A/Port Chalmers/1/73	40	320	2560	320
A/Hanover/61/73	80	640	2560	320
A/Finland/4/74	80	640	1280	320
A/Puerto Rico/2/74	80	160	1280	640

* Antiserum against recombinant A/Hong Kong/8/68(H3)-equine/Prague/1/56(Neq1)
** Antiserum against recombinant A/England/42/72(H3)-equine/Prague/1/56(Neq1)
***Underscoring indicates results of homologous reaction

The HI titers of reference antisera against 138 influenza A isolates were compared with HI titers of these sera with reference strains. The percent of strains demonstrating 4-fold or greater differences in titer from reference strains was considered to reflect the antigenic changes which had occurred in the population of 1973-1974 viral isolates (Table 6). With A/Hong Kong/8/68(H3) antisera, 90% of isolates demonstrated a 4-fold or greater difference in titer from the homologous reference strain. Only 7% of isolates exhibited a 4-fold or greater titer difference from the homologous reference strain when antisera to A/Port Chalmers/1/73(H3N2) was used.

Table 6

Cumulative Distribution of 138 Influenza A Strains
by HI Reactions with Reference Antisera

Fold Difference in HI Titer	A/HK/8/68(H3)*		A/Eng/42/72(H3)*		A/PC/1/73(H3N2)	
	No.	%	No.	%	No.	%
<4x	14	10	70	51	129	93
≥4x	124	90	68	49	9	7
≥8x	57	41	28	21	2	1

* Equine/Prague/1/56(Neq1) recombinants

Antigenic analysis of influenza B isolates received in 1973-1974 indicated that some strains were more closely related to B/Victoria and others were more closely related to B/Hong Kong/5/72 (Table 7). For example, 1 epidemic isolate, B/Georgia/4/74, was more closely related to B/Hong Kong than to B/Victoria. Strains similar to B/Hong Kong, as well as strains reacting with B/Hong Kong antisera at titers 4- to 8-fold lower than the homologous titer, were often isolated from a single outbreak.

Table 7

Hemagglutination Inhibition Test Results with
Selected 1973-1974 Influenza B Viruses

Virus	Antisera			
	B/Vic/98926/70	B/HK/5/72	B/Hanover/3/73	B/Ga/4/74
B/Vic/98926/70	640*	10	80	20
B/HK/5/72	10	160	20	320
B/Hanover/3/73	320	40	160	80
B/Berkeley/9/73	20	80	<10	160
B/Georgia/4/74	20	80	10	160
B/Wisconsin/1/74	10	80	<10	320

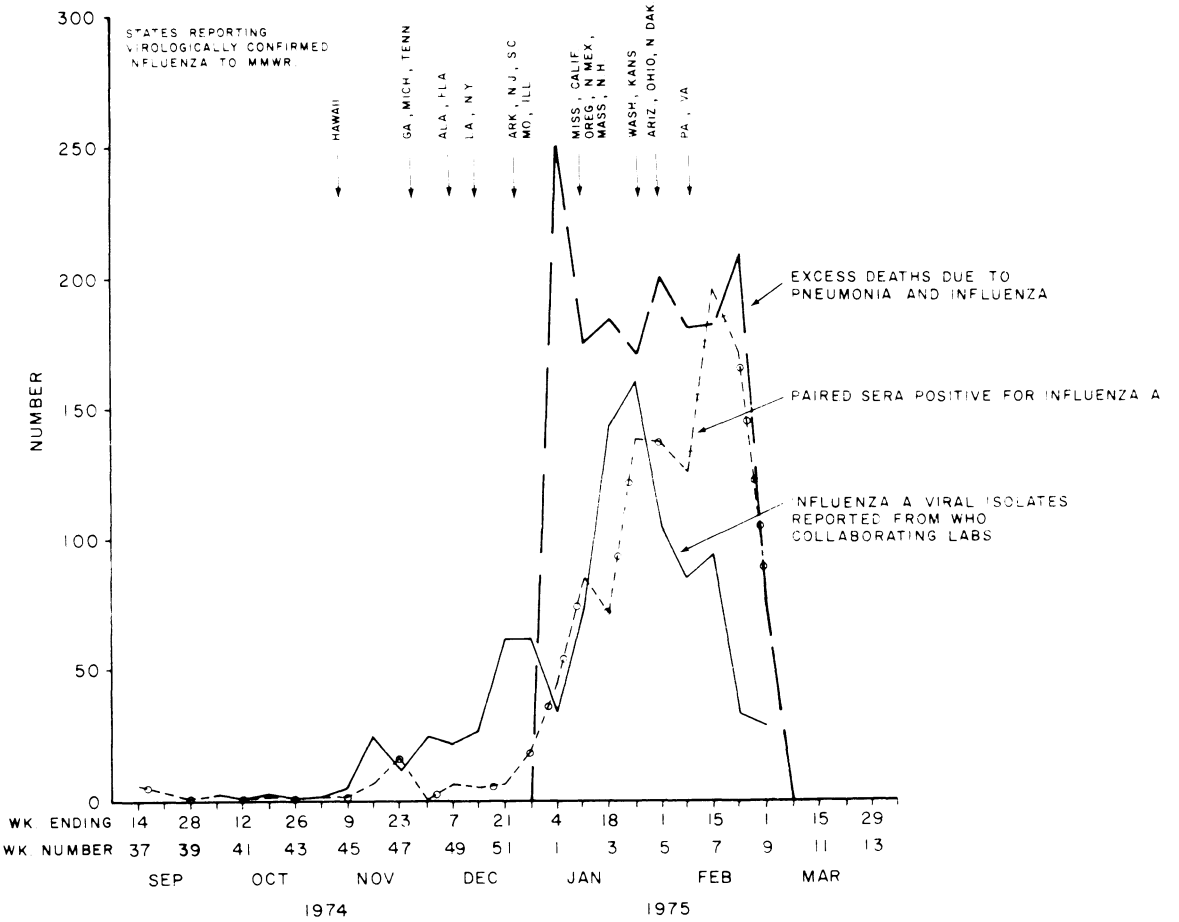
*Underscoring indicates results of homologous reaction

IV. SURVEILLANCE RESULTS, 1974-1975

A. United States

Figure 6 provides influenza activity data for the United States, 1974-1975.

Fig. 6 INFLUENZA ACTIVITY, UNITED STATES, 1974-1975



In November 1974, reports of confirmed influenza A cases were received from California, the District of Columbia, Florida, Georgia, North Carolina, Utah, and Virginia. In all instances, these initial reports were of single isolated cases. On November 25, cases of influenza-like disease associated with isolations of influenza A were reported on the island of Oahu, Hawaii. A clinic on the island of Molokai also reported a marked increase in influenza activity at this time. No further influenza activity was reported until the first week in December, when increases in reported morbidity due to influenza in the South Atlantic states heralded the onset of a 10-week epidemic of influenza A.

