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COMMUNICABLE DISEASE CENTER

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, 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.

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I. SUMMARY

No laboratory confirmed outbreaks of influenza have been reported from any of the 50 States during the fall months of 1962 thus far. A number of reports dealing with relatively restricted A₂ outbreaks occurring during the spring of 1962 have been received, however, and are given here in abstract form. Also described are two outbreaks which have occurred since the last issue of the Influenza Surveillance Report appeared (May 31, 1962) in which the influenza B virus has been implicated.

In anticipation of significant type A₂ outbreaks during the 1962-63 season, the Influenza Surveillance Unit has undertaken a series of vaccine field studies in collaboration with a number of State and local health departments and the Arctic Health Research Center. These investigations are aimed at assessing the importance of such variables as antigenic strength, dosage schedule, type of vaccine (monovalent vs. polyvalent) and route of administration in determining vaccine efficacy--as measured by antibody response and protection in a natural challenge setting. Background information on these studies, a brief description of their design, and a list of participating investigators are given in this report.

Two studies contributing to the problem of the possible role of influenza vaccine in the production of ABO hemolytic disease of the newborn are reported together with a background description of the circumstances of the recent controversy.

In conducting the influenza surveillance program for the 1962-63 influenza season, a system of outbreak reporting similar to that used during the 1957 A_2 outbreaks will be utilized. A description of the surveillance program and examples of the forms currently being used have been included.

The report ends with a summary of the current weekly pneumonia and influenza deaths for the 108 cities.

II. REPORT OF OUTBREAKS - APRIL TO PRESENT

ASIAN INFLUENZA:

Minnesota

Eighty-six cases of relatively mild respiratory disease occurred among patients and employees at the 1014 bed Minneapolis Veterans Administration Hospital during the period May 8 through May 19, 1962. The illness was characterized by temperature elevations to approximately 100-101° F., mild sore throat and malaise. The outbreak was accompanied by an increased incidence of clinically diagnosed pneumonia among the patients. There was, however, no associated increase in crude death rate for the hospital as a whole. Although some hospital employees were affected, there was no obvious involvement of the surrounding community of Minneapolis.

Laboratory confirmation was provided by the Division of Medical Laboratories of the Minnesota Department of Health. Significant titer rises (fourfold or greater) of H. I. antibody to the Asian (Japan 305/57) strain were demonstrated in three of six sets of paired sera. Type A₂ virus was recovered from one of eight throat washings. Other serologic studies including cold agglutinins, and antibody determinations for influenza B, psittacosis and adenovirus infection were consistently negative.

(Herbert P. Reinhardt, Jr., M.D., E.I.S. Officer assigned to Oklahoma State Department of Health; Dean Fleming, M.D., Director of Disease Prevention and Control, Minnesota Department of Health; and Wendall Hall, M.D., Chief of Medical Service, Minneapolis Veterans Administration Hospital).

American Samoa

An outbreak of clinically typical influenza marked by sudden onset, headache, generalized myalgia, non-productive cough, and fever of 102-105° F.lasting 3-4 days occurred on the island of American Samoa in late May and early June 1962. All parts of the island were affected. Retrospective analysis of hospital admissions and outpatient visits and a door to door survey of one village yielded similar "epidemic curves", indicating peak incidence during the two week period from May 20 through June 2. Table 1 gives overall and age specific attack rates from a survey undertaken in two villages on the island. There was no associated increase in death rate above seasonal expectancy for the island as a whole.

Table 1

Age Specific Attack Rates, Influenza Survey American Samoa, 1962

Age	Villages of Pago Pago and Leone						
Group	Population (1960 Census)	Cases		tack Rai (Percent			
0-4	427	137		32	ę . . :		
5-14	736	s – 123 j gragista a 123 j		17			
15-24	491	68		14			
25-34	267	38	1. J. M. H.	14			
35-44	246	47	· · · · · · · · · · · · · · · · · · ·	19			
45-54	132	38	12 J	29			
55 /	144	47		33			
Total	2443	498	an an tha an	20			

Laboratory study of this outbreak was performed by the Respirovirus Unit, Communicable Disease Center. Eleven sets of paired sera were obtained from patients who were first seen near the end of the acute phase of their illness. (The epidemic was very near termination by the time the required personnel had arrived on the island to initiate epidemiologic investigation and no "fresher" cases were available). Two patients demonstrated significant (greater than fourfold) increases of H.I. antibody titer to the Asian (Japan 305/57) strain. Four others showed stable high titers (320-640) on acute and convalescent sera, suggesting recent infection with the Asian strain. Throat washings obtained from seven cases were all negative. (These were of necessity obtained relatively late in the course of the illness and were subjected to known fluctuations in temperature during storage and shipment due to the exigencies of local field conditions).

