

MINUTES, MEETING NO. 11, ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES,
FEBRUARY 13-15, 1968

The Advisory Committee on Immunization Practices met at the National Communicable Disease Center on February 13-15, 1968. Those in attendance were:

Committee

Dr. David J. Sencer, Chairman	Dr. Theodore A. Montgomery
Dr. H. Bruce Dull, Secretary	Dr. Roderick Murray
Dr. Gordon C. Brown	Dr. Jay P. Sanford
Dr. Geoffrey Edsall	Dr. Paul F. Wehrle
Dr. David T. Karzon	

Liaison Member

Dr. Margaret H.D. Smith

Invited Participants

Lt. Col. John D. Marshall, Division of Microbiology, Walter Reed Army Hospital, Washington, D.C.
Dr. Joe Stockard, Deputy Director, International Organizational Affairs, Office of International Health, DHEW, Washington, D.C.

CDC Staff -- Participants and Discussants

Office of the Center Director:	Dr. John R. Bagby, Jr.
Epidemiology Program:	Dr. Alexander D. Langmuir Dr. Philip S. Brachman Dr. William E. Dismukes Dr. Ronald F. Johnson Dr. Adolph Karchmer Dr. Stephen Schoenbaum
Foreign Quarantine Program:	Dr. Arthur Osborne Miss Regina Burns Dr. Robert Latta Dr. James W. Mosley
Immunization Program:	Dr. Robert Freckleton Dr. John J. Witte
Laboratory Program:	Dr. U. Pentti Kokko Dr. Marion Coleman Dr. Walter Dowdle Dr. Steven Mostow

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PLAGUE

Plague Surveillance in SE Asia

The Committee was augmented by Dr. John Marshall who discussed in detail the present status of plague in Southeast Asia, most particularly in the Republic of Viet-Nam (the most plague infested rodent and ectoparasite population presently recognized). Surveys of Viet-Nam (43/47 provinces) suggest that plague is present throughout the country. The usual "plague season" is February-May.

Much of the information on plague initially came from the Pasteur Institutes. More recently, data are derived from military preventive medicine investigations. Granting that there are inaccuracies in the clinical diagnosis of plague from the reports of many non-M.D. health workers, 5,000 cases have been reported in recent years in Viet-Nam, and 400 have been confirmed.

Bubonic plague is most commonly seen, although focal outbreaks of the pneumonic form have been recorded. The amount of plague in non-secure areas can only be speculated. Although plague has not been officially reported from Cambodia, Laos, North Viet-Nam, and Thailand, it is known to exist near the borders of Laos and Cambodia and in the DMZ.

Clinical reports indicate that deaths from plague occur within 6 hours of hospitalization. If patients survive beyond that time, few deaths result because of uniform success of antibiotic therapy (streptomycin plus chloromycetin plus tetracycline).

No chloromycetin-resistant strains of P. pestis have been identified in Viet-Nam; few relatively streptomycin-resistant strains have been reported; and some questionably tetracycline-resistant species are under investigation.

Rodent control activities (only Rattus norvegicus has been identified) have been basic in control programs. DDT is ineffective against rodent fleas; Dieldrin and Diazimon resistance have not been seen. In several areas, vaccination programs have been undertaken in efforts to control focal outbreaks. The effectiveness of vaccine alone has been difficult to interpret as it has generally been part of a general control activity.

Plague Vaccine

Discussion of plague vaccines pointed to the generalities which characterize the field. Various vaccine trials do, however, suggest a short-lived efficacy. Animal models demonstrate moderate protection. The military is presently receiving plague vaccine booster doses every four months. A change to 6-month boosters is under consideration. There is evidence for late, efficient booster recall (in one case up to 25 years after primary vaccination).

Antibody titers in man and animal following plague immunization appear to have little relationship to protection. The mouse neutralization test has some value in quantitating protection, but is costly and difficult to standardize.

The E vaccine and other modifications of standard products are under investigation. Although the available vaccines for use in the United States are inactivated microorganisms, live vaccines are used elsewhere in the world.

A report on a plague outbreak in Nepal in 1967 was presented by Dr. Philip Brachman, who had led a CDC team late in the year to investigate and assist with control.

The previous circulated draft on plague vaccine was reviewed in detail. A working group was appointed to consider revisions and amendments based on the general assessment.

HEPATITIS

Discussion of hepatitis began with historical review of attempts to isolate and identify the etiologic agent. The frustrations of the field are well recognized. Presently, there is modest enthusiasm for a relationship between a virus demonstrable using a marmoset animal model, developed by Dr. F. Deinhardt, and the actual hepatitis virus. However, no established candidate agent gives promise of immediate insight into the specific diagnosis or control of the disease.

