

COMMUNICABLE DISEASE CENTER

INFLUENZA

S U R V E I L L A N C E

TABLE OF CONTENTS

- I. SUMMARY
- II. EPIDEMIC REPORTS
- III. INTERNATIONAL SUMMARY - 1963
- IV. LABORATORY REPORT
- V. SPECIAL REPORT
- VI. WEEKLY PNEUMONIA
AND INFLUENZA DEATHS

PREFACE

Summarized in this report is information received from State Health Departments, university investigators, virology laboratories and other pertinent sources, domestic and foreign. Much of the information is preliminary. It is intended primarily for the use of those with responsibility for disease control activities. Anyone desiring to quote this report should contact the original investigator for confirmation and interpretation.

Contributions to the Surveillance Report are most welcome. Please address to:
Chief, Influenza Surveillance Unit, Communicable Disease Center, Atlanta 22, Georgia.

Communicable Disease Center

James L. Goddard, M.D., Chief

Epidemiology Branch

Alexander D. Langmuir, M.D., Chief

Statistics Section
Surveillance Section

Robert E. Serfling, Ph.D., Chief
Donald A. Henderson, M.D., Chief

Influenza Surveillance Unit

~~James F. Maynard, M.D., Chief~~
Carl Silverman, M.D.

I. SUMMARY

Outbreaks of influenza-like disease have recently been reported from communities in western Washington, from nearby areas on Vancouver Island, British Columbia, and from several areas in the Orient, notably Taiwan and Japan. The Washington epidemic is the first to have been noted in the U. S. this year. Presumptive laboratory confirmation has been obtained in this outbreak - the results indicating an A₂ virus as the etiologic agent. Preliminary serologic studies have also implicated an influenza A virus - probably subtype A₂ - in Taiwan. An influenza B virus appears to be the agent involved in the extensive outbreaks now in progress on the island of Kyushu, Japan.

An international summary of influenza in 1963 is included in this report. It is of some interest that among the last outbreaks to be reported last year were two in Asian countries - the Philippines and Thailand.

Successful application of a method for rapid presumptive identification of the agent in a respiratory disease outbreak is described in the laboratory section of this report.

II. EPIDEMIC REPORTS

Washington State:

Outbreaks of acute febrile respiratory disease, clinically compatible with influenza, have recently been reported from several counties in Western Washington. These are the first such outbreaks to have been noted in the U. S. this year.

Physicians in Skagit County, about 65 miles north of Seattle, began reporting cases in mid-January. They described a syndrome characterized by fever (reaching 103-4^oF in severe cases), dry cough, sore throat, myalgia, and eye pain lasting 3-4 days, followed by a period of fatigue and lassitude lasting several more days. No deaths have been reported.

Most severely affected has been the town of Concrete (pop. 840) where elementary and high school absenteeism reached peak levels of 17-21% during late January, as compared to usual rates of 5-7%. (See Figure 1.) Practitioners in the neighboring communities of Sedro Woolley and Mount Vernon have also been seeing an increasing case load of flu-like illness, but absenteeism in school and industry has remained at normal levels in these areas.

In Whatcom County, just north of Skagit, increased school absenteeism due to flu-like illness has also been observed, particularly in the county seat of Bellingham. In Snohomish County to the south, a slight increase in case reports along with a moderate increase in overall absence rate for county schools have been noted.

A second epidemic focus was noted in early February in the town of Lacey (Thurston County), five miles north of Olympia and about 180 miles south of Skagit County. A boarding school in Lacey with a total enrollment of approximately 300 experienced a sharp outbreak of acute respiratory disease, beginning about January 31. By Monday, February 3, the 15-bed infirmary serving the school was filled to capacity and remained so through February 6. School absenteeism rose sharply at the same time, reaching a peak level of almost 25% on February 4. (See Figure 2.) There is no evidence of increased absenteeism in other schools in Thurston County at present. Laboratory specimens have been obtained from the boarding school outbreak, and are now being processed.

It is of some interest that a 3 day school holiday occurred approximately one week before this outbreak. Two students enrolled at the school were known to have visited Concrete during the holiday period, which coincided with the peak of the Skagit County epidemic.

Figure 1
SCHOOL ABSENTEEISM - CONCRETE, WASHINGTON
 JANUARY, 1964

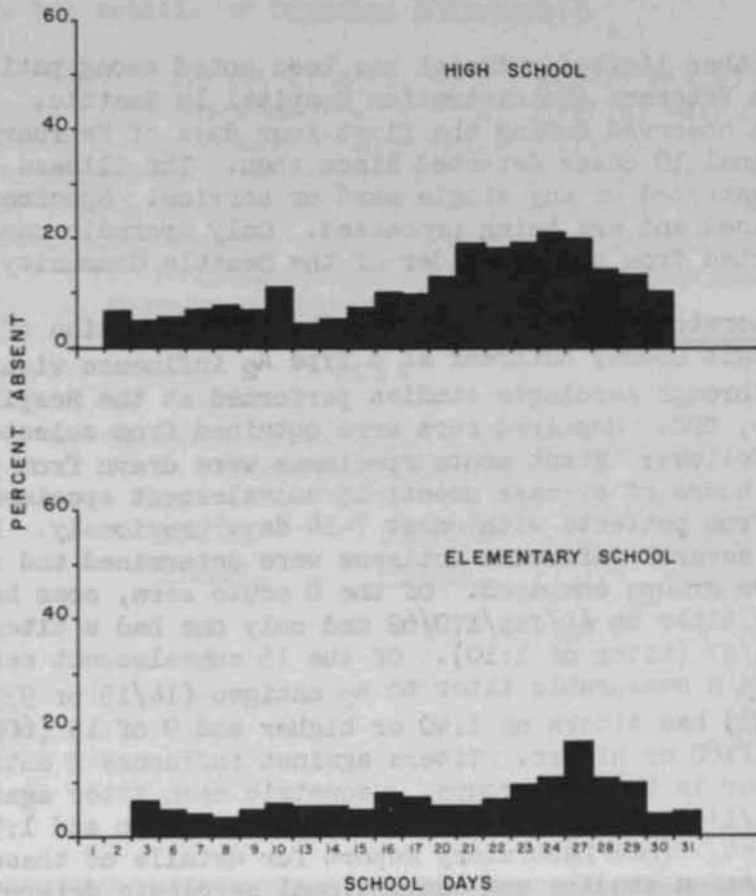
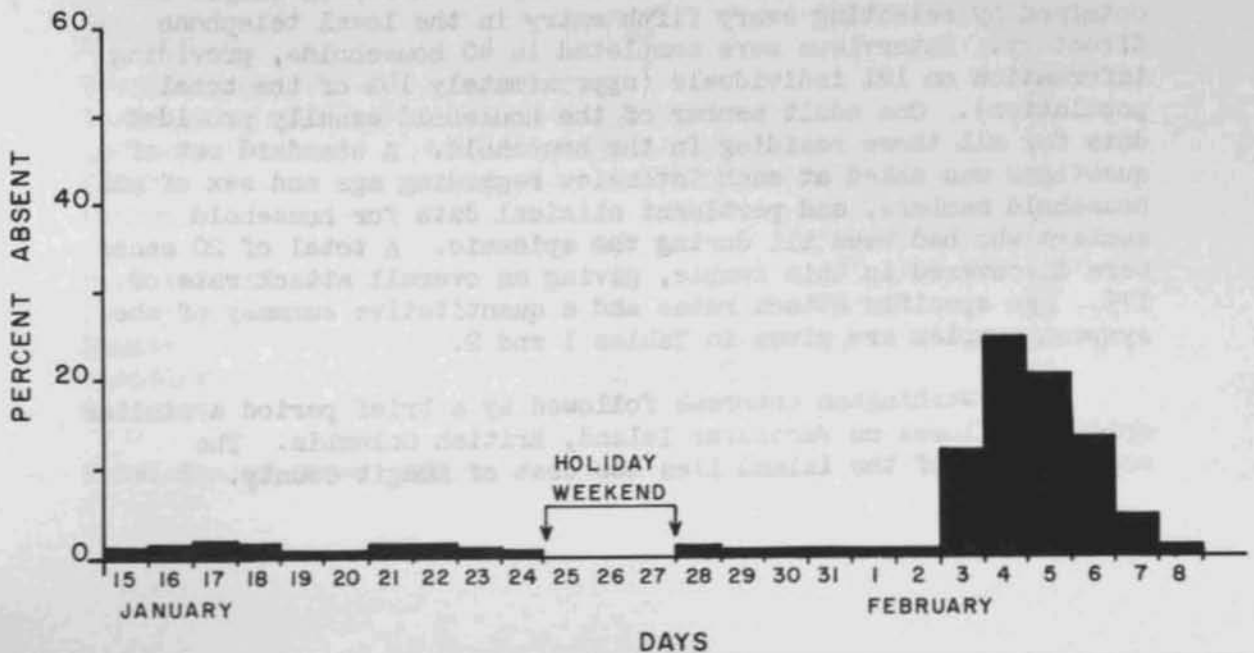