Serologic determinations for influenza B, and para-influenza types 1, 2, and 3, yielded consistently negative results.

(Dorothy Calafiore, R.N., Nurse Epidemiologist, CDC; C. Weldon, M.D., Director of Medical Services, Hospital of American Samoa, Pago Pago, American Samoa).

Illinois

Influenza A_2 virus was isolated from a 20 month old female infant hospitalized during mid-April for presumed chemical pneumonitis following exposure to battery powder. On admission, the patient was febrile and appeared to be having severe respiratory distress. Admission chest films revealed pulmonary ateleclasis. The patient responded well to tracheal suction and other supportive measures, and made a complete recovery. Acute and convalescent sera showed an H.I. titer rise of 1:8 to 1:64 when tested against the A_2 virus. Several members of the patient's family had relatively mild respiratory illnesses at about this time, but there was no evidence of any more extensive outbreak involving the surrounding community.

(Dorothy Hamre, Ph.D., John J. Procknow, M.D., Department of Medicine, The University of Chicago, Chicago, Illinois).

Brazil and Indonesia

A2 isolates from cases of sporadic respiratory illness have been received from Sao Paulo, Brazil and Bandung, Indonesia. Each was obtained from an isolated case seen during the spring of 1962. No outbreaks of influenza-like disease were reported from either area. These isolates were received and confirmed by the Respirovirus Unit of the Communicable Disease Center.

(Dr. Luiz Augusto Ribiero do Valle, Head, Virus Section, Institute Adolf Lutz, Sao Paulo, Brazil; Lo Siauw Goen, M.D., Acting Director, Pasteur's Institute, Bandung, Indonesia).

INFLUENZA B:

Canal Zone

A marked increase in reported cases of upper respiratory infection during the months of May and June 1962 prompted a laboratory investigation of "typical" cases among residents of Paraiso, a non-United States citizen Canal Zone community. The clinical syndrome was characterized by fever (101-104° F.), malaise, myalgia, sore throat, headache and cough, lasting in some cases as long as 10-14 days. The Middle America Research Unit reported isolation of "presumptive Influenza B" virus from five patients residing in Paraiso. Further epidemiologic and laboratory data are now being awaited.

(S. B. Clark, M.D., Chief, Division of Preventive Medicine and Quarantine, Canal Zone Government, Balboa Heights, Canal Zone).

Taiwan

Influenza B virus was recovered from throat washings of two patients residing on Taiwan who became ill in October 1962. Further clinical and epidemiologic data are not as yet available. Follow-up information will appear in subsequent influenza surveillance reports as it is obtained.

(Commander Benjamin F. Gundelfinger, MC, USN, Head, Communicable Disease Branch, Preventive Medicine Division, Bureau of Medicine and Surgery, Department of the Navy, Washington 25, D. C.).

III. VACCINE EVALUATION STUDIES

1. BACKGROUND:

Numerous studies of the immunoprophylaxis of Asian influenza have appeared since 1957 when this strain was first recognized in epidemic form throughout the world. A cooperative field trial at four military training camps was carried out in 1957 under the auspices of the Commission on Influenza of the Armed Forces Epidemiological Board. These studies, employing vaccines of several antigenic strengths, revealed effectiveness ratios varying between 57 and 77 percent. These trials also showed what the authors regarded as a significant difference in effectiveness between vaccines containing 200 CCA units/ml. and those of 400 CCA units/ml. strength--the latter affording greater protection. 1/ Other investigators, however, working with military and adult prison populations, have reported no difference in effectiveness between vaccines containing 200 CCA units/ml. and those containing 500 and 800 CCA units/m1. 2/,3/