A tabulation of the important observations on immune serum globulin for prophylaxis of infectious hepatitis was the basis for considerable discussion of dosage and interval between exposure and administration.

The epidemiologic characteristics of the specific

investigations helped to categorize populations for which globulin prophylaxis would be primarily considered: household, school, institutional, hospital, office, and factory contacts, and foreign travelers.

Definitions of "sufficient" exposure and of the duration of risk were basic in the discussion. It appears from extensive experience that the kinds of contact among family members are epidemiologically most important. More casual exposures as in school or office are not supported as carrying much risk. International travel also is not uniform in its risks and must reflect an understanding of relative levels of potential exposure which exist in various countries or areas of the world. Data on geographic distribution of hepatitis were felt to be important as part of the final recommendations of the Committee.

Dosage of immune serum globulin for overseas travelers had been discussed at the previous ACIP meeting (fall 1967) and was continued. Relatively arbitrary amounts and schedules are being used at the present time by military, Peace Corps, industrial, and other groups. Data are not sufficiently clear to support or negate some of the alternatives. It was felt quite strongly by several members of the Committee that an "optimal" level (0.05 ml./per lb. of body weight) should be discussed before accepting the commonly used 5 ml. per adult recommendation. A working group was appointed to continue preparation of a statement incorporating

the recommended use of immune serum globulin for both infectious and serum hepatitis.

SURVEILLANCE REPORTS

Brief surveillance commentaries on influenza 1967-68, the extent of the U.S. experience and the current vaccine investigations by the CDC were presented by Dr. Walter Dowdle, Chief, Respiratory Virus Infections Unit, Laboratory Program, and his colleagues, Dr. Marion Coleman, Dr. Steven Mostow, and Dr. Stephen Schoenbaum. In general, as predicted by the ACIP, A2 influenza was relatively widespread in the eastern two-thirds of the country (all States except for the Pacific Coast and some parts of the Far West). Mortality reported from all parts of the country except the West Coast rose to peak sharply in January 1968 and then fell abruptly. Influenza was reported to continue at low level in some parts of the country but mortality was now well within expected limits.

Vaccine studies presently being completed include an evaluation of bivalent vs. polyvalent potency, the reactogenicity and potency of standard and purified vaccines in various dosage levels, nasal antibody response to infection and immunization, and laboratory models for characterizing influenza virus strains and vaccine relationships. Results of these investigations will be available by the spring meeting of the ACIP for consideration prior to making influenza vaccine recommendations.

Dr. John Witte summarized the continuing downward trend of measles occurrence in the United States. He presented data on case surveillance and vaccine utilization. Many communities are carrying out widespread measles immunization at the present time as result of focal outbreaks of disease. General effectiveness of present immunization campaigns is expected to help achieve the goal of national measles eradication.

REVIEW OF COMMITTEE RECOMMENDATIONS

Working groups reviewed the recommendations on cholera and typhus vaccines prepared at the October meeting of the ACIP. The corrected drafts were reexamined by the full Committee with minor modifications and were approved for editing and submission to the Surgeon General and approval for publication, (final copy to be circulated).

The newly developed plague vaccine recommendation was discussed and modified with acceptance for final editing and submission to the Surgeon General.

Working drafts on immune serum globulin for prophylaxis of hepatitis will be circulated to Committee members for additional comment prior to accepting final draft.

AGENDA SUGGESTIONS FOR MAY ACIP (May 16 and 17)

The Committee was unable to devote adequate time to discussing the medico-legal aspects of immunization originally scheduled for the present meeting. The Committee, however, was greatly concerned by the implication of litigations which cast shadows on public

and professional acceptance of immunization in its broadest frame. The Committee urged the CDC to pursue its plan for a thorough review of present legislative opinion and to schedule appropriate discussions in the future.

Also to be considered for the May agenda are, of course, influenza vaccine, the rare vaccines program of CDC, simultaneous administration of live virus vaccines, and a general review of all current recommendations of the Committee prior to their joint republication.

With the thanks of the Chairman, the meeting was adjourned.