Figure 2

ABSENTEEISM AT S.M. BOARDING SCHOOL - LACEY, WASHINGTON
 JANUARY, FEBRUARY, 1964



Another limited outbreak has been noted among patients and staff at a Veterans Administration Hospital in Seattle. About 25 cases were observed during the first four days of February, with an additional 10 cases detected since then. The illness has not been concentrated on any single ward or service. Specimens have been obtained and are being processed. Only sporadic cases have been reported from the remainder of the Seattle Community.

Laboratory Studies: Presumptive identification of the agent in the Skagit County outbreak as a Type A₂ influenza virus has been obtained through serologic studies performed at the Respirovirus Laboratory, CDC. Unpaired sera were obtained from selected typical cases as follows: Eight acute specimens were drawn from patients within 48 hours of disease onset; 15 convalescent specimens were obtained from patients with onset 7-14 days previously. H. I. titers to several influenza antigens were determined and results for the two groups compared. Of the 8 acute sera, none had a measurable titer to A₂/Jap/170/62 and only one had a titer to A₂/Jap/305/57 (titer of 1:10). Of the 15 convalescent sera, all but one had a measurable titer to A₂ antigen (14/15 or 93%); 11 of the 15 (73%) had titers of 1:40 or higher and 9 of 15 (60%) had titers of 1:80 or higher. Titers against influenza B antigens were similar in the two groups. Geometric mean titer against the B/Maryland/1/59 strain was 1:48 in the acute group and 1:50 in the convalescent. (See Laboratory Report for details of these results.) Viral isolation studies and conventional serologic determinations on paired specimens are also being performed. These results will be given in a later report.

Epidemiologic Studies: Further epidemiologic information on the Skagit County outbreak was obtained through a telephone survey performed in Concrete on February 2. A random sample was obtained by selecting every fifth entry in the local telephone directory. Interviews were completed in 40 households, providing information on 121 individuals (approximately 14% of the total population). One adult member of the household usually provided data for all those residing in the household. A standard set of questions was asked at each interview regarding age and sex of all household members, and pertinent clinical data for household members who had been ill during the epidemic. A total of 20 cases were discovered in this sample, giving an overall attack rate of 17%. Age specific attack rates and a quantitative summary of the symptom complex are given in Tables 1 and 2.

The Washington outbreak followed by a brief period a similar epidemic illness on Vancouver Island, British Columbia. The southern end of the island lies due west of Skagit County.

(See below for details of Canadian outbreaks.)

(Reported by Ernest A. Ager, M. D., Chief, Division of Epidemiology, State Department of Health, Olympia, Washington; Richard Gross, M. D., Skagit County Health Officer, Mt. Vernon, Washington; Donald R. Peterson, M. D., Epidemiologist, Seattle-King County Health Department, Seattle, Washington; Vincent Guinee, M. D., Epidemiology Branch, C.D.C., Atlanta, Georgia; and Kenrad Nelson, M. D., EIS Medical Epidemiologist, Washington State Department of Health, Olympia, Washington.)

Table 1

Age-Specific Attack Rate - Telephone Survey
Concrete, Washington

| <u>Age Group</u> | <u>No. in Sample</u> | <u>Cases in Sample</u> | <u>Attack Rate for Sample</u> |
|------------------|----------------------|------------------------|-------------------------------|
| 0-4 | 17 | 1 | 6% |
| 5-14 | 18 | 4 | 22% |
| 15-24 | 14 | 4 | 29% |
| 25-34 | 14 | 2 | 14% |
| 35-49 | 26 | 8 | 31% |
| 50-64 | 15 | 1 | 7% |
| 65+ | 17 | 0 | 0% |
| Total | 121 | 20 | 17% |

Table 2

Symptoms of Influenza-like Illness - Telephone Survey
Concrete, Washington - February 2, 1964

| <u>Symptom</u> | <u>Number</u> | <u>Percent</u> |
|---------------------|---------------|----------------|
| Feverishness | 19 | 95 |
| Weakness or malaise | 19 | 95 |
| Headache | 15 | 75 |
| Cough | 13 | 65 |
| Myalgia | 11 | 55 |
| Chills | 10 | 50 |
| Sore throat | 9 | 45 |
| Eye symptoms | 7 | 35 |
| Nausea | 6 | 30 |
| Vomiting | 2 | 10 |
| Diarrhea | 0 | 0 |

Total No. of Cases: 20

Canada:

Epidemic respiratory disease with symptoms typical of influenza has been reported from the community of Lantzville in central Vancouver Island. Peak incidence occurred in mid-January with an estimated 1,000 cases reported during the week ending January 17. Pneumonitis has complicated many of the cases. One death, in a 14-year-old boy, has been reported.

Earlier outbreaks of a similar illness were reported in December from several small villages in the Northwest Territories. The towns of Gjoa Haven, Pelly Bay, and Stence Bay accounted for an estimated 100-150 cases.

(Reported by Dr. E. W. R. Best, Chief, Epidemiology Division, Department of National Health and Welfare, Ottawa, Canada.)

Taiwan:

An extensive respiratory disease epidemic is currently in progress on Taiwan with most severe involvement apparently in the city of Taipei.

The outbreak was first recognized in early January and reached its peak near the end of that month. Clinically, the illness has been characterized by fever, headache, myalgia, and upper respiratory symptoms, each of which has been present in over 60% of the cases analyzed. Epidemiologic investigation has been hampered however by the concomitant occurrence of many milder cases which appear more compatible with the "common cold" syndrome.

At the height of the epidemic in late January, absenteeism at one American high school in Taipei reached 20%, as compared to usual rates of 3-9%. At about the same time, over 40% of the 1200 patients seen daily at one large industrial clinic had complaints referable to acute respiratory disease. (Similar figures from a non-epidemic period are not available for comparison.) The attack rate for this illness among Chinese and American employees at the U. S. Naval Medical Research Unit No. 2 (NAMRU-2), in Taipei has been estimated at about 35%. The outbreak now appears to be waning, without evidence of significant spread beyond Taipei.

