immunization

against disease

1966 - 67

U. S. Department of Health, Education, and Welfare

Public Health Service

Bureau of Disease Prevention and Environmental Control

U.S. National Communicable Disease Center, *Atlanta, Georgia 30333*

IMMUNIZATION AGAINST DISEASE
1966-67

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in the developmental stage, the
supply is limited.

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lasts.

Foreword

The Public Health Service Advisory Committee on Immunization Practices encouraged the National Communicable Disease Center to undertake the preparation of Immunization Against Disease. In their deliberations on communicable disease trends and the optimal role of immunizations, members of the committee agreed that a meaningful analysis of achievements and objectives should be made generally available to the country's public health workers, physicians in private practice, and those in academic medicine.

This first annual summary covers only the basic communicable disease areas in which effective vaccines play an important role. In future editions, additional subjects will be covered to provide a more comprehensive background for sound preventive medical practices.

Readers are encouraged to send comments and suggestions for improving Immunization Against Disease to make it as useful as possible to the professions that are responsible for maintaining the health of the nation.

ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

Secretary

37447

Acknowledgments and Sources of Data

Data in *Immunization Against Disease* are derived from official reports submitted by States and other reporting health jurisdictions. Weekly tallies of the numbers of cases of reportable diseases are sent to the NCDC as part of the established National Morbidity Reporting System and are tabulated in the *Morbidity and Mortality Weekly Report* (MMWR), published regularly by the Center. Official mortality data are provided by the National Center for Health Statistics (NCHS), Washington, D.C.

Collecting information on individual cases of selected diseases, such as poliomyelitis and diphtheria, is a surveillance activity of various Programs at the NCDC. This information comes through epidemiologic and laboratory reporting channels from State and other health jurisdictions. Surveillance data on cases of specific communicable diseases form a very useful resource for careful analysis of disease trends. Case counts from surveillance activities may not always match the official totals because of the inherently different mechanisms of collection. It should be noted that the official data (MMWR, NCHS) are the authoritative and archival counts of cases and deaths, but surveillance records provide additional and valuable insights into the trends and patterns of important communicable diseases and therefore merit attention.

CONTENTS

INTRODUCTION

In recent decades, effective vaccines have become major resources of preventive medicine. Except for antigens of vaccinia and rabies, there were no effective vaccines for common infectious diseases until relatively recently. Use of the variety of inactivated vaccines and live attentuated antigens has resulted dramatically in control or actual eradication of diseases in the United States.

There has been not one confirmed case of smallpox in this country in nearly 20 years, poliomyelitis has virtually been eradicated, measles incidence is already at its lowest point in history, and diphtheria, tetanus, and pertussis are of comparatively minor importance. In the near future, we can expect mumps and other common infectious diseases to be controlled or eliminated through the use of vaccines currently under development.

This immunological basis of preventive medicine implies, however, a major responsibility for the public health and medical professions. Along with the luxury and ease of health provided by artificial antigens must go the commitment for maintaining careful, intensive watch or "surveillance" on their performance. The scope of the surveillance ranges from determining the population's level of protection to assessing the relative effectiveness of alternative antigens.

Vaccines with short durations of protection could merely postpone what were once childhood diseases. Thus, a clear need emerges for regular insight into the adequacy of protection for adults. No longer can reliance be placed on the booster phenomenon resulting from the natural occurrence of diseases. And moreover, contemporary patterns of life and travel provide opportunities for exposure to diseases no longer prevalent in this country.

The commitment of a population protected by immunization against disease is to a complete and current knowledge of the adequacy of its protection and the programs necessary to maintain this protection. "Immunity surveillance," a concept developed out of the commitment to knowledge, implies an awareness of all elements necessary to developing a meaningful immunization pattern.

This edition of *Immunization Against Disease* is the first in a projected annual series. It is a review of the status of infectious diseases important in the United States for which there are effective immunizing agents. The depth of analysis, scope of coverage, and general level of detail will undoubtedly change with added insights and new sources of information. This first edition, primarily covering data summarized through the 1966 calendar year, is addressed to the public health and medical professions; it assesses for them not only achievements in control but also the meaningful obligations for maintaining alertness to present and future needs.

The contents of the summary are divided into two major sections: The first deals with the status of major communicable diseases and the effect vaccines have had on them. The second contains the recommendations of the Public Health Service Advisory Committee on Immunization Practices (ACIP); the United States Immunization Survey sponsored by the National Communicable Disease Center and carried out annually by the Bureau of the Census; and the 1966 Biologics Surveillance Summary, a collaborative effort of the major producers of biologics in the United States and the NCDC.

The first section contains for each disease a brief historical introduction and a current summary with various forms of graphic presentation of data. Explanatory notes accompany the figures and charts.

The other sections contain almost no editorial comments and have considerably more detailed documentation. Each of the recommendations of the ACIP has been previously printed in the *Morbidity and Mortality Weekly Report* published by the NCDC. The compiled recommendations are intended to be a convenient supplement to the disease status summaries. Each one includes an interpretation of the role of immunization in the United States and the practices recommended to public health and preventive medical professions in this country.
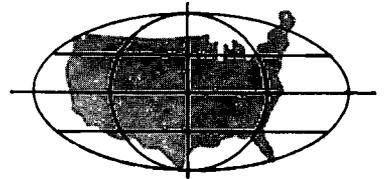
CURRENT REVIEWS–

SELECTED INFECTIOUS DISEASES

DIPHTHERIA

Clinical diphtheria was first described by Bretonnean in 1826, although commentary on a compatible disease syndrome appeared in the Babylonian Talmud (A.D. 400). Klebs described the bacillus, *Corynebacterium diphtheriae*, in 1883, and Loeffler established its etiological relationship in 1884. Soon after, both diphtheria toxin and antitoxin were characterized, and by 1913, toxin neutralized by antitoxin had been used to induce immunity in animals and man. In 1923 Ramon described diphtheria toxoid as being effective for active immunization, and by 1940, the toxoid was in general use.

Widespread immunization of children with diphtheria toxoid has dramatically reduced the incidence of the disease in the United States. In 1966, 209 cases were reported, whereas in 1933, 50,000 cases and 5,000 deaths occurred.

Despite the decline in cases, however, the severity of the disease persists, i.e., the death-to-case ratio — about 10% — has remained essentially unchanged over the past 30 years. Diphtheria continues to be primarily a disease of childhood, although there has been a shift in incidence from preschool to early school age and a moderate increase in cases in the teenage, young adult, and older age groups.

DIPHTHERIA IN 1966

In 1966, 209 cases of diphtheria were reported, a moderate increase over the 164 recorded in 1965. Eighteen deaths were reported in 1965.

The disease was widely scattered, although several parts of the country experienced minor outbreaks among poorly immunized individuals. Children were characteristically most often affected. In investigations of cases, however, mild cases and carrier states in adults as well as children were often identified.

DIPHTHERIA — UNITED STATES, 1920-1966

Morbidity & Mortality Rates
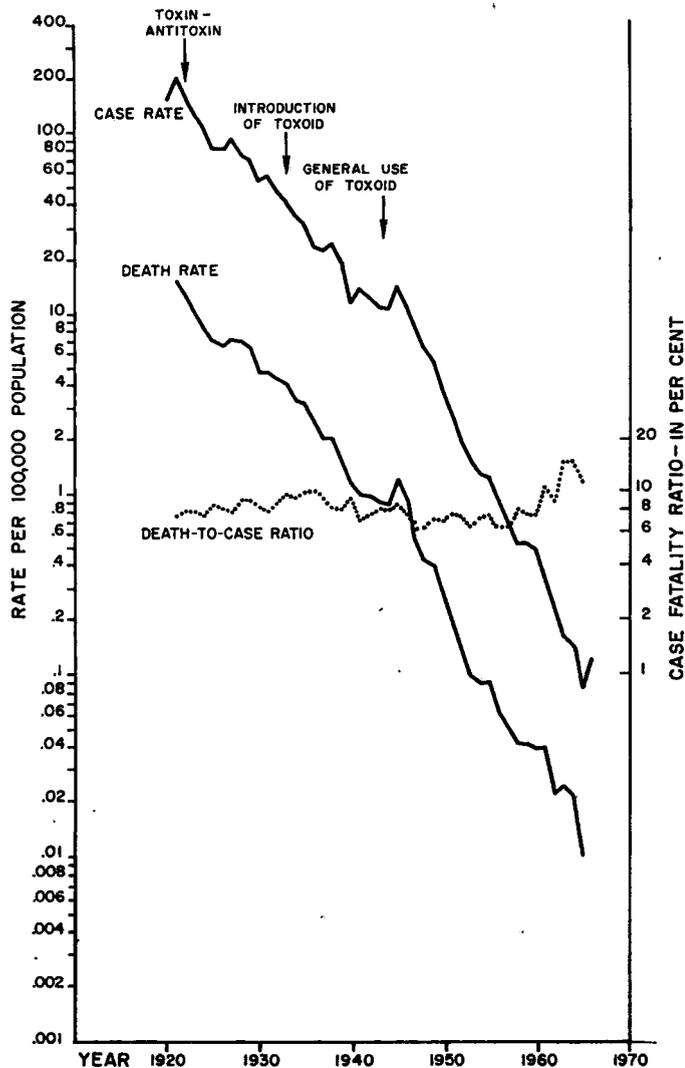
Number of Cases & Deaths
For Selected Years

Year	Cases	Deaths
1933	50,462	4,937
1940	15,536	1,457
1950	5,931	410
1960	918	69
1961	617	68
1962	444	41
1963	314	45
1964	293	42
1965	164	18
1966	209	*Data not available*

Morbidity and Mortality Weekly Report
National Center for Health Statistics

• Since 1920, diphtheria case and death rates have declined dramatically. The availability and use of diphtheria toxin-antitoxin and toxoid contributed to the decline, but concurrent improvements in health care and sanitation undoubtedly also influenced the change. Relative importance of the various factors cannot be completely differentiated.

• Although diphtheria antitoxin therapy deserves some credit for the decrease in diphtheria deaths, widespread use of diphtheria toxoid should be given the major credit for the downward trend.

• Relatively constant death-to-case ratios of about 8% existed until the early 1960's, when a gradual increase (to 14.3% in 1963) occurred. In 1965, the ratio declined to 11%. The reasons for the seemingly increased mortality from diphtheria in recent years appear to be related to a proportionate increase in cases in adults, most of whom were completely unimmunized.

DIPHTHERIA — UNITED STATES, 1966
CASES BY COUNTY

ALASKA

ROSEBUD COUNTY
18

HAWAII

RICHLAND COUNTY
22

ORLEANS PARISH
8

LAFAYETTE PARISH
21

• REPORTED CASE

PUERTO RICO
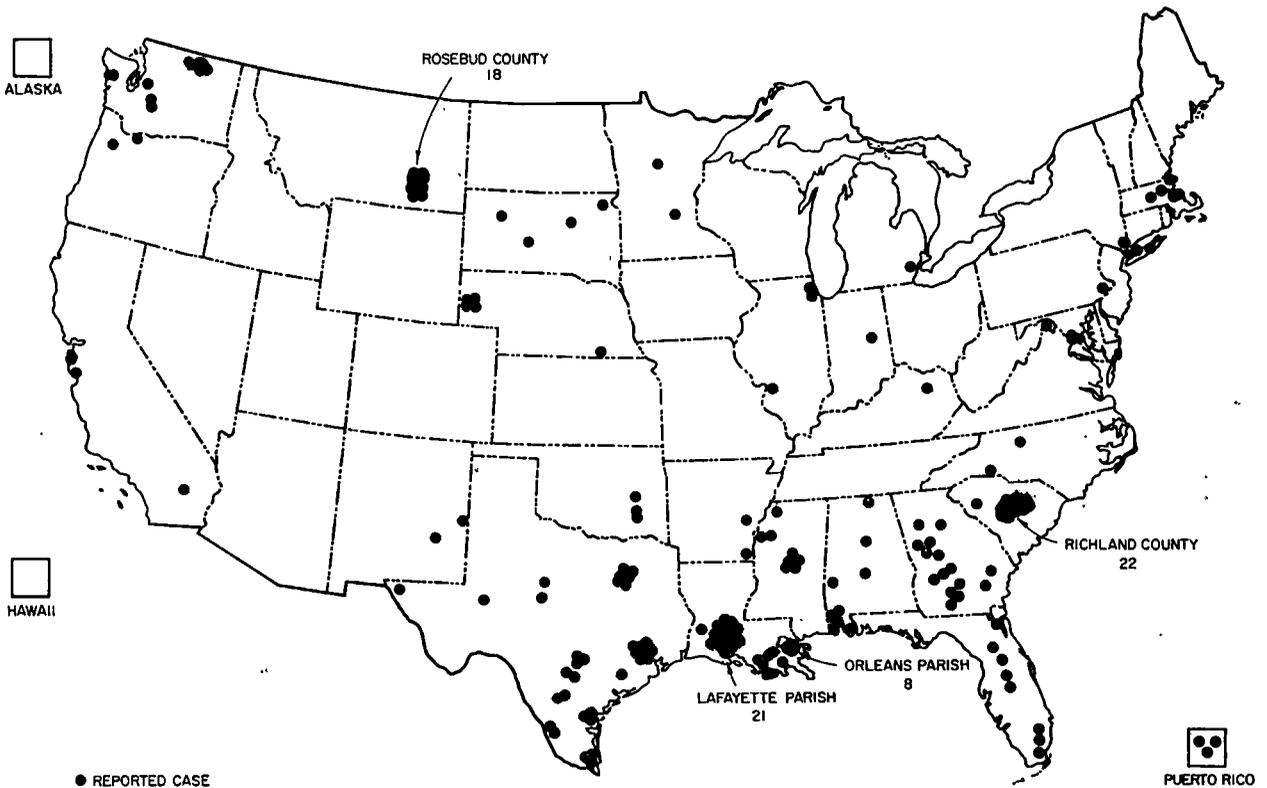
Morbidity and Mortality Weekly Report

• Diphtheria in 1966 was widespread, but a number of somewhat localized epidemics were reported. The majority of outbreaks occurred in the southeastern States and affected primarily unimmunized segments of the population.

• Within urban areas, diphtheria was generally reported in lower socioeconomic populations with inadequate immunization. In rural settings, somewhat less definable population groups were identified, but the relationship of disease to inadequate protection was characteristic.

• In Rosebud County, Montana, an outbreak of diphtheria caused by the intermedius type of *C. diphtheriae* occurred in an Indian population. Outbreaks in Louisiana were caused by a mixture of intermedius, gravis, and mitis types of the organism (the three commonly identified types of *C. diphtheriae*).

DIPHTHERIA — UNITED STATES, 1966
CASES BY AGE GROUPS
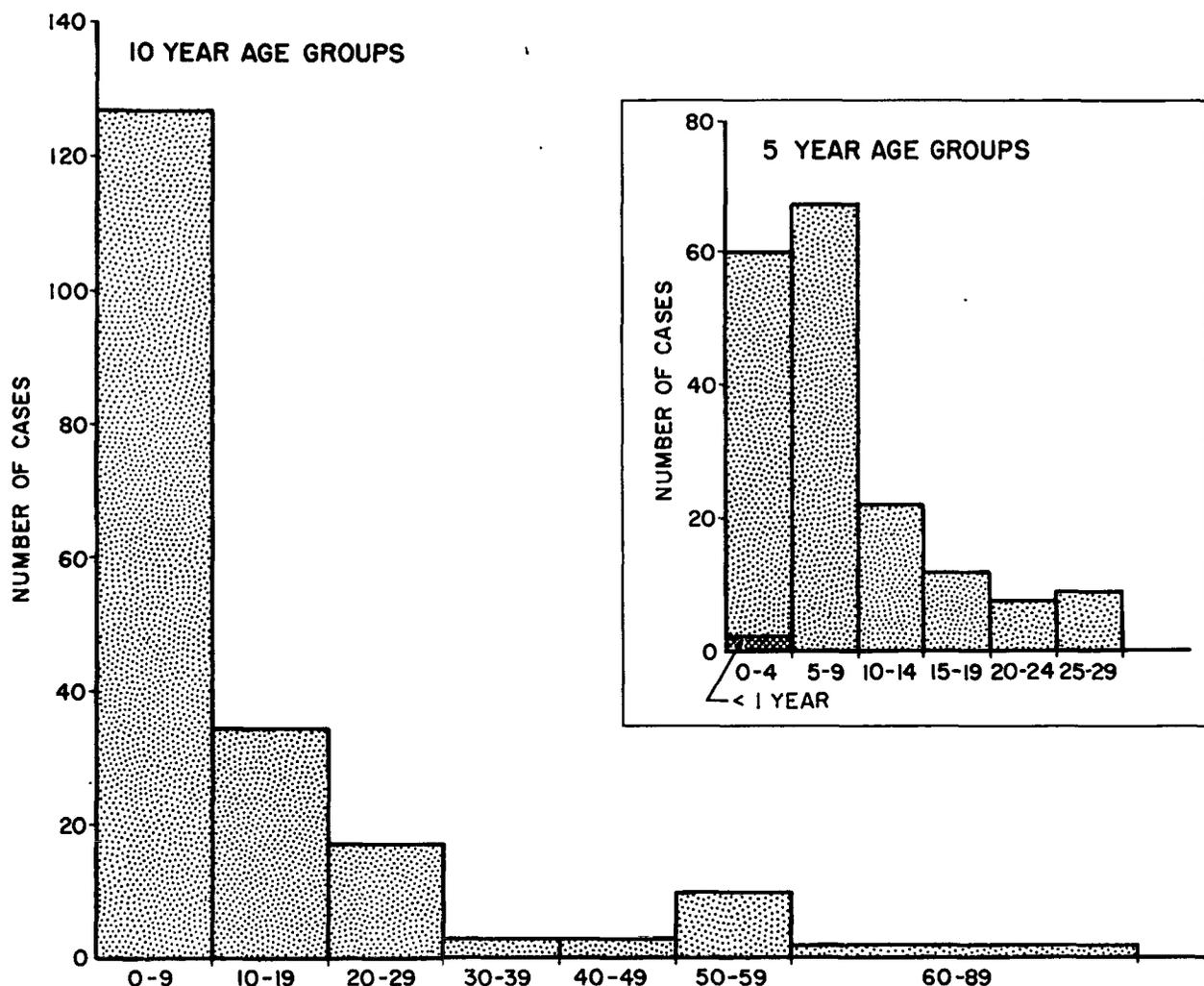
Morbidity and Mortality Weekly Report

• Diphtheria remains primarily a disease of childhood. In 1966, more than 75% of the cases occurred in children under age 15, more than 64% in those under age 10.

• In preschool children (less than 5 years old), only 3% of cases were in children under age 1, which suggests the relative unimportance of diphtheria in infancy and the prominence of cases in the 1-4 year age group. Elementary school children, ages 5-9, were also characteristically affected in 1966.

• Of interest is the distribution of diphtheria cases in adults; there was a persistence of cases in the 20 to 30 year age group and a modest increase in the 50 to 60 year group.

DIPHTHERIA — UNITED STATES, 1965
IMMUNIZATION STATUS OF
DEATHS, NON-FATAL CASES, AND CARRIERS
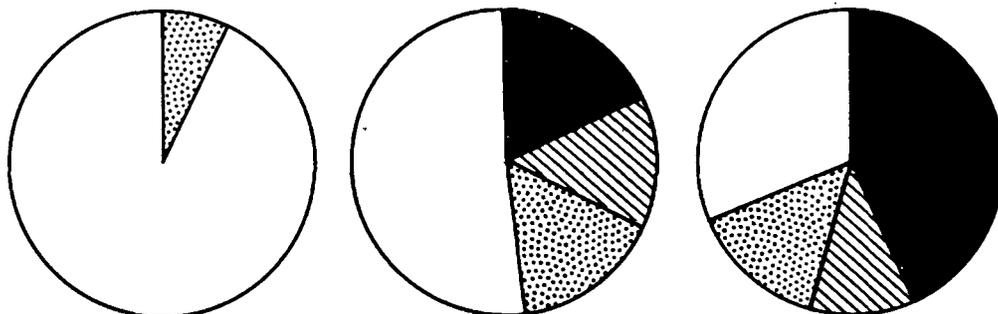
IMMUNIZATION STATUS	NO.	DEATHS %	NO.	NONFATAL CASES %	NO.	CARRIERS %
■ FULLY	0	0	24	17.9	33	44.0
⧄ LAPSED	0	0	19	14.2	6	8.0
▥ INADEQUATE	1	7.1	22	16.4	9	12.0
☐ NONE	13	92.9	69	51.5	27	36.0
TOTAL	14	100.0	134	100.0	75	100.0
UNKNOWN STATUS	2		18		34	
TOTAL REPORTED	16		152		109	

Diphtheria Surveillance, NCDC

• Definition of immunization status represented in this figure depicting 1966 data are as follows:

> **Full** — Primary series (three or more injections, or a primary series plus a booster) completed *within* 4 years prior to onset of illness.

> **Lapsed** — Primary series or a primary series plus booster, completed *more than* 4 years prior to onset of illness.

> **Inadequate** — Uncompleted primary series at any time prior to onset of illness.

> **No** — No diphtheria toxoid prior to onset of illness.

• No *deaths* occurred in individuals with "full" or "lapsed" immunization in 1965. This same observation was made in 1964. In previous years, the few reported deaths in individuals with histories of "full" or "lapsed" immunization generally were complicated cases or occurred in individuals whose immunization histories were of questionable accuracy.

• *Cases* of diphtheria can occur in the fully immunized; *carriers,* identified in investigations of outbreaks, often are fully immunized. These observations indicate that diphtheria immunization *per se* cannot be expected to eliminate the carrier state and thus eradicate the disease.

• Because carriers are generally identified only during investigations of specific outbreaks, a completely objective sample of carrier rates in various segments of the general population cannot be estimated from these data.

TETANUS

Although tetanus was recognized as a clinical entity by Hippocrates, its etiology was not fully understood until the late 19th century, when Nicolaier produced the disease experimentally in animals, Kitasato isolated the organism in pure culture, and von Behring and Kitasato produced tetanus toxin and then tetanus antitoxin. Experiences in World War I confirmed the value of prophylactic passive immunization with antitoxin. In 1925, Ramon introduced tetanus toxoid for active immunization, and in World War II, the incidence of tetanus in troops protected with the toxoid was only 10 percent of what it had been in the previous World War. Since 1945, tetanus toxoid immunization has become almost universal in the United States.

Despite the availability of tetanus toxoid — one of the most effective of the present-day immunizing agents — there has been only a gradual decline in tetanus morbidity and mortality during the past 17 years. In 1950, 486 cases and 336 deaths were reported; in 1966, the reported numbers had fallen only to half.

The persistence of the disease is in part explained by the ubiquitousness of the organism, the lack of natural immunity, and the proportion of the population which is adequately immunized.

TETANUS IN 1966

In 1966, 235 cases of tetanus were reported, a decline from the 300 listed in 1965. A tentative total of 152 deaths in 1966 has been derived from tetanus surveillance reports (NCDC); 181 deaths were officially recorded in 1965. The characteristically high death-to-case ratio persisted.

Although the disease was generally widespread, the East and particularly the Southeast were predominantly affected. Cases occurred in all age groups. Except for cases in the very young age groups, the major importance of tetanus is the frequency with which it affects adults — well over half of the cases in 1966 were in persons over age 50.

Three general groups of tetanus cases emerge: the neonatal tetanus seen in rural areas of the country, particularly in the South and Puerto Rico; tetanus related to accidents and injuries in the general population; and disease in the elderly, where tetanus sometimes complicates chronic lesions, such as those resulting from peripheral vascular disease and diabetes.

TETANUS — UNITED STATES, 1947-1966
CASES AND DEATHS
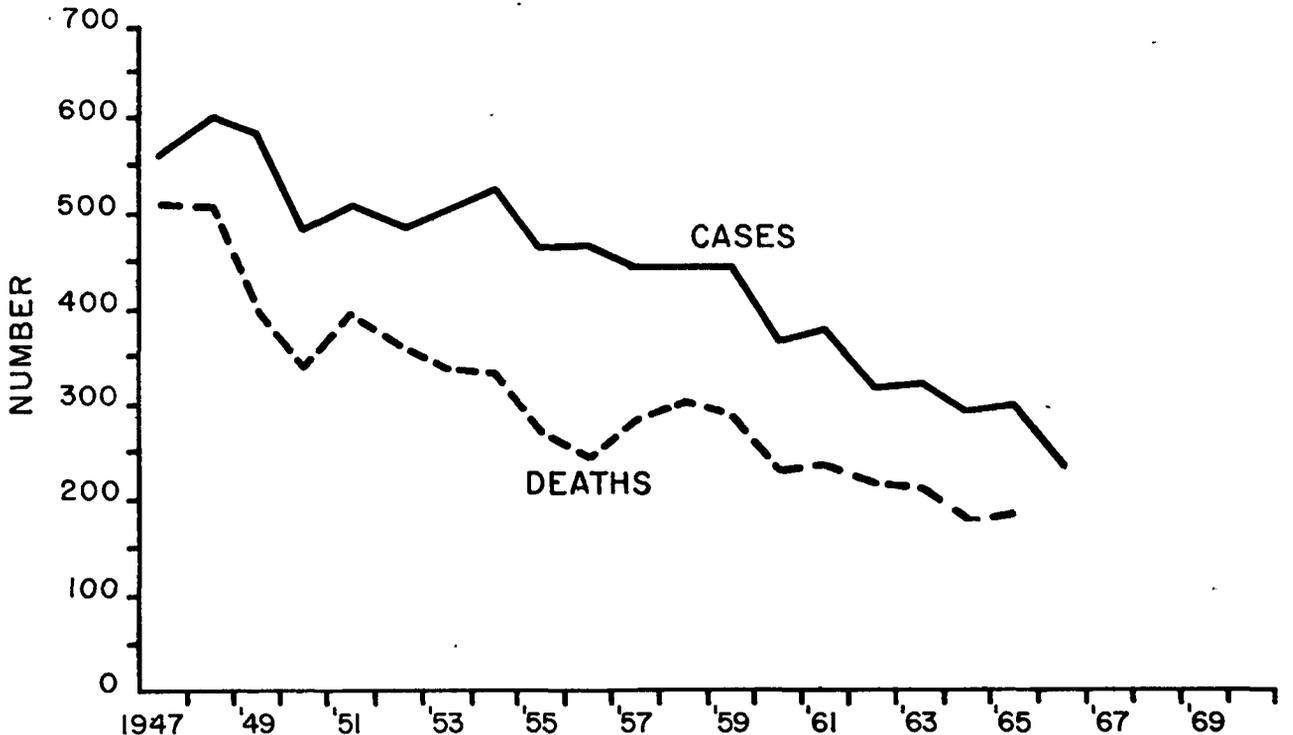
• In the past 20 years, the declines in cases and deaths have been parallel; however, the parallel decline represents a decrease of only about 50%. In view of the highly effective vaccine available for tetanus prophylaxis, the disease has not been brought under control comparable with that seen for the other major communicable diseases, such as diphtheria, poliomyelitis, or petussis.

• The relationship between reported cases and deaths reflects more than a 60% death-to-case ratio. The relative efficiencies in reporting tetanus cases vs. deaths have been suggested to explain this ratio, which some investigators report to be unusually high.

• Tetanus is unique among infectious diseases for which effective vaccines are available — there is no "herd immunity." Each case results from exposure to a source of infection in nature. If the exposed individual is personally unprotected, he can acquire a clinical illness regardless of the general level of protection in the community.