TABLE I

SELECTED STUDIES OF THE VALUE OF IMMUNOGLOBULIN FOR PREVENTION OF INFECTIOUS HEPATITIS

Investigators	Year of Study	Place of Study	Study Situation	Control Population		Immunized Population		Ratio of Attack Rates Immunized:Controls	Dose ml./kg.	Eclipse from Globulin to Onset In Cases Occurring after Immunization		
				No.	Icteric Cases	Attack Rate	No.				Icteric Cases	Attack Rate
Stokes and Neefe (4)	1944	USA	Water-borne epidemic at summer camp	278	125	45.0%	53	3	5.7%	1:7.9	0.33	All 3 by 10th day
Stokes and Others (32)	1948	USA	Person-to-person epidemic in institutions	264	44	16.7%	248	5	2.0%	1:8.4	0.13	4 by 5th day, 1 on 14th day
Stokes and Others (32)	1950	USA	Person-to-person epidemic in institutions	83	45	54.2%	106	3	2.8%	1:19.4	0.02	9th day, 18th day, and 4th month
Drake and Ming (36)	1952	USA	Person-to-person epidemic in institution	152 115	25 24	16.4% 20.9%	86 71	2 3	2.3% 4.2%	1:7.1 1:5.0	0.01 0.02	1 by 7th day, 1 in 3rd week 2 by 7th day, 1 in 6th week
Ashley (37)	1952-53	USA	Household contacts	708	112	15.8%	268	6	2.2%	1:7.2	0.02	3 by 2nd day, 2 on 35th day, 1 on 36th day
Gelperin and Hampton (43)	1952-53	USA	Household contacts	475	37	7.8%	837	9	1.1%	1:7.1	Not given	4 by 7th day, 2 in 2nd week, 1 in 3rd week
Krasna and Radkovsky (46)	1953-56	Czechoslovakia	Person-to-person epidemic in schools	-	-	0.8%	45,546	146	0.3%	1:2.7	0.02	See Table II
Tarantaev and Others (51)	1956-58	Russia	Person-to-person epidemic in schools	1,015	34	3.4%	672 (1,287)	7 6	1.0% 0.5%	1:3.4 1:6.8	0.03-0.05 0.14-0.20	2 by 10th day, 5 between 11 and 50 days All 6 by 10th day
Clark and Others (54)	1955-56	USA	Household contacts	2,109	321	15.2%	2,118	49	2.3%	1:6.6	Not given	Between 6th and 53rd day; details not given
Krugman and Others (55)	1956-63	USA	Person-to-person epidemic in schools	2,988 1,680 636	61 39 31	2.0% 2.3% 4.9%	1,224 1,182 635	9 3 1	0.7% 0.3% 0.2%	1:2.8 1:9.0 1:24.5	0.02 0.13 0.13	Between 2nd and 30th weeks In 5th, 12th, and 50th weeks 1 case within 5 months
Golba and Waluszkiewicz (61)	1960	Poland	Details not available	1,854	132	7.1%	6,429	42	0.7%	1:10.1	0.03	Not available
W. Mosley and Others (65)	1960-61	USA	Household contacts	133	42	31.6%	1,577	12	0.8%	1:39.5	Usually 0.02	7 in 1st week, 2 in 2nd week, 3 thereafter
Krugman and Others (55)	1959	USA	Person-to-person epidemic in schools	15	1-3 A-6	20% 40%	17	1-3 A-6	17.5% 35.3%	1:1.1 1:1.1	.13	1-19th wk(1), 22(1), 26(1) A-5(1), 11(1), 18(1), 20(2), 23(1)
Krugman and Others (12)	1959-60	USA	Person-to-person epidemic in schools	45	1-6 A-11	13.3% 24.4%	40	1-3 A-12	7.5% 30.0%	1:1.8 1: .8	.13	1-5 mos.(1), 6 mos.(2) A- by 2-6 mos.
Mosley and Others (13)	1965-66	Israel	Household contacts	250	16	6.4%	236* 238**	8 2	3.4% 0.8%	1:1.9 1: .8	.02	By 10-33 days By 6 and 45 days