The current recommendation of the Surgeon General's Advisory Committee on Influenza calls for two doses of polyvalent vaccine, each containing 200 CCA units of type A_2 antigen, spaced about two months apart. "Two-dose" schedules have been recommended largely on the basis of antibody studies

performed during the 1957-58 outbreaks. Vaccinees at that time, having had insignificant prior experience with A2 antigens, generally showed poor responses to a single dose of 200 CCA units. A second dose of 200 CCA units induced a satisfactory recall response in a large percentage of subjects. 4/ Similar studies during 1959, however, demonstrated maximal antibody responses 2-4 weeks after the initial injection with relatively little increment in antibody level observed after a second dose. $5^{1/2}$ These findings were thought to reflect this group's prior natural experience with A2 antigens in 1957-58--their response to the first vaccine dose being anamnestic in type. Indeed, prevaccination antibody titers to the Asian strain were measurable in a high percentage of these subjects. It is probable then that the advisability of a "two-dose" vaccine schedule is, in part at least, a function of the prior antigenic experience of the population in question. The extent of this experience may in turn be a function of where, in point of time, one stands relative to the most recent major "antigenic shift" of the virus. Also, it should be emphasized that the studies referred to above were limited to observations on antibody response and did not compare actual protectiveness afforded by each type of schedule.

The commercially distributed vaccine in use today is a polyvalent preparation consisting of four antigenic strains. Such a product is employed largely in order to provide to the vaccinee a wide spectrum of antigenic experience which will presumably be useful to him in subsequent encounters with the natural disease as well as in subsequent immunizations. There is evidence from previous studies $\frac{5}{1}$ that the strain specific antibody response to a given amount of A2 antigen may vary depending on the number and variety of other antigens administered along with it. Specifically, Jensen et al. $\frac{5}{1000}$ have asserted that higher antibody levels are obtained in response to a dose of 400 CCA units of A₂ antigen when it is given as part of a 6-strain polyvalent vaccine than when it is given as part of a 4-strain preparation. (Total CCA units were the same for both vaccines). On the other hand, Hilleman et al. $\frac{11}{}$ have indicated that antibody response to 160 CCA units of A/Japan/305/57 antigen in combination with 1000 CCA units of polyvalent material containing 200 CCA units each of A/Swine/ 1976/30, APR8/34. A¹PR/301/54, B/Lee/40, and B/Great Lakes/ 1739/54, given in a two-dose schedule, gave no greater A2 H.I. antibody response than when the A2 antigen was given alone in a two-dose schedule. The studies described below will attempt to ascertain whether significant differences in vaccine protectiveness exist when monovalent and polyvalent vaccines with identical A2 antigenic components are administered to comparable populations.

Controversy has also surrounded the preferred route of administration of influenza vaccine. Intradermal and subcutaneous routes of administration were compared in an early study of Boger and Liu $\frac{6}{}$ employing volunteers from an elderly population. Only 8 of 22 subjects obtained "adequate" antibody response from 0.1 cc. of vaccine intradermally, as compared with 22 of 28 who developed "adequate" titers from 1 ml. of the same vaccine given subcutaneously. In the fall of 1957, Kirkham 2' in an Iowa community population administered monovalent A2 vaccine in 200 CCA units/ml. concentration in single dosages of 20 or 40 units intradermally and 200 units subcutaneously. In both intradermal and subcutaneous groups, influenza attack rates approximated 10% as opposed to 45% in the group receiving no vaccine. No placebo group was included in this study. Sanger 3/, employing monovalent A2 vaccine containing 200 CCA units per ml., found entirely comparable antibody titers among subjects receiving 1 cc. subcutaneously and 0.1 cc. intradermally. In a study conducted in February 1958 on Navy recruits, Stille, et al. 4/ found that antibody response to a single injection was better by the intradermal route until the dose of inoculation was increased to 5 CCA units intradermally as compared with 50 CCA units subcutaneously. Above these levels, response to subcutaneous injection seemed Buebendorf et al. $\frac{5}{}$ noted only 3 cases among 50 better. medical students vaccinated intradermally with two doses of monovalent A2 vaccine containing 200 CCA units/ml. given in 0.1 ml. doses, separated by a two-week interval. This compared with 20 cases in a comparable control group of 50 students who were unvaccinated. Hilleman et al. 6/, in studying a military population, found comparable antibody responses to 200 CCA units/ml. monovalent vaccine given in two doses when given as 1 ml. subcutaneously and when given as 0.1 ml. intradermally. Candler et al. 7/ also noted adequate antibody levels following two doses of intradermal vaccine given two weeks apart in an industrial population.

The often conflicting conclusions of investigators who have compared intradermal and subcutaneous vaccination are perhaps explained by differences in age and antigenic background of the populations studied and by definite differences in experimental design among the studies, making them not strictly comparable.