TETANUS — UNITED STATES, 1966
CASES BY COUNTY

ALASKA

HAWAII

● REPORTED CASE

PUERTO RICO
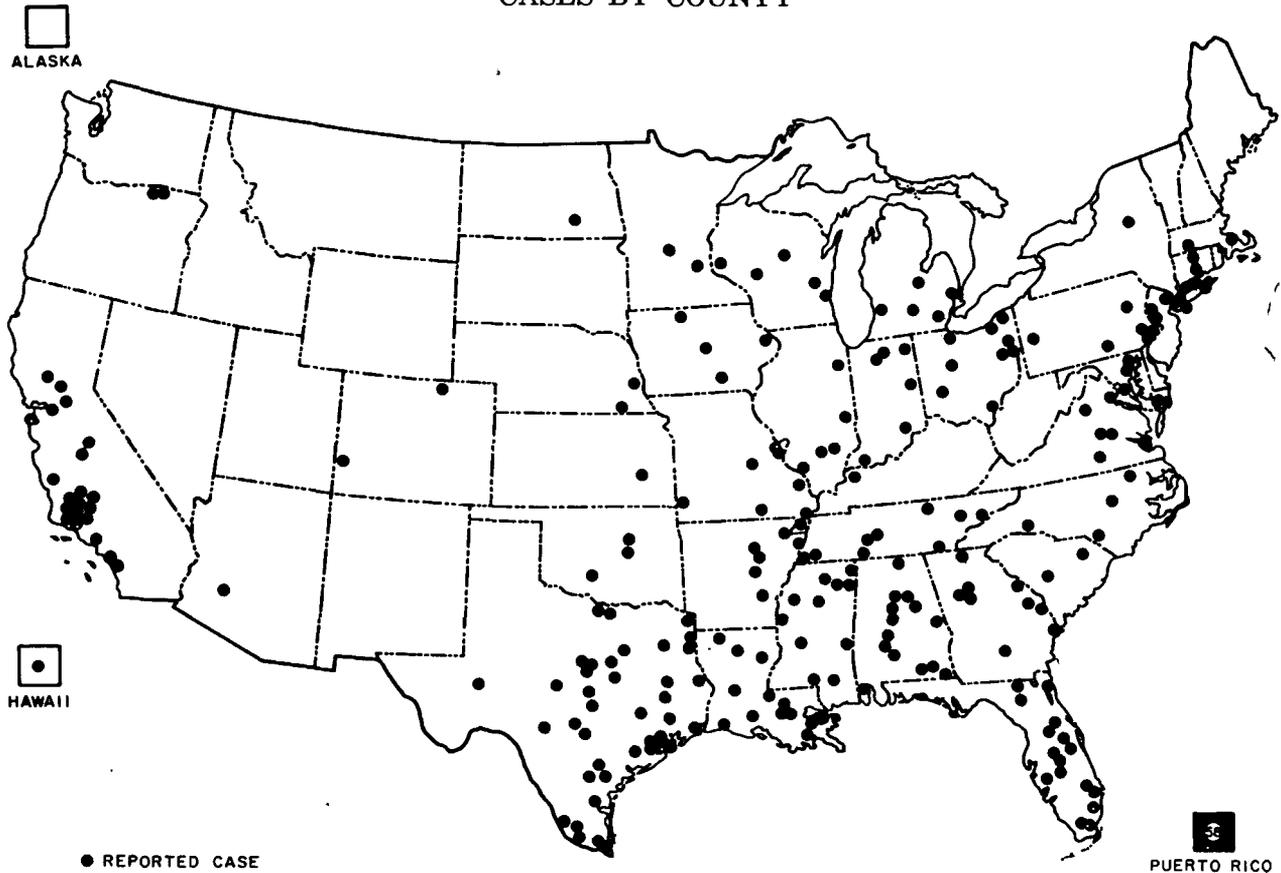
Morbidity and Mortality Weekly Report

● Tetanus cases are reported from all parts of the country, but most of the 235 reported cases in 1966 occurred in the eastern part of the United States, particularly in the southern tier of States. Although tetanus spores are universally distributed, they often abound in areas with extensive farming or grazing.

● The major importance of tetanus in Puerto Rico — 58 cases in 1966 — is related to the high proportion of cases in neonates.

● Neonatal tetanus in the United States has become less prominent in recent years as tetanus immunization among women of child-bearing age became more common and the proportion of births in hospitals or under care of trained personnel increased. In certain parts of the country, particularly the Southeast, neonatal tetanus continues to be recognized.

TETANUS — UNITED STATES, 1966
CASES BY AGE GROUPS

10 YEAR AGE GROUPS

NUMBER OF CASES

(Bar chart: 0-9 ≈54, 10-19 ≈12, 20-29 ≈14, 30-39 ≈20, 40-49 ≈17, 50-59 ≈31, 60-94 ≈35)

5 YEAR AGE GROUPS

NUMBER OF CASES

(Bar chart: 0-4 ≈45 with <1 YEAR ≈34 shaded, 5-9 ≈9, 10-14 ≈7, 15-19 ≈5, 20-24 ≈4, 25-29 ≈10)
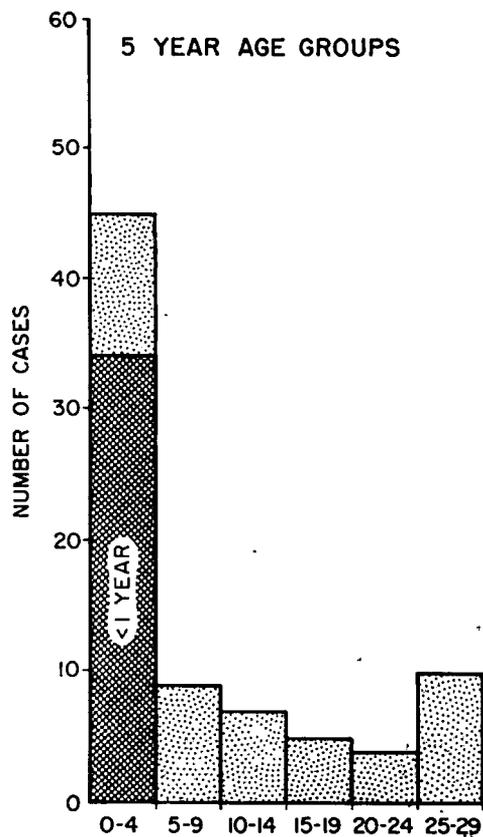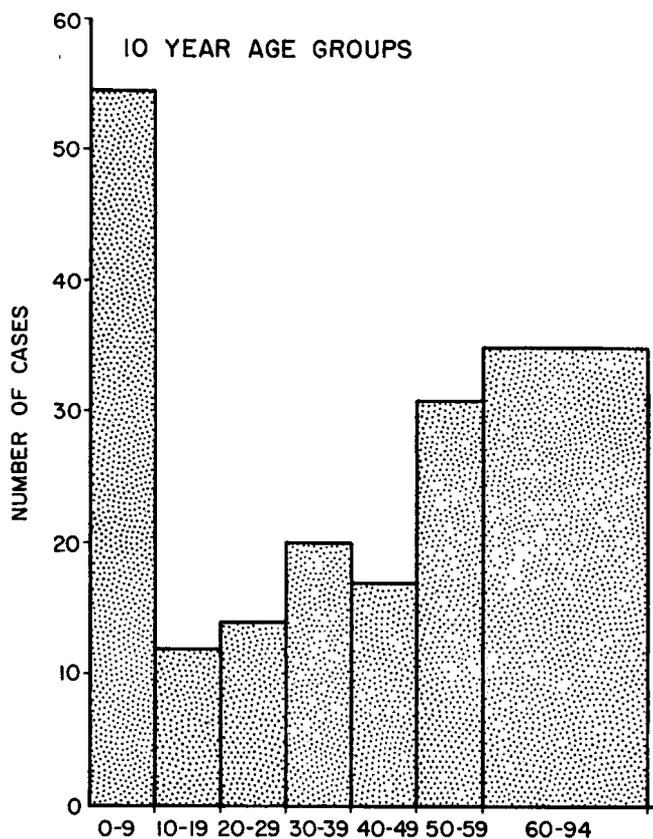
Morbidity and Mortality Weekly Report

• Tetanus occurs in persons of all ages, but particularly in the older adult age groups and in the very young. More than 57% of all reported tetanus cases occurred in adults over age 40, more than 50% in those over age 50, and 37% in those over age 60.

• More than 75% of cases in children under age 5 occurred in the first year of life, largely in the neonatal period.

• Recent investigations of cases reported in 1965 show that essentially all cases were in persons who had had no prior tetanus immunization.

PERTUSSIS

Although pertussis (whooping cough) was described as a clinical entity in 1578 by DeBaillau, not until 1906 was the causative organism isolated by Bordet and Gengou. Pertussis vaccines introduced shortly thereafter varied in their preparation, content, and effectiveness, and therefore had little influence on disease control.

In 1931, Leslie and Gardner demonstrated that changes which occur in the organism's antigenicity and virulence during artificial cultivation partially explain the ineffectiveness of early vaccines. Since the 1940's, pertussis vaccines have been carefully prepared and standardized and have been shown to be effective in preventing illness.

Pertussis is highly communicable; attack rates in reported family outbreaks approach 90%. It occurs in the United States in all seasons but most prominently in winter and spring.

Between 1952 and 1967, both morbidity and mortality rates fell markedly. The disease is still a problem in the United States, however, particularly for the preschool population. In urban communities, 80-90% of reported cases occur in preschool children; and more than half of the total reported cases are in this group. Pertussis continues to be an important cause of infant mortality. Characteristically, more than 70% of pertussis deaths occur in infants.

PERTUSSIS IN 1966

In 1966, 7,717 cases of pertussis were reported, a slight increase over the 6,799 listed in 1965. The disease was widespread but varied somewhat in reported extent in many parts of the country. Although detailed data are not yet available on pertussis deaths in 1966, preliminary summaries point to the usual predominance in infants.

PERTUSSIS — UNITED STATES, 1950-1966
CASES
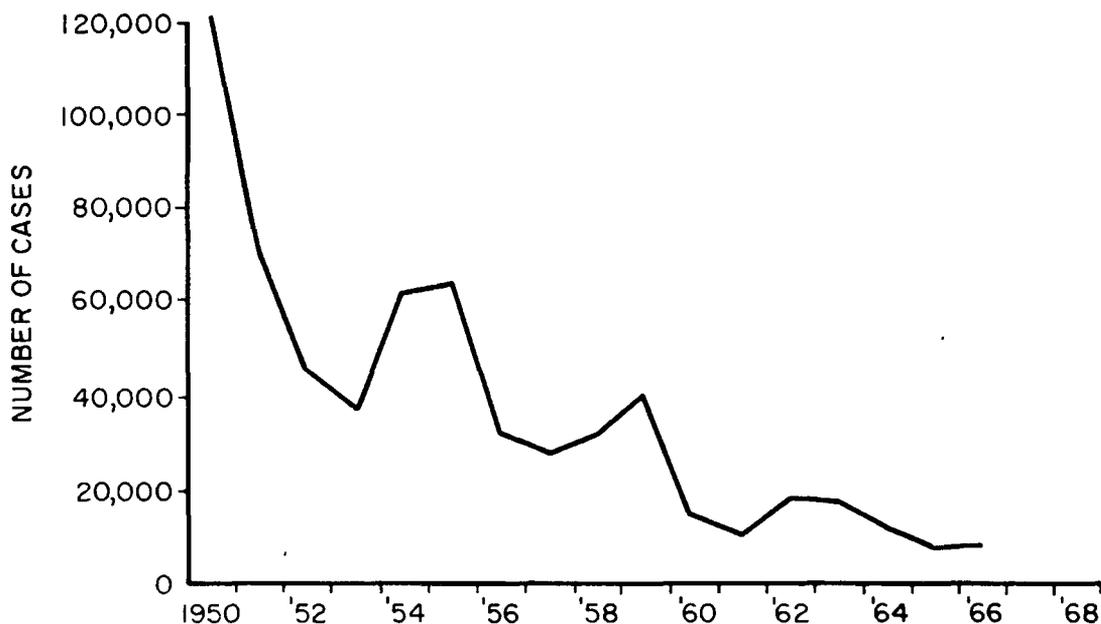
• After 1950, a major decline in reported cases of pertussis was observed. The most marked change occurred between 1950 and 1953, followed by a somewhat irregular and more gradual decline. In 1966, 7,717 cases were reported.

• The temporal trend suggests a cyclical pattern with periodic increases in cases every 4 to 5 years. In the 1960's, however, there has been a damping of this recurring phenomenon.

• Pertussis case reporting is undoubtedly low because of difficulties both in clinical diagnosis in some age groups and in laboratory documentation.

PERTUSSIS — UNITED STATES, 1966
CASE RATES BY STATE
(per 100,000 population)

ALASKA

U. S. REPORTED CASE RATE 4.0

☐ LESS THAN 3

▦ 3 - 5

▨ 6 - 8

■ MORE THAN 8

HAWAII

PUERTO RICO
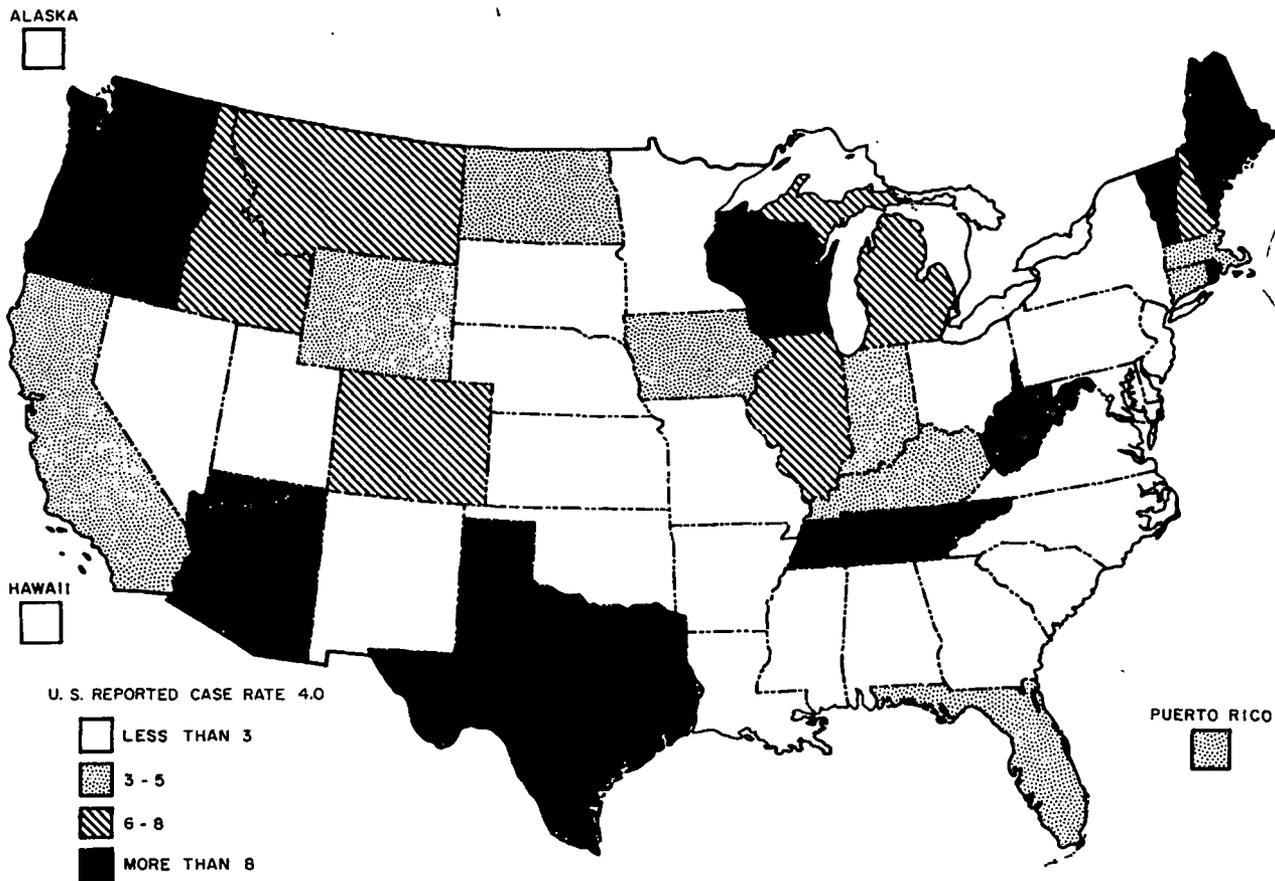
Morbidity and Mortality Weekly Report

• Although pertussis is a widespread disease, its incidence varies considerably from State to State. The variation undoubtedly represents differences in actual occurrence as well as in recognition and reporting.

PERTUSSIS — UNITED STATES, 1950-1965
DEATHS
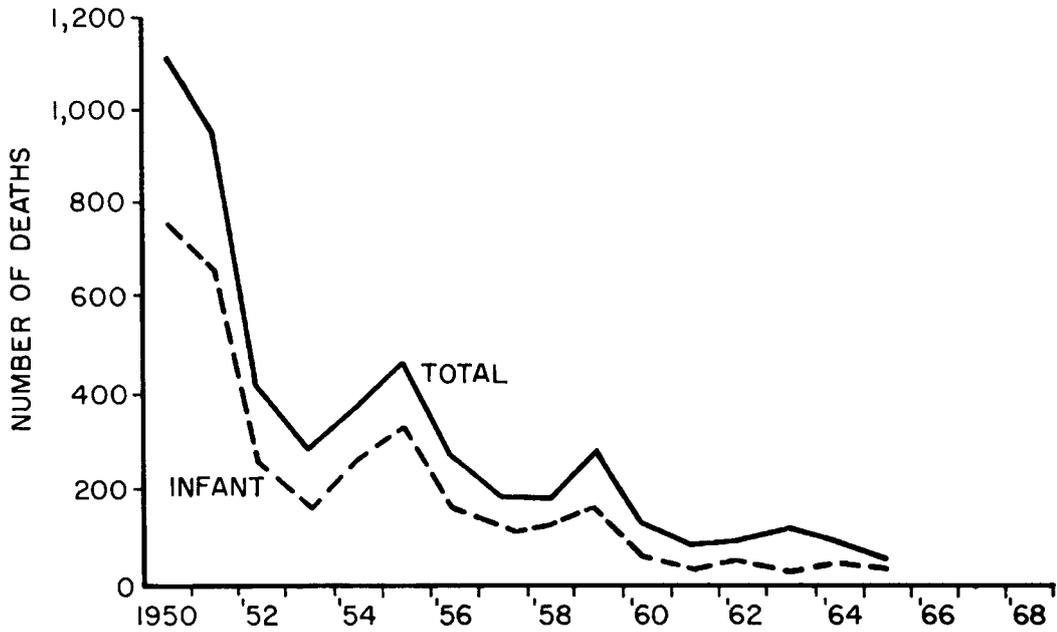
National Center for Health Statistics

- Pertussis deaths declined in direct parallel with pertussis cases from 1950.

- The high death-to-case ratio of pertussis in infants emphasizes the need for early immunization. Importance of the pertussis vaccine component of commonly used DTP is the primary justification for beginning primary immunization at 6 to 8 weeks of age.

PERTUSSIS — UNITED STATES, 1966
DEATHS BY AGE GROUPS
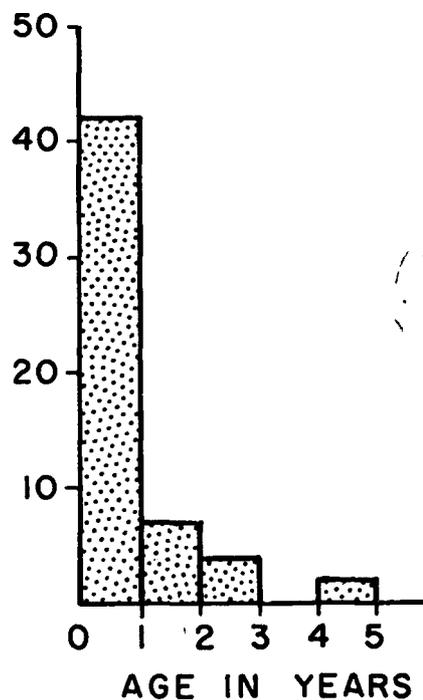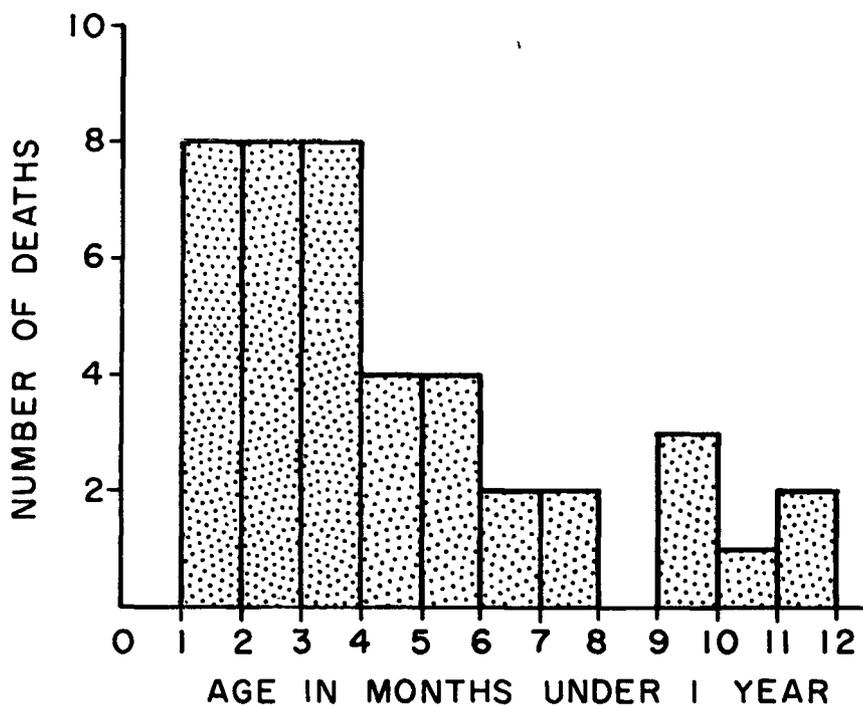
National Center for Health Statistics

• Ages of pertussis patients are not reported nationally. Data on deaths, however, provide insight into the prominence of the disease in infancy, where it is particularly severe.

• Characteristically, 70% or more of the pertussis deaths occur in infants and small children. In 1965 (the most recent year in which mortality data are available) all of the 55 deaths were in children less than 5, and 76% were less than 1 year old.

• Pertussis deaths in children under age 1 occurred primarily in infants less than 4 months of age.

DTP Immunization

DIPHTHERIA, TETANUS, PERTUSSIS IMMUNIZATION
STATUS — UNITED STATES, 1962 AND 1966
AGE GROUPS 1-9 YEARS
(Percent of Groups by Vaccine History)

| | PERCENT BY VACCINE HISTORY | | | | | |
| | 4 Doses | | 3 Doses | | No Vaccine | |
AGE	1962	1966	1962	1966	1962	1966
1	17	19	45	50	17	3
2	31	35	37	39	15	11
3	34	42	37	34	12	10
4	39	50	31	29	12	9
5-9	52	65	24	18	9	5

U.S. Immunization Survey—1966

• Adequate DTP immunization is now defined as four or more doses of vaccine. The generally low proportion (in 1962 and 1966) of children age 1 who had had four or more doses reflects the fact that the fourth dose in the regular series is generally given when children are between 1 and 2 years of age to reinforce immunity.

• Not shown in the table are children under 10 who had received 1 or 2 doses of DTP vaccine; they make up 85% of the total group considered inadequately immunized.

• In 1966, while only 5% of children in the first four years of elementary school were completely *unimmunized* (an improvement over 1962), only 65% of them were *adequately* immunized by current standards.

• The importance of immunization requirements or practices associated with school entrance can be seen in the 15% increase in the number of children who had received four or more doses between age 4 and ages 5-9.

• Thirty-five percent of the early elementary school age groups were inadequately immunized by current standards; of the group, almost 15% had *never* received immunization.

DIPHTHERIA, TETANUS, PERTUSSIS IMMUNIZATION
STATUS — UNITED STATES, 1966

AGE GROUPS 1-9 YEARS — WHITE, NONWHITE
(Percent of groups by vaccine history)

| | PERCENT BY VACCINE HISTORY | | | | | |
| | 4 Doses | | 3 Doses | | No Vaccine | |
AGE	White	Nonwhite	White	Nonwhite	White	Nonwhite
1	21	10	53	33	11	30
2	38	20	40	32	10	23
3	46	22	34	34	9	24
4	53	36	30	24	8	21
5-9	68	47	18	23	4	10

U.S. Immunization Survey—1966

• The immunization status of white children 1-9 years of age was better than that of nonwhites in almost every category — nearly twice as high in many age groups. The most marked difference was in the percentages of those *totally* unimmunized, particularly in the youngest groups.

• Only 47% of nonwhite children under 10 were fully immunized, compared with 68% of white children.

• Despite the difference between the percentage of fully immunized whites and nonwhites, both groups reflect the achievement of immunization practices before or on school entrance. The relatively constant percentages of children of both races at all preschool ages suggests that, in general, many of these children were not provided with completely adequate immunization before entering school.

DIPHTHERIA, TETANUS, AND PERTUSSIS
ANTIGENS — UNITED STATES, 1962-1966
Net Doses (Millions) Distributed Annually

VACCINE	1962*	1963	1964	1965	1966
DIPHTHERIA TOXOID**	19.3	30.4	31.5	29.0	34.5
TETANUS TOXOID**	29.9	49.6	51.8	47.4	53.7
PERTUSSIS VACCINE**	13.8	22.7	22.4	20.9	22.5

*July-December (Biologics Surveillance Program began July 1962)
**Often as combined products

Biologics Surveillance, NCDC

• Most of the vaccine for these three diseases is distributed in combination. The amount of pertussis vaccine used is lowest of the three because it is generally omitted from boosters given older children and adults. More tetanus toxoid is used because of its role in wound management.

• The amounts of these antigens used changed very little in the four full years (1963-1966) in which amounts have been reported.

• Although figures on the distribution of biologics are only an indirect measure of utilization, they give important evidence of yearly trends.

• There is no explanation for the decrease in the amount of all three vaccines distributed in 1965. Since the military supply is included in these figures, one might even expect the amounts to increase in relationship to the number of men inducted into the Armed Forces in recent years.

INFLUENZA

For many centuries, medical historians have recorded numerous intermittent epidemics of respiratory disease now recognized as influenza. The repetitive pattern of these epidemics has become more understandable in the relatively recent past. Identification of the various types of influenza viruses and their variants has given important insights into the disease's epidemic characteristics.

The basic patterns of epidemic influenza are related to the occurrences of its two major virus types — A and B. Each of them undergoes continuing antigenic variation and gradually becomes less and less like the strain which had formerly produced protective antibodies. The variant thus becomes increasingly more capable of causing clinical illnesses once again. Type A viruses appear to undergo variation more rapidly than type B viruses. And epidemiologists have observed a two-to-three-year periodicity for type A viruses, in terms of their ability to cause outbreaks, and a three-to-six-year periodicity for type B.

Influenza, generally a mild disease affecting all age groups, is occasionally a fatal disease. The more serious cases generally occur in the older age groups and especially in those with chronic underlying illnesses of the cardiovascular or respiratory systems. The mortality which accompanies outbreaks of influenza — particularly caused by type A viruses — has become a quantitative measurement of severity and extent.

Type A2 influenza viruses have been prevalent since 1957 when the first A2 (Asian) strains were identified and rapidly replaced the previous A1 viruses. As is characteristic of all influenza viruses, the A2 strains have continued to show minor antigenic variations since 1957 and have produced the characteristic periodic outbreaks. Type B viruses, also present in recent years, have likewise been undergoing antigenic alterations but at the recognized slower rate.

INFLUENZA IN 1966-67

Very little influenza occurred during the 1966-67 influenza season. Although half of the States identified illnesses caused by influenza A2 or B viruses in the winter and early spring months, the general experience was of only very limited outbreaks or incidental cases. Pneumonia-influenza mortality did not rise above the expected seasonal level at any time during the season.

The strains of A2 and B influenza viruses recovered during the year showed continued minor antigenic variation from agents isolated in the preceding year.

Elsewhere in the world, 13 countries, primarily in Europe, identified influenza outbreaks. Nine reported having type A2 virus activity, five reported type B, and one reported both types. Only in the U.S.S.R. and Italy did extensive outbreaks occur; both countries identified type B influenza viruses and involvement of all age groups.