I-Icteric
A-Anicteric
*Globulin Lot A
**Globulin Lot B

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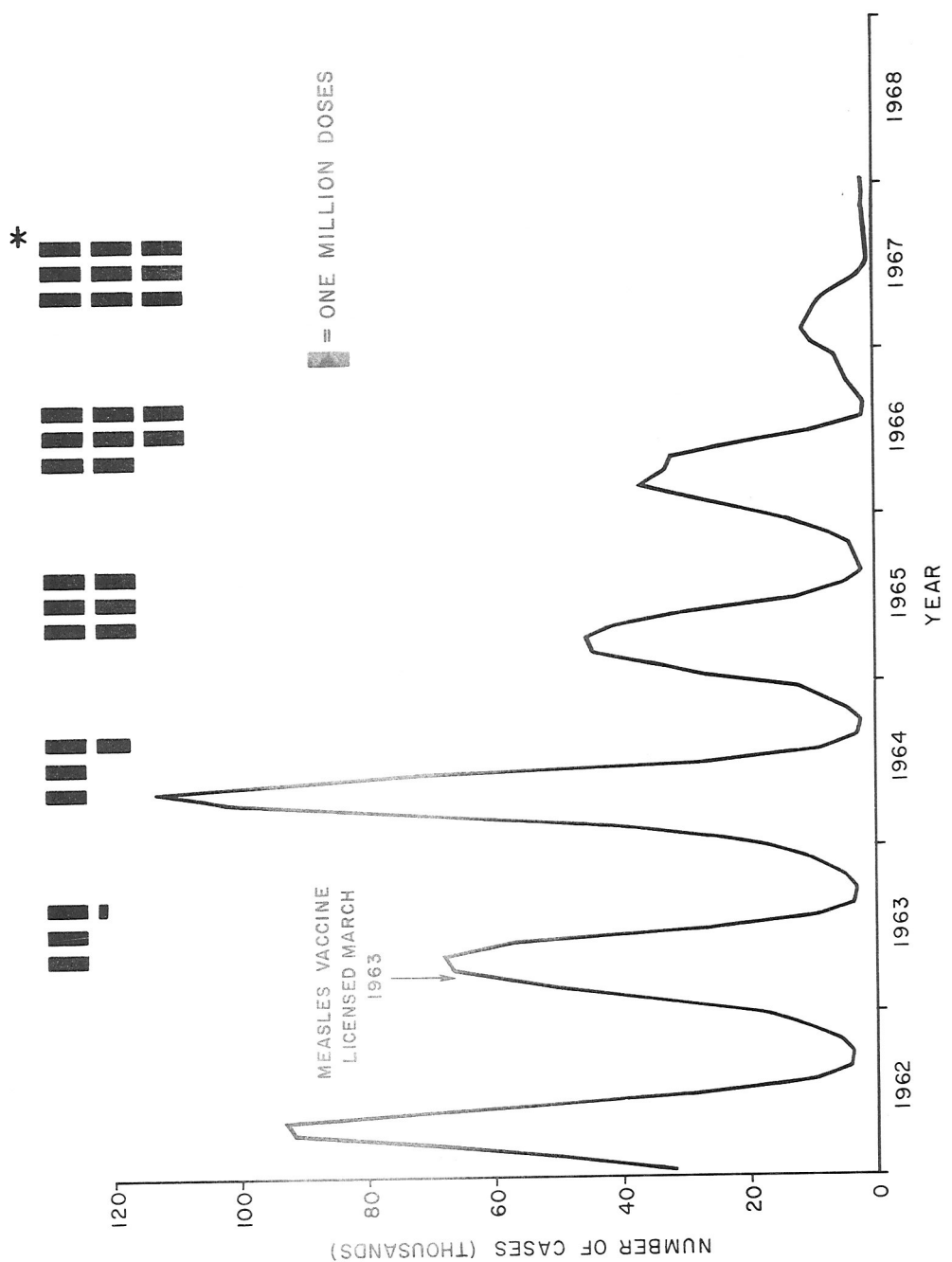
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TABLE 1
Reported Cases of Measles, United States, 1958-1967

YEAR	NUMBER OF CASES	RATIO TO 1967
1958	763,094	12.3
1959	406,162	6.5
1960	441,703	7.1
1961	423,919	6.8
1962	481,530	7.7
1963	385,156	6.2
1964	458,083	7.4
1965	261,904	4.2
1966	204,136	3.3
1967	62,190	1.0

SOURCE: Annual Supplements to MMWR: 1967 Provisional

Figure 1.
REPORTED CASES OF MEASLES BY 4-WEEK PERIODS
WITH PICTOGRAM OF DISTRIBUTION OF LIVE MEASLES VIRUS VACCINE
UNITED STATES, 1962-1967