It is apparent from the above discussion that a number of unresolved issues remain with respect to the optimal vaccine regimen. The present investigations are directed at some of these unanswered questions. The design of these studies is described briefly in the paragraphs below:

2. STUDY PLAN:

The study population consists of junior and senior high school students drawn from six geographic areas. The total population of approximately 6500 is divided into two distinct study groups as follows:

> <u>Study Group I</u> consists of approximately 4500 subjects in eight schools. This investigation is concerned with the effect of varying antigenic strength, dosage schedule, and type of vaccine (monovalent vs. polyvalent) on vaccine effectiveness--using the <u>subcutaneous route</u> of <u>administration only</u>. Each subject receives two vaccine doses of 1 cc. each, separated by an interval of 30 days. The following vaccines are being used:

- (1) Monovalent A₂ (Japan 305/57) aqueous vaccine at potencies of 200 and 400 CCA units/ml.
 - (2) Polyvalent aqueous vaccine of the following composition:

Type	Strain	CCA Units/ml.
A	PR 8	100
A ¹	Ann Arbor 1/57	100
A ₂	Japan 305/57	200
ан алтан алтан 198 8 — В алтан Алтан 298 — Алтан	Great Lakes 1739/54	100

(3) Monovalent B (Great Lakes 1739/54) vaccine at a potency of 100 CCA units/ml. is employed as a placebo.

Students in half the schools have been randomly assigned to one of four treatment groups as follows:

	Dose 1	Dose 2		
1)	Placebo	Monovalent A ₂ 200 CCA Units		
2)	Monovalent A2 200 CCA Units	Monovalent A2 200 CCA Units		
3)	Polyvalent 500 CCA Units	Polyvalent 500 CCA Units		
4)	Placebo	Placebo		

The remaining half of this study group will follow an identical protocol except for the substitution of monovalent A_2 vaccine containing 400 CCA units/ml. for "monovalent A_2 200 CCA units".

A serologic survey is being performed on a 5% sample of this population. First specimens were obtained prior to initial vaccination; a second specimen will be drawn three weeks after the second dose.

<u>Study Group II</u> consists of 2000 students in two schools and is devoted to a comparison of intradermal and subcutaneous routes of administration. Each subject has received a single dose of vaccine only. Subjects were randomly assigned to one of four treatment groups as follows:

- 1) Monovalent A₂ 40 CCA Units intradermally (0.1 cc.)
- 2) Monovalent A₂ 400 CCA Units subcutaneously (1 cc.)
- 3) Placebo 0.1 cc. intradermally
- 4) Placebo 1 cc. subcutaneously.

Monovalent influenza B vaccine again has served as the placebo. A serologic survey of 10% of this population has been completed. Initial specimens were obtained just prior to vaccination and were followed by a second specimen three weeks later.

Techniques for follow-up and influenza surveillance are the same for both study groups. School absenteeism will be followed by means of a daily report of total absences submitted by each school to its local investigator. When absenteeism exceeds a pre-determined level (based on seasonal figures of non-epidemic years), a preliminary investigation is begun. This will consist of a phone survey of selected absentees' homes in an effort to detect and characterize any single syndrome which may be responsible for multiple absences. If an illness clinically consistent with influenza is implicated, a further investigation is undertaken in the form of home visits where further history is obtained and physical examination performed. A limited number of throat washings and paired sera (about 6-12) are obtained from "fresh" cases to provide laboratory confirmation of the suspected etiology of the outbreak. The local investigator will continue to follow school absenteeism daily throughout the outbreak, thus charting an "epidemic curve". When absenteeism has returned to pre-epidemic levels, definitive case finding is obtained through a school

assembly where the clinical features of influenza are described in a standardized manner and students are asked to indicate on a questionnaire whether or not they have had such an illness during the epidemic period. Additional data regarding approximate date of onset, severity and duration of illness are also requested. Attack rates for each treatment group will be calculated from this data, and effectiveness ratios for the several vaccine regimens will be derived.

The following investigators are participating in these studies in collaboration with the Influenza Surveillance Unit of the Communicable Disease Center:

A. B. Colyar, M.D., J. Brody, M.D., R. McAlister, M.D., Arctic Health Research Center, Anchorage, Alaska.

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- E. O. Wicks, M.D., Alaska Department of Health & Welfare, Juneau, Alaska.
- D. Duncan, M.D., Greater Anchorage Health District, Anchorage, Alaska.
- J. O'Brien, M.D., Alaska Department of Health & Welfare, Fairbanks, Alaska.
- Cecil S. Mollohan, M.D. and William Foege, M.D., State Department of Public Health, Denver, Colorado,
- T. O. Vinson, M.D., DeKalb County Health Department, Decatur, Georgia.
- William J. Dougherty, M.D. and Stephen N. Cohen, M.D., New Jersey State Department of Health, Trenton, New Jersey.
- Jacob Koomen, M.D. and George Johnson, M.D., North Carolina State Board of Health, Raleigh, North Carolina.
- Ernest Ager, M.D. and George C. Denniston, Jr., M.D., Washington State Department of Health, Olympia, Washington.