Preliminary serologic studies performed at the NAMRU-2 laboratories indicate that the agent in this epidemic is a Type A

influenza virus - probably subtype A₂. There has been no evidence to implicate the Influenza B/Taiwan/62 strain* in the present outbreak. Further laboratory and epidemiologic investigations are in progress.

(Reported by Capt. Robert Phillips, MC, USN, Officer in Charge, U. S. Naval Medical Research Unit No. 2, Taipei; Capt. Jack W. Millar, MC, USN, Director, Preventive Medicine Division, Department of the Navy; and Robert J. Warren, M. D., Medical Epidemiologist, CDC, Career Development Program.)

Japan:

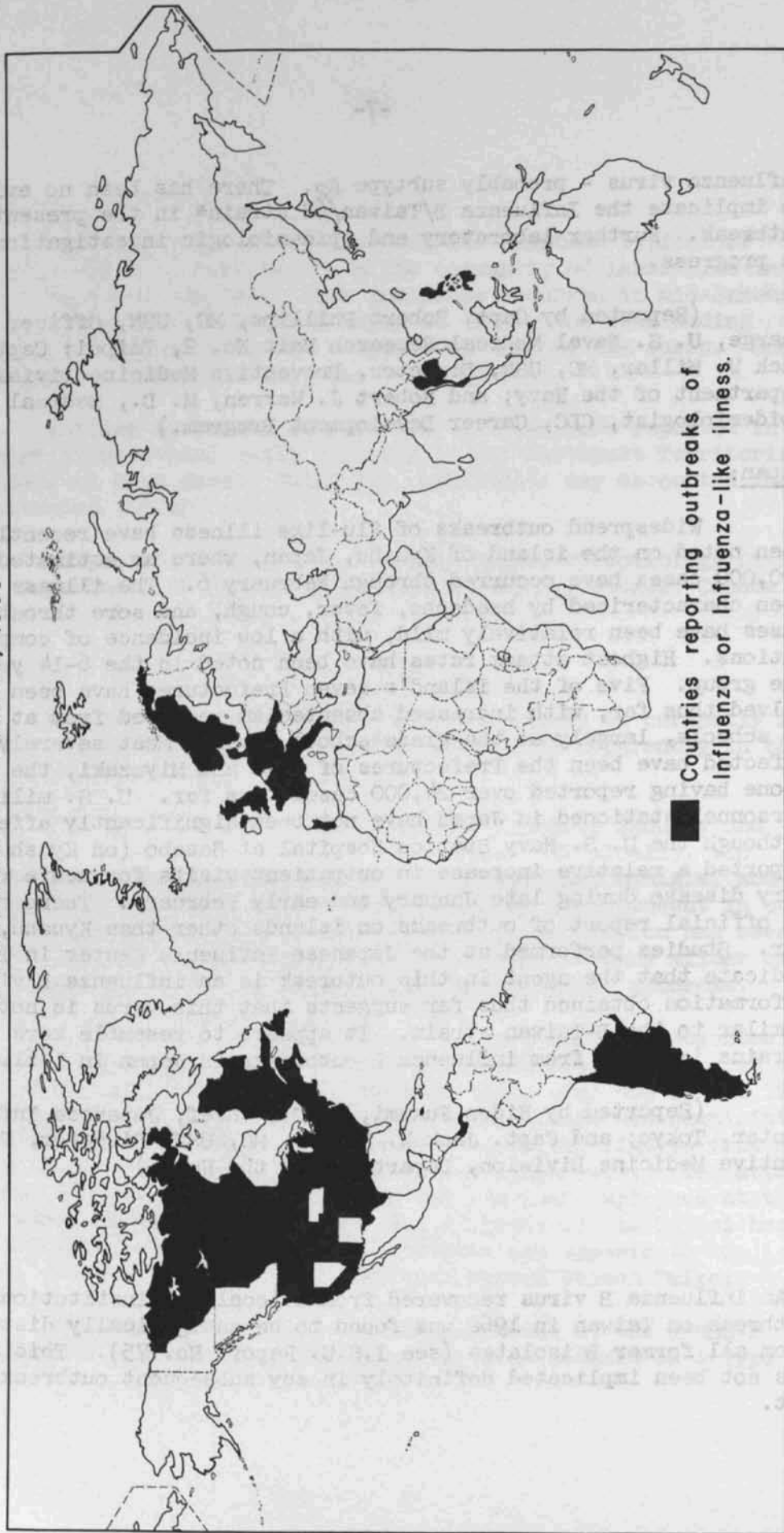
Widespread outbreaks of flu-like illness have recently been noted on the island of Kyushu, Japan, where an estimated 100,000 cases have occurred through February 6. The illness has been characterized by headache, fever, cough, and sore throat. Cases have been relatively mild, with a low incidence of complications. Highest attack rates have been noted in the 6-14 year age group. Five of the island's seven Prefectures have been involved thus far, with increased absenteeism reported from at least 50 schools, largely at the grade school level. Most severely affected have been the Prefectures of Saga and Miyazaki, the latter alone having reported over 24,000 cases thus far. U. S. military personnel stationed in Japan have not been significantly affected, although the U. S. Navy Station Hospital at Sasebo (on Kyushu) reported a relative increase in outpatient visits for acute respiratory disease during late January and early February. There has been no official report of outbreaks on islands other than Kyushu, thus far. Studies performed at the Japanese Influenza Center in Tokyo indicate that the agent in this outbreak is an influenza B virus. Information obtained thus far suggests that this virus is not similar to the B-Taiwan strain. It appears to resemble more closely strains isolated from influenza B outbreaks in Japan in 1961.

(Reported by Hideo Fukumi, M. D., Chief, Japanese Influenza Center, Tokyo; and Capt. Jack W. Millar, MC, USN, Director, Preventive Medicine Division, Department of the Navy.)

* An influenza B virus recovered from a localized institutional outbreak on Taiwan in 1962 was found to be antigenically distinct from all former B isolates (see I.S.U. Report No. 75). This agent has not been implicated definitely in any subsequent outbreaks as yet.

INFLUENZA

INTERNATIONAL SUMMARY, 1963



Countries Reporting Outbreaks of Influenza
1963*

| Country | Peak Months (Estimated) | Remarks |
|---------|----------------------------|--|
| Europe | The Netherlands | January Scattered outbreaks confined to institutional and military populations |
| | United Kingdom | Jan. - Feb., Southern England & Scotland; March, Northern England Early outbreaks reported from London, Glasgow and environs. Northern England affected in March. Influenza deaths reached peak level during week ending March 16. |
| | France | January - March Most outbreaks reported from the Paris and Lyon areas. Also from Departments in Southeastern and Southwestern France. |
| | Germany | February Several outbreaks in Frankfurt am Main, involving adults predominantly. Attack rates reaching 30-40% reported other epidemic foci in Ruhr and North of Hess. |
| | Italy | February Widespread involvement. Forty-one of country's 92 provinces had submitted positive reports by end of February. |
| | Norway | February Increased incidence noted in Rogaland Central section of the country involved principally. Epidemics were mild generally except for a few military outbreaks where high attack rates were observed. |
| | Sweden | February Clinically mild illness involving communities in all sections of the country. Incidence appeared highest in school age children. |
| | Portugal | February - March Almost all cantons involved with those in Eastern part of the country most severely affected. |
| | Switzerland | March Relatively mild disease clinically, involving several parts of the country |
| | Denmark | March - April |