INFLUENZA — UNITED STATES, 1966-67 SEASON
STATES REPORTING TYPE A2

ALASKA

HAWAII

PUERTO RICO

☐ NO ACTIVITY RECOGNIZED

▨ ISOLATED CASES OR OUTBREAKS

■ REGIONAL INVOLVEMENT

Influenza Surveillance, NCDC

• Data for determining geographical extent and temporal relationships of influenza outbreaks are based largely on appraisal summaries submitted by State health officials at the conclusion of the influenza season. (Information through May 30, 1967.)

• Type A2 influenza was identified in 19 States, predominantly States in the eastern half of the country. Although minor in extent, the disease was most prominent in March and April, the end of the usual influenza season. Sporadic cases occurred in Texas, but no clear peak incidence was recognized.

• Only in Georgia was there evidence of widespread illness with identification of more than localized cases or limited outbreaks. In some States, only individual serological identifications were reported.

• Type A2 influenza was last notable in the eastern two-thirds of the country in the 1964-65 season when the New England and Atlantic States in particular were affected, except for several of the large metropolitan areas. In the following year, 1965-66, type A2 virus was widely prevalent in the Far West, particularly in States along the Pacific and in the Southwest. In that same season, type B influenza was occurring in the East and only in scattered parts of the Midwest and Northwest. Influenza in 1966-67 was therefore not expected to be extensive, since in recent years most of the States had experienced both virus types.

INFLUENZA — UNITED STATES, 1966-67 SEASON
STATES REPORTING TYPE B

ALASKA

HAWAII

PUERTO RICO

☐ NO ACTIVITY RECOGNIZED

▨ ISOLATED CASES OR OUTBREAKS

■ REGIONAL INVOLVEMENT

Influenza Surveillance, NCDC

- Type B influenza was recognized in 11 States in the late winter. In Colorado, sporadic cases without a recognizable peak incidence were reported.

- In general, type B influenza occurred as isolated cases or localized outbreaks. Contiguous counties' involvement with widespread disease occurred only in the Southwest.

- In the previous influenza season, 1965-66, type B influenza was widespread in the eastern half of the country but recognized in only a few parts of the Far West late in the year. Its appearance in 1966-67 in the Far West essentially completes its affecting the entire country in two years.

PNEUMONIA — INFLUENZA DEATHS
122 UNITED STATES CITIES, 1964-1967 SEASONS

• During influenza outbreaks, particularly those caused by type A viruses, mortality attributable to pneumonia and influenza is generally a direct measure of the severity and extent of the disease. In 1962-63, a major epidemic of A2 influenza occurred, with considerably increased mortality. No subsequent years have had comparable influenza epidemics.

• A weekly estimate of the geographic distribution of epidemic influenza is evidenced in pneumonia-influenza deaths reported currently from 122 U.S. cities cooperating with the NCDC in influenza surveillance.

• The expected weekly number of deaths calculated from a series of previous years' reports form a baseline with which to compare current reports. The "epidemic threshold" is a statistical measurement for determining epidemics based on variation from the baseline.

• In the 1964-65 and 1965-66 influenza seasons, modest excursions above the "epidemic threshold" were correlated directly with outbreaks of influenza. In 1964-65, the contributing epidemics were caused by type A2 virus occurring primarily in the eastern part of the country. In 1965-66, the excess pneumonia-influenza mortality associated with type A2 influenza occurred in the Far West and Southwest. The type B outbreaks of 1965-66 which affected the East did not contribute substantially to the increased mortality.

• In 1966-67, there was no evidence whatever of increased pneumonia-influenza deaths, and indeed the reported mortality was generally below the expected amount. These observations on pneumonia-influenza deaths from 122 cities correlate directly with epidemiologic observations of minimal influenza in this country.

PNEUMONIA — INFLUENZA AND TOTAL EXCESS MORTALITY — UNITED STATES, 1934-1965
DEATH RATES BY MONTH AND DURING EPIDEMIC PERIODS

Monthly Rates - Annual Base

PNEUMONIA-INFLUENZA DEATHS PER 100,000

TOTAL EXCESS DEATHS PER 100,000

Type A Epidemics

Type B Epidemics

ALL CAUSES
PNEUMONIA-INFLUENZA

Influenza Surveillance, NCDC

• Using pneumonia-influenza death rates as an index of epidemic influenza, the regular but variable increases in the winter-spring influenza season are evident. When the causative influenza virus — either type A or type B — is related to the excess death rate, a periodic and somewhat cyclical pattern for both type A and type B epidemics is revealed.

• In general, from 1934, type A epidemics occurred every two to three years and type B every three to six years.

• Type A epidemics are generally associated with a greater proportion of deaths than type B outbreaks are.

• Whether measuring excess deaths due to all causes or those due to pneumonia-influenza, one can demonstrate a direct correlation between the severity of the epidemic in broad epidemiologic terms and the associated mortality.

• Forecasts of influenza outbreaks are based on knowledge of the periodicity and other characteristics of the disease.

EXCESS PNEUMONIA-INFLUENZA MORTALITY — UNITED STATES, FEBRUARY-MARCH 1963 BY AGE GROUPS

FEBRUARY - MARCH 1963
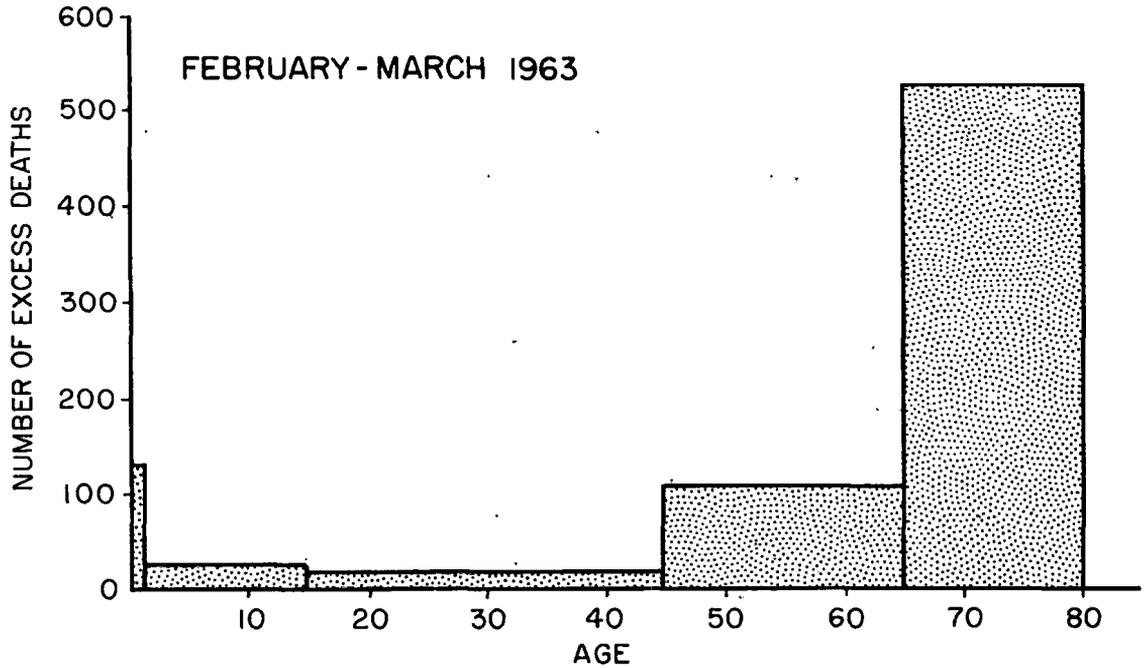
Morbidity and Mortality Weekly Report

• Looking at one specific epidemic period, February through March 1963 (the period of the last major United States epidemic associated with type A2 influenza virus), the characteristic mortality in older people is apparent. The major burden was borne by those over age 45 and particularly those over 65.

• In all age groups experiencing increased mortality during influenza outbreaks, those individuals with underlying chronic illnesses — cardiovascular, pulmonary, and metabolic disorders — appear to be particularly susceptible to complications and to death.

INFLUENZA VACCINE — UNITED STATES, 1962-1966
Net Doses (Millions) Distributed Annually

Vaccine	1962*	1963	1964	1965	1966
Influenza Vaccine	42.7	44.4	9.8	10.5	20.9

*July-December (Biologics Surveillance began in July 1962)

Biologics Surveillance, NCDC

• When the expectation is for only the usual seasonal increase of influenza, immunization is recommended for only those individuals in high risk groups — the older age groups and the chronically ill.

• The substantially greater-than-average distribution of influenza vaccine in 1962 and 1963 is related to the emphasis on immunization for that particular season, in which a major increase in influenza was expected. As predicted, a widespread outbreak of type A2 influenza did occur in the United States in the 1962-63 season. In subsequent years, lesser amounts of influenza were expected, and general immunization was not recommended.

MEASLES (RUBEOLA)

Some historians claim that the first recorded epidemic of measles was described about 1,000 years ago by Rhazes, a Persian physician. However, medical records describing syndromes compatible with measles suggest that the disease was often confused with smallpox, particularly during the Middle Ages, when severe epidemics of measles-like disease with many associated deaths swept through Western Europe.

In 1846, Panum investigated an outbreak of measles in the Faro Islands, many years after the last epidemic. His notes and analysis are an epidemiologic clasic. Panum documented a number of the identifying features of measles: its characteristic incubation period, high infectivity, respiratory route of spread, higher mortality in infants, and apparently life-long immunity following clinical illness.

For a century following publication of Panum's report, no significant advances were made toward a complete understanding of measles. At last, Enders and Peebles isolated the measles virus in cell culture in 1954, and it became possible for the first time to develop a vaccine that could alter the characteristic pattern of measles in human populations.

Measles has been a universal infection. Mortality from the disease has always been generally low in the United States and Europe, while a major cause of death in certain age groups in other parts of the world. Proportionately, measles is not a highly fatal illness; however, the infection was so common that it caused 400 or more deaths each year in the United States before the vaccine was developed.

Measles complications, such as pneumonia and otitis media, continue to be relatively common. Encephalitis develops with approximately one of every 1,000 measles cases; about one-third of the patients with encephalitic complications die, and another one-third suffer permanent central nervous system damage. Death occurs in approximately one of every 10,000 cases of measles. (The 10-fold higher ratio derived from reported deaths and cases in past years results from the inaccuracy in case reporting.)

Measles is primarily a disease of infants and young children, with the elementary schools serving as the primary focus of community outbreaks and the reservoir from which disease is transmitted to preschool children and infants. The disease has been so common in the first seven or eight years of life that often 95% or more of the individuals reaching early adolescence have serological evidence of immunity.

Measles immunization programs since 1963 have already markedly altered the characteristic pattern of measles epidemics. A direct relationship is seen between the extent of vaccination and the decline in measles cases and deaths.

MEASLES IN 1966-67

Because measles is primarily a disease of late winter and early spring, incidence during a measles season, or "epidemiologic year," beginning in mid-autumn is more easily interpreted than that during the calendar year. Much of the subsequent discussion will be based on this epidemiologic time period.

During the latter half of 1966, a major effort was launched in the United States to eradicate measles. This effort resulted not only in accelerated programs of immunization but also in improved reporting of measles cases and outbreaks of the disease. As a result of these programs, less than one-third as many cases were recorded in the first half of 1967 (54,629) as in the first half of 1966 (178,678), the previous "low." This marked reduction in reported incidence is probably a low estimate of the true reduction, for reporting of measles cases has also greatly improved in the past years.

In some States, where high levels of immunization have been achieved, measles has essentially disappeared. In other areas, where vaccination has been less widespread and where epidemic control programs have been less actively pursued, the reported incidence of measles has declined only slightly.

MEASLES — UNITED STATES, 1956-1966
CASES BY FOUR-WEEK PERIODS
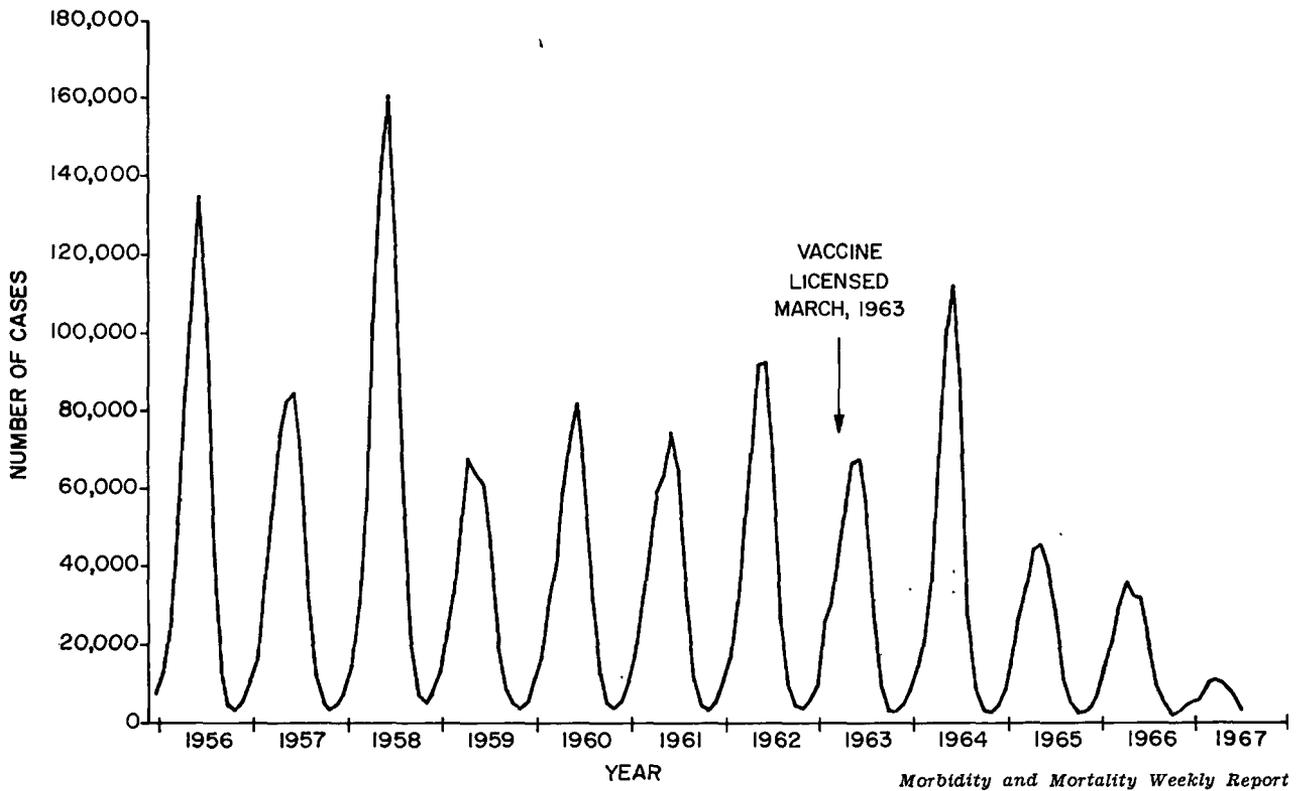
Morbidity and Mortality Weekly Report

- The pattern of measles cases in the United States is characterized by a recurrent late winter-spring peak each year. Incidence in the spring of 1964 reflects an unknown admixture of rubella, which was unusually epidemic at that time. In smaller and more circumscribed populations, such as small States or single metropolitan areas, measles shows a characteristic two-to-three-year periodicity.

- It has been estimated that over the past decade only about 10% of the measles actually occurring has been reported. It is known that some 90% of our adolescent and young adult populations have immunity to measles; such levels of natural immunity could be achieved only if some 4,000,000 cases occurred annually rather than the 400,000 reported annually until 1945.

- The impact of measles vaccination was suggested in the incidence figures in 1965, became evident in 1966, and is dramatic in 1967. The number of cases presently being reported is the lowest since measles reporting began early in the century (1912).

MEASLES — UNITED STATES
CASES AND DEATHS

Cases by Four-Week Periods
1964-1967
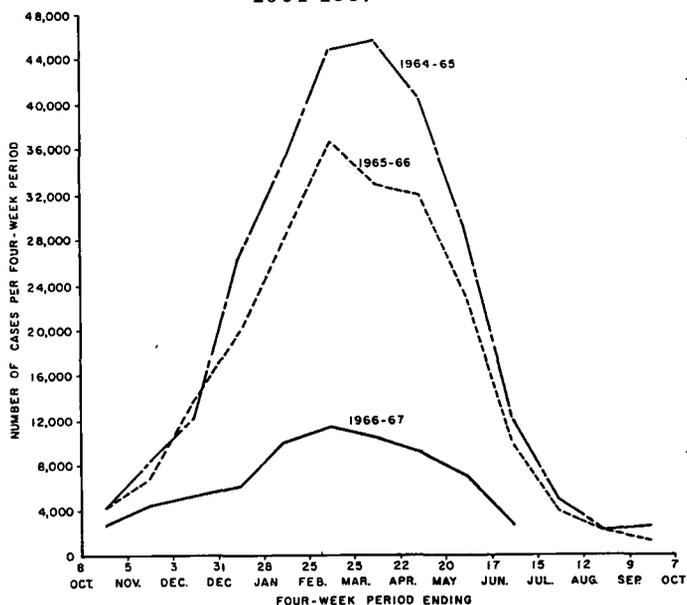
Selected "Epidemiologic Years"*

"YEAR"	CASES (thousands)	DEATHS
1959-60	441	375
1960-61	425	421
1961-62	482	430
1962-63	391	365
1963-64	461	430
1964-65	262	265
1965-66	217	*Data not available*
1966-June 67	67	*Data not available*

*October-September

• The characteristic winter epidemic of measles is most easily recognized in this figure based on a period relevant to the disease — beginning in October.

• The regular decline in measles during the last three years was dramatic in the 1966-67 epidemiologic year (through June 1967). Even its seasonal characteristic was somewhat damped in the winter months.

• In 1966-67, the number of reported measles cases was approximately one-third the number reported in a comparable period of 1965-66, the previous "low" in the United States measles records.

MEASLES DEATHS — UNITED STATES, 1955-1964
PERCENT DISTRIBUTION BY AGE FOR 10-YEAR PERIOD

National Center for Health Statistics
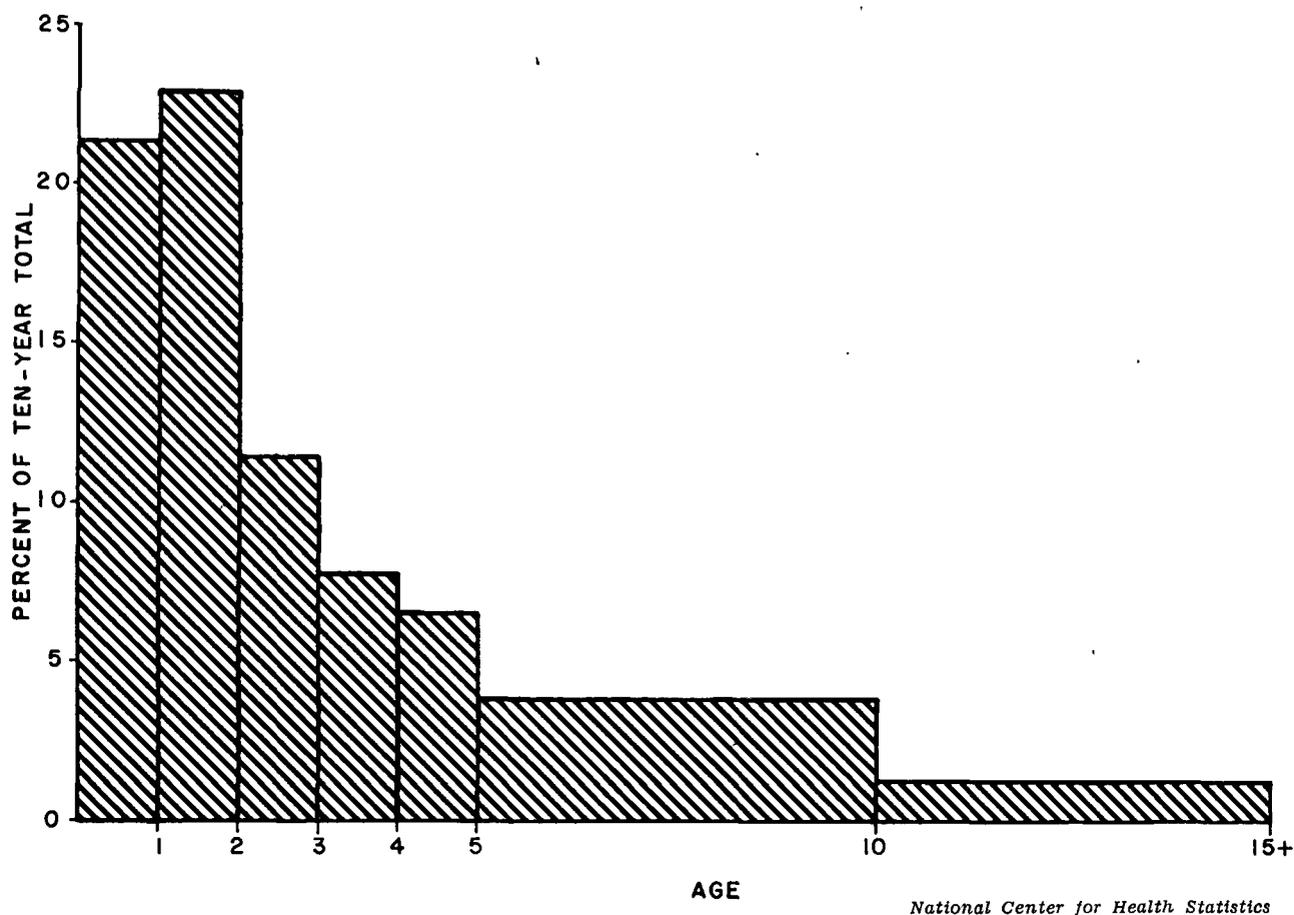
• In the 10 years beginning with 1955, the annual number of measles deaths by calendar year ranged from 345 (1955) to 552 (1958) with the mean of 421. The 10-year total number of deaths was 4,208. With widespread use of measles vaccine since 1964, the number of deaths has declined — 421 were reported in 1964 and 276 in 1965. The data are not available for 1966.

• More than forty-five percent of measles deaths in the 10-year period 1955-1964 occurred in infants, and 70% occurred in children less than 5 years old.

• Measles deaths occur almost exclusively in children. Rarely is an adult death reported. Most measles fatalities occur in patients with central nervous system or respiratory tract complications.

MEASLES — UNITED STATES
ESTIMATED PROPORTION OF IMMUNES BY AGE

Four Investigations of Measles Illness

ATLANTA, 1961
BLACK, 1959
COLLINS, 1942
COLLINS, 1929
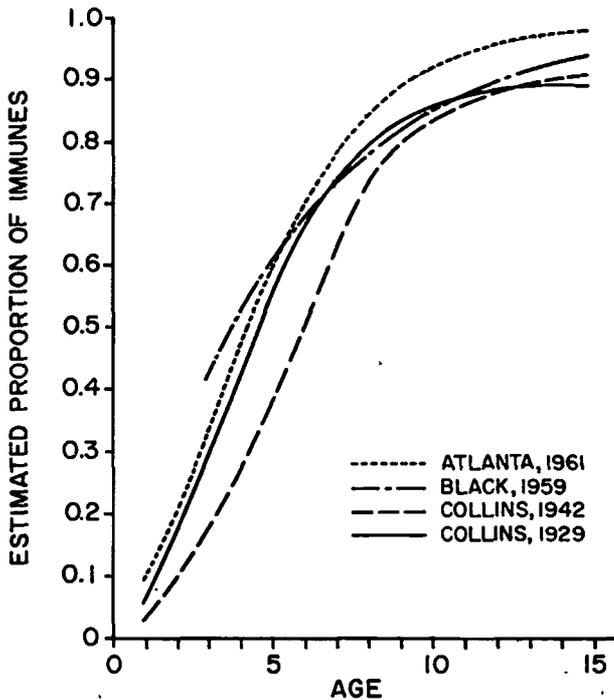
Histories of Measles Illness and Measles Vaccine
1965 and 1966

| YEAR | AGE | PERCENT OF GROUP | |
		History of Measles Illness	History of Measles Vaccine
1965	< 1	2.0	6.5
	1-4	19.7	33.2
	5-9	54.3	19.3
1966	< 1	2.0	9.1
	1-4	16.5	45.5
	5-9	49.0	28.0

U.S. Immunization Survey, 1966

• The chart relating measles and age is derived from four different surveys carried out between 1929 and 1961 (before measles vaccine). The highly consistent findings show that by age 10 nearly 85% of the population had a history of measles. Serologic surveys confirm the accuracy of historical data on measles immunity and often increase the proportion of immunes in the population to 95% by early adolescence.

• There is an almost straight-line increase in the proportion of children between ages one and eight who give a history of measles illness — increasing at a rate of about 10% per year.

• The table compares histories of measles *illness* with measles *vaccination* in 1965 and 1966 surveys. In only one year's time, all age groups showed a moderate rise in the proportion with history of measles vaccine, and all but one showed a decline in history of measles illness.

• In 1965, 51% of the 1-4 year age group and 70% of the 5-9 year age group had had either measles illness or vaccine. In 1966, the respective totals were 59% and 73%. In order for measles to be eradicated, the total proportion of immune children will need to be increased and maintained at relatively high levels.

MEASLES VACCINES — UNITED STATES, 1963-1966
Net Doses (Millions) Distributed Annually

VACCINE	1963*	1964	1965	1966
Measles Virus Vaccine, Inactivated	0.7	0.5	0.3	0.2
Measles Virus Vaccine, Live, Attenuated	3.2	3.8	6.0	7.9

*Production began during the year

Biologics Surveillance, NCDC

- From 1963, when measles virus vaccines became available, to 1966, 1.7 million doses of the inactivated vaccine and 20.9 million doses of the live, attenuated vaccine were distributed in the United States.

- Use of inactivated measles virus vaccine has always been considerably less than use of the live, attenuated vaccine; distribution of the inactivated product has declined steadily since 1963. The decline reflects the growing preference for the live, attenuated antigen which gives lasting protection with only a single dose.

- Because only one dose of the live, attenuated vaccine is needed for complete immunization, it is possible to estimate broadly the decline in susceptibles from information on distribution of vaccine. Obviously a factor to account for unused material must be introduced into calculations, because not all doses of vaccine distributed are used, and many are not returned to the producers. Some observers suggest that possibly 10% of live, attenuated measles virus vaccine distributed is not used.

- Multiple doses of inactivated measles virus vaccine and regular booster doses are required for protection. The doses of this product distributed cannot, therefore, give very meaningful estimates of the number of individuals who are adequately protected as a result of its use in immunization activities.

POLIOMYELITIS

Following the recognition of poliomyelitis as a clinical entity by Heine (1840) and Medin (1891), Wickman and Frost characterized the disease epidemiologically in the early 1900's. Not until early in this century did Landsteiner (1909) establish the viral etiology of poliomyelitis. In 1949, Howe, Badian, and Morgan identified the three serotypes of poliovirus; and Enders, Weller, and Robbins demonstrated that polioviruses could be propagated in tissue culture. Finally, Horstmann and Bodian (1954) showed that a viremic stage of the disease occurs. The foundation was thus laid for the development, first, of inactivated poliomyelitis vaccine (IPV), licensed in 1953, and then of live oral poliovirus vaccine (OPV), licensed in 1961.

Over the past decade, because of the·availability and general use of effective polio vaccines, the epidemiologic pattern of poliomyelitis in the United States has altered markedly: First, the annual incidence of the disease has declined dramatically — in 1955, there were 14,850 cases of paralytic poliomyelitis and 1,053 deaths, in contrast, in 1966, there were only 108 paralytic cases and seven deaths. Second, poliomyelitis cases now occur primarily in unimmunized preschool children in lower socioeconomic groups rather than affecting all ages and socioeconomic groups. Third, there have been no major outbreaks of poliomyelitis within limited geographic areas since 1963.