By mid-March, a marked decrease in influenza activity had occurred throughout the United States. Excess pneumonia and influenza deaths occurred from the 2nd to the 10th week of 1975. Reports of viral isolates from WHO Collaborating Laboratories in the United States peaked in the week ending February 7, near the middle of the excess mortality period.

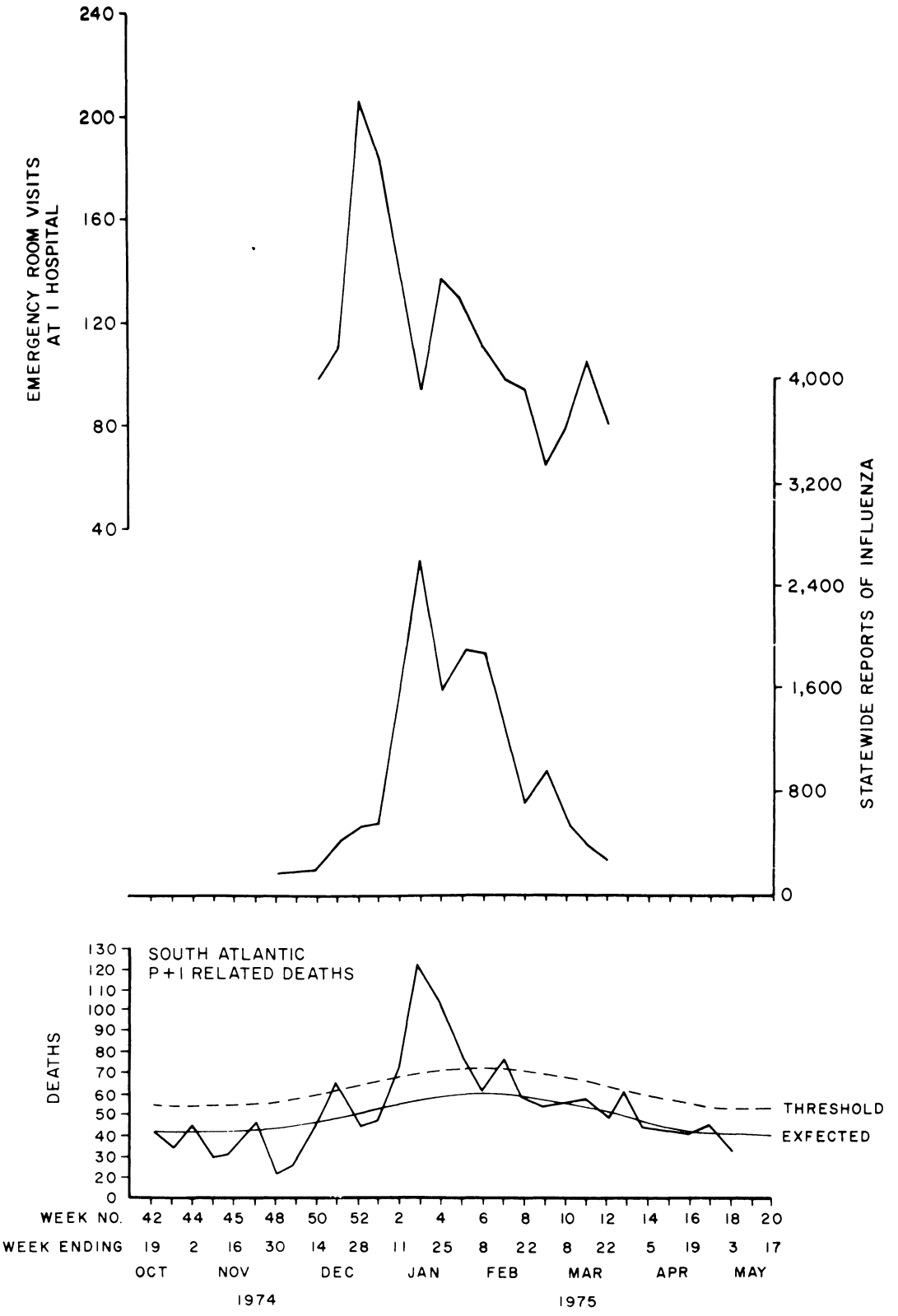
1. Regional Summaries.

a. South Atlantic: In the first week of December, 26 of 45 employees (58%) of a suburban Atlanta, Georgia, post office were reported absent from work with an influenza-like disease. Influenza A virus was isolated from 2 persons. Additional reports of influenza activity throughout north Georgia were received the next week. Physicians at the outpatient clinic of Grady Memorial Hospital in Atlanta noted a marked increase in patient visits. Visits due to respiratory complaints in which fever greater than 100°F was recorded (febrile respiratory/total respiratory x 100%) increased from the baseline of 40% to 67% in the week ending December 22, 1974, and to 79% in the week ending December 29. In the last week of December, the number of adults seen at the medical clinic was 1,906. This number was greater than the number seen during the maximum week of the A/England epidemic in 1972-1973 but smaller than the 2,300 seen during the peak week of the 1968-1969 Hong Kong epidemic (B/Hong Kong/8/68). Influenza A virus was isolated from a number of individuals who had febrile upper respiratory illness (7). Reports of influenza-like disease from Whitfield, Floyd, Richmond, and Polk counties indicated that school absenteeism as high as 34% had occurred.

Influenza also was noted in Memphis and Shelby counties in Tennessee the first week of December. Isolation of influenza A virus and morbidity reports indicated large numbers of students at the University of Tennessee had been affected.

Influenza activity had spread to all of the South Atlantic states by early January. Florida was one of the most heavily involved states, as indicated by reports of greatly increased absenteeism and emergency room visits (Figure 7). Statewide influenza reports from physicians followed increased emergency room visits by about 2 weeks and peaked in the 2nd week of January, simultaneously with the peak in pneumonia and influenza deaths in the South Atlantic states. Influenza activity decreased in late January and early February in Florida. Pinellas County Health officials conducted an uncontrolled survey of 5,607 adults and found that 47% of individuals experienced a flu-like illness (8).

Fig. 7 INFLUENZA SURVEILLANCE, FLORIDA, 1974-1975



b. Middle Atlantic: The initial outbreak in this area occurred in Hamburg, New York (near Buffalo), in December. Further New York state outbreaks occurred in Albany and Buffalo in the middle of January. Increased school absenteeism was noted.

An outbreak of febrile upper respiratory disease in patients of a New York City nursing home was documented the last week in December. Of 115 patients, 28 had febrile clinical influenza. Five of the 28 contracted pneumonia and 1 of the 5 died. Four of 11 throat washings grew influenza A virus. Sporadic outbreaks of influenza in New Jersey occurred in early January. An outbreak of nosocomial influenza in 1 floor of a hospital in Trenton, New Jersey, was reported the first week in January 1975. Sixteen patients and 6 hospital staff members had influenza-like disease, and isolates of influenza A were obtained.

c. East South Central: During mid- and late December, marked increases in influenza-like illness were noted in Louisiana, Mississippi, and Arkansas, indicating the westward spread of influenza.

d. East North Central: Although the main focus of influenza activity early in the year was in the South Atlantic states, a report was received the 3rd week of December that a number of influenza cases had occurred at the State University at Marquette, Michigan. An interesting fact is that Canadian Laboratory surveillance indicated a marked rise in the number of influenza A isolates in the province of Ontario in the latter part of December, corresponding in time to this outbreak across the border in the United States (9). Subsequent influenza activity in Michigan was sporadic.