Continued

Countries Reporting Outbreaks of Influenza
1963*

| | Country | Peak Months (Estimated) | Remarks |
|-----------------|-----------------|----------------------------|--|
| The Americas | Czechoslovakia | March-April | Moderately widespread. School and military populations most severely affected. |
| | Jamaica | March | Island wide epidemic with overall attack rate about 28%. "Flattened" age specific attack rate curve resembling that seen in U. S. outbreaks in 1963. |
| | Canada | March | Widespread outbreaks |
| | Chile | June | Most cases reported from Santiago and Concepcion |
| | Argentina | August | Outbreaks reported from Federal Capital area and Misiones, Catamarca, Santa Cruz, and Corrientes provinces. No laboratory confirmation reported. |
| | Panama | September | Influenza A ₂ virus recovered |
| Asia | The Philippines | September-October | Outbreaks in Manila and its suburbs. |
| | Thailand | October-December | Isolates more closely related to 1957 strains than to other 1963 isolates. |

* Data from the weekly Epidemiological Bulletin of the World Health Organization. Influenza A₂ virus was implicated as etiologic agent in one or more outbreaks from each of the countries listed, except where otherwise indicated.

III. LABORATORY REPORT

Rapid Characterization of an Influenza Outbreak

It is often possible to make a rapid presumptive characterization of an outbreak of respiratory disease suspected of being caused by an influenza virus. This is done by comparison of antibody titers determined by the hemagglutination inhibition test using unpaired acute and convalescent serum specimens.

A presumptive determination of type A influenza virus etiology was recently made during an outbreak of respiratory disease reported from the state of Washington on January 31. This was done by collecting sera from a number of carefully selected typical cases whose onset of illness was within the past 48 hours. In addition, sera were collected from a number of typical associated cases whose onset was between 7 and 14 days previously. Sera were transported to this laboratory on February 3. Results of hemagglutination inhibition tests performed on February 4 are given in Table 1.

It is quite evident that influenza A, presumably sub-type A₂, is responsible for this outbreak in that none of the acute sera contained appreciable levels of A₂ virus antibody while most of the convalescent sera contained substantial levels of antibody measurable with all A₂ virus antigens. Type B influenza was excluded on the basis of type B antibody common to both acute and convalescent sera. Virus isolation studies are in progress.

Such data do not replace those obtained in conventional procedures since results are not always as clear cut. However, when possible, early knowledge of the type of influenza virus involved is valuable in considering problems associated with influenza immunization as well as subsequent attempts at virus isolation. Serologic characterization of an influenza outbreak should never be considered a substitute for isolation of the virus involved. Virus recovery still remains the most important function of influenza surveillance laboratories.

Table 1

Titers of Unpaired Sera Determined by Hemagglutination Inhibition Test

| Serum Specimen | Date Collected | Date of Onset | Influenza Virus Antigen | | | | |
|---------------------|----------------|---------------|-------------------------|-----------------|------------------------|-----------------|---------------|
| | | | A2/Japan/305/57 | A2/Japan/170/62 | A2/North Carolina/1/63 | B/Maryland/1/59 | B/Taiwan/2/62 |
| <u>Acute</u> | | | | | | | |
| 1 | 2-3 | 2-2 | *0 | 0 | 0 | 20 | 10 |
| 2 | 2-3 | 2-2 | 0 | 0 | 0 | 20 | 0 |
| 3 | 2-3 | 2-1 | 0 | 0 | 0 | 80 | 0 |
| 4 | 2-3 | 2-1 | 0 | 0 | 0 | 40 | 10 |
| 5 | 2-3 | 2-1 | 0 | 0 | 0 | 40 | 0 |
| 6 | 2-3 | 2-1 | 0 | 0 | 0 | 80 | 20 |
| 7 | 2-3 | 2-1 | 0 | 0 | 0 | 80 | 0 |
| 8 | 2-2 | 2-1 | 0 | 10 | 10 | 80 | 10 |
| <u>Convalescent</u> | | | | | | | |
| 1 | 2-3 | 1-24 | 640 | 640 | 640 | 80 | 10 |
| 2 | 2-3 | 1-22 | 320 | 640 | 320 | 0 | 0 |
| 3 | 2-3 | 1-19 | 20 | 40 | 40 | 10 | 0 |
| 4 | 2-3 | 1-21 | 160 | 160 | 240 | 80 | 10 |
| 5 | 2-3 | 1-19 | 0 | 0 | 0 | 40 | 0 |
| 6 | 2-3 | 1-24 | 40 | 80 | 80 | 160 | 40 |
| 7 | 2-3 | 1-20 | 80 | 160 | 80 | 80 | 0 |
| 8 | 2-3 | 1-20 | 80 | 80 | 80 | 10 | 0 |
| 9 | 2-3 | 1-27 | 20 | 40 | 40 | 80 | 10 |
| 10 | 2-3 | 1-20 | 320 | 480 | 480 | 80 | 0 |
| 11 | 2-3 | 1-24 | 160 | 320 | 320 | 20 | 0 |
| 12 | 2-3 | 1-27 | 40 | 80 | 40 | 20 | 20 |
| 13 | 2-3 | 1-18 | 320 | 640 | 640 | 0 | 0 |
| 14 | 2-3 | 1-17 | 80 | 80 | 80 | 40 | 0 |
| 15 | 2-2 | 1-27 | 20 | 20 | 20 | 160 | 20 |

* Less than 1:10, the initial serum dilution

SPECIAL REPORT: A Study of Vaccine Efficacy in Pregnant Women

(The following report has been abstracted from material kindly provided by Dr. J. F. Hulka, Assistant Professor of Obstetrics and Gynecology, University of Pittsburg, Pittsburgh 13, Pennsylvania.)

Introduction

Pregnant women have long been regarded as a high risk group during influenza epidemics and have therefore been included among those for whom immunization is specifically advised. This recommendation has been based largely on studies of morbidity and mortality among pregnant women during the pandemic of 1918 and 1957. Studies performed during outbreaks of Asian influenza in New York City, subsequent to 1957, however, failed to demonstrate a significant increase in mortality rate associated with pregnancy. ¹ Investigation on the effect of influenza during pregnancy on fetal outcome have likewise yielded conflicting results. ^{2,3,4} The need for including pregnant women in a high risk category, along with the aged and chronically ill, has therefore been questioned in recent years. The most recent recommendations of the Surgeon General's Advisory Committee on Influenza still include pregnant women among those "... at greatest risk of death or severe morbidity should they acquire the disease," but a qualifying phrase is added, indicating that the evidence is less clear-cut in this group than in other "high risk" populations.

The question of the effectiveness of vaccine in preventing disease among pregnant women has largely been neglected amid the controversy over their high risk status. The present study addresses itself to this specific question.

Materials and Methods

All ward service patients presenting at the ante partum and gynecology clinics of the Magee-Women's Hospital in Pittsburgh, from October 1962 through January 1963, were offered participation in the study. A total of 720 subjects volunteered during this period. Of these, 544 were pregnant and 176 non-pregnant. Although random assignment of subjects to vaccine and placebo groups was planned originally, this was not possible due to technical delays in preparation of the latter product, which was not available until December. Consequently, all subjects entering the study during October and November received vaccine, and those entering during December and January received a saline placebo.