PARALYTIC POLIOMYELITIS IN 1966

The number of cases of paralytic poliomyelitis in the United States increased from 61 in 1965 to 108 in 1966. Two-thirds (73) of the 1966 cases represented one dispersed type 1 poliovirus outbreak in Texas. The Texas cases were distributed among 30 counties, with no one county reporting more than 10 cases.

The 35 cases occurring outside Texas in 1966 were widely scattered in 16 States and Puerto Rico. No single poliovirus type predominated.

That most cases occurred in the summer was due primarily to the Texas outbreak, which reached its peak in July. Eighty-one of the 108 cases (75%) were in preschool children, most of whom were either totally unimmunized or were inadequately immunized.

POLIOMYELITIS — UNITED STATES, 1941-1966
CASES

Morbidity and Mortality Weekly Report
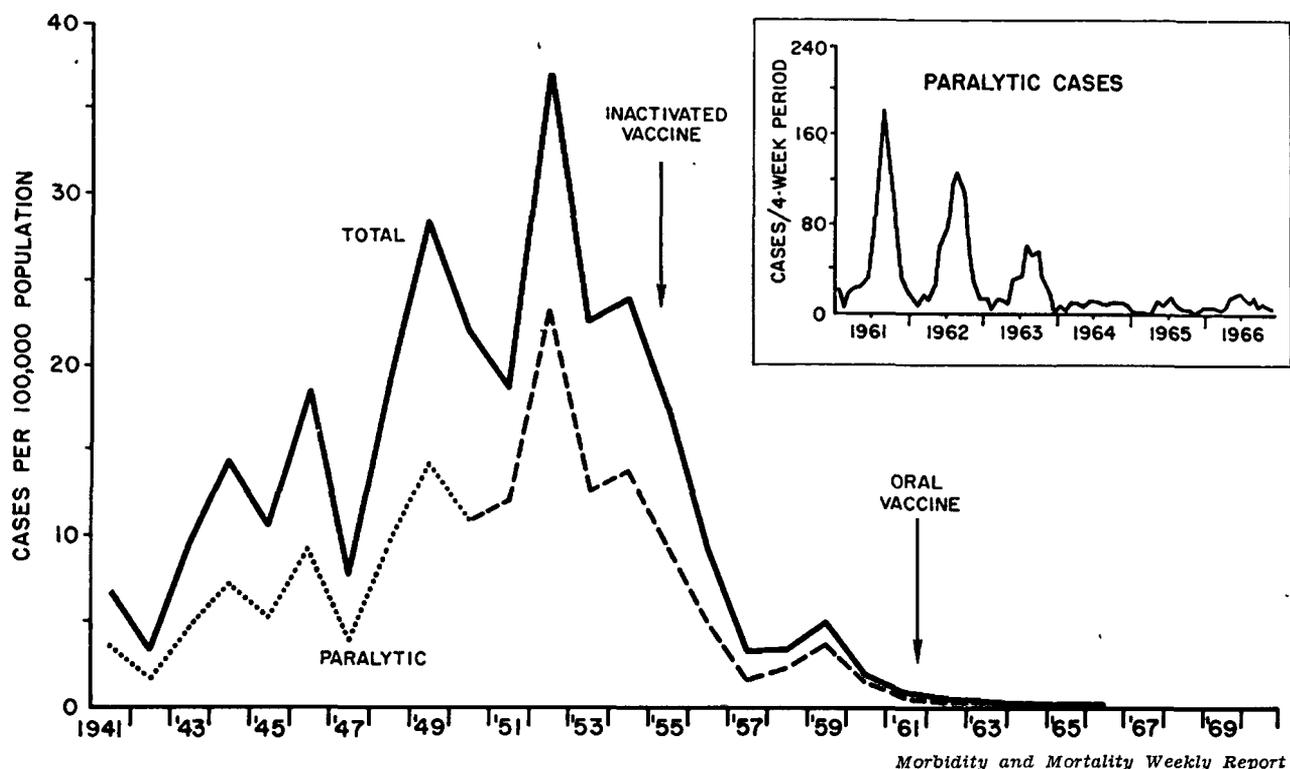
• Widespread use of effective vaccines has resulted in virtual eradication of poliomyelitis in the United States. Although inactivated vaccine appears initially to have altered incidence more dramatically than oral vaccines, the predominent use of oral vaccines in recent years has further reduced occurrence of the disease (see insert).

• Prior to 1951, *paralytic* poliomyelitis was not differentiated within the total reported cases. In this figure, it is assumed that paralytic cases represented 50% of the total number reported before 1951.

• The high reported incidence of poliomyelitis in the late 1940's and early 1950's was due in part to improved disease reporting with the admixture of cases of polio-like disease caused by ECHO and Coxsackie viruses.

• The characteristic peak incidence of poliomyelitis in temperate climates in late summer and fall can still be discerned (see insert). The summer predominence in 1966 was due primarily to the outbreak in Texas.

• Decrease in the proportion of cases reported as non-paralytic poliomyelitis in the past 10 years is partially attributable to improvement in identifying the actual etiologies of syndromes formerly ascribed clinically to poliovirus infection.

PARALYTIC POLIOMYELITIS — UNITED STATES, 1966
CASES BY COUNTY

ALASKA

HAWAII

● REPORTED CASE

ZAVALA AND
MAVERICK COUNTIES
9

STARR, HILDAGO,
AND CAMERON COUNTIES
18

BEXAR COUNTY
10

PUERTO RICO
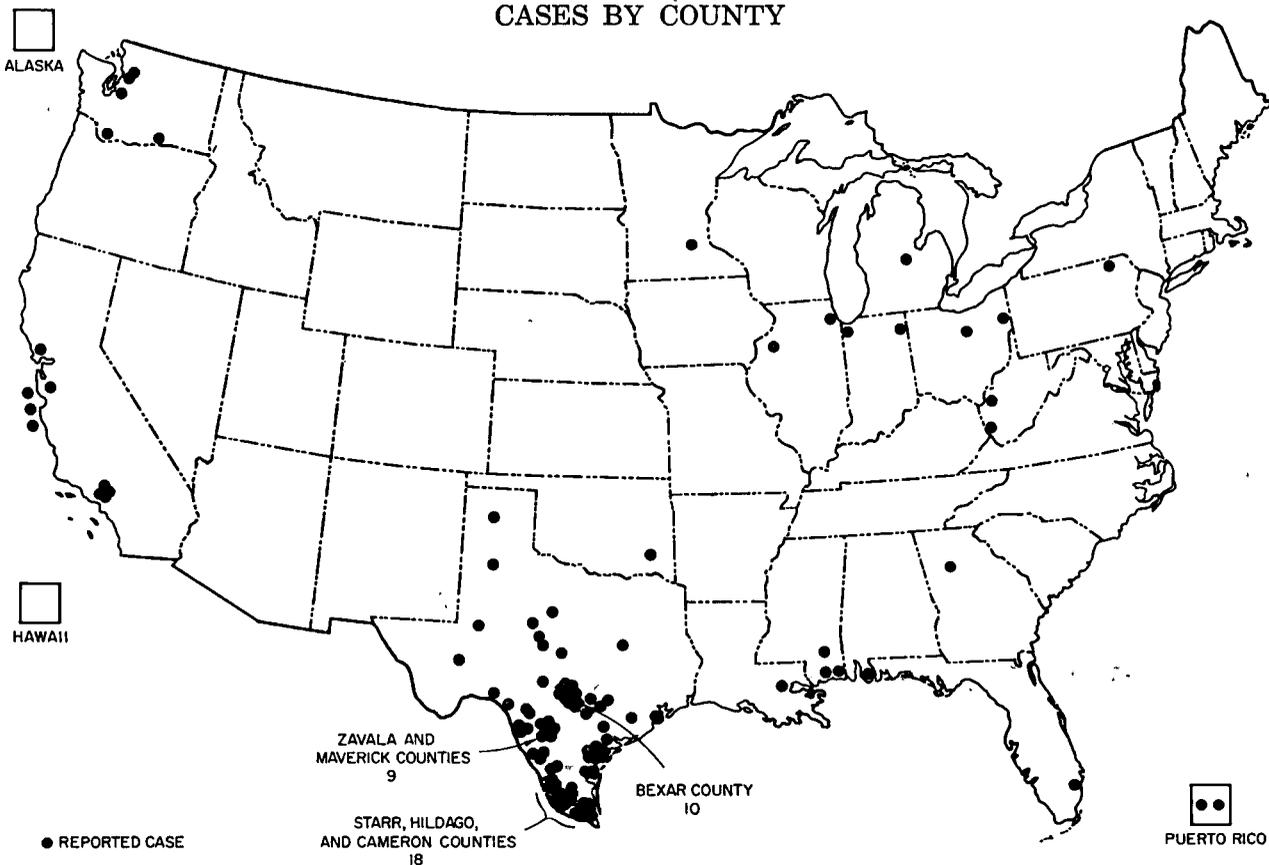
Morbidity and Mortality Weekly Report

● Two-thirds of the 108 cases of paralytic poliomyelitis in 1966 were reported from Texas, where a type 1 poliovirus epidemic occurred.

● The Texas outbreak was not limited to a single area: the 73 cases were distributed among 30 counties. Cases were concentrated primarily in the southern part of the State, with the earliest cases occurring along the Mexican border.

● Cases outside Texas occurred in 16 States and Puerto Rico, with no more than three cases identified in a single county.

● Despite the appearance of wild poliovirus in 30 Texas counties and in 16 other States and Puerto Rico, *no* focal outbreaks resulted.

PARALYTIC POLIOMYELITIS — UNITED STATES, 1966
CASES BY AGE AND IMMUNIZATION STATUS
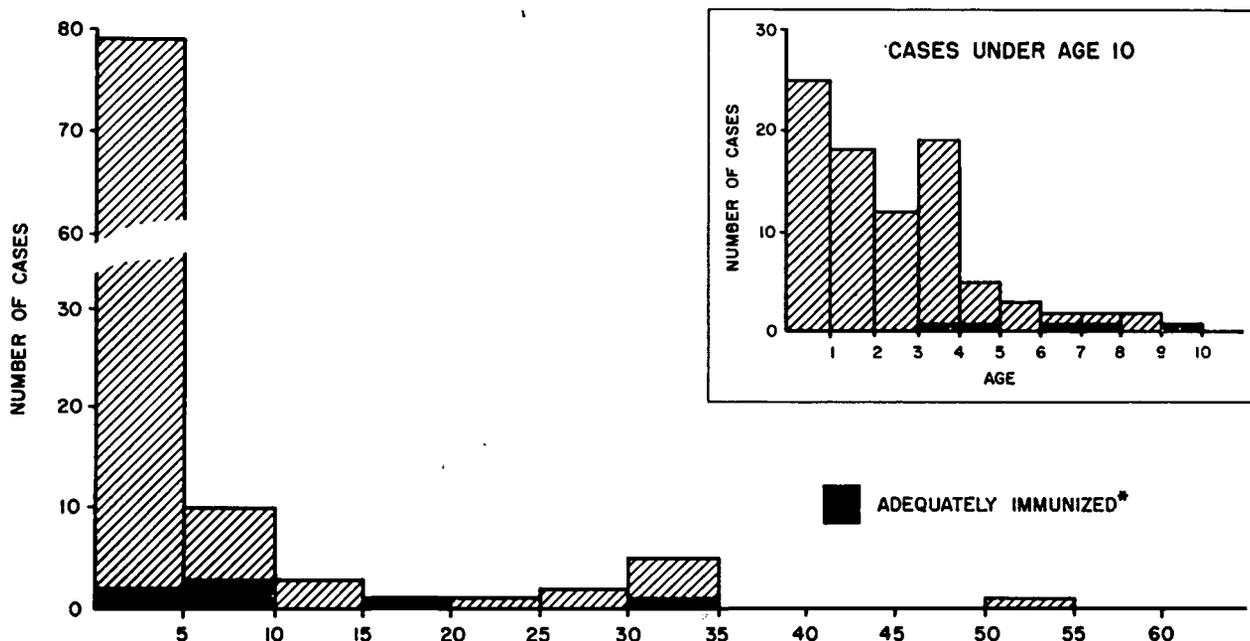
✦ FULL SERIES OF ORAL VACCINE AND/OR FOUR OR MORE DOSES OF INACTIVATED VACCINE MORE THAN 30 DAYS PRIOR TO ONSET.

Neurotropic Disease Surveillance, NCDC

- Immunization histories and other epidemiologic data are provided on individual cases of poliomyelitis for surveillance activities, NCDC, by State health departments. In these reports, cases are defined as "paralytic" when there is *residual paralysis* 60 days after onset. Cases initially reported as paralytic but not followed up at 60 days are also included in this category. (These, however, account for only a small proportion of cases.)

- The 102 cases of poliomyelitis reported on NCDC surveillance forms fulfilling these criteria of "paralytic" are described in this figure. The six-case discrepancy between this total and the 108 cases reported in the *Morbidity and Mortality Weekly Report* is attributed to the difference in mechanics of collection and the definition applied to analysis.

- Seventy-five percent of the 1966 paralytic patients had never received any polio vaccine; only seven had histories of adequate polio immunization.

- Twenty-five percent of the cases were in infants (less than 1 year old); five were less than 6 months old. In Texas, all but three of the 66 cases were in children less than 6 years old, but of the cases occurring outside Texas only half were in preschool children.

- Only one of the nine adult patients was adequately immunized. One-third of the adult cases occurred in contacts of individuals receiving oral vaccine.

- Ten "vaccine associated" cases of polio were among the 102 reported. "Vaccine associated" is defined as paralytic polio in individuals living outside an epidemic area with onset of illness between 4 and 30 days after administration of poliovaccine. One of the 10 "vaccine associated" cases in 1966 was related to the administration of inactivated poliovaccine, the other nine to oral vaccine.

POLIOMYELITIS IMMUNIZATION STATUS — UNITED STATES,
1965 and 1966
AGE GROUPS 1-19 YEARS
(Percent of Group by Vaccine History)

AGE GROUP	PERCENT BY VACCINE HISTORY					
	Adequate*		Incomplete		No Vaccine	
	1965	1966	1965	1966	1965	1966
1-4	74	70	16	18	10	11
5-9	90	88	7	9	3	3
10-14	92	90	6	8	2	2
15-19	88	86	8	10	4	4

*Full series of oral vaccine and/or at least THREE doses of inactivated vaccine.

U.S. Immunization Surveys, 1965 and 1966

• Among the age groups surveyed, the proportion of individuals in each category in 1966 did not change significantly from that found in 1965.

• Both in 1965 and 1966, the least adequately immunized is the 1-4 year age group, the preschool population. The 1-4 group also has the largest proportionate segment of children who are *completely* unimmunized.

• By the time they enter elementary school, nearly 90% of children have completed at least the primary polio immunization series.

• Individuals with only partial immunization are considered incompletely protected; although if they received OPV they should have adequate protection against at least one or two types of poliovirus.

(U.S. Immunization Survey, September 1965, Supplement to C.D.C. Poliomyelitis Surveillance Report #288, June 1, 1966).

POLIOMYELITIS IMMUNIZATION STATUS —
UNITED STATES, 1966
COMPARISON OF IMMUNIZATION "ADEQUACY"
AGE 'GROUPS 1-19 YEARS
(Percent of Group by Vaccine History)

| AGE GROUP | PERCENT BY VACCINE HISTORY | | |
	"ADEQUACY"*		
	Complete OPV or at least 3 IPV	Complete OPV or at least 4 IPV	No Vaccine
1-4	70	57	11
5-9	88	80	3
10-14	90	82	2
15-19	86	77	4

*See explanation in comments.

U. S. Immunization Survey, 1966

• Historically, "adequate" polio immunization has been defined as receipt of a full series of OPV or at least 3 doses of IPV. Because the recommendation for primary immunization with IPV is 4 doses, this table compares the relative proportion of groups with at least 3 doses of IPV with those with at least 4.

• The more stringent definition of immunization "adequacy" with respect to IPV decreases by less than 10% the proportion of all except the youngest age group considered to be adequately protected. In the 1-4 year age group, however, a 13% difference exists. This difference may be partly explained by the fact that some 1-year-olds have not reached the usual age for giving the fourth dose of IPV.

POLIOMYELITIS IMMUNIZATION STATUS —
UNITED STATES, 1966
AGE GROUPS 1-19 YEARS — WHITE, NONWHITE
(Percent of Group by Vaccine History)

AGE GROUP	PERCENT BY VACCINE HISTORY					
	Adequate*		Incomplete		No Vaccine	
	White	Nonwhite	White	Nonwhite	White	Nonwhite
1-4	60	47	31	33	10	21
5-9	82	72	16	24	3	4
10-14	82	78	16	19	2	2
15-19	78	71	18	23	4	6

*Full series of oral vaccine and/or at least FOUR doses of inactivated vaccine.

U.S. Immunization Survey, 1966

• This table is based on defining adequate immunization as a full series of OPV or at least 4 doses of IPV.

• There is a difference ranging from 4% to 13% in the proportion of the white and nonwhite of each age group considered to be adequately immunized. The major difference exists in the youngest group.

• The most striking contrast between the white and nonwhite groups is in the 1-4 year age group without history of any polio immunization.

• The marked improvement in immunization status between the 1-4 year and the 5-9 year age groups may be associated with school entrance requirements or school health programs. It may also reflect the result of mass immunization programs carried out in 1962 and 1963 when the 5-9 year age group was a preschool population.

POLIOMYELITIS VACCINES — UNITED STATES, 1962-1966
Net Doses (Millions) Distributed Annually

VACCINE	1962*	1963	1964	1965	1966
Poliomyelitis Vaccine (inactivated)	15.3	19.0	8.8	7.5	5.5
Poliovirus Vaccine, Live, Oral					
Type 1	33.1	38.7	24.9	4.7	1.4
Type 2	37.0	34.2	29.8	3.4	1.3
Type 3	13.7	54.2	28.4	3.7	1.4
Trivalent	....	4.2**	24.0	17.4	24.0

*July-December (Biologics Surveillance Program began July 1962)
**Production began during year

Biologics Surveillance, NCDC

• Use of IPV steadily declined, until in 1966 distribution reached 35% of the 1962 level.

• From the introduction of oral polio vaccines in 1961-62, the amount of monovalent OPV used annually declined markedly while proportionate increases in the use of trivalent OPV occurred.

• Large amounts of polio vaccine, particularly OPV, were used in the early 1960's in major immunization campaigns and community-wide programs. Regular immunization alone since 1965 accounts for the lower use of vaccines.

RABIES

Rabies is one of the oldest diseases known to man. Perhaps the earliest reference to it is in the Pre-Mosaic Eschnunna Code, written before the 23rd century B.C. The disease in animals was described with amazing accuracy by Democritus in the 5th century B.C., and in A.D. 100 Celsus pointed out that man is also susceptible.

Rabies spread throughout Europe in the 19th century and first appeared in North America in 1753; it had reached the Mississippi River by 1860 and California by 1899.

Pasteur's classic investigations in the 1880's showed that rabies virus could be modified in the laboratory to induce immunity without producing disease; they are milestones in the progress of immunology as a basic tool of preventive medicine. Although Pasteur's original rabies vaccine has been modified, the name "Pasteur treatment" is still used.

Cases of rabies in humans are now rare in the United States; however, more than 30,000 people receive rabies prophylaxis each year. The incidence of rabies in humans declined from an average of 22 cases per year, 1946-1950, to one or two cases per year, 1963-1966.

Rabies in domestic animals also diminished. In 1946, there were more than 8,000 reported cases of rabies in dogs; in 1966 there were only 412. Consequently, the likelihood of being exposed to rabies by domestic animals has decreased greatly. Bites by dogs and cats, however, continue to be responsible for the overwhelming majority of antirabies treatments.

In contrast, the disease in wildlife — especially skunks, foxes, and bats — has become increasingly prominent in recent years. And today wild animals constitute the most important source of infection for both domestic animals and man in the United States.

Two types of inactivated rabies vaccines are available for post-exposure use in humans; duck embryo vaccine (DEV) and nervous tissue vaccine (NTV). Hyperimmune serum is also given for severe exposures.

RABIES IN 1966

One case of rabies in a human — a 10-year-old boy in South Dakota — was reported in 1966. Symptoms of rabies developed 24 days after he had been bitten by a rabid skunk, and he died nine days later, despite intensive therapy.

A total of 4,197 laboratory confirmed cases of rabies in animals were reported; 47 States, all but Delaware, Hawaii, and Rhode Island, reported animal rabies. The 448 rabid animals reported by Texas constituted the largest total for any State. Skunks and foxes accounted for 57% of the animal rabies in the United States in 1966.

Nearly one million individual doses of human antirabies vaccines were distributed in 1966. In addition, 150,000 ml of equine origin antirabies serum were distributed. Approximately 8,000 of the estimated 30,000 persons who received antirabies vaccine also received antirabies serum.

RABIES — UNITED STATES, 1946-1966
DEATHS (HUMAN)
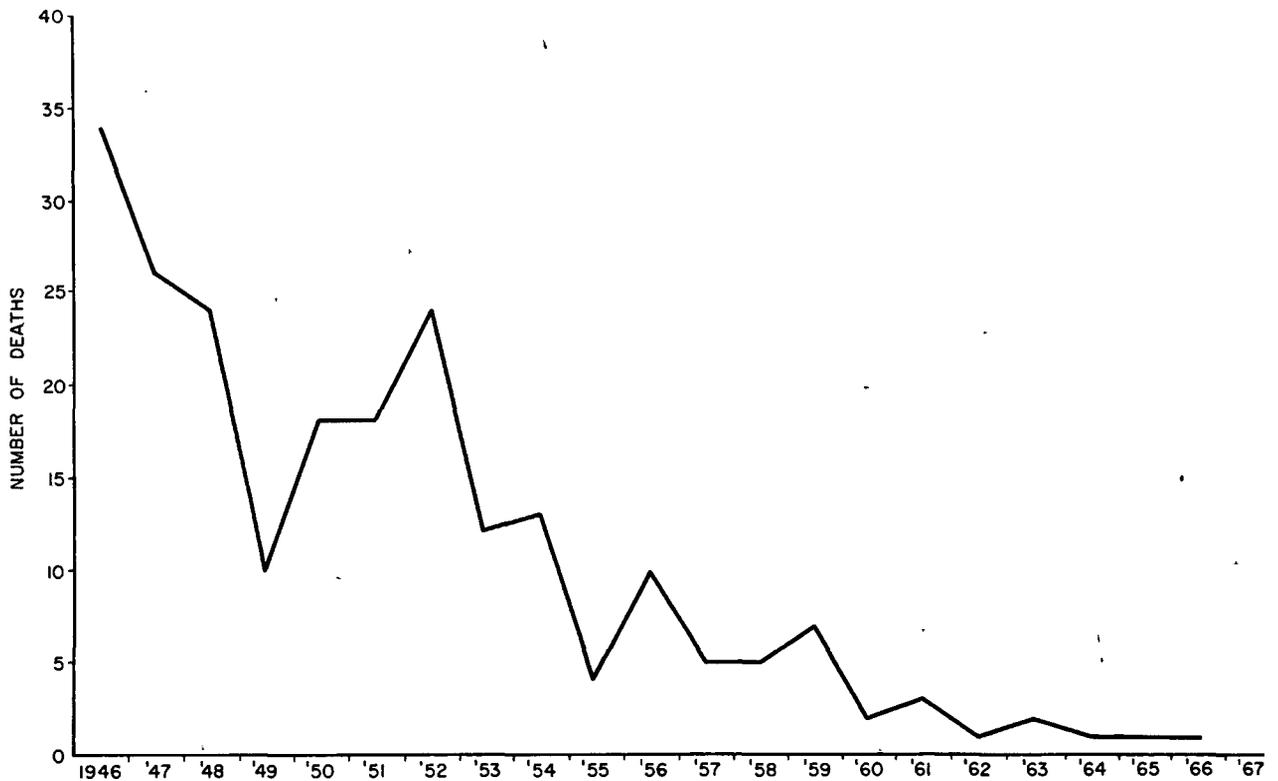
National Center for Health Statistics

• In the years 1946 through 1966, 221 persons died of rabies in the United States. Once clinically apparent, essentially all cases of rabies are fatal.

• The number of human deaths from rabies declined from 34 in 1946 to only one or two per year for the past five years, 1962 through 1966. This decline probably resulted from reduction — through immunization — of the incidence of rabies in dogs.

• The animals responsible for infection were identified in 150 of the rabies deaths reported in the past 21 years. Domestic animal sources were identified in 130 instances and wildlife sources in the remaining 20. All 20 deaths traced to rabid wildlife were reported after 1951.

RABIES — UNITED STATES, 1950-1966
DEATHS (HUMAN) BY 5-YEAR AGE GROUPS AND SEX
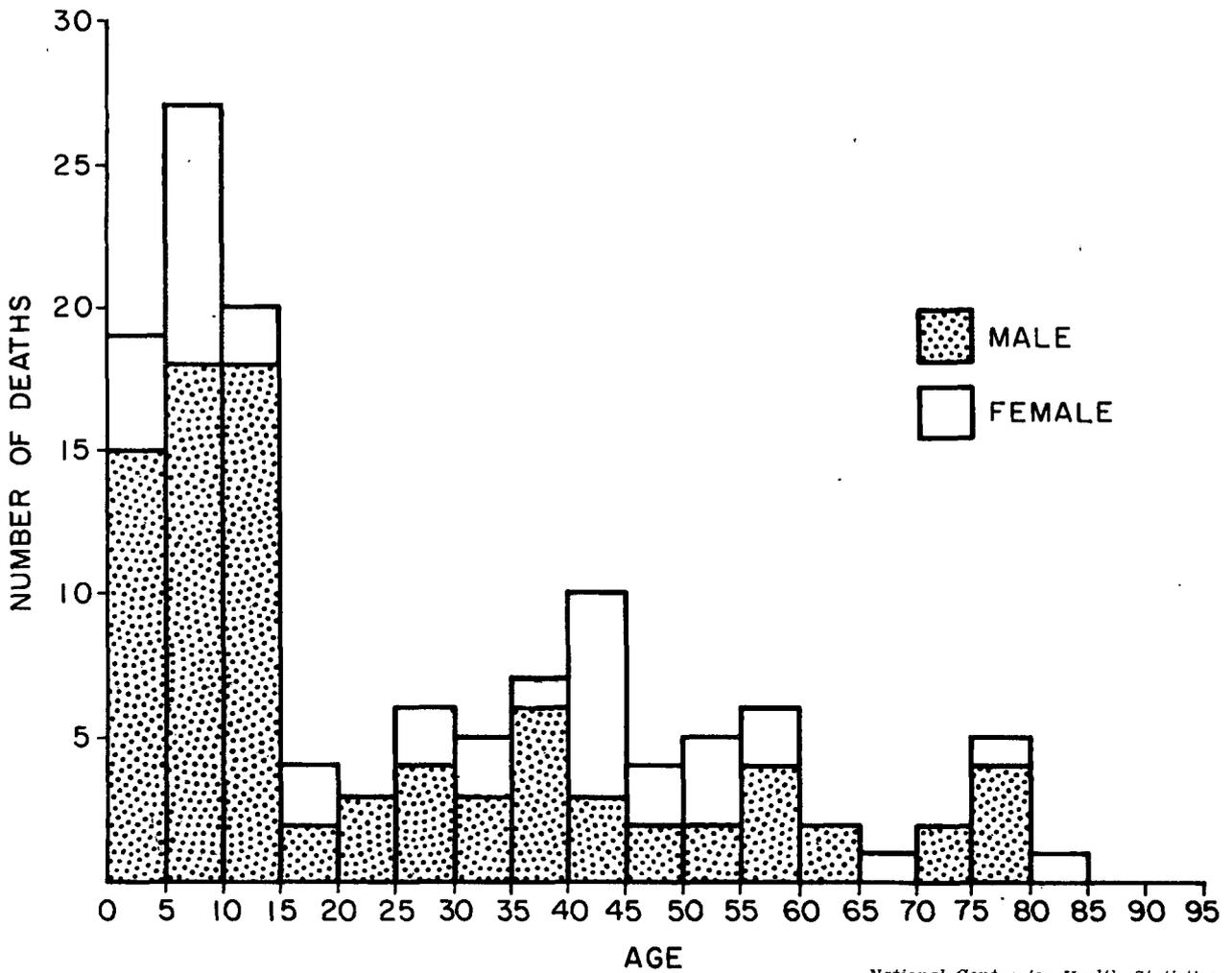
National Center for Health Statistics

- Of the 127 persons who died of rabies in the 16-year period from 1950, more than half were less than 15 years of age; 15% were less than 5.