Industrial absenteeism, viral isolates, emergency room visits, and mortality due to pneumonia and influenza in Illinois all peaked between the 2nd and 8th week of 1975 (Figure 8). Overall, however, activity was moderate as indicated by both the small number of isolates obtained by the state laboratory and by lack of sustained excess mortality in this area.

e. West North Central: Private physicians' reports and school absenteeism indicated outbreaks of illness in Missouri in January (Figure 9). Isolations of influenza virus were obtained between January 25 and March 15. Interestingly, the peak in pneumonia and influenza mortality in the West North Central states tended to precede the reports of increased absenteeism and reports of viral isolations. The peak in mortality was broad and spread from the 1st through the 5th weeks in 1975.

f. Mountain States: In Colorado cases of influenza reported to the state health department increased markedly in the week ending February 1, 1975. Other parameters, such as emergency room visits to Denver General Hospital, showed no evidence of a definite peak (Figure 10). Isolates of influenza A virus were obtained in March and April at the state health department laboratory. The peak in excess mortality in the Mountain states occurred the week ending March 1, 4 weeks after the peak in influenza cases reported in Colorado.

g. Pacific States: Sporadic cases of influenza had been documented in California before January and sporadic outbreaks occurred in January. Many influenza A viruses were isolated from mid-December through mid-March in California. Mortality remained above the epidemic threshold for 15 of the first 17 weeks in 1975. A detailed surveillance system at the Kaiser-Permanente Hospital in Portland, Oregon, indicated that increased influenza activity occurred from the 6th through the 10th weeks of 1975, and the maximum incidence occurred in the 8th week at a rate of 26 contacts due to influenza-like illness per 10,000 persons. About 1% of the population served by the Kaiser-Permanente Hospital visited the clinic with signs and symptoms of influenza during the epidemic. Sporadic outbreaks of influenza A in Washington state were reported. In some communities, young high school students seemed most affected.