* ESTIMATED TOTAL FOR 1967

Figure 2
REPORTED CASES OF MEASLES BY 4-WEEK PERIODS-UNITED STATES
EPIDEMIOLOGIC YEAR 1967-68, COMPARED WITH 1966-67

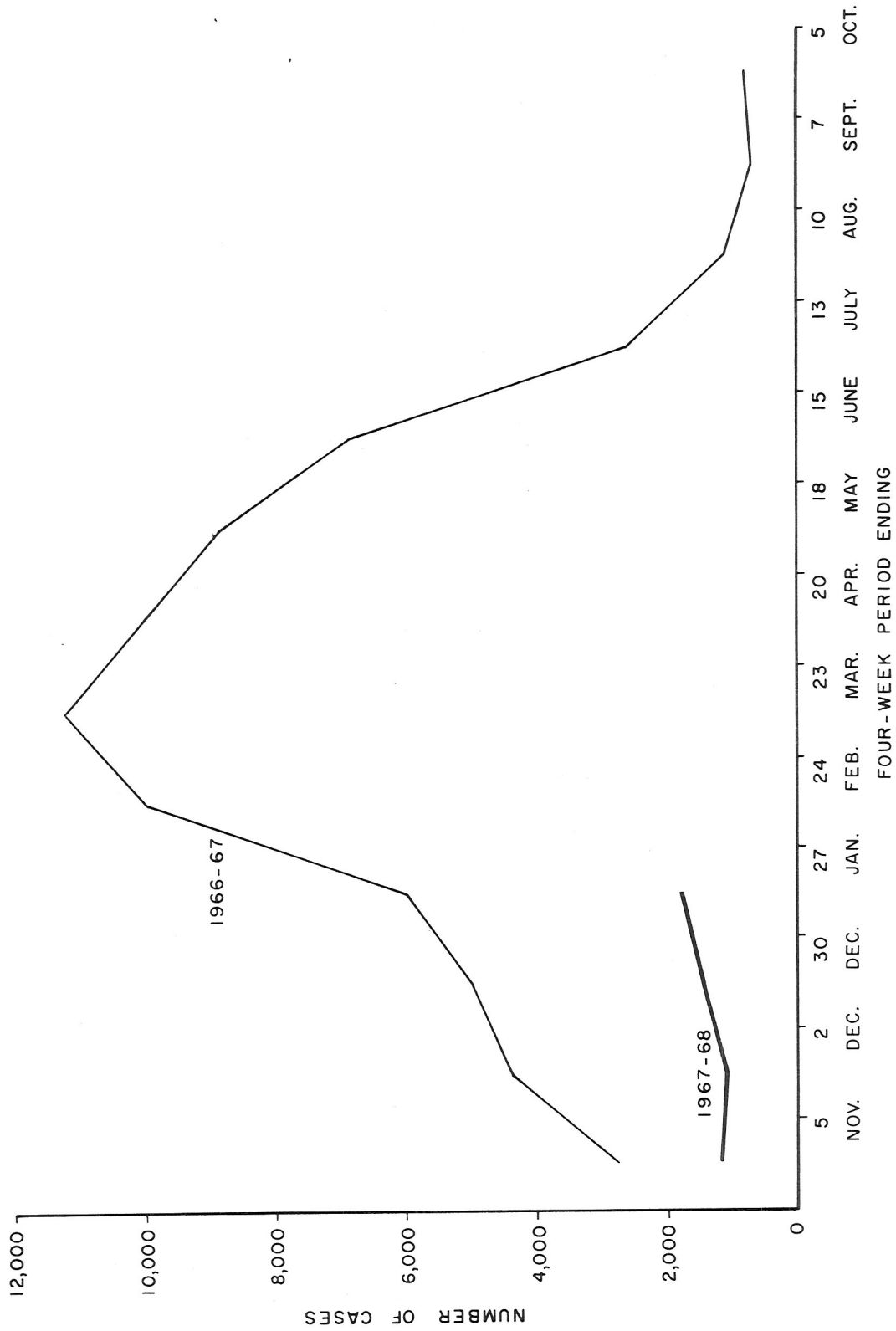


Figure 3

REPORTED CASES OF MEASLES BY 4-WEEK PERIODS