All subjects designated as immunized received 1 ml. of commercial polyvalent vaccine subcutaneously at their first clinic visit, followed by a second 1 ml. dose one month later. Control subjects received a single 1 ml. dose of saline placebo at their first visit.

All subjects were questioned during subsequent clinic visits with regard to occurrence of local pain and/or malaise in the first 2-3 days following inoculation. They were also asked whether or not they "took to bed" because of the latter symptom. Paired sera were obtained on all immunized subjects, the first sample having been drawn immediately prior to their first vaccine dose, and the second sample one month after the second dose. A single blood sample was obtained from control subjects just prior to their inoculation. The composition of the study population is summarized in Table 1.

Participating subjects were surveyed with postcard questionnaires in April 1963, after the winter epidemic had subsided. Subjects were asked to indicate whether or not they had experienced "the flu with fever" at any time during the winter. Subjects who failed to return the card and those who answered affirmatively were telephoned, the details of any illness discussed, and a judgment made as to whether or not this was a febrile respiratory disease. Also, the number of days in bed due to the illness was recorded.

A high drop-out rate, particularly among control subjects, necessitated the enlargement of this group to include unimmunized subjects who did not receive placebo injections. All patients seen at the ante partum and gynecology clinics during the month of April who had not been part of the original study population and who had not received flu shots privately, were surveyed retrospectively for incidence of "flu with fever." Illness data on this group were combined with those of the original control population in calculating attack rates.

The prevalence of influenza virus in the community was followed by weekly analysis of pooled sera obtained from representative populations. Beginning in January, pools of 35 sera were obtained each week from patients registering with the ante partum clinic and influenza antibody titer determined for each pool. Similar observations were made in a non-pregnant population through analysis of serum pools obtained weekly in V.D. Clinics and jails throughout Allegheny County. These populations represented the same age groups and socio-economic strata as those which characterized the study population, and for the most part, came from the same district of the city that the study subjects came from. Sera obtained from study subjects were analyzed individually to evaluate vaccine induced antibody

response and were also grouped into pools of 35, collected weekly, in order to estimate antibody prevalence in the community during the early months of the study period. C. F. antibody titers were measured using A₂ Japan/305/63 antigen isolated during the outbreak in Allegheny County.

III. Results

A. Evidence of Asian Influenza Epidemic in Allegheny County.

1. Viral Identification

A virus antigenically related to the A₂ Japan/305/57 Prototype strain was recovered from a patient in an Allegheny County Hospital on February 10, 1963. This virus served as the antigen in all serologic studies reported here. Several additional viral isolations were obtained later in the month.

2. Serologic Data

Pooled sera from non-immunized pregnant and non-pregnant women were analyzed with respect to antibody titers against A₂ Japan/305/63 influenza antigen throughout the winter months. These titers are shown in Figures 1 and 2. Titers in the non-immunized population showed a slight rise as early as November, and reached peak levels in February for both pregnant and non-pregnant women.

3. Mortality in the county due to respiratory disease increased markedly in mid-February, and reached a six-year high during the week ending March 8. No maternal mortalities were reported.

4. Absenteeism in schools and industry increased markedly in the county during February and March, subsiding to normal levels by April.

B. Vaccine Reactions

1. Local. The incidence of local pain at the injection site in the various study groups is summarized in Table 2. Eighty-three percent of subjects receiving influenza vaccine reported some local pain as compared to 40% in the placebo group. It can be estimated therefore that the true incidence of local pain attributable to the vaccine was approximately 83 minus 40, or 43%.

2. Systemic. The incidence of malaise and number of days spent in bed due to this symptom, following inoculation, is given in Table 3. Whereas 20% of immunized subjects reported some systemic reaction, less than 2% of those given placebos reported similar symptoms. Fifteen percent of immunized subjects took to bed because of the reaction, accounting for a total of 108 bed days. Dividing this figure by the total number of subjects receiving vaccine (269), one obtains a rate of 0.4 days in bed per subject "at risk" of incurring a vaccine reaction.

C. Incidence of Influenza-like Disease During the Winter Months.

The incidence of influenza-like disease in the various study groups is given in Table 4.

The overall attack rates for immunized and unimmunized subjects were 15% and 23% respectively, giving an overall effectiveness ratio of 35%. Illness appeared to be somewhat less severe among immunized subjects, who experienced 0.38 bed-days per subject at risk, as compared to 1.05 bed-days per subject in the unimmunized group. Incidence and severity of disease appeared to be diminished somewhat among pregnant women, independent of their vaccine status. In the immunized group, pregnant women experienced an attack rate of 11% as compared to 22% among the non-pregnant. In the unimmunized group the comparable rates were 20% and 26% respectively. Vaccine protectiveness appeared to be enhanced in the pregnant group where a 44% effectiveness ratio was observed, as compared to a 14% ratio among non-pregnant subjects. No explanation for the apparent influence of pregnancy on disease susceptibility and responsiveness to vaccine is apparent from these data.

The combined effects of vaccine reactions and illness in producing morbidity, as measured by days in bed per subject at risk during the study period is given in Table 5. In the immunized group, subjects spent an average of 0.78 days in bed due to the combined effects of vaccine reactions and influenza-like illness, whereas in the unimmunized group the figure was only slightly higher - 1.089.

Table 1

Composition of Initial Study Population

| | <u>Pregnant</u> | <u>Non-Pregnant</u> | <u>Total</u> |
|------------------|-----------------|---------------------|--------------|
| <u>Immunized</u> | 363 | 138 | 501 |
| <u>Control</u> | 181 | 38 | 219 |
| <u>Total</u> | 544 | 176 | 720 |