Fig. 8 INFLUENZA SURVEILLANCE, ILLINOIS, 1974-1975

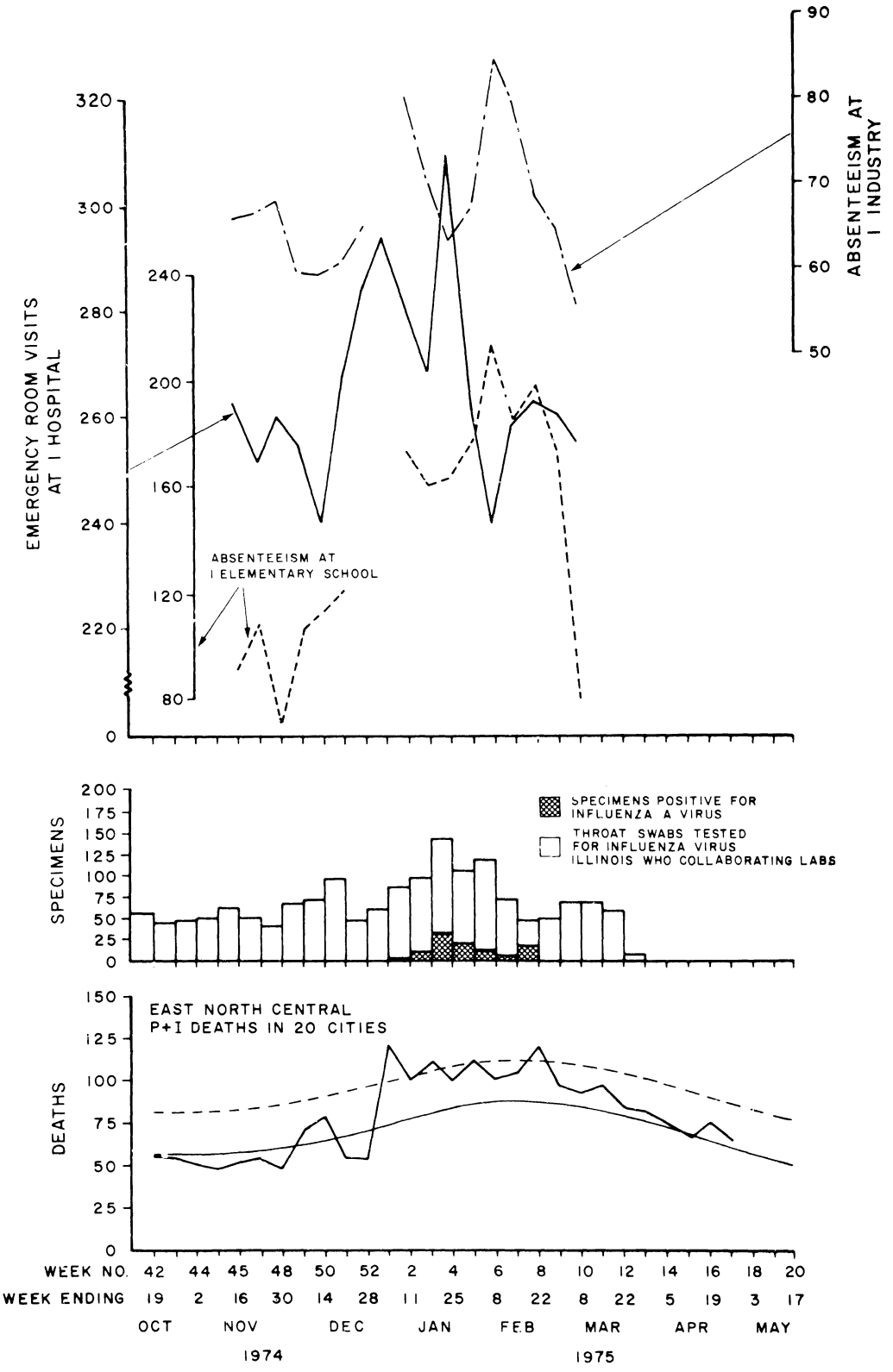


Fig. 9 INFLUENZA SURVEILLANCE, MISSOURI, 1974-1975

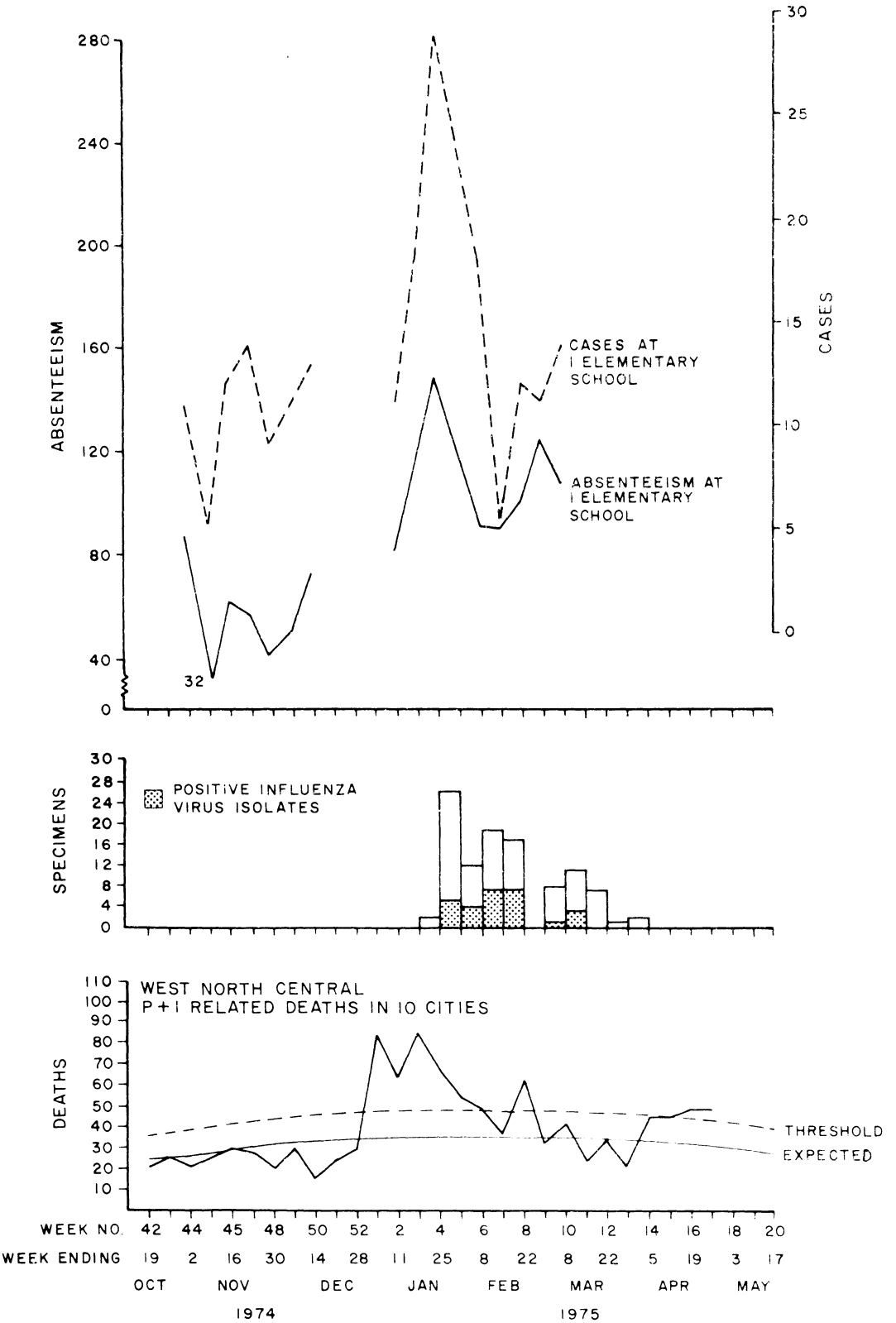
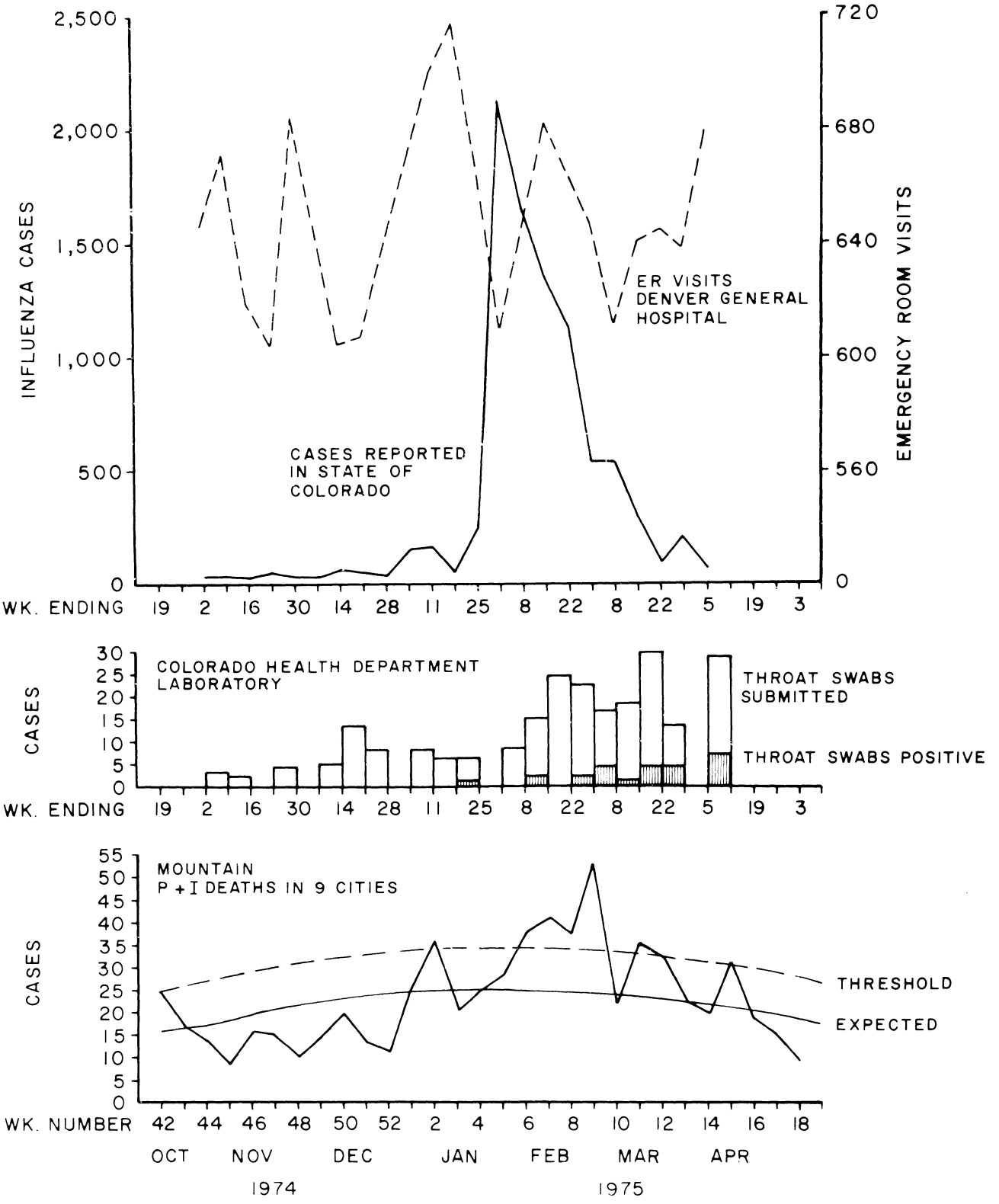