- Seventy percent of deaths occurred in males, and proportionately, nearly 60% of the males who died were boys less than 15 years old. Rabies deaths in females occurred in somewhat older individuals — only 38% were less than 15.

- Among adults, death occurred at all ages with a slight predominance between age 40 and 45.

RABIES — UNITED STATES, 1953-1966
CASES (ANIMAL)
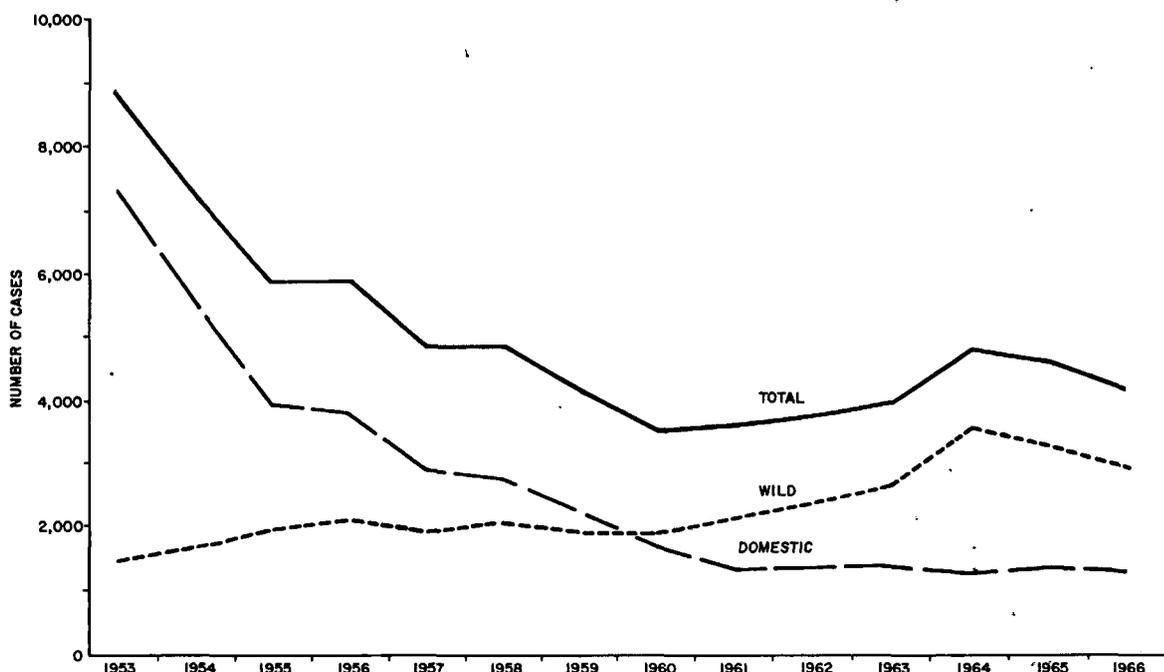
- The total number of laboratory-confirmed cases of rabies in animals declined from 8,837 in 1953 to 4,197 in 1966.

- Rabies in domestic animals diminished sharply from 7,344 cases in 1953 to only 1,251 in 1966 — the major explanation for the overall decrease of rabies in animals.

- Reported cases of wildlife rabies increased from 1,479 in 1953 to 2,946 in 1966, an absolute as well as a proportionate rise, according to surveillance and laboratory information.

- At least 1 million animal bites occur in the United States each year. Of all animal bites, approximately 3% (30,000) are considered possible rabies exposures calling for specific rabies prophylaxis. Approximately one-third of the bites that prompt antirabies treatment are inflicted by wild animals, and the remaining two-thirds by domestic animals, including dogs, cats, and livestock.

RABIES — UNITED STATES, 1966
CASES (ANIMAL) BY COUNTY

ALASKA

HAWAII

GUAM

PUERTO RICO

VIRGIN ISLANDS

STATES REPORTING RABIES — 47
COUNTIES REPORTING RABIES — 1,180
TOTAL CASES — 4,197
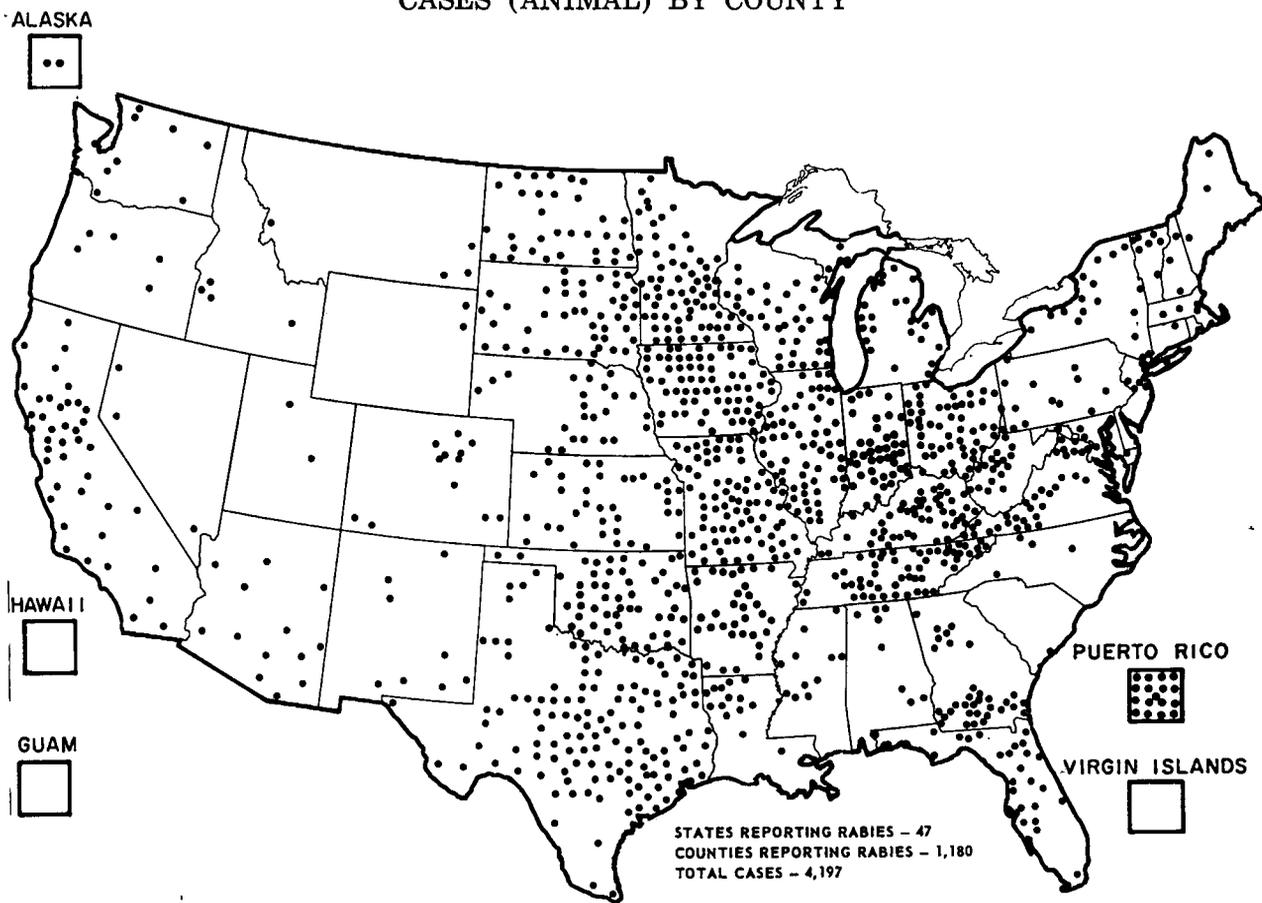
Zoonoses Surveillance, NCDC

• Domestic animals (dogs, cats, and livestock) accounted for 1,251 of the 4,197 cases of animal rabies reported in 1966 (30%); the remaining cases were in wildlife species.

• The four States along the Mexican border reported 34% of all dog rabies in the United States. Three other States, Kentucky, Missouri, and Tennessee, reported an additional 26% of the rabies in dogs.

• More than one-third of all the 1966 rabies cases in animals were in skunks. Texas reported 180 cases, Ohio 160, and California 154. Recognition of rabies in skunks was particularly frequent in agricultural areas because of the correlation of dense skunk populations and livestock.

• Thirty States reported rabies in foxes in 1966. Of the 864 reported cases, Tennessee listed 192, and Virginia 168.

• In 1966, 377 rabid bats were identified. California reported 54, more than any other of the 40 States reporting rabid bats.

RABIES — UNITED STATES, 1953-1966
CASES (WILDLIFE)
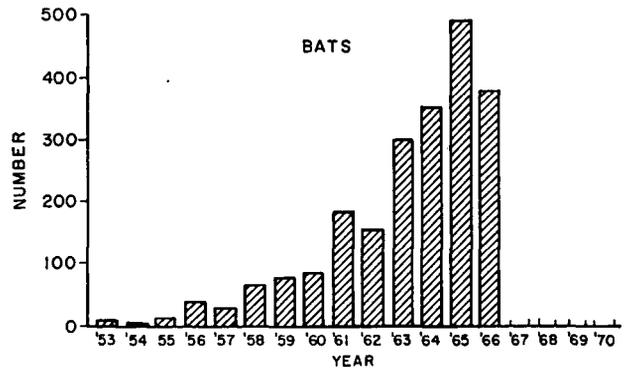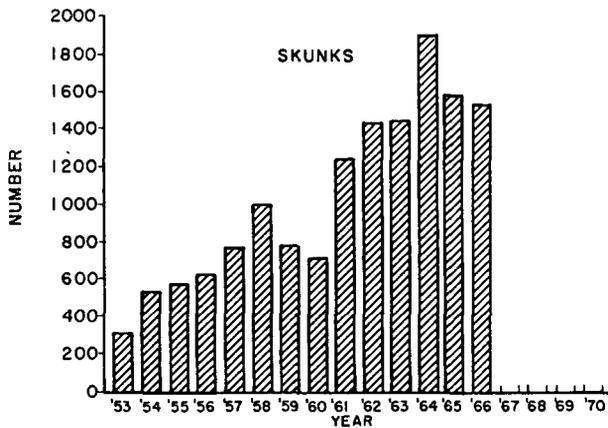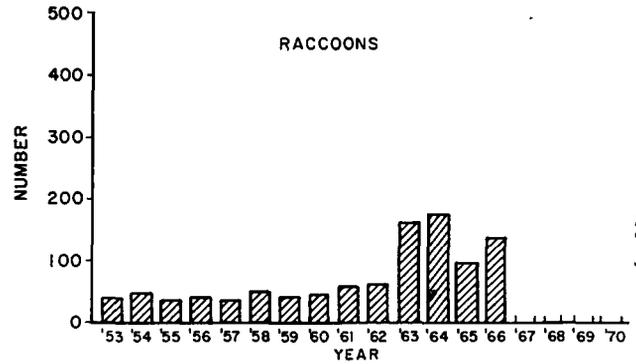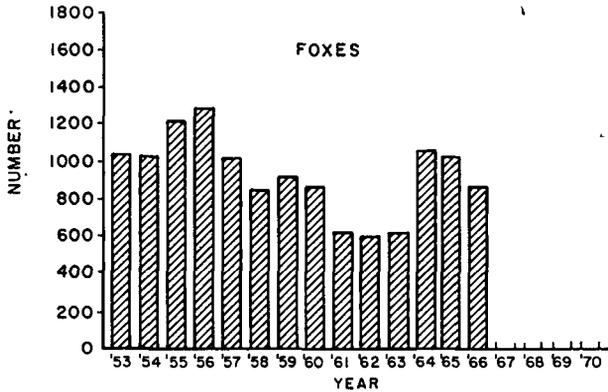
Zoonoses Surveillance, NCDC

• In recent years, rabies in wildlife, particularly in skunks and bats, has been increasing. Nationally, there have been no cycles in the occurrence of rabies in any wildlife species since 1953.

• Fox rabies persisted at a level of 850 to 1,200 cases during 11 of the 14 years up to 1967; in 1961-1963, 594 to 622 cases were recorded annually. Foxes ranked second only to skunks as the most frequently rabid wildlife species in the six-year period 1961-1966.

• Rabies increased more rapidly in skunks than that in foxes. In 1961-1966, there were more laboratory-confirmed cases of rabies in skunks than in any other species.

• Raccoons were the most frequently reported rabid species in some southeastern States (Florida since 1953 and Georgia since 1963). Rabid raccoons are seldom recognized in other States.

• The first rabid bat was identified in the United States in 1953. Since then, 48 of the 50 States have reported rabies in 26 of the 39 species of insectivorous bats found in the United States. Only Alaska and Hawaii have not reported rabid bats.

RABIES VACCINES — UNITED STATES, 1962-1966
Net Doses (Thousands) Distributed Annually

VACCINE	1962*	1963	1964	1965	1966
NTV	41	159	84	83	83
DEV	191	343	456	461	887

*July-December (Biologics Surveillance Program began July 1962)

Biologics Surveillance, NCDC

• Nervous tissue antirabies vaccine (NTV) was the only type available in the United States until 1957, when duck embryo vaccine (DEV) was licensed. Since then, the preference for DEV has increased annually. In 1966, 91% of the commercially produced antirabies vaccine used in the United States was DEV.

• In 1962-1966, approximately 425,000 doses of rabies vaccine were used each year by civilian physicians. Estimating that an average of 14 doses were given each person treated, approximately 30,000 people received post-exposure antirabies prophylaxis annually.

• In 1966, 430,000 more doses of antirabies vaccine were used in the United States than in any of the preceding four years. This increase is based largely on more pre-exposure immunizations and additional requirements of the military.

• The military used five times more antirabies vaccine in 1966 than in either of the two preceding years. Rabies is epizootic among dogs in Southeast Asia, and pre-exposure immunization has become a widely adopted prophylactic measure.

SMALLPOX

Vaccinia virus was the first agent to be used widely for human immunization, Jenner's term *Variola vaccinae* (smallpox of the cow) was the basis of the term "vaccination." In 1800, two years after Jenner published his initial report, Benjamin Waterhouse introduced vaccination into the United States. Smallpox had been rampant in the early history of this country and decimated many Indian tribes as it spread west. Waterhouse was supported by Dr. Oliver Wendell Holmes and by Thomas Jefferson in the fight to establish vaccination as a routine public health procedure.

Throughout the 1800's, variola major, with its high death rate, apparently coexisted with variola minor, or alastrim, in many parts of the United States. At the turn of the century, however, the case-fatality ratio reported for smallpox was low, which suggests that most of the cases were then due to variola minor.

The major decline in smallpox incidence in the United States took place during the 1930's, but occasional cases were reported even as late as 1957. The last definitive focal outbreaks of smallpox occurred in 1946, 1947, and 1949. It is likely that the reservoir of smallpox in the continental United States disappeared during World War II and that importation was responsible for the last few reported outbreaks.

SMALLPOX IN 1966 (WORLDWIDE)

In 1966, the provisional total of 50,797 cases of smallpox was reported to the World Health Organization, Geneva. Known to be under-reported in parts of the world because of limited diagnostic and health communications resources, smallpox is still a disease of major international importance.

Increased population mobility has increased the risk of reintroducing smallpox where it is no longer indigenous. With more people traveling frequently and far, international surveillance of smallpox and efforts to control the disease in areas of endemicity take on added importance. A number of European countries, smallpox-free for some years, have recently experienced limited smallpox epidemics following reintroduction by international travelers: Great Britain, Sweden, and Germany are among those countries recording well-documented epidemics in the 1960's. These outbreaks demonstrated the now characteristic pattern of spread from an unsuspected initial case to numerous patients and staff members of the medical facility in which he sought treatment. Important in the transmission of smallpox was the inadequate immunization of the predominantly exposed groups in hospitals.

SMALLPOX — WORLDWIDE, 1947-1966
CASES
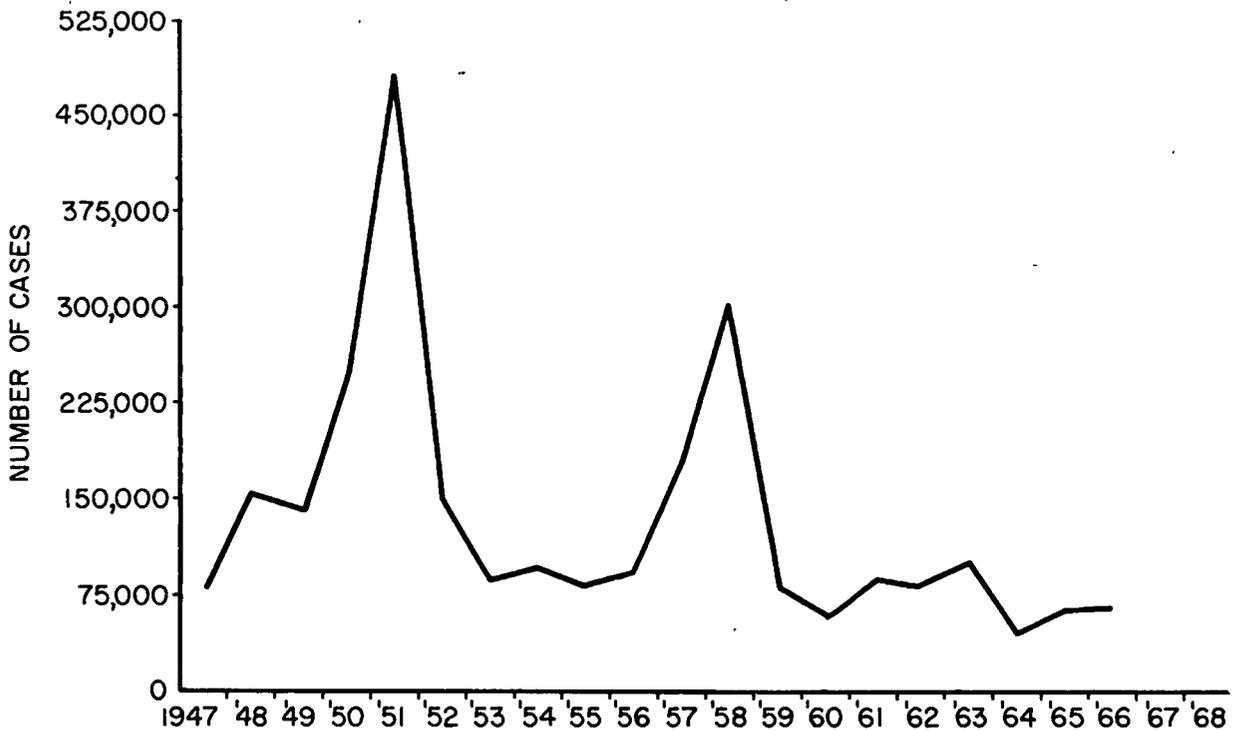
World Health Organization

• The 20-year trend of worldwide smallpox 1947-1966 was gradually downward. This is particularly meaningful in light of the great increase in world population and the probable increase in the completeness of disease reporting.

• Epidemic peaks in the late 1940's and 1950's are largely attributable to epidemics in the Asian sub-continent. An epidemic in the early 1960's suggested by the curve may have been aborted by immunization programs in many parts of Southeast Asia.

• While the general trend of smallpox has been downward, international travel is expanding so rapidly that the risk of smallpox importation may be rising rather than falling. The regular occurrence of smallpox along many of the main travel and trade routes of South America, Africa, and Asia poses a continuing threat of importation of the disease into the United States.

SMALLPOX — WORLDWIDE, 1955 AND 1965
ENDEMIC AREAS

■ Endemic Area—1965

░ Endemic Area—1955

World Health Organization

- During the decade from 1955, the reservoir of endemic smallpox diminished considerably. Major foci remain only in Brazil, Africa (south of the Sahara), the sub-continent of Asia, and Indonesia. In 1945, smallpox was also endemic in the United States, Mexico, Europe, and the Middle East, and was more extensive in Southeast Asia and the Orient.

- Preliminary 1966 data indicate the geographical extent of smallpox: 13,192 cases were reported from Africa, 36,974 from Asia, 558 from the Americas, and 73 from Europe. The European cases resulted entirely from reintroduction of smallpox from countries, such as India and Pakistan, with large reservoirs of disease. India reported more than 22,000 cases, Indonesia more than 10,000, and Pakistan somewhat fewer than 4,000.

- As part of the worldwide smallpox eradication program of the World Health Organization, all smallpox endemic areas are now planning or are engaged in eradication campaigns.

- Use of heat-stable, lyophilized smallpox vaccine has made eradication programs possible in tropical climates where no refrigeration is available.

SMALLPOX — UNITED STATES, 1922-1966
CASES

Morbidity and Mortality Weekly Report
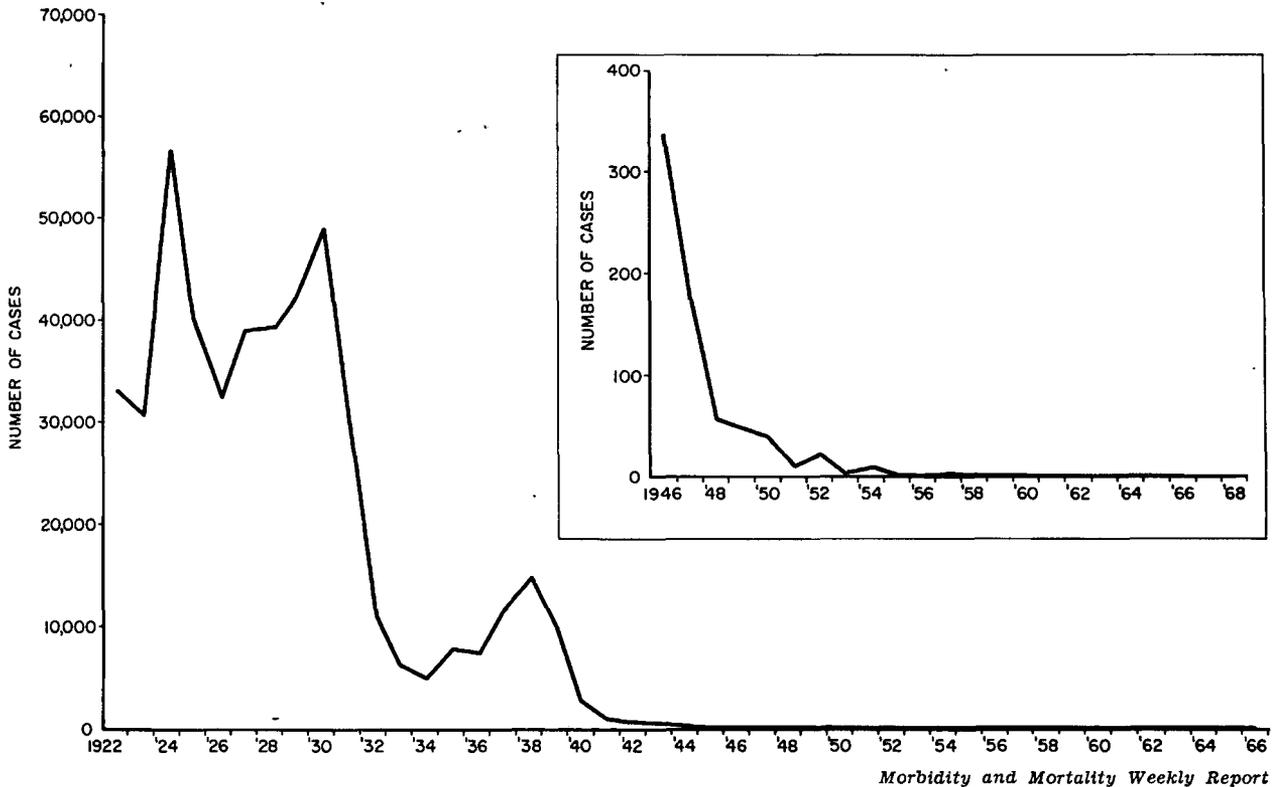
- 1926 was the last year of extensive smallpox outbreaks in the United States. During the 1920's and 1930's, the case-fatality ratio was approximately 1%.

- The reasons for the rapid decline of smallpox in the 1930's are not completely clear. Immunization may not have been solely responsible, for surveys showed that 60 percent of the rural inhabitants of the United States and more than 25 percent of those living in selected cities with over 100,000 population were not immunized against the disease.

- Small numbers of smallpox cases were officially reported in the late 1940's and early 1950's. However, none of the cases after 1949 fulfilled the usual clinical criteria for smallpox, and no laboratory evidence was presented. The last documented cases in the United States occurred in outbreaks in Seattle in 1946, New York in 1947, and the lower Rio Grande Valley in 1949. All of these outbreaks were traced to importation.

- In the Seattle and New York City outbreaks, as in recent outbreaks in Europe, the risk of developing smallpox was much greater for patients, physicians, nurses, and other hospital employees than for the population at large.

SMALLPOX IMMUNIZATION STATUS — UNITED STATES, 1964
AGE GROUPS
(Percent of Groups by Vaccine History)

Per Cent

PER CENT VACCINATED DURING LIFETIME

PER CENT VACCINATED WITHIN PAST 12 MONTHS

AGE 5   10   15   20   25   30   35   40   45   50   55   60   65   70   75   80   85

U.S. Immunization Survey, 1964
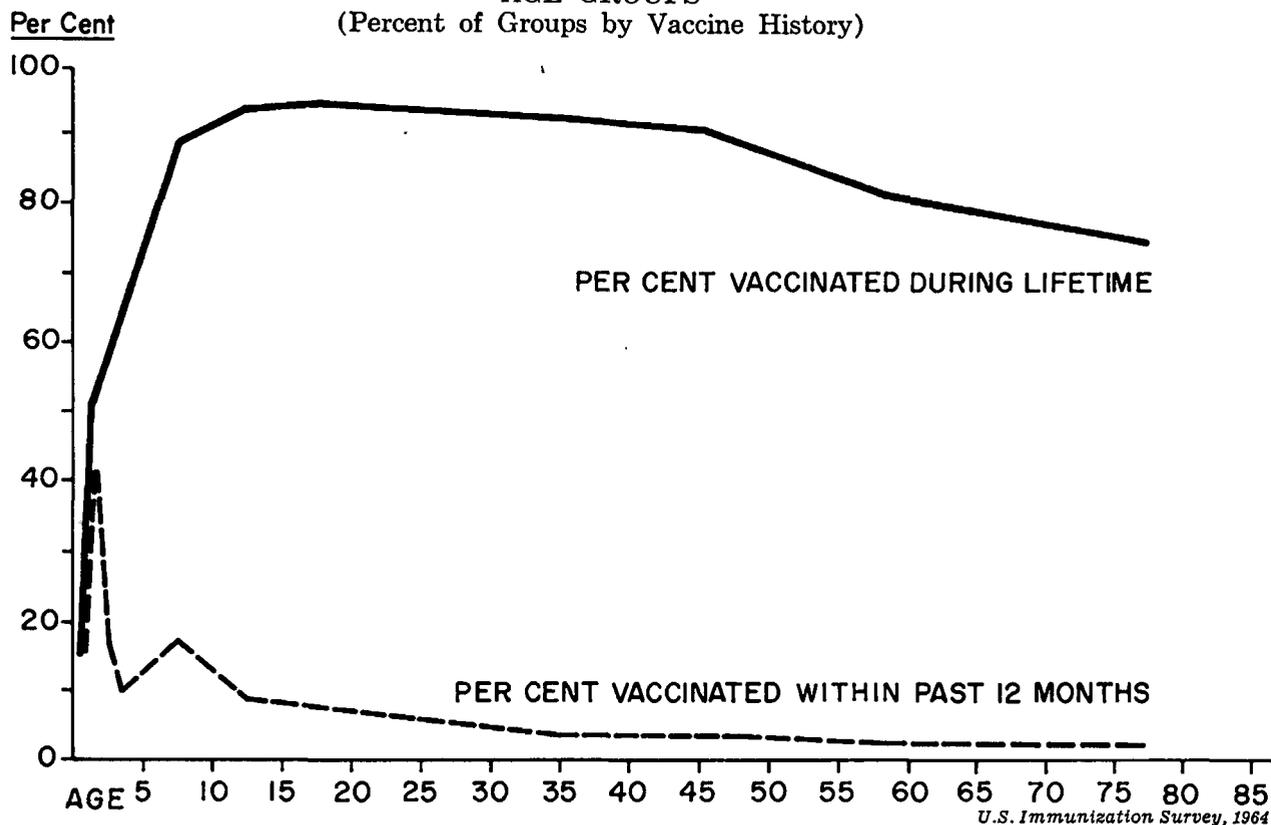
- In 1964, an estimated 5,421,000 of 13,360,000 smallpox vaccinations were primary vaccinations, 7,374,000 were revaccinations, and 565,000 were administered to individuals having an unknown prior vaccination history. Although 7.4% of the population in 1964 had been vaccinated within the preceding year, many of the vaccinations were given to travelers, military personnel, and others who are revaccinated frequently. Less extensive surveys in smaller areas suggest that less than 20% of the population has had a vaccination in the last 3 years.