IN 3 STATES CONDUCTING A STATEWIDE CAMPAIGN
1962 - 1967

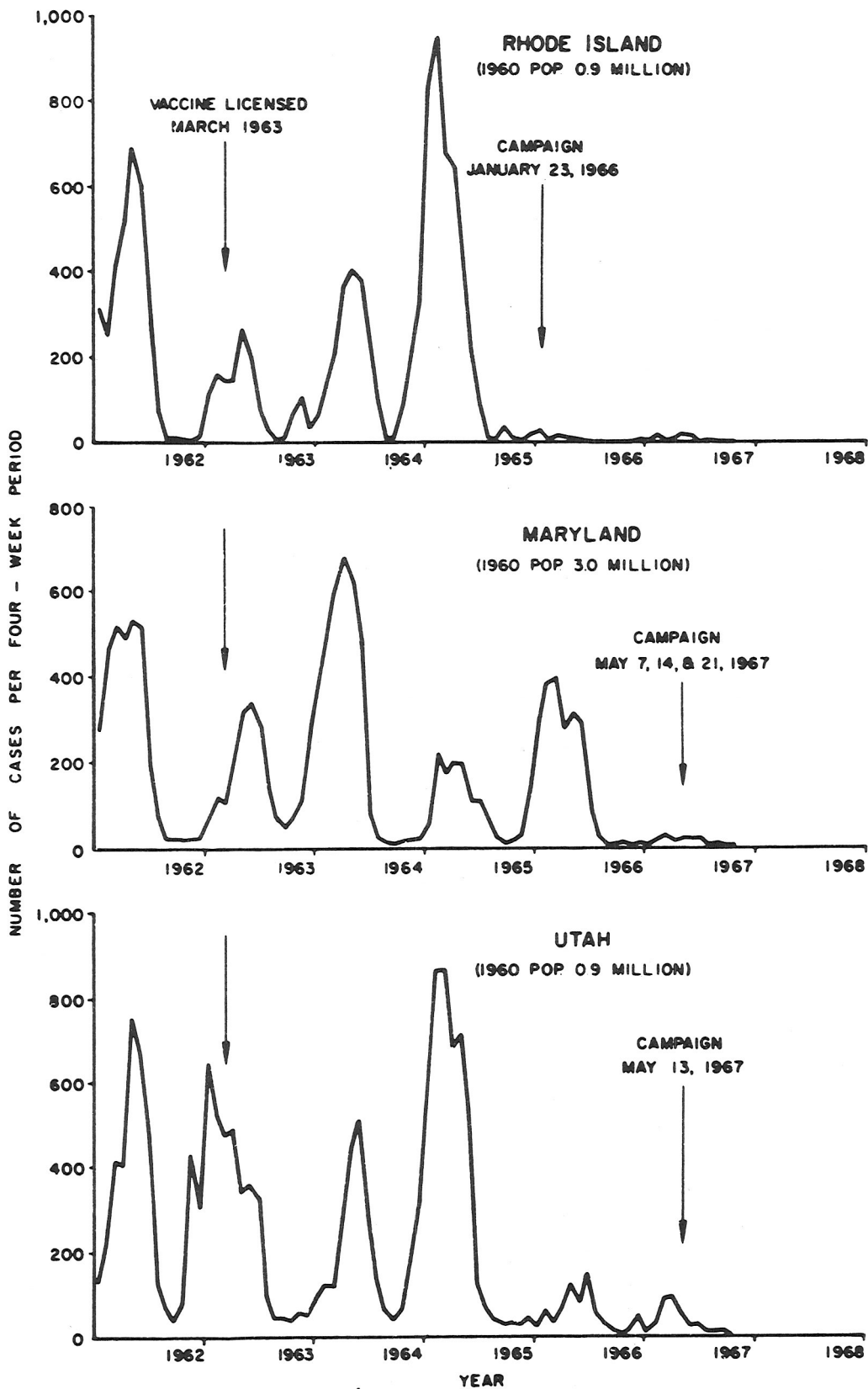


Figure 4
 REPORTED CASES OF MEASLES BY 4-WEEK PERIODS
 IN 3 STATES WITH ON-GOING AND COMMUNITY-WIDE
 IMMUNIZATION PROGRAMS
 1962 - 1967