Fig. 10 INFLUENZA SURVEILLANCE, COLORADO, 1974-1975



2. Excess Mortality.

Figure 11 shows pneumonia-influenza deaths for the 121 reporting cities 1972-1975 and for the individual geographic areas 1974-1975. Excess mortality occurred between the 2nd and 10th weeks of 1975, a total of 1,600 deaths in 121 cities which report to the MMWR. If the deaths occurring in these cities with a total population of 70 million are extrapolated to the entire population of the United States, 4,800 excess deaths due to pneumonia and influenza can be estimated for the influenza season. The South Atlantic and East South Central regions were affected earliest, followed by the West North Central and West South Central regions. Finally, the Mountain, Pacific, and Middle Atlantic states were affected. The New England states had a small amount of excess mortality in February and March.

Compared with the A/England epidemic of 1972-1973, in which 6,700 excess pneumonia and influenza deaths occurred, this year's epidemic had less of an impact in terms of mortality (Table 8). Comparison of data from 1973 through 1975 should be made with caution, since data on earlier epidemics were obtained from National Center for Health Statistics death certificates, while data for 1973-1975 were obtained from the CDC's pneumonia and influenza surveillance. Some differences in regional involvement exist also. In general, states most heavily affected in the 1974-1975 epidemic (South Atlantic, East South Central, and West North Central) were among the least affected in the 1972-1973 epidemic. However, of the 3 divisions most heavily affected in the 1972-1973 epidemic (Pacific, West South Central, and Mountain), 2 (Pacific and West South Central) were also heavily affected in the 1974-1975 epidemic. In the 12 epidemics between 1957 and 1975, 6 epidemics were associated with a higher rate of excess deaths per 100,000 population than the epidemic in the 1974-1975 season.

Table 8

Excess Mortality Due to Pneumonia and Influenza
1957-1975

Period of Excess Mortality	Population (1,000's)	Estimated Number of Excess Deaths Due to Pneumonia and Influenza	Rate of Excess Per 100,000	Type of Influenza
Oct. 1957-Mar. 1958	173,232	18,500	10.7	A(Asian)
Mar.-Apr. 1959	176,420	1,400	0.8	A(Asian)
Jan.-Mar. 1960	179,323	12,700	7.1	A(Asian)
Jan.-Mar. 1962	185,890	3,500	1.9	B
Feb.-Mar. 1963	188,658	11,500	6.1	A(Asian)
Feb.-Mar. 1965	193,818	2,900	1.5	A(Asian)
Feb.-Apr. 1966	195,875	3,700	1.9	A(Asian)
Jan.-Feb. 1968	199,846	9,000	4.5	A(Asian)
Dec. 1968-Jan. 1969	201,921	12,700	6.3	A(HK)
Jan.-Feb. 1970	203,736	3,500	1.7	A(HK)
Jan.-Feb. 1972	208,232	5,600	2.7	A(HK)
Jan.-Feb. 1973*	209,851	6,700	3.2	A(HK-Eng)
Jan.-Feb. 1975*	211,390	4,800	2.3	A(HK-PC)

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

B. International Influenza Surveillance

Influenza A activity was prominent in many countries in 1974-1975. Table 9 summarizes data excerpted from numerous issues of the Weekly Epidemiological Record (WER) during the 1974-1975 influenza season. The data presented are greatly abbreviated, and more detailed summaries can be found in the WER.

TABLE 9

INFLUENZA IN THE WORLD: 1974-1975*

Continent/Country	Start	Peak	End	Remarks	Attack Rate	Virus
AFRICA						
Kenya	Nov. 1974	Dec. 1974	Jan. 1975	Clinically mild except in old people		A
South Africa	March 1975		July 1975	Clinically mild illness in Johanessburg and Pretoria	20-40%	A/Port Chalmers
Tunesia	Dec. 1974		Jan. 1975			A
SOUTH AMERICA						
Argentina	June 1974		July 1974	Occurred in sentinel military barracks		A
Brazil		July 1974				A/Port Chalmers/ 1/73
Chile	May 1974	June 23, 1974		General population of Santiago		A
Uruguay	July 1974					A
NORTH AMERICA						
Canada	Dec. 1974		Feb. 1975	Spreading in a generally east-west pattern similar to that seen in the United States	10-50% school absenteeism	A/Port Chalmers/ 1/73
ASIA						
India				Late 1974 and early 1975		A/Scotland/840/74
Israel	Dec. 1974			Moderate severity in Tel Aviv area		A/Port Chalmers/ 1/73
Japan	Dec. 1974			School absenteeism to 16%		A/Port Chalmers/ 1/73 with some A/Scotland/ 840/74 in late 1974 and early 1975
Korea	March 1975			Children and adults		
AUSTRALIA AND NEW ZEALAND						
Australia	May 1974	June		Most activity due to A virus, though one outbreak of B reported		A/Port Chalmers/ 1/73 but one B outbreak reported
Australia	Sept. 1974			This strain proved to be A/Scotland/840/74-like		A/Australia/54/74