- According to immunization surveys in 1963 and 1964, the proportion of individuals in each vaccination category did not change significantly in the intervening year.

- Survey data (1964) indicate geographic differences in vaccination rates. More than 90% of the residents of New England and the Atlantic States had been vaccinated, in contrast to less than 80% of those in the West-North Central, East-South Central, and West-South Central States.

- Approximately 16% of children less than one year of age received primary vaccination in 1964. Another 41% received primary vaccination in the second year of life. Some 60% of children have been vaccinated by the time they reach the age of five; and in the early school years, vaccination programs brought the proportion vaccinated to 88%. In the age groups that include those entering military service, approximately 8% are vaccinated each year. However, only 3% of those over 30 are vaccinated annually, largely for international travel.

(U.S. Immunization Survey, September 1964, supplement to C.D.C. Poliomyelitis Surveillance Unit Report #287, June 1, 1965.)

SMALLPOX VACCINE — UNITED STATES, 1962-1966
Net Doses (Millions) Distributed Annually

VACCINE	1962*	1963	1964	1965	1966
SMALLPOX	8.8	14.7	18.1	19.4	17.1

*July-December (Biologics Surveillance Program began July 1962)

<div align="right">Biologics Surveillance, NCDC</div>

• These data refer to smallpox vaccine distributed for both domestic and military use. Some of the increased use of vaccine can be ascribed to military needs and the rest to civilian travel and other domestic requirements.

• The proportion of lyophilized smallpox vaccine distributed in the United States is unknown. Lyophilized vaccine is more uniformily potent and has a better rate of response than the traditional calf lymph.

• U.S. Immunization Survey estimates of the total numbers of smallpox vaccinations given in 1963 and 1964 correspond to the total number of doses of vaccine distrbuted in the same years.
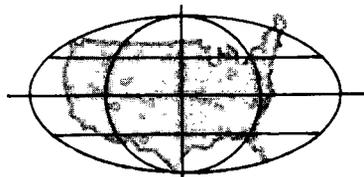
UNITED STATES

IMMUNIZATION SURVEY–1966

United States
Immunization Survey—1966

The annual United States Immunization Survey conducted each September by the Bureau of the Census under sponsorship of the National Communicable Disease Center has evolved from exploratory and specialized investigations begun in 1957. Since 1963, the general format and comprehensive analyses have been consistent with those presented here. Previous survey reports were distributed as supplements to the Poliomyelitis Surveillance Reports prepared by the Center.

The survey has focused on various vaccines, describing patterns of usage by age and other population groupings. The general content of the annual survey is based on the current need for information about immunization activities.

In the 1966 survey, information was sought on polio immunization, both with oral and inactivated products, of persons under 20 years of age, on diphtheria-tetanus-pertussis immunization of children under 10, on history of measles illness and measles vaccination of children under 11. The Statistics Section, Epidemiology Program, NCDC, analyzed the data and prepared the tables.

Estimates for each age group in each table were independently rounded without the tables' totals' being adjusted. This procedure accounts for minor discrepancies in the tabular presentation.

TABLES OF DATA ARE PRESENTED IN THE FOLLOWING SECTIONS:

SECTION A. TABLES 1-5
Summary Tables, Poliovaccine Immunization Status, Ages Under 20 Years

SECTION B. TABLES 6-10
Diphtheria-Tetanus-Pertussis Immunization Status, Ages 1-9 Years

SECTION C. TABLE 11
Immunization Status, Infants (Under 1 Year)

SECTION D. TABLES 12-13
Measles History and Measles Vaccine History, Ages Through 10 Years

SECTION E. TABLES 14-15
Standard Error Tables, Computed by the Bureau of the Census

TABLE 1A POLIOVACCINE STATUS — UNITED STATES, 1966
Ages Under 20 Years
Oral Poliovaccine (OPV) and Inactivated Poliovaccine (IPV)
Percent of Population with Doses as Specified

Age	3 OPV and 3 or more IPV	3 OPV and less than 3 IPV	Less than 3 OPV and 3 or more IPV	Total	2 OPV and 0,1,2 IPV	Cumulative Total	All other combinations except Never Vaccinated	Never Vaccinated
1-4	17.2	31.5	21.5	70.2	8.6	78.9	9.8	11.3
5-9	43.8	21.0	23.3	88.2	4.3	92.4	4.7	2.9
10-14	46.7	18.0	25.3	90.0	3.7	93.7	3.9	2.3
15-19	42.3	16.2	27.9	86.4	3.6	89.9	5.9	4.1

TABLE 1B. POLIOVACCINE STATUS — UNITED STATES, 1966
Ages Under 20 Years
Oral Poliovaccine (OPV) and Inactivated Poliovaccine (IPV)
Number (Thousands) of Persons in the Population

Age	Population	3 OPV and 3 or more IPV	3 OPV and less than 3 IPV	Less than 3 OPV and 3 or more IPV	Total	2 OPV and 0,1,2 IPV	Cumulative Total	All other combinations except Never Vaccinated	Never Vaccinated
1-4	16,091	2,772	5,072	3,458	11,302	1,391	12,693	1,573	1,825
5-9	20,436	8,959	4,287	4,769	18,015	877	18,892	952	592
10-14	19,694	9,204	3,541	4,985	17,730	733	18,463	776	455
15-19	17,250	7,303	2,786	4,807	14,896	615	15,511	1,024	715

Note: for all tables on poliomyelitis immunization status:
"OPV" includes both monovalent and trivalent vaccines.
Column headed "All Other Combinations" (of IPV and OPV doses received) includes persons with unknown immunization status and those with unknown number of doses.

TABLE 2A. POLIOVACCINE STATUS — UNITED STATES, 1966
Ages Under 20 Years — White
Oral Poliovaccine (OPV) and Inactivated Poliovaccine (IPV)
Percent of Population with Doses as Specified

Age	3 OPV and 3 or more IPV	3 OPV and less than 3 IPV	Less than 3 OPV and 3 or more IPV	Total	2 OPV and 0,1,2 IPV	Cumulative Total	All other combinations except Never Vaccinated	Never Vaccinated
1-4	17.5	32.6	22.8	72.9	8.7	81.6	8.9	9.5
5-9	44.9	20.1	24.6	89.6	3.9	93.5	3.8	2.7
10-14	47.4	16.9	26.6	90.9	3.3	94.1	3.6	2.3
15-19	43.1	15.4	29.0	87.4	3.2	90.6	5.5	3.9

TABLE 2B. POLIOVACCINE STATUS — UNITED STATES, 1966
Ages Under 20 Years — White
Oral Poliovaccine (OPV) and Inactivated Poliovaccine (IPV)
Number (Thousands) of Persons in the Population

Age	Population	3 OPV and 3 or more IPV	3 OPV and less than 3 IPV	Less than 3 OPV and 3 or more IPV	Total	2 OPV and 0,1,2 IPV	Cumulative Total	All other combinations except Never Vaccinated	Never Vaccinated
1-4	13,493	2,356	4,393	3,083	9,832	1,179	11,011	1,199	1,283
5-9	17,427	7,822	3,510	4,280	15,612	684	16,296	661	470
10-14	16,912	8,024	2,850	4,492	15,366	554	15,920	603	389
15-19	15,021	6,467	2,315	4,352	13,134	479	13,613	819	589

TABLE 3A. POLIOVACCINE STATUS — UNITED STATES, 1966
Ages Under 20 Years — Nonwhite
Oral Poliovaccine (OPV) and Inactivated Poliovaccine (IPV)
Percent of Population with Doses as Specified

Age	3 OPV and 3 or more IPV	3 OPV and less than 3 IPV	Less than 3 OPV and 3 or more IPV	Total	2 OPV and 0,1,2 IPV	Cumulative Total	All other combinations except Never Vaccinated	Never Vaccinated
1-4	16.0	26.1	14.5	56.6	8.2	64.8	14.3	20.8
5-9	37.7	25.8	16.3	79.8	6.4	86.2	9.7	4.1
10-14	42.4	24.8	17.8	85.0	6.4	91.4	6.2	2.4
15-19	37.5	21.1	20.4	79.1	6.1	85.1	9.2	5.7

TABLE 3B. POLIOVACCINE STATUS — UNITED STATES, 1966
Ages Under 20 Years — Nonwhite
Oral Poliovaccine (OPV) and Inactivated Poliovaccine (IPV)
Number (Thousands) of Persons in the Population

Age	Population	3 OPV and 3 or more IPV	3 OPV and less than 3 IPV	Less than 3 OPV and 3 or more IPV	Total	2 OPV and 0,1,2 IPV	Cumulative Total	All other combinations except Never Vaccinated	Never Vaccinated
1-4	2,601	416	680	377	1,473	213	1,686	373	542
5-9	3,011	1,136	777	490	2,403	193	2,596	292	123
10-14	2,782	1,180	691	494	2,365	178	2,543	173	66
15-19	2,228	836	471	455	1,762	135	1,897	205	126

TABLE 4. POLIOVACCINE STATUS — UNITED STATES, 1966
Ages Under 20 Years
Oral Poliovaccine (OPV) and Inactivated Poliovaccine (IPV)
Percent of Population with Doses as Specified
Standard Metropolitan Statistical Areas

Age	Population (thousands)	3 OPV and 3 or more IPV	3 OPV and less than 3 IPV	Less than 3 OPV and 3 or more IPV	Total	2 OPV and 0,1,2 IPV	Cumulative Total	All other combinations except Never Vaccinated	Never Vaccinated
				Central Cities — Total					
1-4	4,634	15.6	30.2	22.3	68.1	7.9	76.0	11.4	12.6
5-9	5,481	39.0	22.0	25.0	86.0	5.5	91.5	6.1	2.4
10-14	5,313	42.7	18.7	26.8	88.2	5.1	93.3	4.7	2.0
15-19	4,878	37.9	15.8	30.2	83.9	3.8	87.7	7.9	4.3
				Central Cities — White					
1-4	3,265	16.3	32.3	24.4	73.0	7.5	80.5	9.7	9.7
5-9	3,931	41.0	21.5	26.3	88.8	4.1	92.9	4.7	2.4
10-14	3,983	45.2	16.8	27.7	89.7	4.2	93.9	4.2	2.0
15-19	3,810	39.4	15.3	31.2	85.9	3.1	89.0	7.2	3.8
				Central Cities — Nonwhite					
1-4	1,369	13.9	25.3	17.3	56.5	8.7	65.2	15.3	19.6
5-9	1,550	33.9	23.1	21.7	78.7	9.2	87.9	9.9	2.3
10-14	1,330	35.3	24.4	24.2	84.0	7.7	91.7	6.2	2.0
15-19	1,068	32.4	17.8	26.6	76.8	6.5	83.2	10.7	6.1
				Remaining Population in SMS Areas					
1-4	5,471	19.0	32.7	22.0	73.7	10.1	83.8	9.1	7.1
5-9	7,336	46.5	20.5	23.5	90.5	4.3	94.8	3.5	1.7
10-14	7,108	47.4	17.1	27.1	91.5	3.3	94.8	3.2	2.0
15-19	6,005	44.6	15.8	28.1	88.5	3.5	92.0	5.1	2.9
				Population Outside SMS Areas					
1-4	5,989	16.9	31.5	20.3	68.7	7.9	76.6	9.2	14.2
5-9	7,618	44.7	20.7	22.0	87.4	3.4	90.8	4.8	4.4
10-14	7,271	49.1	18.3	22.5	89.9	3.1	93.0	4.1	2.9
15-19	6,369	43.6	16.7	25.9	86.2	3.4	89.6	5.2	5.1

TABLE 5. POLIOVACCINE STATUS — UNITED STATES, 1966
Ages Under 20 Years
Oral Poliovaccine (OPV) and Inactivated Poliovaccine (IPV)
Percent of Population with Doses as Specified
Geographic Divisions

Age	Population (thousands)	3 OPV and 3 or more IPV	3 OPV and less than 3 IPV	Less than 3 OPV and 3 or more IPV	Total	2 OPV and 0,1,2 IPV	Cumulative Total	All other combinations except Never Vaccinated	Never Vaccinated
New England
1-4	1,031	17.5	40.9	16.0	74.4	7.4	81.8	9.8	8.4
5-9	1,289	47.6	24.7	16.6	88.9	2.9	91.9	6.1	2.1
10-14	1,337	49.3	19.2	22.0	90.5	3.6	94.1	4.3	1.6
15-19	1,125	42.3	14.3	26.4	83.0	5.2	88.3	7.9	3.8
Middle Atlantic
1-4	2,714	19.4	27.9	28.2	75.5	8.2	83.7	9.1	7.1
5-9	3,415	44.9	16.0	29.0	89.8	3.1	93.0	4.9	2.1
10-14	3,220	47.9	14.3	28.5	90.7	2.8	93.5	4.2	2.2
15-19	2,947	40.2	11.5	37.6	89.3	2.0	91.4	5.4	3.2
East North Central
1-4	3,230	14.3	21.5	30.2	66.1	9.8	75.9	11.6	12.5
5-9	4,337	37.9	15.0	33.3	86.2	6.1	92.3	4.4	3.3
10-14	4,271	35.8	12.5	39.0	87.4	5.0	92.4	4.8	2.8
15-19	3,636	33.2	12.3	38.4	83.9	3.6	87.4	8.2	4.3
West North Central
1-4	1,236	7.8	26.3	27.6	61.7	12.7	74.4	10.9	14.6
5-9	1,568	31.0	18.2	33.8	83.0	7.4	90.4	4.5	5.2
10-14	1,554	35.4	18.1	34.3	87.8	5.9	93.8	3.0	3.3
15-19	1,461	35.0	14.1	37.2	86.3	5.1	91.4	5.4	3.2
South Atlantic
1-4	2,456	22.9	32.5	15.1	70.5	7.5	78.1	10.3	11.7
5-9	2,991	47.8	25.1	17.5	90.4	3.8	94.2	3.5	2.3
10-14	2,896	55.8	20.2	16.6	92.6	2.7	95.3	2.9	1.8
15-19	2,460	46.3	19.6	19.0	84.9	5.0	89.8	4.6	5.6
East South Central
1-4	1,184	21.2	41.4	10.0	72.6	5.3	77.9	8.9	13.3
5-9	1,489	55.3	24.8	8.7	88.7	2.6	91.3	4.7	4.0
10-14	1,407	61.3	20.5	10.0	91.8	1.3	93.1	3.7	3.2
15-19	1,292	56.1	19.2	14.0	89.3	1.8	91.1	3.1	5.8

TABLE 5. (cont.) POLIOVACCINE STATUS — UNITED STATES, 1966

Ages Under 20 Years
Oral Poliovaccine (OPV) and Inactivated Poliovaccine (IPV)
Percent of Population with Doses as Specified
Geographic Divisions

Age	Popu-lation (thou-sands)	3 OPV and 3 or more IPV	3 OPV and less than 3 IPV	Less than 3 OPV and 3 or more IPV	Total	2 OPV and 0,1,2 IPV	Cumu-lative Total	All other combi-nations except Never Vacci-nated	Never Vacci-nated
West South Central
1-4	1,487	14.9	35.6	14.9	65.4	7.7	73.0	9.1	17.9
5-9	1,855	42.9	27.4	14.7	84.9	3.7	88.6	6.8	4.5
10-14	1,740	46.9	27.7	13.8	88.4	4.8	93.2	4.3	2.6
15-19	1,499	48.4	24.9	12.7	86.1	4.3	90.3	5.3	4.4
Mountain
1-4	652	20.1	44.3	16.7	81.1	4.1	85.3	6.0	8.7
5-9	837	51.0	27.6	12.4	91.0	2.2	93.2	4.1	2.7
10-14	819	51.9	27.7	11.0	90.6	3.8	94.4	4.8	0.9
15-19	684	50.3	26.5	11.8	88.6	1.6	90.2	6.1	3.7
Pacific
1-4	2,107	16.1	36.4	18.4	70.9	10.9	81.8	9.0	9.2
5-9	2,654	45.4	23.7	21.3	90.5	4.3	94.8	4.0	1.2
10-14	2,464	48.9	17.2	25.6	91.7	3.2	94.9	3.4	1.7
15-19	2,148	46.2	16.2	25.3	87.7	3.4	91.0	5.7	3.3

TABLE 6.

DTP IMMUNIZATION STATUS — UNITED STATES, 1966
Ages 1-9 Years

Age	Population (thousands)	Number of Injections						Percent with		
		0	1-2	3	≥4	Unknown No.	Unknown Status	0	3	≥4
1	3,747	500	577	1,865	709	66	30	13.3	49.8	18.9
2	4,036	441	485	1,569	1,416	84	41	10.9	38.9	35.1
3	4,124	433	438	1,396	1,724	80	54	10.5	33.9	41.8
4	4,184	370	368	1,203	2,104	107	31	8.8	28.8	50.3
1-4	16,091	1,744	1,868	6,033	5,953	337	156	10.8	37.5	37.0
5-9	20,436	961	1,523	3,733	13,307	661	251	4.7	18.3	65.1

TABLE 7.

DTP IMMUNIZATION STATUS — UNITED STATES, 1966
Ages 1-9 Years
Percent with Specified Doses by Race

	Total	White	Nonwhite
Ages 1-4			
Percent with no vaccine	10.8	8.6	22.5
Percent with 3 doses	37.5	38.8	30.8
Percent with 4 or more	37.0	39.9	22.1
Percent with 3 or more	74.5	78.6	52.9
Ages 5-9			
Percent with no vaccine	4.7	3.8	10.2
Percent with 3 doses	18.3	17.5	23.0
Percent with 4 or more	65.1	68.3	46.8
Percent with 3 or more	83.4	85.7	69.8

TABLE 8.

DTP IMMUNIZATION STATUS — UNITED STATES, 1966
Ages 1-9 Years
Standard Metropolitan Statistical Areas

	Percent with Specified Number of Injections			
	0	3	4 or More	3 or More
Ages 1-4				
Central Cities	11.2	34.3	34.5	68.8
White	8.5	35.8	39.6	75.4
Nonwhite	17.8	30.9	22.3	53.2
Remaining SMS Areas	6.5	41.6	40.6	82.2
Areas Outside SMS Areas	14.5	36.2	35.7	71.8
Ages 5-9				
Central Cities	4.2	18.6	61.9	80.5
White	2.9	16.7	67.3	84.0
Nonwhite	7.4	23.2	48.2	71.4
Remaining SMS Areas	3.1	17.6	68.7	86.3
Areas Outside SMS Areas	6.6	18.7	63.9	82.6

TABLE 9.

DTP IMMUNIZATION STATUS — UNITED STATES, 1966
Ages 1-9 Years
Major Geographic Divisions

Age	Percent with Specified Number of Injections											
	0	1-2	3	≥4	0	1-2	3	≥4	0	1-2	3	≥4
	New England				*Middle Atlantic*				*East North Central*			
1-4	7.6	8.0	38.5	42.9	8.1	13.2	37.7	37.5	11.5	12.6	41.1	32.1
5-9	2.6	5.8	14.7	75.1	4.1	9.4	18.7	62.0	4.5	7.7	18.2	66.1
	West North Central				*South Atlantic*				*East South Central*			
1-4	11.6	12.0	44.1	29.9	11.0	11.7	34.0	39.6	13.0	11.3	34.4	38.2
5-9	6.1	9.8	20.0	61.0	3.3	5.9	18.6	66.6	6.4	5.6	22.0	58.8
	West South Central				*Mountain*				*Pacific*			
1-4	19.6	11.0	26.5	39.3	10.3	7.4	44.6	35.9	7.0	11.3	38.6	40.3
5-9	10.0	7.2	17.2	61.6	6.2	8.6	17.0	65.3	2.6	6.6	17.3	69.3

TABLE 10.

DTP IMMUNIZATION STATUS — UNITED STATES, 1966
Percent of Children 1-4 Years with Specified Number of DTP
Injections, by Single Years of Life, by Race

Age	Population (thousands)	Number of Injections			
		0	1-2	3	≥4
White					
1	3,123	11.0	15.2	53.1	20.7
2	3,389	9.8	12.0	40.2	38.0
3	3,429	.9.4	10.9	33.9	45.8
4	3,551	7.6	10.0	29.6	52.8
Nonwhite					
1	624	29.8	26.6	33.3	10.3
2	647	23.3	24.9	31.8	19.9
3	695	23.6	20.6	33.8	22.0
4	633	21.0	19.0	24.0	36.0

Note: In this table, children reported as having an unknown number of injections are included in the percentages computed for 1 dose; those reported with status unknown, in percentages computed for 0 doses.

TABLE 11.

IMMUNIZATION STATUS, INFANTS (UNDER 1 YEAR) — UNITED STATES, 1966

	Population (thousands)	Percent with 1 or More		
		OPV Doses	IPV Injections	DTP Injections
United States, Total	3,666	41.6	18.5	63.9
Geographic Divisions				
New England	230	44.3	12.2	65.2
Middle Atlantic	618	46.3	24.1	71.4
East North Central	731	28.5	22.7	60.9
West North Central	283	40.3	18.4	63.3
South Atlantic	520	37.5	19.2	62.3
East South Central	266	53.0	11.7	61.3
West South Central	358	41.1	12.8	53.4
Mountain	123	52.8	11.4	72.4
Pacific	536	49.8	17.4	67.4
Standard Metropolitan Statistical Area Classification				
Central Cities, SMS Areas	1,088	41.6	19.4	63.2
Remaining SMS Areas	1,281	43.8	20.7	70.3
Areas Outside SMS Areas	1,297	39.5	15.7	58.1

Note: In this table, infants reported as having an unknown number of doses or injections are considered to have had 1 dose or injection.

TABLE 12.

PERCENT OF PERSONS REPORTING HISTORY OF MEASLES ILLNESS — UNITED STATES, 1966
Ages 0-10 Years

Age	Population (thousands)	Percent Reporting History	
		8-Day Measles	3-Day Measles
<1	3,666	2.0	4.6
1	3,747	8.1	16.1
2	4,036	13.2	20.3
3	4,124	19.2	27.6
4	4,184	24.4	35.5
5	4,251	32.9	38.7
6	4,000	42.7	46.0
7	4,146	49.7	53.3
8	3,954	56.6	57.9
9	4,084	63.8	63.8
10	4,204	67.3	63.7

TABLE 13.

PERCENT OF PERSONS REPORTING HISTORY OF MEASLES VACCINE — UNITED STATES, 1966
Ages 0-9 Years

Age	Population (thousands)	Percent with History of Measles Vaccine
<1	3,666	9.1
1-4	16,091	45.5
5-9	20,436	28.0

TABLE 14.*
STANDARD ERROR OF THE ESTIMATED PERCENTAGE
A. of persons who received inactivated poliovaccine and of persons who received DTP immunization
(68 chances out of 100)

Estimated Percentage	Base of Percentage (000)							
	500	1,000	2,500	5,000	10,000	25,000	50,000	100,000
2 or 98	1.4	1.0	0.6	0.4	0.3	0.2	0.1	0.1
5 or 95	2.1	1.5	1.0	0.7	0.5	0.3	0.2	0.2
10 or 90	3.0	2.1	1.3	0.9	0.7	0.4	0.3	0.2
25 or 75	4.3	3.0	1.9	1.4	1.0	0.6	0.4	0.3
50	4.9	3.5	2.2	1.6	1.1	0.7	0.5	0.3

B. of persons who received oral poliovaccine and of persons who contracted measles
(68 chances out of 100)

Estimated Percentage	Base of Percentage (000)							
	500	1,000	2,500	5,000	10,000	25,000	50,000	100,000
2 or 98	1.1	0.8	0.5	0.3	0.2	0.2	0.1	0.1
5 or 95	1.7	1.2	0.8	0.5	0.4	0.2	0.2	0.1
10 or 90	2.3	1.6	1.0	0.7	0.5	0.3	0.2	0.2
25 or 75	3.3	2.4	1.5	1.1	0.7	0.5	0.3	0.2
50	3.9	2.7	1.7	1.2	0.9	0.5	0.4	0.3

C. of persons who received both oral and inactivated poliovaccine
(68 chances out of 100)

Estimated Percentage	Base of Percentage (000)						
	250	500	1,000	2,500	5,000	10,000	25,000
2 or 98	1.7	1.2	0.9	0.6	0.4	0.3	0.2
5 or 95	2.7	1.9	1.4	0.9	0.6	0.4	0.3
10 or 90	3.7	2.6	1.9	1.2	0.8	0.6	0.4
25 or 75	5.4	3.8	2.7	1.7	1.2	0.9	0.5
50	6.2	4.4	3.1	2.0	1.4	1.0	0.6

*The standard errors provide an indication of the order of magnitude of the standard errors rather than precise values for any specific item. A number of approximations had to be used to derive standard errors that would be applicable to the wide variety of items that could be prepared at moderate cost.

TABLE 15.*

STANDARD ERROR OF LEVEL OF ESTIMATES OF THE NUMBER OF PERSONS IMMUNIZED BY TYPE OF IMMUNIZATION
(68 chances out of 100)

Level of Estimate (000)	Standard Error (000)		
	Inactivated Poliovaccine and DTP	Oral Poliovaccine and Measles	Oral Poliovaccine and Inactivated Poliovaccine
250	35	27	31
500	49	39	44
1,000	69	54	61
2,500	109	85	92
5,000	152	120	120
10,000	210	165	140
25,000	305	245	
50,000	360	305	

The standard errors provide an indication of the order of magnitude of the standard errors rather than precise values for any specific item. A number of approximations had to be used to derive standard errors that would be applicable to the wide variety of items that could be prepared at moderate cost.

Illustrations of How to Use the Tables of Standard Errors
(all numbers in thousands)

Table 1A shows that 25.3 percent (4,985/19,694) of children in the age group 10-14 had received less than 3 doses of OPV and 3 or more injections of IPV. Using Table 14C, the standard error of 25.3 percent based on 19,694 children is found by taking 25 percent (in the first column) as approximately equal to 25.3 percent and interpolating between the standard errors, 0.9 and 0.5, given in the body of the table under bases 10,000 and 25,000 respectively. Taking the interpolated value as 0.6 of a percentage point, the chances are 68 out of 100 that a complete census would have shown a result between 24.7 and 25.9 percent of children age 10-14 with less than 3 doses of OPV and 3 or more injections of IPV; and 95 out of 100 that a census result would have been between 24.1 and 26.5 percent.