Figure 1

C.F. ANTIBODY TITERS AGAINST TYPE A₂ INFLUENZA ANTIGEN
IN SERUM POOLS FROM PREGNANT PATIENTS

MAGEE - WOMENS HOSPITAL, NOVEMBER 1962 - MARCH 1963

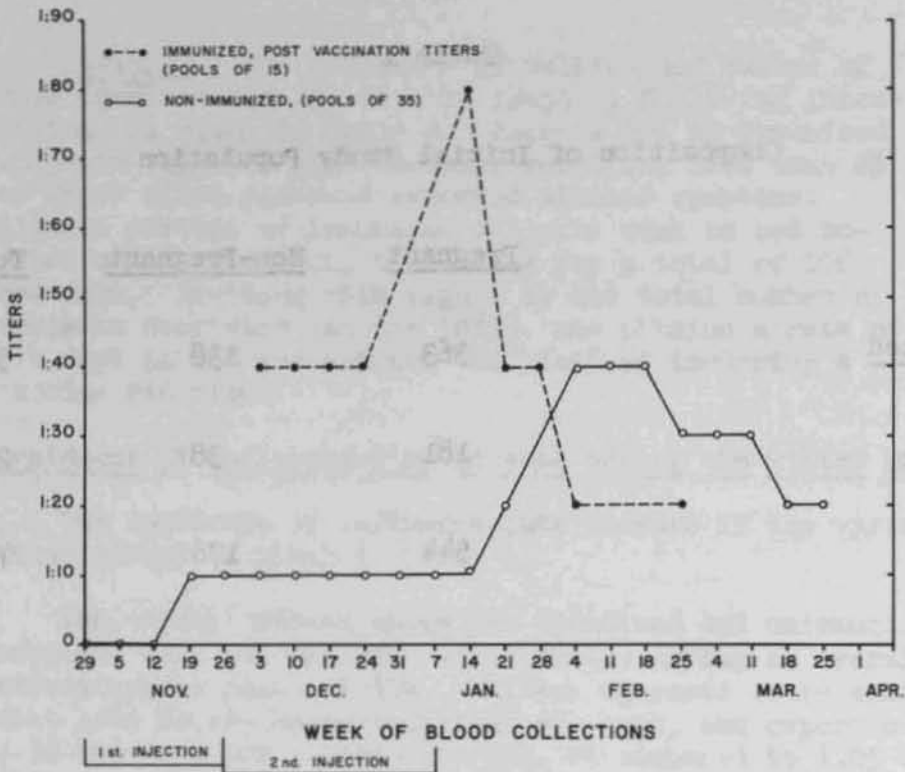


Figure 2

C.F. ANTIBODY TITERS AGAINST TYPE A₂ INFLUENZA ANTIGEN
IN SERUM POOLS FROM NON-PREGNANT PATIENTS

MAGEE - WOMENS HOSPITAL, NOVEMBER 1962 - MARCH 1963

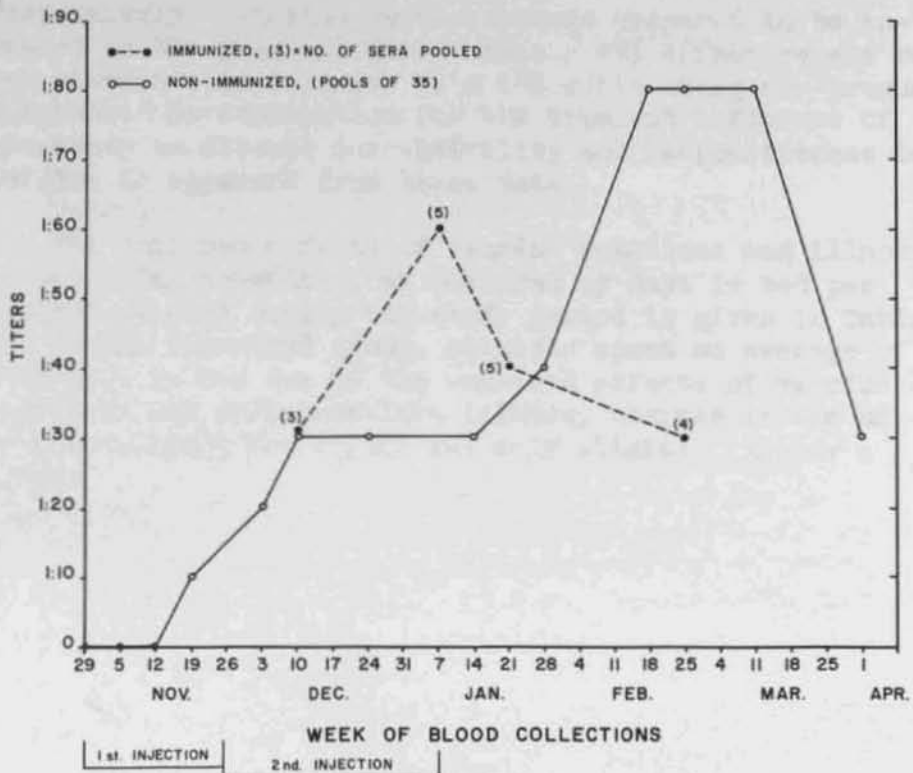


Table 2

Incidence of Local Pain at Injection Site

| | Vaccine Group | | | Placebo Group | | |
|-------------------|---------------|--------------|-------|---------------|--------------|-------|
| | Pregnant | Non-pregnant | Total | Pregnant | Non-Pregnant | Total |
| Number reporting | 225 | 44 | 269 | 95 | 25 | 120 |
| Number with pain | 187 | 37 | 224 | 39 | 9 | 48 |
| Percent with pain | 83% | 84% | 83% | 41% | 36% | 40% |

Table 3

Incidence and Severity of Malaise Following Inoculation

| | Vaccine Group | | | Placebo Group | | |
|---------------------------------|---------------|--------------|----------|---------------|--------------|----------|
| | Pregnant | Non-pregnant | Total | Pregnant | Non-pregnant | Total |
| Number patients answering | 225 | 44 | 269 | 104 | 25 | 129 |
| Number with malaise | 42 (19%) | 13 (30%) | 55 (20%) | 2 (1.9%) | 0 | 2 (1.6%) |
| Number requiring bed rest | 32 (14%) | 9 (20%) | 41 (15%) | 1 (1.0%) | 0 | 1 (0.8%) |
| Total bed days | 93 | 15 | 108 | 5 | 0 | 5 |
| Bed days per subject inoculated | 0.41 | 0.34 | 0.40 | 0.048 | 0 | 0.039 |

Table 4

Incidence of Influenza-like Disease Among Study Subjects

| | Immunized | | | Unimmunized* | | |
|------------------------------------|-----------|--------------|-------|--------------|--------------|-------|
| | Pregnant | Non-pregnant | Total | Pregnant | Non-pregnant | Total |
| Number responding | 214 | 112 | 326 | 181 | 166 | 347 |
| Number with influenza-like illness | 24 | 25 | 49 | 36 | 43 | 79 |
| Attack rate | 11% | 22% | 15% | 20% | 26% | 23% |
| Total bed days | 54 | 69 | 123 | 137 | 228 | 365 |
| Bed days per subject | 0.25 | 0.63 | 0.38 | 0.75 | 1.38 | 1.05 |

* Includes subjects given saline placebo plus unvaccinated controls.

Table 5

Bed Days Per Subject at Risk During the Study Period

| | Immunized | | | Unimmunized | | |
|--------------------------------|-----------|--------------|-------|-------------|--------------|-------|
| | Pregnant | Non-pregnant | Total | Pregnant | Non-pregnant | Total |
| Bed days from vaccine reaction | 0.41 | 0.34 | 0.40 | 0.048 | 0.0 | 0.039 |
| Bed days from illness | 0.25 | 0.63 | 0.38 | 0.75 | 1.38 | 1.05 |
| Total bed days | 0.66 | 0.97 | 0.78 | 0.798 | 1.38 | 1.089 |

REFERENCES

1. Widelock, D. et al.: Influenza, Pregnancy, and Fetal Outcome. Public Health Reports 78:1, January 1963.
2. Campbell, W. A. B.: Influenza in Early Pregnancy. Effects on the Foetus. Lancet 1:173, 1953.
3. Coffey, V. P., and Jessop, W. J. F.: Maternal Influenza and Congenital Deformities: A Prospective Study. Lancet 2:935, 1959.
4. Abramovitz, L. J.; The Effect of Asian Influenza on Pregnancy. South African Medical Journal 32:1155, 1958.

VI. WEEKLY PNEUMONIA AND INFLUENZA DEATHS

During the late summer and fall months, pneumonia-influenza deaths were generally below or at expected weekly levels. During the first three weeks of January, the number of deaths increased to slightly above the epidemic threshold, rising to a marked elevation during the second week and has since shown a steady week-to-week decline.