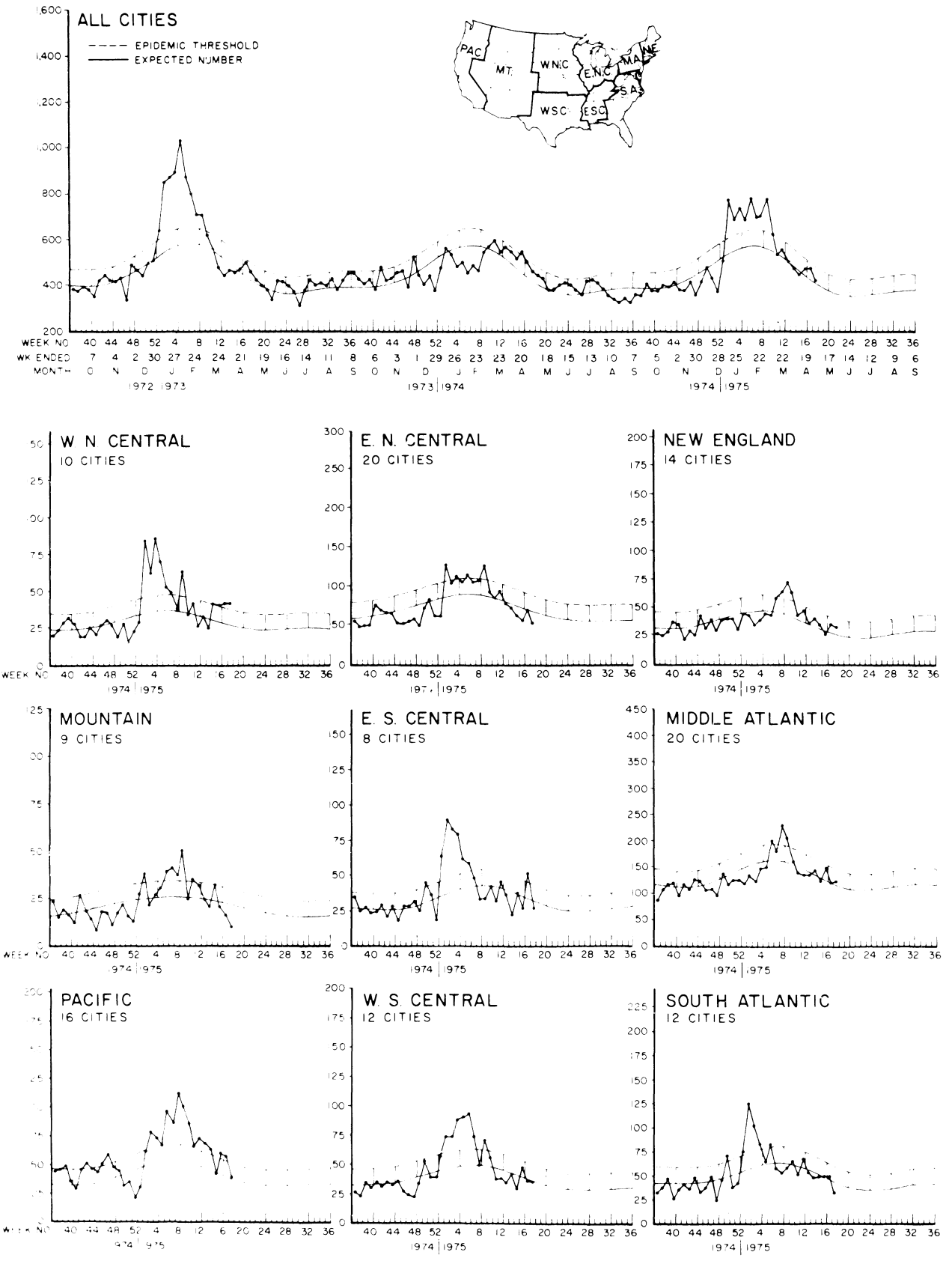
TABLE 9

INFLUENZA IN THE WORLD: 1974-1975 (cont'd.)*

Continent/Country	Start	Peak	End	Remarks	Attack Rate	Virus
New Zealand	June 1974	July 1974 September 1974		Dunedin		B A
EUROPE						
Austria	Dec. 1974	Feb. 1975			2-3%	A
Bulgaria	Dec. 1974	January 1			15% age 0-7	
Federal Republic of Germany	Jan. 1974		March 1975		2.5% of those >95	
France	Nov. 1974	Dec.	Jan. 1975			A/Port Chalmers/1/73
German Democratic Republic	Dec. 1974		March 1975		14.7%	A
Iceland	Jan. 4, 1975		Feb.13, 1975	Seeding from crew of a U.S. military airplane		
Italy				Few isolates		A/Scotland/840/74
Netherlands				Few isolates		A/Scotland/840/74
Norway	Jan. 18, 1975		Feb.22, 1975			
Poland	Dec. 1974		March 1975	Age 0-7, 14.9% attack rate Age 8-18, 52.2% attack rate	14.6% overall	A
Scotland	Dec. 1974		Feb. 1975	By mid February 59% of A strains isolated in the United Kingdom were A/Scotland-like		A/Port Chalmers/1/73 at first, then A/Scotland/840/74 towards the end of the outbreak
Spain	Nov. 22, 1974		Dec. 1974	All age groups A/Scotland isolated late in epidemic	9% in Barcelona	A/Port Chalmers/1/73 and A/Scotland/840/74
Sweden	Feb. 1975	End of Feb.	March 1975	Whole country		A/Port Chalmers/1/73
Switzerland	Nov. 1974		Jan. 1975			A

*Summarized from Weekly Epidemiological Record 18(48); 49(24-33, 37-44, 47, 50, 51, 52); 50(1-15, 22).

Fig. 11 PNEUMONIA-INFLUENZA DEATHS IN 121 UNITED STATES CITIES



C. Laboratory Results

1. Influenza Laboratory Surveillance in the United States. For 33 weeks from September 13, 1974, through May 2, 1975, approximately 50 WHO Collaborating Laboratories in the United States submitted weekly summaries of the results of their influenza diagnostic tests. In this period 8,441 specimens were tested for the presence of respiratory virus and no B virus strains were isolated (Table 10). The largest number of strains isolated in any week--686--were isolated in the week ending January 24, 1975. A total of 8,604 paired sera were tested for 4-fold or greater rises in HI or CF antibody titers; 1,472 pairs were positive for influenza A, and 9 were positive for influenza B.

Table 10

Influenza Laboratory Surveillance for the United States
September 1974 - April 1975

Week Ending	No. of Labs	Viral Isolation			Paired Sera		
		No. Tested	No. Isolates		No. Tested	No. Positive	
			A	B		A	B
9/13/74	1	0	0	0	3	3	0
9/20/74	1	5	0	0	2	1	0
10/4/74	6	63	0	0	39	0	0
10/11/74	16	175	2	0	155	1	0
10/18/74	15	130	0	0	122	0	0
10/26/74	23	176	2	0	249	1	0
11/2/74	20	136	0	0	185	1	2
11/9/74	21	161	0	0	176	1	0
11/16/74	23	235	5	0	258	1	0
11/23/74	28	180	24	0	208	3	0
11/30/74	25	159	12	0	188	18	1
12/7/74	23	326	24	0	241	0	0
12/14/74	26	290	21	0	247	7	0
12/21/74	29	312	26	0	213	5	1
12/27/74	26	279	61	0	174	7	0
1/3/75	35	368	61	0	217	19	2
1/11/75	37	400	39	0	288	45	0
1/18/75	40	518	86	0	410	84	0
1/24/75	35	686	142	0	327	71	0
1/31/75	45	639	160	0	500	139	0
2/7/75	39	576	104	0	512	137	0
2/15/75	32	513	84	0	443	124	0
2/21/75	38	437	94	0	511	195	1
2/28/75	35	373	31	0	581	170	0
3/7/75	30	420	32	0	450	114	1
3/14/75	27	272	11	0	488	95	0
3/21/75	22	210	4	0	352	79	0
3/28/75	20	126	2	0	367	58	1
4/4/75	13	109	1	0	223	34	0
4/11/75	14	96	2	0	254	35	0
4/18/75	9	46	2	0	140	12	0
4/25/75	6	25	0	0	72	12	0
5/2/75	1	0	0	0	9	0	0
TOTALS		8,441	1,032	0	8,604	1,472	9

During the 1974-1975 influenza season, diagnostic serology at CDC was performed routinely by HI tests using influenza A/Hong Kong/8/68(H3N2), A/Port Chalmers/1/73 (H3N2), A/Georgia/1/75(H3N2)--a Port Chalmers-like current epidemic strain--and B/Hong Kong/5/72 antigens and by CF tests using influenza A and B ribonucleoprotein antigens. A total of 82 diagnostic (4-fold or greater) antibody titer rises to influenza A were obtained in paired sera by HI and/or CF testing (Table 11). The HI test detected 96% of the total number of diagnostic rises, compared with 62% of the rises which were detected by CF testing. The CF test failed to detect 31 of the 79 rises measured by HI testing, while the HI test missed only 3 of the 51 rises detected by the CF test. Thus, HI testing with 3 antigens was considerably more effective in detecting titer rises than the CF test, which is in contrast to the 1973-1974 influenza B experience, when the CF test was more effective in detecting influenza B antibody titer rises than the HI test using 2 antigens.