All laboratory studies connected with this investigation will be performed at the Respirovirus Unit of the Communicable Disease Center under the supervision of Roslyn Q. Robinson, Ph.D., Chief.

3. REFERENCES:

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- 2/ Stille, W. T., et al., Combinations of Asian Influenza Virus and Adenovirus Vaccine in the Prophylaxis of Respiratory Illness of Navy Recruits (Part II), Amer. J. Public Health 52(2):275, Feb. 1962.
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- 4/ Meiklejohn, G., and Morris, A. J., Influenza Vaccination, Ann. Intern. Med., 49:529, Sept. 1958.
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- 7/ Kirkham, L. J., Asiatic Influenza in Midwestern Town: With Comparison of Intradermal and Subcutaneous Vaccination, J. Iowa Med. Soc. <u>48</u>:593-598, 1958.
- 8/ Sanger, M.D., Immunization After Intradermal and Subcutaneous Injection of Asian Influenza Vaccine, Ann. Allergy <u>17</u>:173-178, 1959.
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- 11/ Hilleman, M. R., et al., Antibody Response in Volunteers to Asian Influenza Vaccine, J.A.M.A. 166:1134-1140, 1958.
- 12/ Candler, M. L., et al., Intradermal Vaccination in Healthy Adults With Type A Asian Strain Influenza Vaccine, Proc. Soc. Exp. Biol. Med. 103:151-154, 1960.

IV. INFLUENZA VACCINE AND ABO INCOMPATIBILITY

Of particular interest during the preceding months, has been the publicity and controversy relating to a news release in early October, attributed to Dr. Georg F. Springer and Mr. Harvey Tritel (Immunochemistry Section, William Pepper Laboratory and Department of Medical Microbiology, University of Pennsylvania), purporting to indicate that expectant mothers of blood type 0 who receive influenza vaccine, run some risk of bearing fetuses with hemolytic disease if the fetuses are of blood type A. Subsequent to this news release, an article on the subject of anti blood group A antibodies produced in volunteers by influenza vaccine was published by the above authors in Science 138:687-688, 1962.

It has long been known that substances with some antigenic resemblance to blood group A substance occur freely in nature and are present in porcine byproducts, such as hog peptones, used in bacterial preparations. It has also been observed that substances of this kind exist in eggs and may be contained in egg prepared influenza vaccines. Springer, by injection of a concentrated treated portion of commercial polyvalent influenza vaccine, was able to produce 4 to 8 fold rises in human blood group anti A_1 and A_2 titers in all of five human volunteers of blood group B or O receiving the injections. The article did not relate these titers to hemolytic disease of the newborn and, as noted in a memorandum issued by CDC on October 24 to readers of the Influenza vaccine and the incidence of ABO hemolytic disease of the newborn is lacking.

Subsequent to Dr. Springer's study, Dr. Fred Davenport, in cooperation with Dr. Henry Gershowitz of the Department of Human Genetics, University of Michigan, Ann Arbor, and Capt. L. F. Miller and Commander R. O. Peckinpaugh, NAMRU 4, Great Lakes, Illinois, collected sets of sera from naval recruits of blood types B and O participating in an immunization program. Serum was obtained on individuals before, about 2 weeks, and up to 8 weeks after the immunization schedule was begun. Four groups were defined. Two groups contained individuals of blood group 0 or B who did not receive influenza vaccine, but received all other vaccines currently given to incoming naval recruits. The other two groups of blood group O or B received 1 cc. of military influenza vaccine containing a total of 1000 CCA units/ml, in addition to the vaccines given in the first two groups. All samples were tested for anti A antibodies.