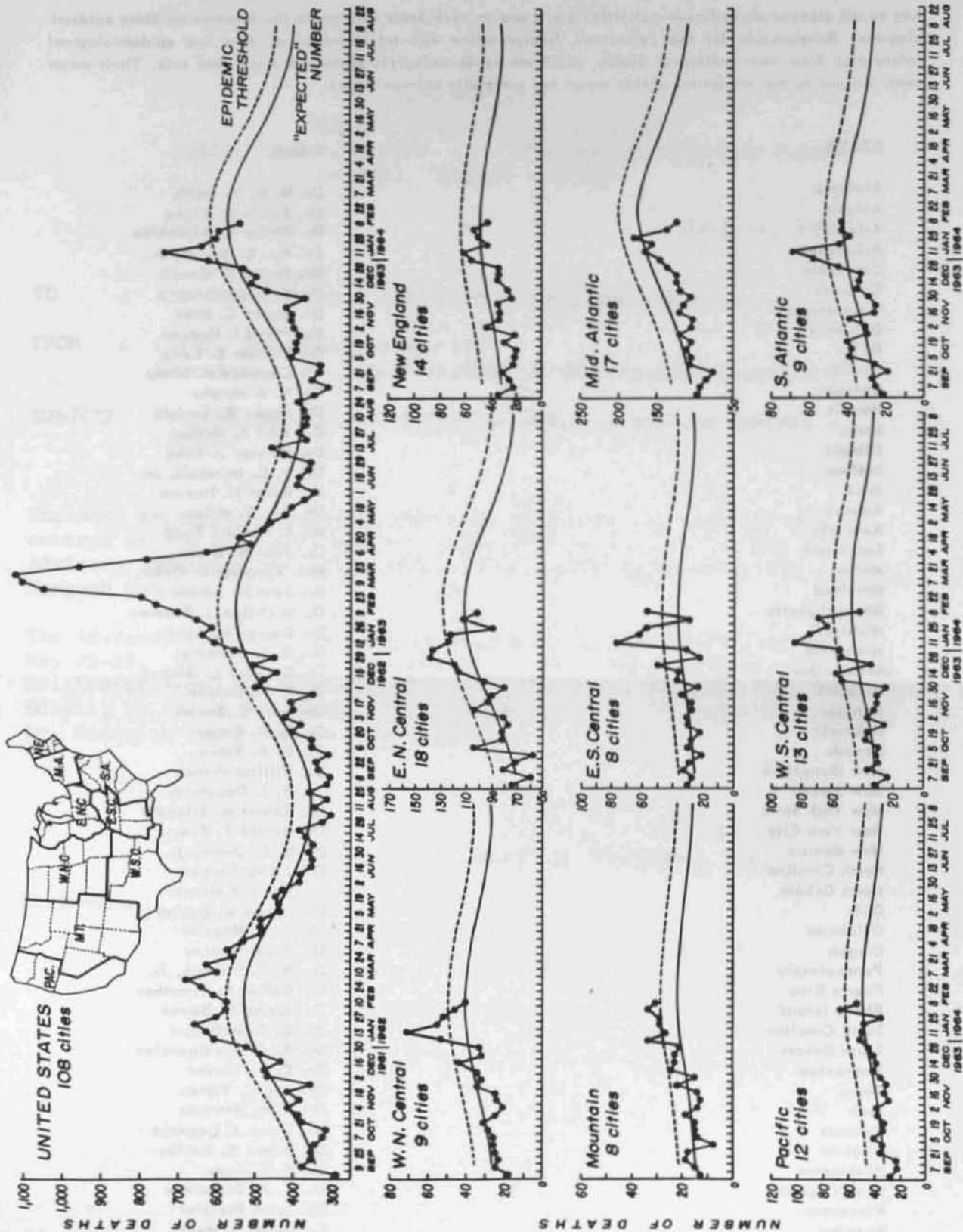
The increased number of pneumonia-influenza deaths during the early weeks of January included end of the year "close-outs" on the part of several cities which advised that delayed 1963 death certificates were added to the reports for these weeks.

During the current week (February 8), the number of influenza-pneumonia deaths were below or at expected levels except for the East South Central States which showed an elevation above the epidemic threshold following a week in which the number had fallen to below the expected; and the Mountain States Division which has now reported numbers above the epidemic threshold for four consecutive weeks. This elevation reflects small increases reported in succeeding weeks by the cities in the Division, but with no concentration either by week or by city.

The table below shows observed and expected numbers for the past four weeks:

| | Week Ending | | | | 4-Week Total | Weekly Average |
|----------|-------------|------|-----|-----|-----------------|-------------------|
| | 1/18 | 1/25 | 2/1 | 2/8 | | |
| Observed | 636 | 598 | 590 | 534 | 2,358 | 589 |
| Expected | 560 | 564 | 566 | 567 | 2,257 | 564 |
| Excess | 76 | 34 | 24 | -33 | 101 | 25 |

WEEKLY PNEUMONIA AND INFLUENZA DEATHS



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 epidemiological 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.

| STATE | NAME |
|----------------|-------------------------|
| Alabama | Dr. W. H. Y. Smith |
| Alaska | Dr. Edwin O. Wicks |
| Arizona | Dr. Philip M. Hotchkiss |
| Arkansas | Dr. Wm. L. Bunch, Jr. |
| California | Dr. Philip K. Condit |
| Colorado | Dr. C. S. Mollohan |
| Connecticut | Dr. James C. Hart |
| Delaware | Dr. Floyd I. Hudson |
| D. C. | Dr. William E. Long |
| Florida | Dr. Clarence M. Sharp |
| Georgia | Dr. W. J. Murphy |
| Hawaii | Dr. James R. Enright |
| Idaho | Dr. John A. Mather |
| Illinois | Dr. Norman J. Rose |
| Indiana | Dr. A. L. Marshall, Jr. |
| Iowa | Dr. Ralph H. Heeren |
| Kansas | Dr. Don E. Wilcox |
| Kentucky | Mr. J. Clifford Todd |
| Louisiana | Dr. John M. Bruce |
| Maine | Mrs. Margaret H. Oakes |
| Maryland | Dr. John H. Janney |
| Massachusetts | Dr. Nicholas J. Fiumara |
| Michigan | Dr. George H. Agate |
| Minnesota | Dr. D. S. Fleming |
| Mississippi | Dr. Durward L. Blakey |
| Missouri | Dr. E. A. Belden |
| Montana | Dr. Mary E. Soules |
| Nebraska | Dr. E. A. Rogers |
| Nevada | Dr. B. A. Winne |
| New Hampshire | Dr. William Prince |
| New Jersey | Dr. W. J. Dougherty |
| New York State | Dr. Robert M. Albrecht |
| New York City | Dr. Harold T. Fuerst |
| New Mexico | Dr. H. G. Doran, Jr. |
| North Carolina | Dr. Jacob Koomen |
| North Dakota | Mr. Kenneth Mosser |
| Ohio | Dr. Harold A. Decker |
| Oklahoma | Dr. F. R. Hassler |
| Oregon | Dr. Grant Skinner |
| Pennsylvania | Dr. W. D. Schrack, Jr. |
| Puerto Rico | Dr. Rafael A. Timothee |
| Rhode Island | Dr. James E. Bowes |
| South Carolina | Dr. G. E. McDaniel |
| South Dakota | Dr. G. J. Van Heuvelen |
| Tennessee | Dr. C. B. Tucker |
| Texas | Dr. Van C. Tipton |
| Utah | Dr. Elton Newman |
| Vermont | Dr. Linus J. Leavens |
| Virginia | Dr. James B. Kenley |
| Washington | Dr. E. A. Ager |
| West Virginia | Dr. L. A. Dickerson |
| Wisconsin | Dr. Josef Preizler |
| Wyoming | Dr. Helen A. Moore |

CHIEF, SURVEILLANCE SECTION 10c 1-7
46
6 64
EPIDEMIOLOGY BRANCH

DEPARTMENT OF
HEALTH, EDUCATION AND WELFARE
Public Health Service Communicable Disease Center
Atlanta, Georgia 30333

July 22, 1964

TO : All Subscribers - Influenza Surveillance Reports

FROM : Chief, Surveillance Section
Secretary, Advisory Committee on Immunization Practice

SUBJECT: Recommendations for Influenza Immunization and Control -
1964-65

Enclosed are recommendations regarding influenza immunization and control in the civilian population for 1964-65 prepared by the Advisory Committee on Immunization Practice and approved by the Surgeon General.