Table 11

Results of Hemagglutination Inhibition (HI) and Complement Fixation (CF) Tests for the Serodiagnosis of Influenza A, 1974-1975

Serologic Test	Diagnostic Rises* No.	%
HI** and/or CF*** (Totals)	82	100
HI	79	96
CF	51	62
HI (CF negative)	31	38
CF (HI negative)	3	4

* ≥4-fold rise in antibody titer
** A/Hong Kong/8/68, A/Port Chalmers/1/73, and/or A/Georgia/1/75
*** Influenza A ribonucleoprotein

2. Geographic Distribution and Antigenic Analysis of Isolates. From July 1974 through June 1975, the WHO Collaborating Center for Influenza, Bureau of Laboratories, CDC, examined 591 influenza A and 3 influenza B isolates which were received from 79 collaborating laboratories in the United States and 16 other countries (Table 12). All of the influenza A isolates from North, Central, and South American and Caribbean laboratories, including Hawaii, were closely related to A/Port Chalmers/1/73(H3N2), except for 1 isolate from Minnesota, A/Mayo Clinic/4/75 (Table 13). This isolate appeared to be unique, as other isolates from this same laboratory resembled A/Port Chalmers, and no similar variants were obtained from the United States or foreign laboratories.

In early December, viruses recovered from outbreaks of influenza in Scotland showed a drift away from the A/Port Chalmers hemagglutinin antigen. Viruses similar to the representative A/Scotland/840/74(H3N2) strains were isolated with increasing frequency in England from December through February and similar strains were recovered in Western Europe, India, and Australia. HI tests which used antisera to the hemagglutinin of A/Port Chalmers and an unrelated equine neuraminidase revealed only moderate antigenic drift away from that of A/Port Chalmers. Another isolate, A/Norway/1/75(H3N2), also showed evidence of antigenic drift away from A/Port Chalmers by HI testing, although this strain was not isolated in other areas.

Table 12

Influenza Isolates Examined July 1974-June 1975

Geographic Origin	Influenza Type	
North America	A	B
AK	6	
AZ	17	
AR	12	
CA	9	
CT	2	
FL	3	
GA	104	
ID	6	
IL	15	
IN	4	
IA	13	
KS	1	
KY	12	
LA	2	
MA	12	
ME	1	
MD	15	
MI	2	
MN	19	
MO	43	
MT	3	
MS	3	
NC	4	
ND	1	
NH	14	
NJ	11	
NM	4	
NY	9	
OH	21	
OR	4	
PA	37	
RI	1	
SC	2	
TN	6	
TX	21	
UT	1	
VA	4	
VT	1	
WA	10	
WI	9	
Canada	12	
Mexico	1	—
TOTAL	477	0

Geographic Origin	Influenza Type	
Caribbean	A	B
Jamaica	8	
Trinidad	14	
Central America		
Panama Canal	2	
South America		
Argentina	15	
Brazil	12	
Chile	1	
Uruguay	3	1
Pacific and Far East		
Hawaii	23	
Hong Kong	3	
Kuala Lumpur	1	
Philippine Islands	3	
Singapore	12	
Europe	16	
Africa	1	2
TOTAL	114	3

Table 13

Hemagglutination Inhibition Test Results*, 1974-1975
Influenza A Viruses

Virus Strains	Ferret Antisera A/Hong Kong/8/68	A/England/42/72	A/Port Chalmers/1/73	A/Scotland/840/74	A/Georgia/101/74	A/Georgia/1/75	A/Norway/1/75	A/Mayo Clinic/4/75
A/Hong Kong/8/68	3840	2560	120	120	80	160	80	30
A/England/42/72	240	2560	240	120	80	240	160	40
A/Port Chalmers/1/73	60	320	960	160	80	640	240	120
A/Scotland/840/74	30	80	240	1920	40	240	80	80
A/Georgia/101/74	80	80	320	80	160	160	80	20
A/Georgia/1/75	60	320	480	120	40	540	240	120
A/Norway/1/75	30	120	240	60	20	240	240	40
A/Mayo Clinic/4/75	20	40	60	30	20	80	80	960

*Average of 2 tests

No significant difference was found between A/Port Chalmers and A/Scotland neuraminidase antigens in NI tests with antibody to A/equine(Heq1)-A/Port Chalmers(N2) (Table 14). Although not shown, the neuraminidase antigens of A/Mayo Clinic/4/75 and A/Norway/1/75 were also similar to A/Port Chalmers/1/73.

Table 14

Neuraminidase Inhibition Test Results*

Virus Strains	Chicken Antisera A/HK/8/68**	A/Eng/42/72**	A/Pt. Ch./1/73**
A/Hong Kong/8/68	2471	717	94
A/England/42/72	631	4677	661
A/Port Chalmers/1/73	380	316	903
A/Scotland/840/74	479	346	479
A/Allegheny/101/74	436	724	1096
A/Georgia/1/75***	296	480	436
A/Georgia/4/75***	457	1047	603

* Average of 2 tests
** Recombinant possessing A/equine/Prague/1/56(Heq1) and and indicated N2 antigen
*** Isolates resembling A/Port Chalmers by HI testing

Only 3 influenza B isolates were received, and none were received from the United States (Table 15). These isolates--B/Entebbe/129/74, B/Johannesburg/9/75, and B/Uruguay/1/75--did now show any significant antigenic drift away from the wild-type, low passage B/Hong Kong/5/72 strain.