The standard error of the number of 10-14-year-old children, 4,985, who had received less than 3 doses of OPV and 3 or more injections of IPV can be estimated from Table 15. Referring to this table, the number 4,985 falls between 2,500 and 5,000 in the column "Level of Estimate," so the standard error of the estimate (fourth column, OPV and IPV) lies between 92 and 120. By linear interpolation, the standard error of the 4,985 children in the 10-14 age group who were reported to have had less than 3 doses of OPV and 3 or more injections of IPV is 120 (thousand). The chances are 68 out of 100 that a complete census would have differed by less than 120 thousand, and 95 out of 100 that the difference would have been less than 240 thousand.
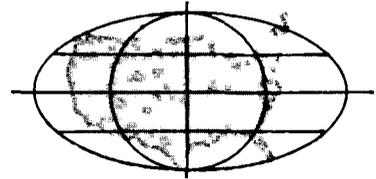
BIOLOGICS SURVEILLANCE –

1966 SUMMARY

Biologics Surveillance—
1966 Summary

In July 1962, the Public Health Service and the major U.S. producers of biologics agreed to collaborate on compiling data pertaining to the distribution of the most common biologics used for immunization in the United States. Of course, doses distributed are not necessarily doses used, but distribution figures are among the most reliable indicators of month-to-month trends in vaccine utilization.

The following summary of the distribution of biologics is the first to be made generally available. Each major antigen is represented by a line graph showing for 1965 and 1966 the net monthly distribution, which represents the total initial distribution of vaccine minus recordable returned doses, by private manufacturers or State laboratories.

To maintain confidentiality of an individual commercial manufacturer's report for economic and production reasons, current tabulations are available only when at least three producers market and report figures for essentially the same product. This is a basic agreement of the Biologics Surveillance Program.

In some instances, where adequate time has elapsed since production and distribution, manufacturers have allowed the data to be released when not all the criteria of confidentiality could be met. Addition of these data to the summaries completes the "natural history" of early patterns of vaccine utilization.

Abstracts of the data included in this summary are included in the individual disease presentations of *Immunization Against Disease*. The more detailed tables and figures that follow give additional insight into monthly and seasonal patterns.

BIOLOGICS SURVEILLANCE PROGRAM PARTICIPANTS

Courtland Laboratories	*The Philadelphia Blood Center*
Cutter Laboratories	*Phillips Roxane, Inc.*
Hyland Laboratories	*Pitman-Moore Company*
Lederle Laboratories	*Squibb, E. R., & Sons*
Lilly, Eli and Company	*Wyeth Laboratories*
Merck Sharp & Dohme	*Illinois Department of Public Health*
The National Drug Company	*Massachusetts Department of Public Health*
Parke, Davis & Company	*Michigan Department of Health*
Pfizer, Chas. & Company	*Texas State Department of Health*

BIOLOGICS — UNITED STATES, 1965-1966
Net Doses Distributed Annually

Biologics	Net Total Doses	
	1965	1966
Influenza Virus Vaccine	10,548,058	20,894,652
Diphtheria Toxoid	28,986,870	34,458,928
Pertussis Vaccine	20,885,893	22,501,029
Tetanus Toxoid	47,352,918	53,721,526
Poliomyelitis Vaccine*	7,462,277	5,547,702
Poliovirus Vaccine, Live, Oral, Type 1	4,651,015	1,425,035
Poliovirus Vaccine, Live, Oral, Type 2	3,352,754	1,314,645
Poliovirus Vaccine, Live, Oral, Type 3	3,708,360	1,373,905
Poliovirus Vaccine, Live, Oral, Trivalent	17,379,175	23,999,654
Measles Virus Vaccine, Inactivated	335,920	166,641
Measles Virus Vaccine, Live, Attenuated	5,732,907	7,929,239
Smallpox Vaccine	19,370,819	17,050,240
Rabies Vaccine	543,796	970,454
Immune Serum Globulins (human)	9,438,069	11,615,499

Inactivated (Salk Type)

COMBINED BIOLOGICS* — UNITED STATES, 1965-1966
Net Doses Distributed Annually

| Biologics	Net Total Doses	
	1965	1966
Diphtheria Toxoid with Tetanus Toxoid	3,121,807	3,559,962
Diphtheria and Tetanus Toxoids with Pertussis Vacine	19,942,388	21,725,597
Diphtheria Toxoid with Pertussis Vaccine	**	**
Tetanus Toxoid with Diphtheria Toxoid (adult)	5,064,430	8,472,070
Diphtheria-Tetanus Toxoids and Poliomyelitis Vaccine Combined: Diphtheria-Tetanus Toxoids and Pertussis and Poliomyelitis Vaccines Combined	260,391	410,660

Also shown above as doses of separate antigens.
**Not shown since fewer than three producers reported.*

DIPHTHERIA AND TETANUS TOXOIDS, PERTUSSIS VACCINE
UNITED STATES, 1965-1966 (Net Distribution by Month)

DIPHTHERIA TOXOID*

1966

1965

TETANUS TOXOID*

1966

1965

MILLIONS OF DOSES

PERTUSSIS VACCINE*

1966

1965

JAN   FEB   MAR   APR   MAY   JUN   JUL   AUG   SEP   OCT   NOV   DEC
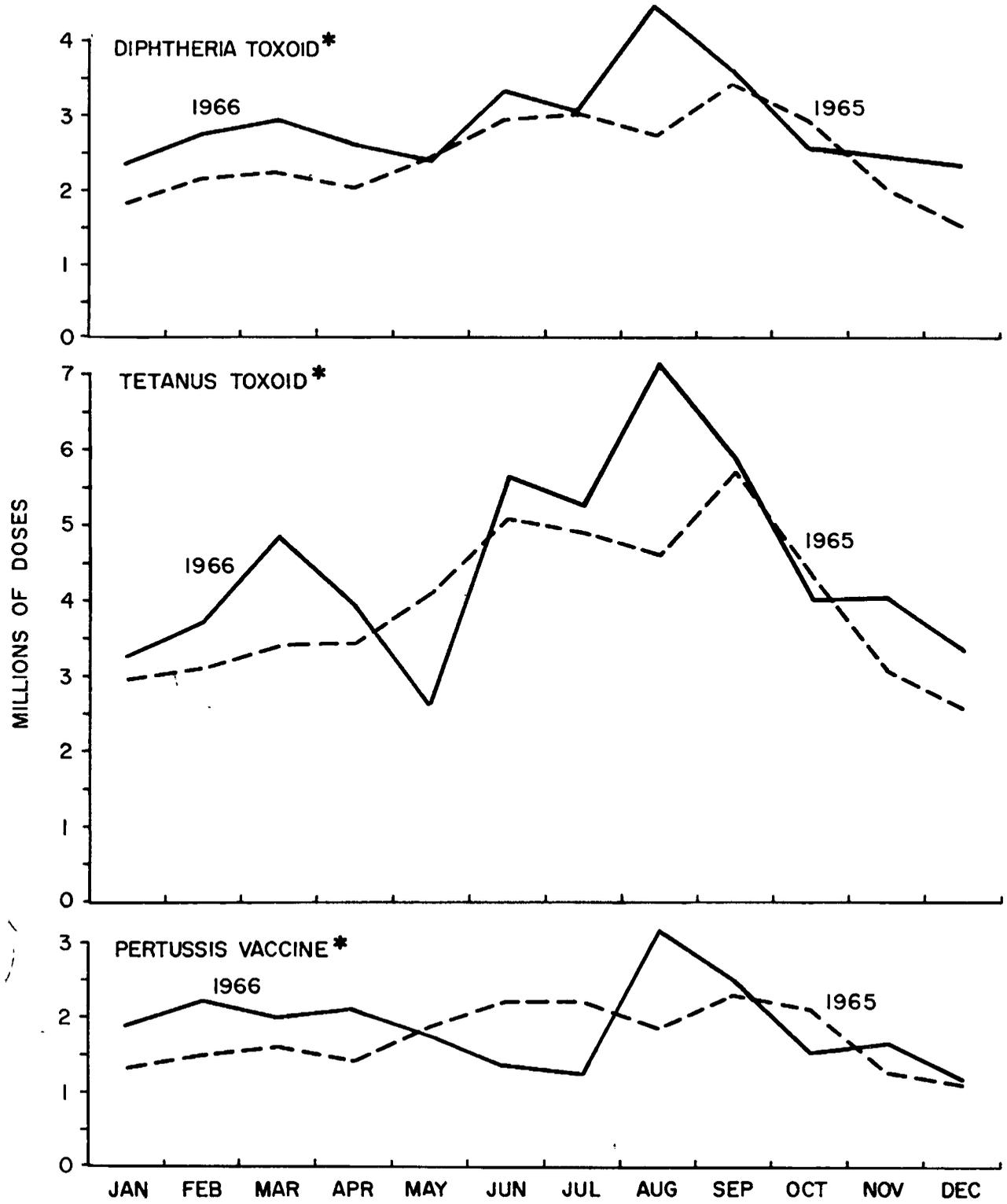
* INCLUDES ALL PRODUCTS CONTAINING THESE ANTIGENS

INFLUENZA VIRUS VACCINE - UNITED STATES, 1965-1966
(Net Distribution by Month)
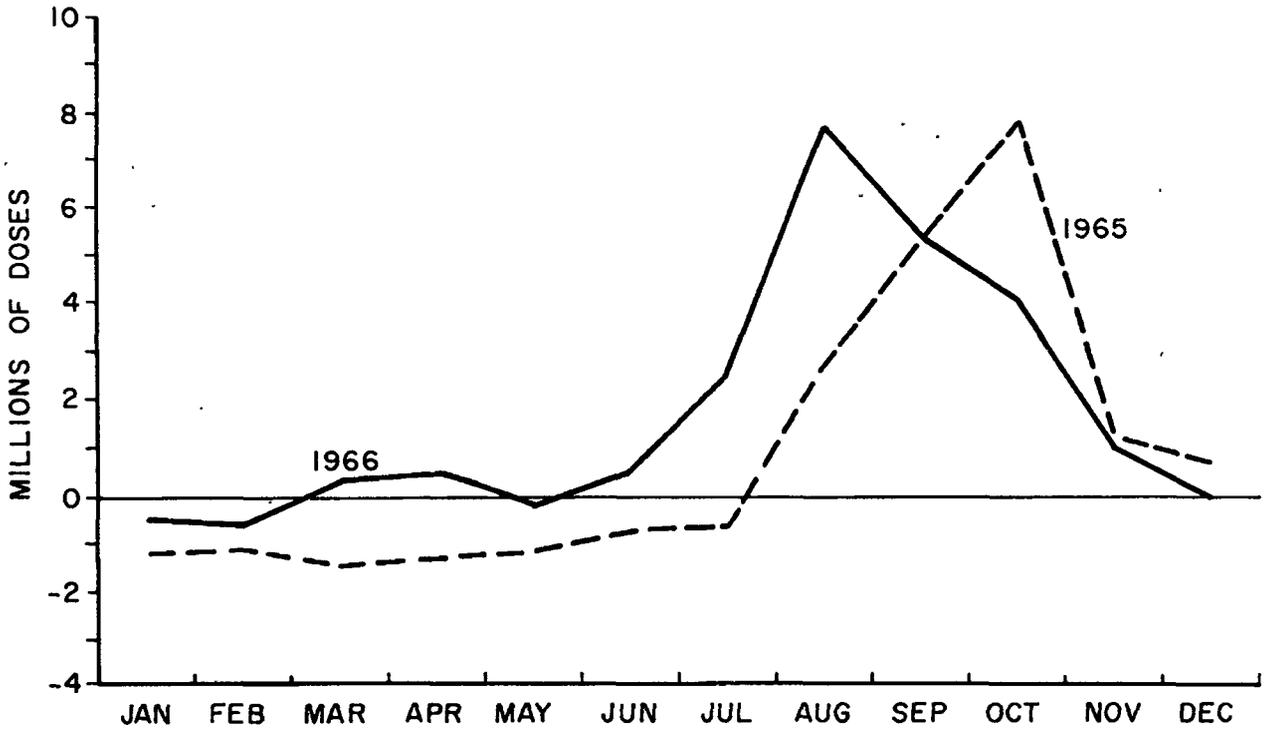
MEASLES VIRUS VACCINE, LIVE, ATTENUATED
UNITED STATES, 1965-1966
(Net Distribution by Month)
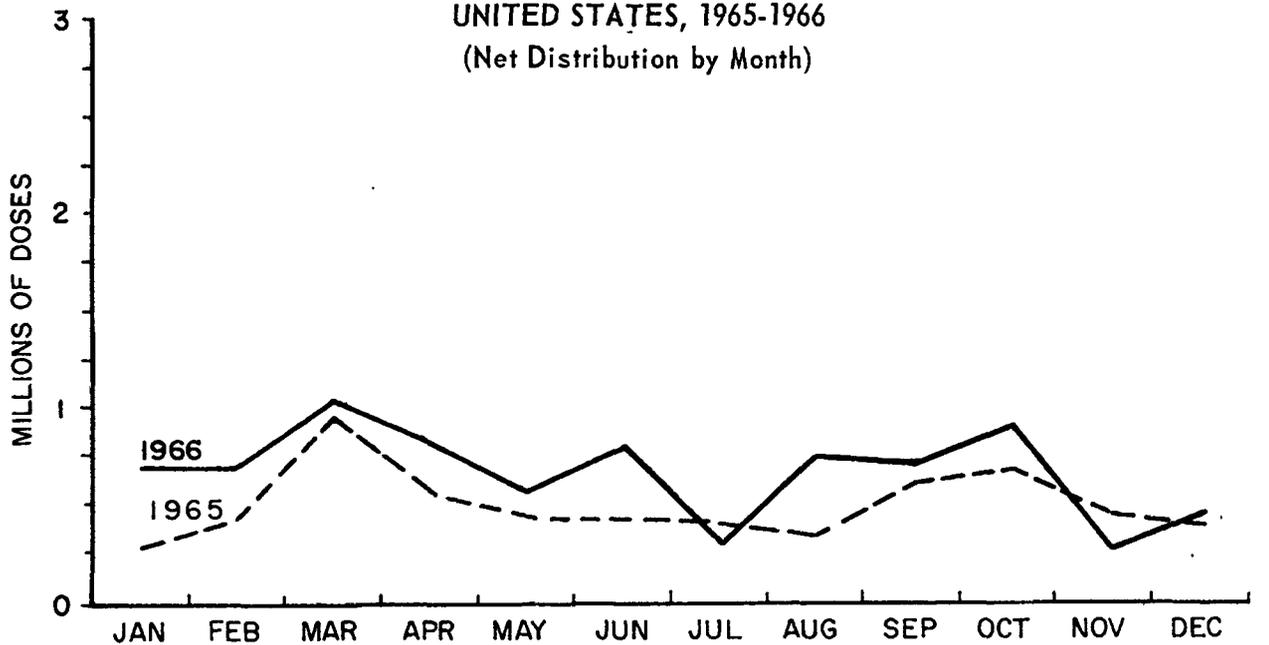
POLIOVIRUS VACCINES, LIVE, ORAL - UNITED STATES, 1965-1966
(Net Distribution by Month)
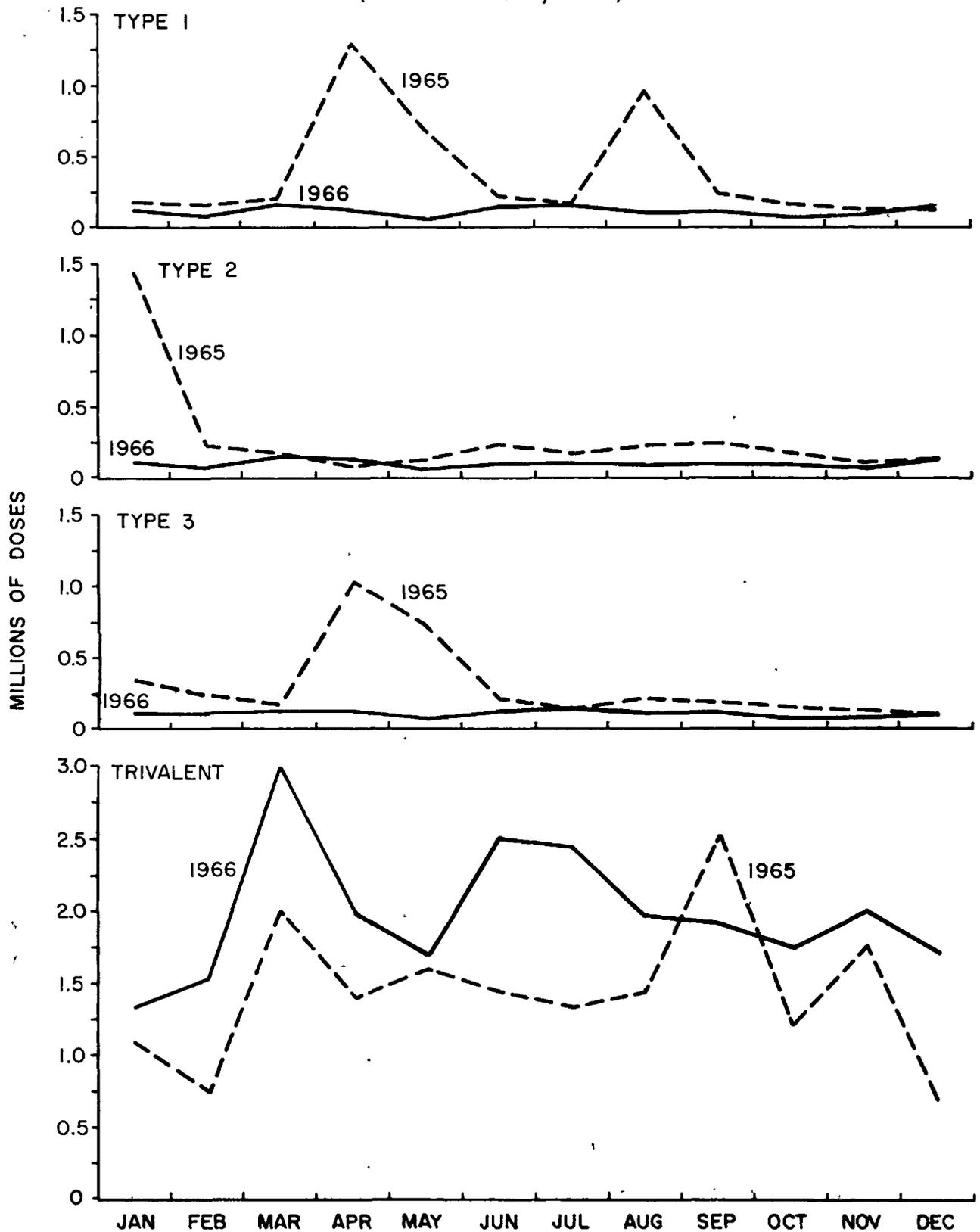
POLIOMYELITIS VACCINE*-UNITED STATES, 1965-1966
(Net Distribution by Month)
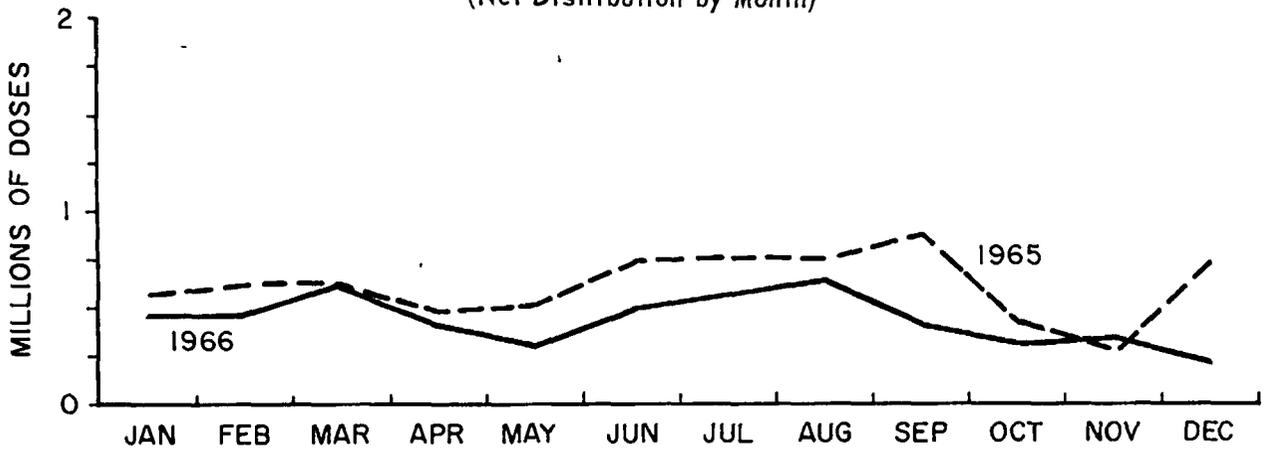
**INACTIVATED (SALK TYPE), INCLUDING ALL PRODUCTS CONTAINING POLIOMYELITIS VACCINE.

RABIES VACCINE - UNITED STATES, 1965-1966
(Net Distribution by Month)
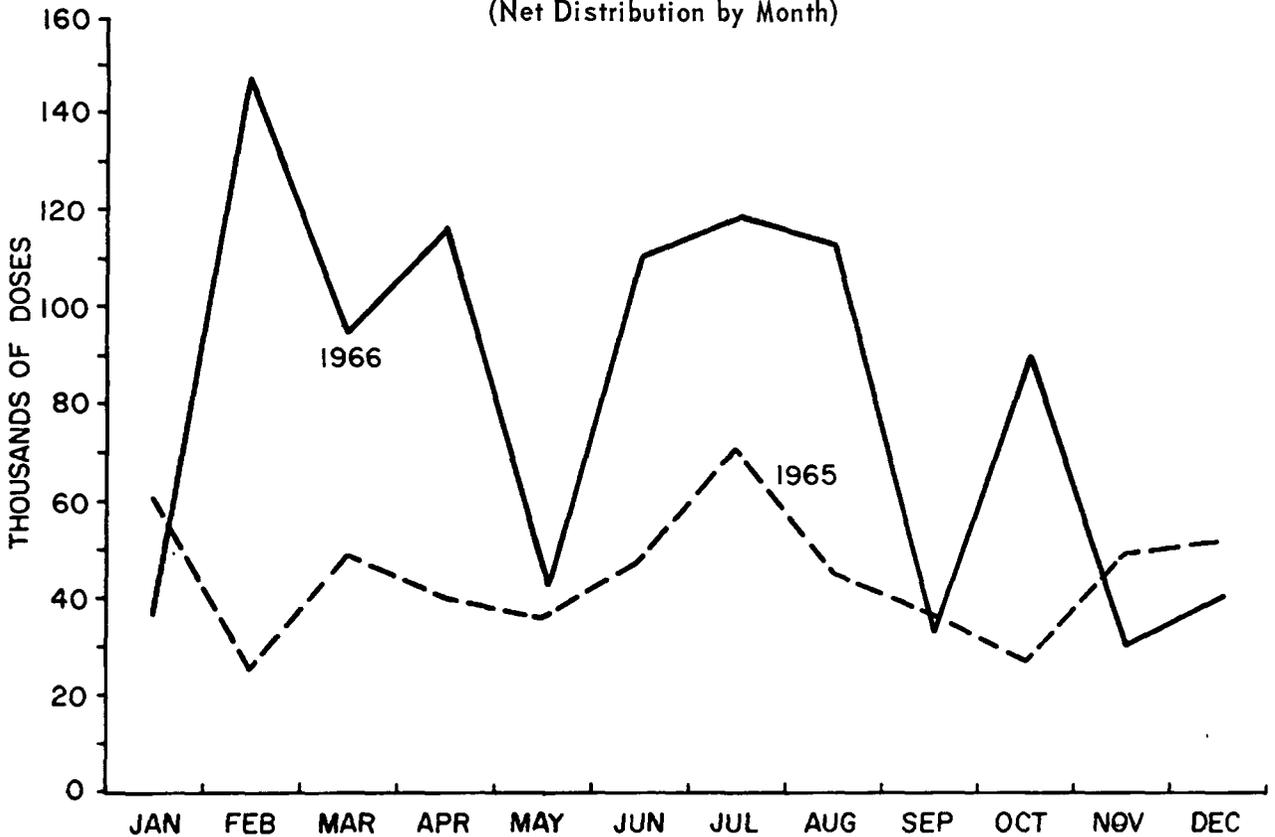
SMALLPOX VACCINE - UNITED STATES, 1965-1966
(Net Distribution by Month)
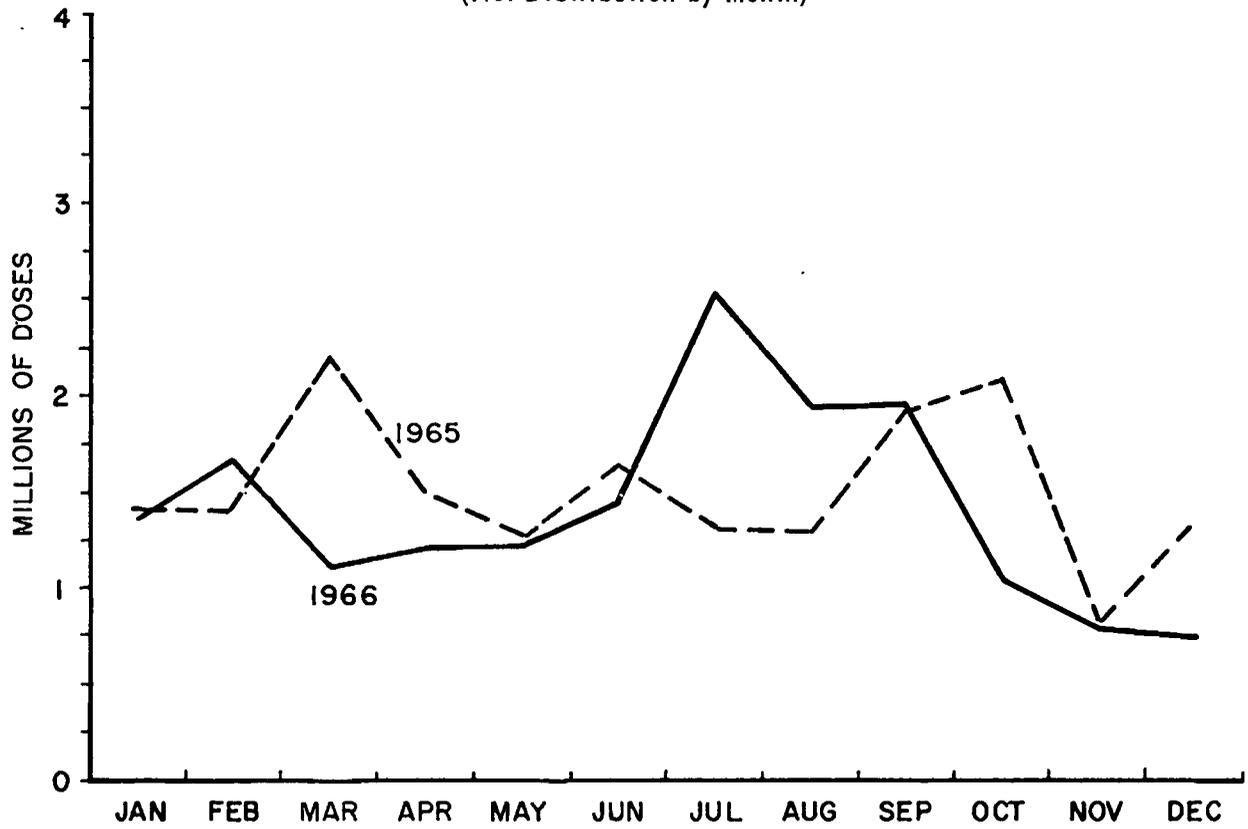
IMMUNE SERUM GLOBULINS (HUMAN)
UNITED STATES, 1965-1966
(Net Distribution by Month)
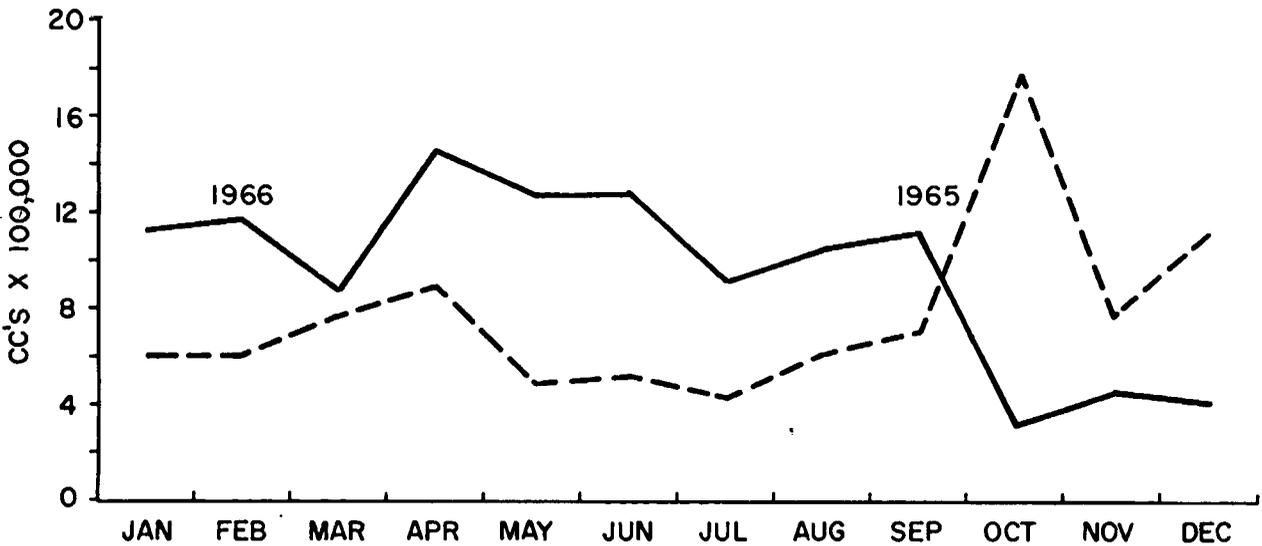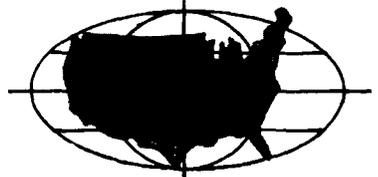
RECOMMENDATIONS –

PUBLIC HEALTH SERVICE

ADVISORY COMMITTEE

ON IMMUNIZATION PRACTICES

Advisory Committee on Immunization Practices

In 1964, the Surgeon General of the Public Health Service, Luther L. Terry, M.D., established the Advisory Committee on Immunization Practices (ACIP) and charged its members to keep him apprised of the status of diseases for which effective vaccines are available and to advise regularly on immunization practices relevant to these diseases. The committee has carefully reviewed the status of pertinent communicable diseases and appraised available vaccines in terms of optimal use in public health and preventive medical practice in the United States. Once released, recommendations of the ACIP are published in the *Morbidity and Mortality Weekly Report* (MMWR) prepared by the Epi-

Serving on the ACIP are physicians and other specialists engaged in the practice of medicine and public health, and in teaching and research. The committee is responsible to the Surgeon General, and it is supported in its deliberations by special consultants and staff members of the National Communicable Disease Center. It maintains regular liaison with the major medical and public health organizations, particularly those actively engaged in making recommendations on immunization practices.

demiology Program of the National Communicable Disease Center.