The Advisory Committee on Immunization Practice met in Atlanta on May 25-26. The Committee is composed of: Dr. James Goddard, Chairman; Dr. Ernest Ager, Dr. Gordon Brown, Dr. Alice Chenoweth, Dr. Geoffrey Edsall, Dr. D. A. Henderson, Dr. David Karzon, Dr. Theodore Montgomery, Dr. Roderick Murray and Dr. Paul Wehrle.


Donald A. Henderson, M.D.

Enclosure

1964-65 Recommendations for Influenza Immunization and Control
 in the Civilian Population

Advisory Committee on Immunization Practice

1. Expected Occurrence of Influenza During 1964-65

a. Influenza A₂

Widespread outbreaks of influenza A₂ occurred in 1962-63 in most areas of the United States except for the West Coast. During 1963-64, influenza A₂ was widely prevalent along the West Coast; limited outbreaks occurred also in Southern Minnesota. Although influenza A commonly occurs in two to three year cycles, it would seem, in the face of the extensive 1962-1963 outbreak and the West Coast involvement in 1963-64, that a major outbreak would be unlikely this year. As in other inter-epidemic years, however, focal outbreaks might be anticipated.

b. Influenza B

A nation-wide epidemic of influenza B was last observed in the United States during 1961-62. During 1963-64, influenza B in epidemic proportions was observed in Japan. The strain involved was related to previous strains isolated in the United States and was unrelated to the sharply modified B strain recovered in Taiwan in 1962 during an institutional outbreak. This strain has not since been isolated. Possibilities that the Japanese influenza B epidemics might herald outbreaks on the West Coast during the coming year or that the Taiwan B strain might reappear cannot be completely dismissed. It seems

unlikely, however, in view of the relatively rare occurrence of major epidemics of influenza B, that the United States would experience more than scattered, limited outbreaks of influenza B during 1964-65.

2. Vaccine Efficacy

Since its introduction, influenza vaccine has been shown, in repeated control trials, to confer substantial protection (60 to 80 percent) against the epidemic disease. Notable exceptions were observed when major shifts occurred in the antigenic composition of the virus (1947 and 1957) and more recently, when more gradual antigenic changes within the A₂ family of viruses have evolved, as occurred between 1957 and 1962. It would appear that, in general, the greater the similarity between viruses incorporated in the vaccine and naturally occurring strains, the better the degree of protection. Since influenza viruses are constantly undergoing antigenic change, the incorporation of recent isolates into the vaccine has merit. The incorporation of recent A₂ and B isolates in the 1963-64 vaccine and the increase in their concentration during 1964-65 should result in a vaccine capable of conferring substantial protection in 1964-65. There has yet, however, been no opportunity to evaluate the newly constituted vaccine under conditions of a natural challenge.

That influenza vaccine prevents mortality from influenza, particularly among the aged and chronically ill, is based upon inference. It is presumed that vaccine protection demonstrated in studies among younger persons is similar among the aged and

chronically ill, the group at particular risk of death should they acquire the disease. It is further assumed that such protection against clinical disease serves to protect them also against mortality associated with epidemic influenza. No studies, however, have yet been reported which measure the efficacy of the vaccine in prevention of influenza-associated mortality.

3. High Risk Groups

Immunization should be considered and generally recommended for persons in groups who experience high mortality from epidemic influenza. Such groups include:

a) Persons at all ages who suffer from chronic debilitating disease, e.g., chronic cardiovascular, pulmonary, renal or metabolic disorders; in particular:

1. Patients with rheumatic heart disease, especially those with mitral stenosis.
2. Patients with other cardiovascular disorders such as arteriosclerotic heart disease and hypertension, especially those with evidence of frank or incipient cardiac insufficiency.
3. Patients with chronic bronchopulmonary disease, for example, chronic asthma, chronic bronchitis, bronchiectasis, pulmonary fibrosis, pulmonary emphysema, pulmonary tuberculosis.
4. Patients with diabetes mellitus and Addison's disease.

b) Persons in older age groups. During three successive recent epidemics a moderate increase in mortality has been demonstrated

among persons over 45 years and a marked increase among those over 65 years of age.

c) Pregnant women - It is to be noted that some increased mortality was observed among pregnant women during the 1957-58 influenza A₂ epidemic both in this country and abroad. It has not, however, been demonstrated in subsequent years.

4. Time of Vaccination

Vaccination should begin as soon as practicable after September 1 and ideally should be completed by mid-December. In any case a two week delay in the development of antibodies may be expected and it is important, therefore, that immunization be carried out before influenza occurs in the immediate area.

5. Vaccine Composition

Recent isolates of both the A and B strains demonstrate a continuing alteration in antigenic structure. Accordingly, it is noted that more recent strains of both the influenza A₂ and B strains have been added in increased amounts. The antigenic composition of the vaccine for the 1964-65 season is as follows:

| <u>Type</u> | <u>Strain</u> | <u>CCA Units per cc.</u> |
|----------------|----------------|--------------------------|
| A | PR8 | 100 |
| A ₁ | Ann Arbor 1/57 | 100 |
| A ₂ | Japan 170/62 | 200 |
| B | Maryland 1/59 | <u>200</u> |
| | | 600 |

6. Dose and Schedule of Vaccination by Age (for those for whom immunization is recommended).

- a) Primary Series - Those not vaccinated since July 1963 should receive a subcutaneous dose of polyvalent vaccine followed by a second dose about two months later. It is to be pointed out, however, that even a single dose can afford significant protection; a second dose given as early as two weeks following the first will enhance the protection.
- b) Revaccination - Those revaccinated since July 1963 need receive but a single dose of the vaccine.
- c) Dosage
1. Adults and children over 12 - 1.0 ml. (600 CCA units)
 2. Children 6 to 12 years* - 0.5 ml. (300 CCA units)
 3. Children 3 months to 5 years*
- Primary series should consist of 0.1-0.2 ml. (60-120 CCA units) of vaccine given subcutaneously on two occasions separated by one to two weeks followed by a third dose of 0.1-0.2 ml. about two months later. For those previously vaccinated, a single booster of 0.1-0.2 ml. is recommended.
- * Since febrile reactions in this age group are common following influenza vaccination, an antipyretic may be indicated.
- d) Contraindication - Since the vaccine viruses are produced in eggs, the vaccine should not be administered to those who are hypersensitive to eggs or egg products.

7. Future Studies

Constant vigilance, nationally and internationally, is important if early detection of strains showing a marked antigenic shift is to be accomplished. Should such strains be detected, it is important that some isolations be made in systems compatible with subsequent vaccine production. Such systems would include cercopithecus monkey kidney tissue culture or eggs.

Controlled field studies of vaccine efficacy among elderly persons and other high risk groups are of vital importance. As previously noted, evidence that influenza-associated mortality is prevented among such groups by vaccination has not been directly documented. Since use of the vaccine is not without costs, the protective value of the procedure demands further documentation.