Results were the following: Three of 24 individuals of blood group 0 who were vaccinated against influenza showed a fourfold or greater rise in anti A titer. The titer rises observed were 1:8 - 1:256, 1:64 - 1:256, 1:16 - 1:64. Among 24 persons of blood type B who received influenza vaccine, only one showed a significant anti A titer increase from 1:8 - 1:32. Of the 19 persons in the blood type B group that did not receive influenza vaccine, one individual exhibited an anti A titer increase from 1:16 - 1:64. None of the 24 blood group O subjects who did not receive influenza vaccine showed a significant anti A titer change. In summary, Dr. Davenport remarks that the high frequency (100%) of stimulation of anti A titers shown by Dr. Springer following administration of two doses of an autoclaved dialyzed concentrate of commercial polyvalent influenza vaccine was not observed when influenza virus vaccine containing twice the antigenic mass of vaccines authorized for civilian use was given once to young military recruits of the same blood types.

Another small review study bearing on this subject was published recently (Editorial, Dallas Medical Journal, November 1962) by Dr. Sol Haberman, Director of Microbiology, Department of Pathology, Baylor University Medical Center. Dr. Haberman reviewed the data from an influenza vaccine evaluation study done in 1957 among 177 pregnant women. At the time of delivery at Baylor University Medical Center, ABO, Rh-Hr, and Coombs studies were done as routine on all infants. Of the 177 pregnant women, there were 19 group O mothers with A infants; 5 group B mothers with A infants; and 2 group B mothers with AB infants. In only one case, an O mother with an A child, was a positive Coombs test on the baby found. Haberman states that in his experience anti A isoimmunization in pregnancy might be expected in 9.3% of instances in which an O or B mother gives birth to an A or AB child. In the study only 1 of 26 showed immunization to the A antigen, a proportion below that expected under normal circumstances and not indicative of a significant difference between the vaccine group and the general population, Haberman concludes that his data lend no credence to the conclusions of the press release attributed to Dr. Springer. Of importance to the interpretation of the Haberman data would be a resolution of the question of the significance of the direct Coombs test in the diagnosis of ABO hemolytic disease.

In order to shed further light upon the overall problem, the Influenza Surveillance Unit, in connection with its current vaccine evaluation studies, is making available for blood group A antibody determinations pre and post vaccination sera from O and B blood group individuals in the studies. Results of these determinations should indicate whether undiluted commercial influenza vaccine given in both a one and the recommended two-dose schedule is capable of producing rises in anti A antibody titers in these individuals.

A basic difficulty in understanding the role that exogenous sources of blood group A-like substances may play in hemolytic disease of the newborn is the present uncertainty regarding the pathogenesis of the condition. The question of whether ABO erythroblastosis is due primarily to isoimmunization of the mother by incompatible fetal cells and blood antigen rich fetal secretions or to reaction to maternal heteroimmune antibody produced by the extra human sources of substances antigenically related to blood group A substance is in doubt. Wiener, in his article on the pathogenesis of ABO hemolytic disease (Amer. J. Obstet. Gynec. 79:567, 1960), indicates his belief in the existence of both heteroimmune and isoimmune anti A antibodies and implicates the isoimmune mechanism in the production of ABO hemolytic disease of severe nature requiring exchange transfusion. He also indicates the possible involvement of the heteroimmune mechanism in the mild ABO hemolytic condition not usually requiring treatment, called "Icterus Praecox" by Halbrect.

The matter becomes further involved, since Wiener also postulates the existence of an A B cross reacting antibody substance called "anti C". This substance is thought to be found in the serum of blood group 0 mothers and not in the serum of type B mothers. He feels that this antibody may be more directly related to the production of ABO hemolytic disease than either the anti A or anti B antibody complexes and, through its absence in group B mothers, may explain the relative lack of ABO hemolytic disease in blood group A fetuses born to them.

It is clear that the final answer to the question of the role that exogenous blood group A-like substances may play in the production of hemolytic disease (the possible A-like content of influenza vaccine being only one aspect of the total problem) must rest, in part, upon a more complete elucidation of the pathogenetic mechanisms involved in the production of this condition.

V. NATIONAL INFLUENZA SURVEILLANCE, 1962-63

After conference of Epidemiology Branch staff with members of the Executive Committee of the Conference of State and Territorial Epidemiologists in Atlanta, September 14, 1962, a cooperative protocol for the State-Federal surveillance of influenza was agreed upon for the 1962-63 respiratory disease season.