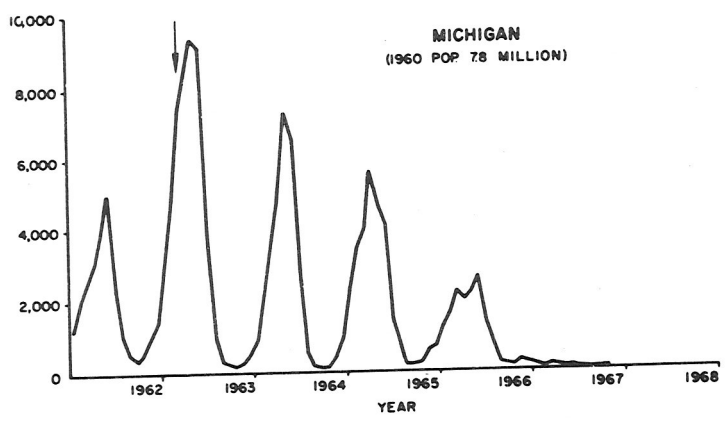
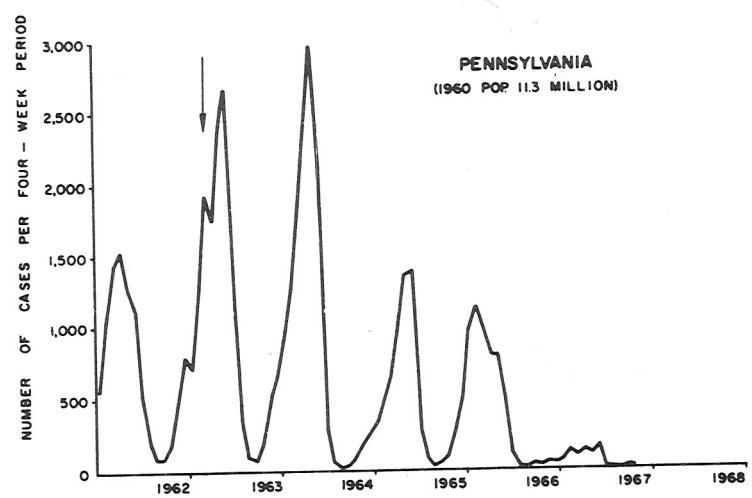
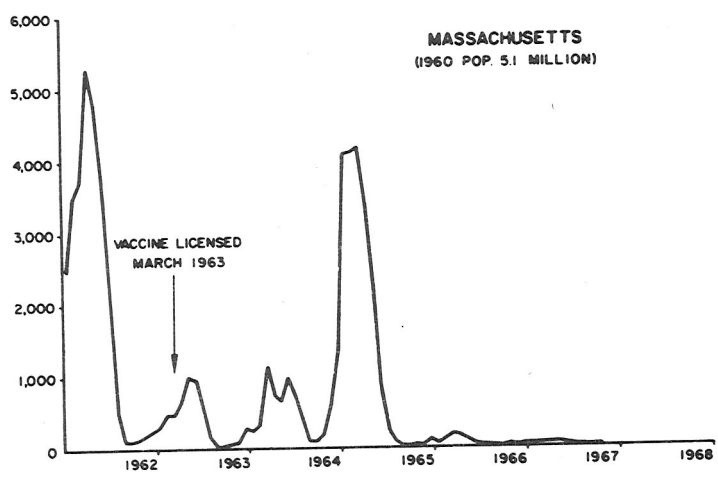
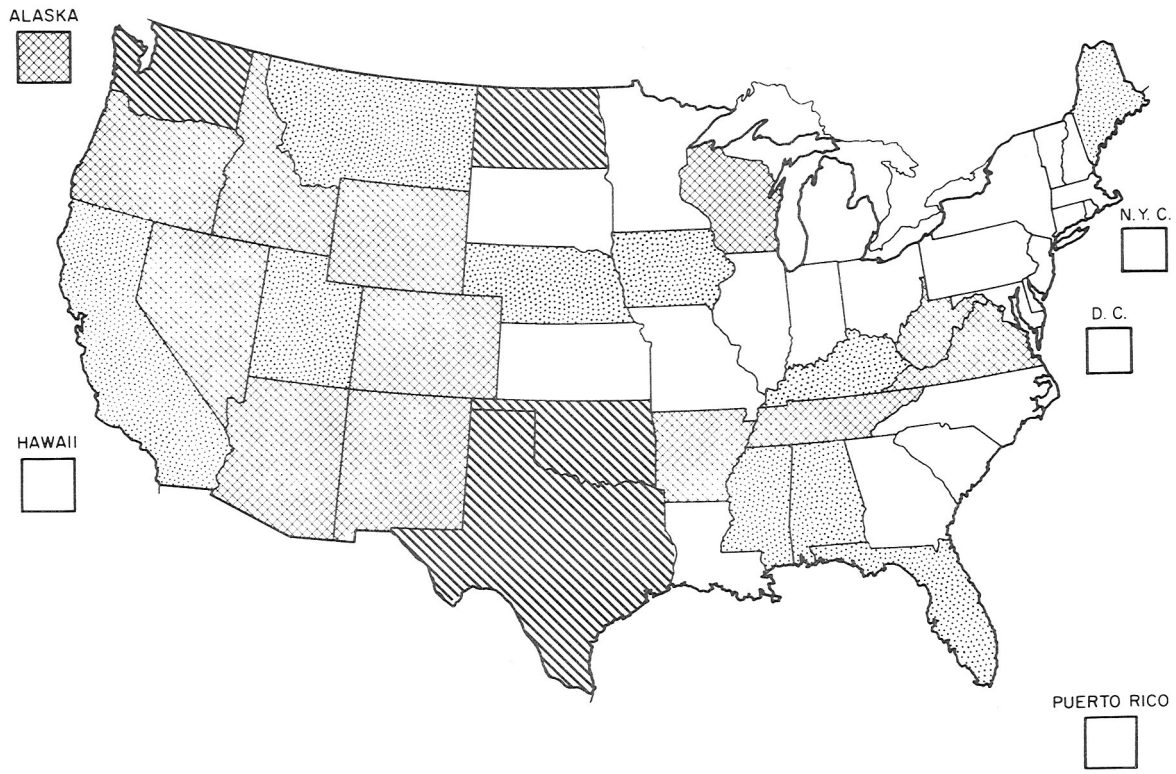
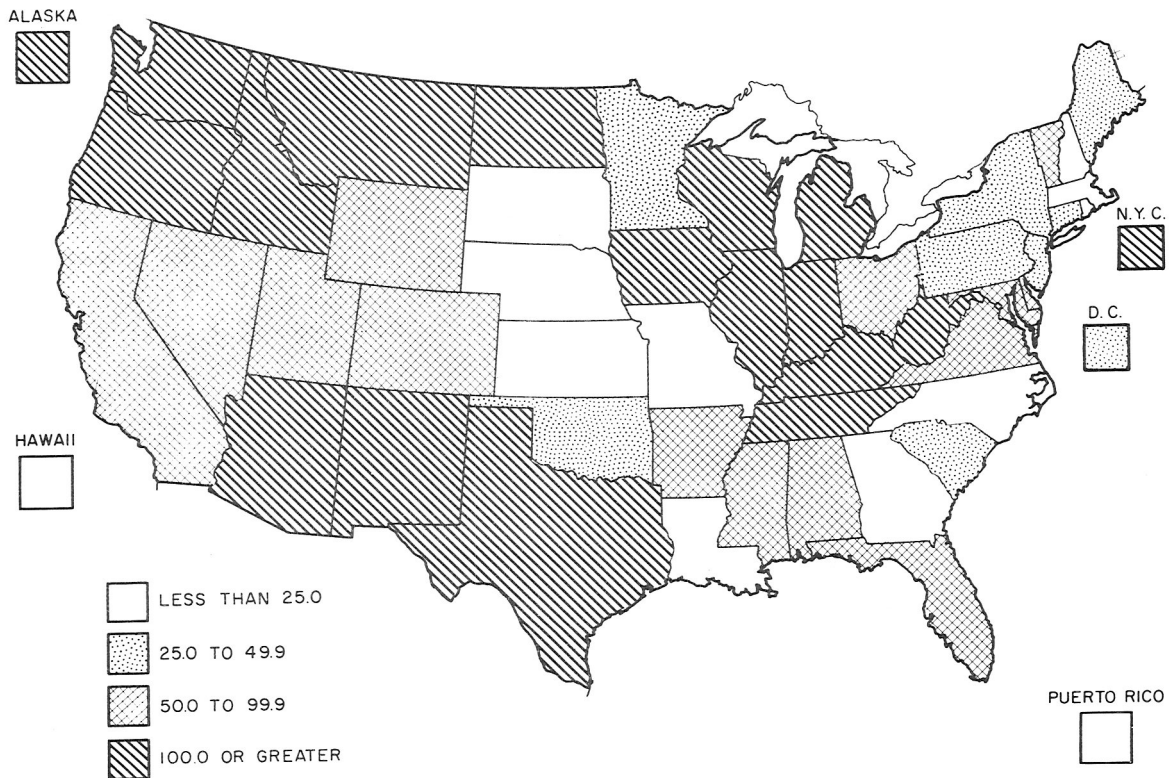


Figure 5
 REPORTED MEASLES CASES PER 100,000 POPULATION
 UNITED STATES, 1967



UNITED STATES, 1966



Reported Cases of Measles, Chicago, Illinois
 October 1967 - February 1968

<u>Month</u>	<u>Number of Cases</u>	<u>No. Community Areas Involved</u>
October 1967	53	21
November	135	26
December	167	35
January 1968	276	46
February (1-7)	61	-

Community Area Number 8 - Located
 on "Near North Side"

Total Population	75,500
Population <10 years	13,900
White <10 years	4,600
Negro <10 years	9,300

Number of Cases by Month of Onset

October	3
November	15
December	29
January	33
February (1-7)	<u>8</u>
Total	88

Age Distribution of Cases Reported Through January 31

<u>Age</u>	<u>Number of Cases</u>	<u>Percent</u>
<1	7	9
1-4	41	52
5-14	29	36
15+	2	2
Unknown	<u>1</u>	<u>1</u>
Total	80	100

Cases by Race

	<u>Number</u>	<u>Percent</u>
White	3	3.8
Negro	70	87.2
Unknown	7	9.0