Table 15

Hemagglutination Inhibition Reactions of Representative Influenza B Viruses Isolated Since March 1975 Received at CDC

Influenza B Strains	Chicken Antisera	
	B/HK/5/72	B/Joh/9/75
B/Hong Kong/5/72 (BX-1, antibody avid)	1280	1280
B/Hong Kong/5/72 (low passage, non-avid)	160	240
B/Entebbe/129/74	80	240
B/Johannesburg/9/75	160	640
B/Uruguay/1/75	160	480

V. METHOD FOR DIAGNOSIS OF INFLUENZA OUTBREAKS

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

As the public generally believes all febrile upper respiratory disease is the "flu," the isolation of the influenzavirus is important. The diagnosis of influenza must initially be made either serologically or by virus isolation. Facilities for such diagnosis are available in almost every state and large city, and private practitioners are encouraged to use these facilities if they suspect an outbreak of influenza. Only when a virus has been isolated during an outbreak can the type of influenzavirus causing the outbreak and its relationship to previous types be established with certainty. Even though multiple virus isolates obtained from the same epidemic will undoubtedly confirm that the epidemic is caused by a specific influenzavirus, virus isolation is neither a convenient nor practical means of laboratory documentation of epidemics. Theoretically, it should be possible to isolate and identify an influenzavirus in as little as 48 hours; but, in practice, it may take a week or more before an isolate is identified. Multiple blind passages of virus may be required before an isolation is made. Finally, it is much easier to demonstrate a diagnostic rise in antibody than to isolate a virus from a single infected person.

Serologic diagnosis of influenza infection is most readily made by the HI or by the CF tests. CF or HI tests can be run within a 24-hour period; however, there is a considerable time lag in making a serologic diagnosis since collection of acute and convalescent sera from the same individual takes 2 to 3 weeks. To minimize this time lag, a number of investigators (10-12) have compared groups of acute and convalescent sera taken from 1 epidemic, but from different persons.

By the time the presence of an epidemic has been established, there are usually a number of individuals in the community who are already convalescent from the illness, while a number of other persons are in the early acute stages. At one point in time, 10 or more acute specimens and 10 or more convalescent specimens can easily be collected. Since influenza antibody levels vary by age and by influenza vaccination status, the acute and convalescent groups should be equivalent with respect to age and preferably consist of unvaccinated individuals.

The same serologic test (CF or HI) is performed in a single run on each of the sera in each group. Geometric mean titers are then calculated for the acute and the convalescent groups. Although for any single individual, a 4-fold rise in titer

constitutes a diagnostic rise, a 4-fold rise in geometric mean titer is clearly too stringent a criterion for documentation of an epidemic: for example, if 6 to 10 persons involved in the same outbreak had exactly a 4-fold rise in influenza antibody and the remaining 4 had no rise, one would not hesitate to make the diagnosis of an influenza outbreak even though the geometric mean titer rise for the group of 10 was less than 4-fold.

The statistical significance of a comparison between acute geometric mean titers (GMT) and convalescent GMT must be made by using log titers because of the marked non-normality of titer data. A conventional student's t test is then performed on the log titers.

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

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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

INFLUENZA VACCINE

INTRODUCTION

Cases of influenza occur in the United States every year, but there is great variation in incidence and geographic extent. Periodically, influenza becomes epidemic. This appears to occur when antibody levels wane or when the antigens of prevalent influenza viruses have changed enough to render the population susceptible. More epidemics are caused by type A influenza viruses than by type B, and type A epidemics are generally more severe.

Inactivated influenza vaccine, the best available means of protection against influenza, has been variably effective, and vaccine-induced antibody appears to be relatively short-lived. Consequently, public health recommendations on influenza immunization in the United States are oriented toward protecting those at greatest risk of serious disease and death by emphasizing the selective vaccination of "high-risk" groups.

Repeated observations during most influenza epidemics indicate that fatalities are almost completely restricted to the chronically ill and the elderly, especially persons over age 65. Epidemics caused by type A influenza viruses, but rarely those caused by type B, are notable for inducing mortality in excess of what is normally expected.

People in the "high-risk" group should be vaccinated annually regardless of the amount of influenza expected in any specific geographic area. In this way, those at particular risk can maintain the highest possible level of protection. Vaccination of the "high-risk" group should be emphasized by public health authorities; now only 10-15 percent of this group are vaccinated each year.

Influenza control through widespread vaccination of the general population is not currently a public health objective for several reasons: the variable effectiveness and short-lived antibody with available influenza vaccines, the relatively low attack rates of influenza in community outbreaks, and the low frequency of serious complications from the disease in healthy people in the general population.

INFLUENZA VIRUS VACCINE

Bivalent Vaccine*

The Bureau of Biologics, Food and Drug Administration, reviews influenza vaccine formulation regularly and recommends reformulation with contemporary antigens when indicated. Bivalent influenza vaccine this year will contain type A and type B influenza viruses representative of currently prevalent strains. Each adult dose of the 1975-76 vaccine will contain not less than 1200 chick cell agglutinating (CCA) units of antigen in the following proportion: 350 CCA units of a type A strain comparable to the prototype A/Port Chalmers/1/73(H3N2)**, 350 CCA units of a type A strain comparable to the prototype A/Scotland/840/74(H3N2) and 500 CCA units of a type B strain B/Hong Kong/5/72.

*Official name: Influenza Virus Vaccine, Bivalent.

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

VACCINE USAGE

General Recommendations

Annual vaccination is strongly recommended for persons who have such chronic conditions as 1) heart disease of any etiology, particularly with mitral stenosis or cardiac insufficiency, 2) chronic bronchopulmonary diseases, such as asthma, chronic bronchitis, bronchiectasis, tuberculosis, and emphysema, 3) chronic renal disease, and 4) diabetes mellitus and other chronic metabolic disorders.

Annual vaccination is recommended for older persons, particularly those over age 65 years, because influenza outbreaks are commonly associated with excess mortality in older age groups.

Vaccination may also be considered for persons who provide essential community services if local priorities justify. However, before undertaking such an immunization effort, those responsible should take into account a number of reasonable constraints: difficulties inherent in predicting influenza epidemics, variability in vaccine effectiveness, availability of vaccine, and cost.

Vaccination of patients not at "high risk" in an attempt to reduce their chances of acquiring influenza is a decision for practicing physicians.

Pregnancy is not an indication for or against influenza vaccination.

Schedule

The primary series of bivalent influenza vaccine has traditionally been 2 doses. Data indicate that with the more potent influenza vaccines available in recent years, the second dose provides little additional benefit. It is, therefore, reasonable to give a single dose of vaccine for either primary or annual booster vaccination. Dose volumes for adults and children and the recommended route of administration are specified in the manufacturers' package labeling.

Influenza vaccine should be administered by mid-November.

Reactions

Influenza vaccines from all manufacturers are highly purified and should produce few severe adverse effects. Local reactions such as erythema and tenderness at the injection site, however, are relatively common. Mild systemic reactions, including low-grade fever, chills, myalgias, or headache, reportedly occur in up to 20 percent of adult recipients. Fever appears to be more common in children than in adults, and febrile convulsions in children under 3 years of age have been described. This possible adverse reaction must be recognized in vaccinating infants and young children who are in the "high-risk" group (see General Recommendations). As an adjunct to influenza vaccine, antipyretic therapy may be considered.

Precautions

Influenza vaccine is prepared from viruses grown in embryonated eggs and should not be administered to persons clearly hypersensitive to egg protein, ingested or injected.

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STATE EPIDEMIOLOGISTS

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

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