This surveillance will be based primarily upon the pattern developed in previous years. Since influenza is not a reportable disease in many States, and since the clinical diagnosis of influenza on an individual basis is often difficult, the agreed upon epidemiologic unit will again be the existence of an influenza outbreak or outbreaks at the local county or comparable health jurisdiction level. Two forms, similar to those used in 1957-58, may be utilized. One form entitled, "Influenza Epidemic Summary" would be used by health officers, in the local jurisdictions, for the reporting of influenza epidemics to the State health departments. The States, in turn, would summarize this data on a second form, "Current Report of Influenza Outbreaks" to be submitted weekly to the Influenza Surveillance Unit. Examples of these forms are appended to this surveillance report. It is realized that a surveillance system of this kind can give only the most general portrayal of the temporal and geographic spread of disease in this country. One of its most important benefits will hopefully be its ability to provide the current intelligence necessary to the undertaking of extremely important supplementary studies of specific epidemics. These studies should include precise descriptions of clinical syndrome and general severity of illness, analyses of age specific attack rates, the relating of clinical illness to the presence or absence of disease in 1957 or 1959-60, and the analyses of school and industry absentee data as well as mortality data in the community epidemic situation.

In addition to the above general surveillance mechanism, the Influenza Surveillance Unit is subscribing, this year, to a nation-wide press clipping service which will provide clippings on outbreaks of acute respiratory disease. It is hoped that the service will increase our overall intelligence regarding influenza. Information derived from this source will be made available to the States for validation and comment.

VI. WEEKLY PNEUMONIA AND INFLUENZA DEATHS

The current pneumonia-influenza mortality charts are linear extrapolations of the charts used in 1960-61. These were based on 1954-60 experience. As in the 1960-61 charts (CDC Influenza Surveillance Report No. 61, December 19, 1961) the "epidemic threshold" is placed at a distance of 1.65 standard deviations above "normal expectancy". In endemic periods it is unusual for the number of weekly deaths to exceed the epidemic threshold for more than two successive weeks.

Since mid-April of this year, as shown in the accompanying chart, the numbers of deaths due to pneumonia and influenza reported weekly by 108 United States Cities have fluctuated around levels somewhat lower than expected on the basis of the 1954-60 experience. For the week ending December 1, the number of deaths exceeded expected levels but the excess was largely a reflection of delayed reports from the preceding (Thanksgiving holiday) week. Such delays are customary during major holiday periods. The average for the two weeks coincides with the expected number of pneumoniainfluenza deaths at this time of year.

In Table 2 the number of pneumonia-influenza deaths is shown for the past six weeks for the nine geographic divisions.

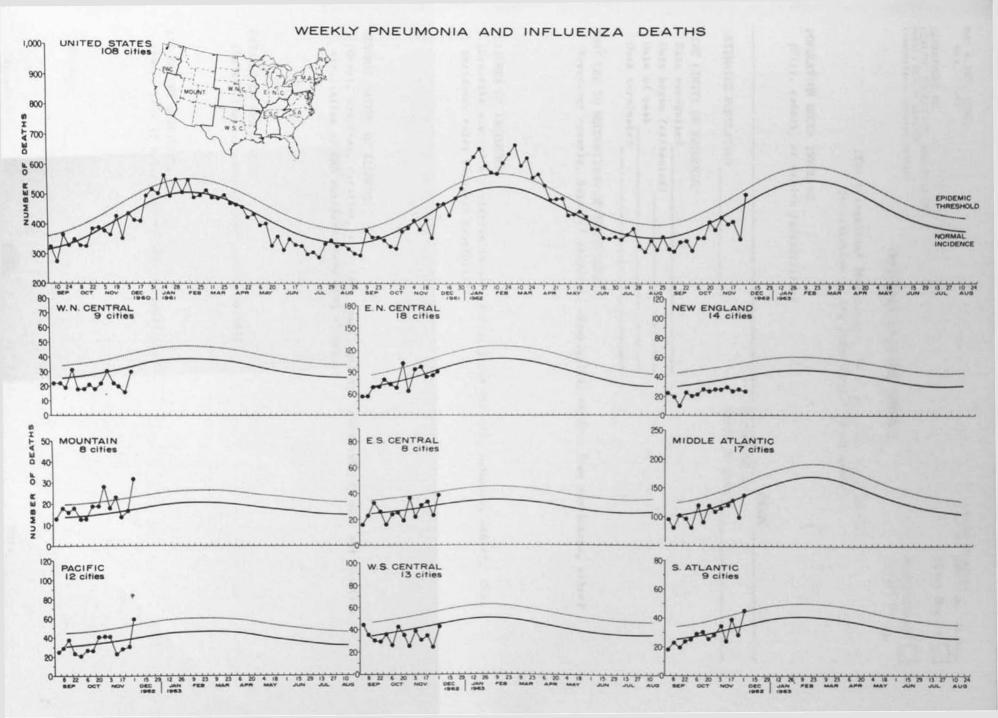
Table 2

Current Analysis of Influenza and Pneumonia Mortality* Current Influenza and Pneumonia Deaths in 108 United States Citles

Division	Number of Cities in Deaths (Including Estimates**) During Weeks Ending:							
Division	Study Reporting This Week	12-1-62 (107 Cities)	11-24-62 (108 Cities)	11-17-62 (108 Cities)	11-10-62 (108 Cities)	11-3-62 (108 Cities)	10-27-62 (108 Cities	
ll Divisions	107	501	350	409	400	422	381	
New England	14	25	27	25	29	27	27	
Mid. Atlantic	17	136	98	129	120	115	108	
E. North Central	18	91	86	84	97	194-194 194-194	64	
W. North Central	9	30	16	20	22	30	22	
S. Atlantic	9	45	28	39	24	.35	28	
E. South Central	8	39	23	34	31	22	37	
W. South Central	13	43	24	35	31	39	25	
Mountain	8	32	17	14	23	. 18	28	
Pacific	11	60**	31	29	23	42	42	

*Prepared by the Statistics Section, CDC.

**The number of deaths given includes estimates for cities not reporting in a given week. The table is corrected for preceding weeks after receipt of late reports.



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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE		First Report
COMMUNICABLE DISEASE CENTER	INFLUENZA EPIDEMIC SUMMARY	Supplemental 🗌 Report No
1-		
	ttal from county, city, or other local ction to the State Health Department.	
POPULATION GROUP INVOLVED:		
(City, county, or health jur	isdiction)	
		STATE
	ESTIMATED NO.	•
ESTIMATED POPULATION	CASES TO DATE	an a
TIME LIMITS OF EPIDEMIC:		
Date recognized Date began (estimated)	yer war waar an	
liate of neak		
Date terminated		
WHAT LED TO RECOGNITION OF THE	FDIDEMIC.	
	crowding, absenteeism, reports from p	hysicians, other)
MEASURES OF INCIDENCE:		
(Describe unusual absenteeism incidence rates whenever pos	n in any special group (school, indust ssible.)	ry, other). Give
GENERAL NATURE OF ILLNESS:		
	severity, complications, Particularly ations with illness.)	note any possible
DETAILS ON ANY DEATHS:		
(Submit copy of autopsy report	rt when possible)	
LABORATORY SPECIMENS: (Where sent if collected; re:	sults if available)	
	,	
COMMENTS:		

Signed

Title_____ Date____

In anticipation of probable widespread epidemic influenza in the United States during the winter of 1962-63, these forms have been proposed to serve as a relatively simple procedure for summarizing the main qualitative features of epidemics in specific health jurisdictions. It is suggested that these forms be used for relaying this information to the State Health Departments. Review of the forms as they are received will provide the States with a current picture of the scope of the influenza problem within their borders. In turn the States will summarize these reports and submit essential data in tabular form to the Communicable Disease Center. These data will become part of the Influenza Surveillance Program which has been established to provide ready recognition of any unusual change in the characteristics of the disease. Supplementary reports are indicated when unusual observations are made relating to ages of individuals attacked, severity, duration, symptoms, and complications in the individual influenza epidemics.

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CURRENT REPORT OF INFLUENZA OUTBREAKS

STATE

Week

ending_____

Reports should be sent each Friday to: Influenza Surveillance Unit Communicable Disease Center Atlanta 22, Georgia

	County	Indicate if First	Estimate of Epi			Laboratory Con- firmation (Indi-	Populations Involved: 1) School, 2) Industry,	Remarks:
	and/or	or Sup-	First		1 1	cate if Specimens		4
	City	plemental	Recog-	Peak		Collected and Any	wide. (Give Related Attack	2) Severity and Complications, 3) Associated
		Report	nized				Rates, If Possible)	Deaths, 4) Associated CNS Manifestations
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*Subject to revision in subsequent reports.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE -

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This form has been prepared for use during the anticipated influenza epidemic in the winter of 1962-63. Weekly reporting on this form will provide the Public Health Service with current regional data which will be of considerable value in the National Influenza Surveillance Program. Of particular importance in this program will be information relating to severity of the disease, frequency of complications, secondary bacterial agents, and influenza associated deaths. Supplementary reports relating to these items should be appended whenever possible.