ACIP membership as of July 1967:

Chairman: David J. Sencer, M.D.
Director
National Communicable Disease Center

Secretary: H. Bruce Dull, M.D.
Assistant Director
National Communicable Disease Center

Members: Gordon C. Brown, Sc.D.
Professor of Epidemiology
School of Public Health
University of Michigan

Geoffrey Edsall, M.D.
Superintendent
Institute of Laboratories
Massachusetts Department of Public Health

David T. Karzon, M.D.
Professor of Pediatrics
University of New York at Buffalo

Theodore A. Montgomery, M.D.
Chief
Division of Preventive Medical Services
California Department of Public Health

Ira L. Myers, M.D.
State Health Officer
Alabama Department of Public Health

Jay P. Sanford, M.D.
Professor of Internal Medicine
University of Texas Southwestern Medical School

Paul F. Wehrle, M.D.
Professor of Pediatrics and Head of the Infectious Disease Division
Los Angeles County General Hospital

Ex officio: Alice D. Chenoweth, M.D.
Chief
Program Services Branch
Childrens Bureau, DHEW

Roderick Murray, M.D.
Director
Division of Biologics Standards
National Institutes of Health

Liaison representative: Margaret H. D. Smith, M.D.
Professor of Pediatrics
Tulane University School of Medicine

(Chairman, Committee on the Control of Infectious Disease, American Academy of Pediatrics)

RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

The Public Health Service Advisory Committee on Immunization Practices meeting on October 11, 1966, issued the following recommendations on diphtheria, tetanus, and pertussis vaccination practices and tetanus prophylaxis in wound management for the United States. (Reprinted from MMWR, Vol. 15, No. 48, week ending December 3, 1966.)

DIPHTHERIA AND TETANUS TOXOIDS AND PERTUSSIS VACCINE

TETANUS PROPHYLAXIS IN WOUND MANAGEMENT

Introduction

Routine immunization against diphtheria, tetanus, and pertussis during infancy and childhood has been widely advocated and generally practiced in the United States during the past 20 years. The effectiveness of these programs is reflected in the decreasing incidence and mortality due to these diseases. The following recommendations regarding immunization have been developed on the basis of this experience and accumulated epidemiologic and immunologic data.

Diphtheria

There has been an accelerated decline in the annual incidence of diphtheria since the end of World War II, and diphtheria is now a rare disease in many areas of the United States. In 1965, fewer than 175 cases were reported. However, localized outbreaks continue to appear, accompanied by serious complications and a case-fatality ratio often greater than 10 percent.

The great majority of cases occur in inadequately immunized individuals. Although most diphtheria is in children, cases and deaths occur in all age groups. Diphtheria toxoid, when administered according to recommended schedules, prevents deaths and greatly reduces clinical illness and complications. Following adequate immunization, protective levels of antitoxin have been observed to persist for 10 years or more.

Tetanus

Although its incidence in the United States has declined in recent years, tetanus remains an important public health problem which can only be eliminated through universal active immunization. In 1964, nearly 300 cases of tetanus were reported, the majority in unimmunized adults. Of these, 180 died, a death to case ratio of more than 60 percent. Adequate immunization with tetanus toxoid provides effective and durable protection against the disease. Furthermore, prior active immunization eliminates the need for passive therapy at the time of injury, thus preventing the considerable morbidity resulting from use of heterologous animal serum. In addition, universal active immunization will prevent the significant proportion of cases occurring after trivial injury or with unrecognized portals of entry. Other benefits include the prevention of neonatal tetanus and protection to individuals in various high risk groups.

Tetanus toxoid is highly effective and almost completely free of side effects. Since it also provides long-lasting protection, it is an almost ideal immunizing agent. Because there is neither natural immunity to tetanus, nor any general contraindication to tetanus toxoid, and since the organism is unbiquitous, the need for immunization is universal.

Pertussis

Pertussis with its associated high mortality is the major rationale for DTP immunization in early infancy. The disease is highly communicable, with attack rates up to 90 percent among unimmunized household contacts. Most cases are reported in infants and young children. In 1964, nearly three-fourths of pertussis deaths occurred in those under age one — some 40 percent of the total number in infants three months of age or younger. Immunization is very effective in reducing both incidence and case fatality. The mortality rate has declined precipitously since the widespread use of standardized pertussis vaccines beginning in the mid 1940's. Since the incidence and mortality decrease with age, while local and systemic reactions to the vaccine increase, pertussis immunization is not recommended above the age of six years.

Preparations Used for Immunization

Diphtheria and tetanus toxoids are prepared by formaldehyde treatment of the respective toxins. Pertussis vaccine is made from a killed bacterial suspension or a bacterial fraction. The toxoids and pertussis vaccines are available in both fluid and adsorbed forms. Comparative tests have shown that the adsorbed toxoids are clearly superior in antibody titer produced and in the durability of protection achieved. The promptness of antibody responses following the administration of either fluid or adsorbed toxoids as boosters is not sufficiently different to be of clinical importance. Therefore, adsorbed toxoids are the agents of choice for all primary and booster immunization.

These antigens are available in various combinations and concentrations for specific purposes. Three antigens are important for public health use:

1) Diphtheria and Tetanus Toxoids and Pertussis Vaccine (DTP)
2) Tetanus and Diphtheria Toxoids, Adult Type (Td)
3) Tetanus Toxoid (T)

All preparations contain comparable amounts of tetanus toxoid, but the diphtheria component in the adult type of tetanus and diphtheria toxoids (Td) is only about 10 percent of that contained in the standard DTP preparation used in infants and young children.

Dosage

Since the antigen concentration varies in different products, the manufacturers' package inserts provide specific information regarding the volume of single doses.

Schedules

Recommendations regarding usage of these vaccines are based upon immunologic and epidemiologic considerations, taking into account the special circumstances of school entrance and other factors important in disease transmission.

Primary Immunization

Children 2 months through 6 years (Ideally beginning at age 2-3 months or at the time of a 6-week "check-up" if such timing is an established routine.)

DTP — The recommended single dose given intramuscularly on *three* occasions at 4-6 week intervals with a reinforcing dose approximately one year after the third injection.

Adults and children over 6 years

Td* — The recommended single dose given intramuscularly or subcutaneously on *two* occasions at 4-6 week intervals with a reinforcing dose approximately one year after the second.

Booster Immunization

Children 3 through 6 years, (Preferably at time of school entrance, kindergarten or elementary school.)

DTP — The recommended single dose intramuscularly.

Thereafter and for all other individuals

Td* — The recommended single dose intramuscularly or subcutaneously every 10 years. (When administered as part of wound management — see specific

recommendations — a 10-year interval is determined from *that* date). More frequent routine booster doses are not indicated and may be associated with increased reactions.

Tetanus Prophylaxis in Wound Management

An important part of the management of wounds is prevention of tetanus. The physician is often faced with decisions concerning use of tetanus toxoid for active protection and tetanus antitoxin or tetanus immune globlin (human) for passive protection. The available evidence demonstrates that primary immunization with tetanus toxoid (initial doses plus the reinforcing dose) provides a longlasting basis for active protection against tetanus. Passive protection need be considered only for the individual without a valid history of at least one injection of tetanus toxoid; indeed, there is evidence that persons who have received a single dose will respond adequately to a single booster dose, even after an interval of several years.

The following outline summarizes recommendations for the use of active and passive tetanus immunization in wound management:

1. Primary immunization or booster dose *less than* one year prior to injury:
   a. No tetanus prophylaxis required.
2. Primary immunization or most recent booster *more than* one year prior to injury:
   a. Td** — The recommended single dose intramuscularly or subcutaneously.
3. Incompletely immunized:
   a. Complete primary immunization (See Dosage and Schedules).
4. Unimmunized:
   a. Initiate primary immunization (See Dosage and Schedules).
   b. The decision to use concomitant passive prophylaxis will depend upon medical judgment after evaluating such factors as location, type and severity of the wound, degree and kind of contamination and the time elapsed between injury and medical attention. If passive therapy is elected, tetanus immune globulin (human) is strongly preferred to equine or bovine antiserum. It offers the advantages of longer protection and freedom from undesirable reactions. The currently recommended prophylactic dose of tetanus immune globulin (human) is 250 units for wounds of average severity. When used concurrently, toxoid and antitoxin should be given in separate syringes and at separate sites.

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*Td is considered the agent of choice for immunization at ages over 6 years on the basis of data regarding its effectiveness in primary immunization of older children and adults and because of increasing reactions to full doses of diphtheria toxoid with age. The use of this preparation obviates the need for Schick or Moloney testing prior to immunization.

**If there is any reason to suspect hypersensitivity to the diphtheria component, tetanus toxoid (T) should be substituted for Td (adult type).

Should tetanus immune globulin (human) be unavailable, equine or bovine antitoxin may be used. The usual dose is from 3,000 to 5,000 units. Administration should always be preceded by careful screening for sensitivity. The following schema is derived from recommendations by the Committee on Trauma, American College of Surgeons:[1]

Determining Sensitivity to Equine or Bovine Serum
History
1. Inquire specifically regarding previous injections of equine or bovine serum. Sensitivity frequently develops after the first injection of animal serum. *If an adverse reaction occurred previously following either serum, do not consider its further use.* (The alternative product can then be subjected to the sensitivity testing described below.)
2. Question the patient with regard to sensitivity to horse dander or beef products. Either may be considered a signal for caution.

Skin Tests (Equine or Bovine Antitoxin)
1. Inject *intracutaneously* 0.02-0.03 ml. of 1:10 normal saline dilution of the tetanus antitoxin.* The area of infiltration should be about the size of the head of a pin. A control test with the same volume of saline should be done for comparison.
2. In 15 minutes or less, a *positive reaction* will be manifested by a hive-like wheal and erythema. The larger the reaction, the greater the sensitivity. A 0.5 cm. wheal may represent a nonspecific response which may be confirmed by the presence of a comparable reaction to the saline alone.

Eye Tests
1. Place a drop of 1:10 normal saline dilution of the tetanus antitoxin in the conjunctival sac of one eye at the time the skin test using the same material is performed. A drop of normal saline in the other eye can serve as a useful control.

2. Within 30 minutes, a *positive reaction* will be indicated by redness of the conjunctiva.
3. If no conjunctival reaction occurs following use of the antitoxin, the eye test may be considered *negative*.
4. After the result is apparent, a drop or two of epinephrine 1:1000 should be instilled in the test eye.

Interpretations
1. If a *positive reaction* occurs with skin and/or eye test, the animal serum employed in the testing *should not* be administered. Desensitization *should not* be attempted. The physician may either test for sensitivity to the other animal serum or endeavor to obtain tetanus immune globulin (human).
2. Following a *positive reaction* to one animal serum, the other should be subjected to the same skin and eye tests before considering its use in tetanus prophylaxis.
3. If history and both skin and eye tests are *negative*, the likelihood of a reaction to a *standard dose* of the animal serum tested is small, and it may be administered.*

(As an additional precaution encouraged by some, 0.1 ml. of a 1:10 normal saline dilution of antitoxin may first be injected *subcutaneously*.* If no untoward reaction is observed in 30 minutes, the prophylactic dose may be given.)

Wherever animal serum is administered parenterally either for test or treatment, a syringe with 1 ml. of epinephrine 1:1000 should always be immediately available.

REFERENCE:

[1]*Early Care of Acute Soft Tissue Injuries.* The Committee on Trauma of the American College of Surgeons. W. B. Saunders Co., Philadelphia and London, 1965, pp. 25-26.

RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

The Public Health Service Advisory Committee on Immunization Practices meeting on May 26, 1967, issued the following recommendation regarding influenza immunization and control in the civilian population. (Reprinted from MMWR, Vol. 16, No. 26, July 1, 1967)

INFLUENZA — 1967-68

Influenza Prospectus — 1967-68 — United States

During the winter and spring of 1966-67, the influenza reported in the United States was limited to minor outbreaks and individual cases. Type A2 influenza virus was recovered only from several small outbreaks in the eastern States. Type B virus was identified in the Southwest, particularly in California and Arizona. Excess mortality attributed to pneumonia and influenza did not reach the national "epidemic threshold" at any time, and it did not remain elevated for more than a single week in any of the country's geographic divisions.

No significant antigenic changes were demonstrated in the relatively few strains of type A2 influenza virus recovered during the year in the United States and abroad. Type B strains were similar to those isolated in the 1965-66 season but did show antigenic differences from earlier type B strains.

The relatively little disease caused by A2 influenza viruses in the 1966-67 season permitted the general level of susceptibility to increase, particularly in the eastern States where the last major outbreaks of A2 illness were observed in 1964-65. Thus, substantial numbers of cases of A2 influenza can be expected to occur during the 1967-68 season, especially in the eastern part of the country. Because in 1965-66 and 1966-67 most areas of the United States experienced type B influenza caused by strains related to those still prevalent, no significant amount of type B infection is likely to occur in the coming year.

Influenza Viruses and Vaccine Formulation

Influenza viruses are known to undergo continual antigenic change. Minor variations, as discerned by laboratory procedures, occur frequently. Moderate changes can result in increased numbers of influenza cases, presumably on the basis of the population's heightened susceptibility to the variant. Major antigenic shifts occur infrequently. When they do, they may produce widespread or even pandemic disease. The most recent major type A influenza virus variant is the A2 (Asian) strain which appeared in 1957.

The protection afforded by a particular influenza vaccine antigen, like that conferred by natural infection, is directed primarily against the same or similar infecting strains. This relationship has been most easily observed at the time of major antigenic shifts, although the relative effectiveness of vaccines may also be reduced when less marked changes occur.

During the 25 years since development of inactivated influenza vaccines, the appearance of three major antigenic variants emphasizes the need for regular up-dating of vaccine formulations. When A1 influenza virus appeared in the United States in 1947, vaccine containing only A antigen gave very little protection. Similarly, marked ineffectiveness of type A1 antigen was observed in 1957 when the A2 strain appeared; and when an essentially distinct strain of type B influenza virus appeared in 1954, vaccines containing the previous type B strains were no longer satisfactory.

In general, it has been recognized that the relative effectiveness of influenza vaccine depends on the degree of similarity between strains incorporated in the vaccine and the viruses prevalent in the community. Yearly review of epidemiologic and laboratory data on vaccines and prevalent viruses is required to ensure that the proposed vaccine formulation is suitable for the next year's forecast.

Influenza Vaccines — 1967-68

Two influenza vaccine formulations will be available for use in the 1967-68 season. A newly introduced bivalent vaccine containing only contemporary A2 and B strains is for general use to provide greater protection against current strains of influenza. The traditional polyvalent vaccine incorporates older strains (types A and A1) as well as newer A2 and B antigens in order to stimulate a broader immunologic response. The older strains do not play a significant role against the currently prevalent viruses.

Both the bivalent and polyvalent vaccine formulations contain the same total quantity of influenza antigens — 600 chick cell agglutinating (CCA) units. This limit is set in order to minimize the frequency of local and systemic reactions. The bivalent vaccine includes considerably greater representation of contemporary A2 and B strains than is possible in polyvalent vaccine which retains A and A1 antigens. Bivalent vaccine should provide greater protection against current strains of influenza than has previously been possible.

The A2 strains included in both vaccine formulations are the same as were used in 1966-67. Because of antigenic changes in prevalent type B strains, however, B,'Maryland,'1,'59 has been replaced by B 'Massachusetts,'3,'66.

Bivalent (A2 and B Strains) Influenza Virus Vaccine—1967

Type	Strain	CCA Units per ml	
A2	{Japan,'170,'62 {Taiwan, 1,'64	{150 {150	300
B	Massachusetts, 3,'66		300
Total			600

Polyvalent (A, A1, A2, and B Strains) Influenza Virus Vaccine—1967

Type	Strain	CCA Units per ml
A	PR/8/34	100
A1	Ann Arbor/1/57	100
A2	{ Japan/170/62 Taiwan/1/64	{ 100 100 } 200
B	Massachusetts/3/66	200
Total		600

Vaccine Usage

Annual influenza immunization is not currently indicated for all individuals, but should be given to persons in groups known to experience high mortality from epidemic influenza. In particular, immunization with bivalent vaccine is recommended for persons in older age groups and for all individuals with chronic illnesses such as those discussed below:

Chronically Ill

Persons of all ages who suffer from chronic debilitating diseases including cardiovascular, pulmonary, renal, or metabolic disorders; in particular:

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

Older Age Groups

During major influenza outbreaks, especially those caused by type A viruses, increased mortality has regularly been recognized in persons over 45 years of age and even more notably in those over 65. This association has been particularly marked when underlying chronic illnesses were also evident.

Persons in Institutions

Patients residing in nursing homes, chronic disease hospitals, and comparable environments should be considered at particular risk since their living arrangements may allow greater spread of disease once an outbreak has been established.

Some increased mortality was observed among pregnant women during the 1957-58 influenza A2 epidemic both in this country and abroad. Subsequently, there has been no indication of increased risk. Routine influenza immunization during pregnancy is not recommended unless the individual also falls into one of the "high risk" categories noted above.

Physicians contemplating general vaccination programs for industrial, school, and other such groups must weigh the expense of the programs against the likelihood of extensive illness. When widespread epidemics of influenza are forecast, officials responsible for maintaining community services are justified in recommending the use of influenza vaccine in selected adult groups if above-average levels of absenteeism would disrupt satisfactory operations.

Dosage and Schedule

Persons Not Vaccinated Since July 1963

Persons who require immunization and have not been vaccinated since July 1963 should receive a primary immunization series of bivalent vaccine. The primary series consists of an initial subcutaneous dose, followed by a second, two months later. It may be noted that even a single dose can afford some protection. A second injection as early as two weeks after the first one will enhance the antibody response.

Immunization should begin as soon as practicable after October 1 and ideally should be completed by early December. It is important that immunization be carried out before influenza occurs in the immediate area, because there is a two-week interval between vaccination and maximal development of antibodies.

Summary

Adults and children 10 and older
1.0 ml subcutaneously on two occasions as specified above.

Children 6 to 10 years*
0.5 ml subcutaneously on two occasions as specified above.

Children 3 months to 6 years*
0.1-0.2 ml 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.

Persons Vaccinated After July 1963

Only a single booster of bivalent vaccine at the dosage level specified for the primary series is necessary for individuals requiring immunization who have been vaccinated as recently as July 1963. This booster dose is best given in early December, before the onset of the anticipated influenza season.

For those in older age groups who have previously experienced undue reactions to influenza vaccine, a booster dose of 0.1 ml given by careful intracutaneous injection can be expected to induce an antibody response which is somewhat comparable to that induced by the 1.0 ml subcutaneous dose. The intracutaneous route is not recommended, however, in other circumstances.

Contraindication

Since the vaccine viruses are propagated in eggs, the vaccine should not be administered to anyone who is hypersensitive to eggs or egg products.

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*Since febrile reactions in this age group are common following influenza vaccination, an antipyretic may be indicated.

RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

The Public Health Service Advisory Committee on Immunization Practices meeting on May 26, 1967, issued the following recommendation on measles vaccines, the second revision of the initial recommendation which appeared in the MMWR, Vol. 14, No. 7 (February 20, 1965). (The first revision appeared in the MMWR, Vol. 14, No. 36, September 11, 1965.)

MEASLES VACCINES

Introduction

Highly effective, safe vaccines are available for eliminating measles in the United States. Collaborative efforts of professional and voluntary medical and public health organizations are directed toward eradicating the disease in 1967. Unless protected by vaccine, virtually all children will at some time have clinically evident measles. Measles is often a severe disease; it is of particular concern because of frequent complications, including bronchopneumonia, middle ear infection, and encephalitis. Encephalitis, which follows measles in approximately one of every 1,000 cases, often causes permanent brain damage and subsequent mental retardation. An average of one measles death occurs for every 10,000 cases.

All susceptible children—those who have not had natural measles or measles vaccine—should be immunized. It is particularly important to immunize children that are still susceptible on entering nursery school, kindergarten and elementary school, because they are often responsible for transmission of measles to other children in the community. Communities should establish programs directed toward vaccinating all children at about one year of age.

Live Attenuated Measles Virus Vaccine (Edmonston and Schwarz Strains)

Live attenuated measles virus vaccine* prepared from the Edmonston or Schwarz (further attenuated) measles virus strains is widely used in the United States. The Edmonston strain is propagated in either chick embryo or canine renal cell culture; it may be given alone or with Measles Immune Globulin according to the manufacturers' directions. The Schwarz strain is prepared only in chick embryo cell culture; it is suitable for administration without Measles Immune Globulin.

The live attenuated measles virus vaccines produce a mild or inapparent, non-communicable infection. Fifteen percent of those receiving either the Edmonston strain with Measles Immune Globulin or the Schwarz strain experience fever, with temperatures of 103°F (rectal) or higher, beginning about the sixth day after vaccination and lasting no longer than 5 days. About twice as many (30 percent) of those receiving Edmonston strain without Measles Immune Globulin have similar responses. The great majority of reports indicate that even children with high fevers experience relatively little discomfort and

*The official name of the product in use is: Measles Virus Vaccine, Live, Attenuated.

minimal toxicity. As a result, febrile reactions often go unnoticed by the parents.

An antibody response develops in virtually all susceptible children who are given live attenuated measles virus vaccines. Edmonston strain vaccine administered without Measles Immune Globulin induces a level and persistence of antibody corresponding to that seen following regular measles. Antibody titers in response to Edmonston strain with Measles Immune Globulin or to Schwarz strain are slightly lower. However, all three of these vaccine schedules appear to confer lasting protection against naturally occurring measles.

Experience with more than 20 million doses administered in the United States by early 1967 indicates that live attenuated measles virus vaccines are among the safest immunizing agents available. To date, serious reactions associated with their use have been very rare.

Recommendations for Vaccine Use

Age

For maximum efficacy, live attenuated measles virus vaccine should be administered when children are at least 12 months old. It can be given to infants at 9 to 12 months of age realizing that the proportion of vaccine responses may be slightly reduced. The proportion is further decreased if Measles Immune Globulin is administered with the vaccine. Vaccination of adults at the present time is rarely necessary, because nearly all individuals are immune by age 15. Limited data indicate that reactions to vaccine are no more common in adults than in children.

High Risk Groups

Immunization against measles is particularly important for children with chronic illnesses, such as heart disease, cystic fibrosis, and chronic pulmonary diseases, as well as for children with malnutrition and those living in institutions.

Prevention of Natural Measles Following Exposure

Live attenuated measles virus vaccine can usually prevent disease if administered before or on the day of exposure to natural measles. Limited studies reported to date indicate that protection is not conferred when vaccine is administered after the day of exposure, nor are adverse effects induced by measles immunization following exposure.

Precautions in the Use of Live Attenuated Measles Virus Vaccines

Severe Febrile Illnesses
Vaccination should be postponed until recovery is complete.

Tuberculosis
The exacerbations of tuberculosis that have been related to natural measles infection, by analogy might accompany infection with live attenuated measles virus. Therefore, any individual with known active tuberculosis should be under treatment when given measles vaccine. Although tuberculin skin testing is desirable as part of ideal health care, it need not be a routine prerequisite in community measles immunization programs. The protection against natural measles outweighs the theoretical hazard of possible exacerbation of tuberculosis infection by the administration of vaccine.

Recent Immune Globulin Administration
After administration of immune globulin, immunization should be deferred for 3 months. Persistence of measles antibody from the globulin may interfere with response to the vaccine.

Marked Hypersensitivity to Vaccine Components
Measles vaccine produced in chick embryo cell culture should not be given to children hypersensitive to ingested egg proteins. Similarly, vaccine produced in canine cell culture should not be administered to children highly sensitive to dog hair or dog dander. To date, no reactions of the anaphylactic type following measles vaccine have been reported in the United States.

Contraindications to Use of Live Attenuated Measles Virus Vaccine

Leukemia, Lymphomas, and Other Generalized Malignancies
Administration of live attenuated measles virus vaccine to children with leukemia has occasionally been followed by severe complications such as fatal giant cell pneumonia. Theoretically, attenuated measles virus infection might be potentiated by other severe underlying diseases, such as lymphomas and generalized malignancies.

Altered Resistance from Therapy
Steroids, alkylating drugs, antimetabolites, and radiation may predispose to untoward complications due to altered resistance.

Pregnancy
Purely on speculative grounds, physicians are reluctant to risk causing fetal damage that might theoretically be related to attenuated measles virus infection.

Management of Patients with Contraindications to Live Attenuated Measles Virus Vaccines
If immediate protection against measles is required for persons in whom use of live attenuated measles virus vaccine is contraindicated, passive immunization with Measles Immune Globulin (dose 0.25 ml/kg) should be given as soon as possible after a known exposure. It is important to note, however, that the preventive dosage of Measles Immune Globulin effective in normal children may not be equally so in children with acute leukemia. Inactivated measles virus vaccines* may induce longer lasting protection than provided by Measles Immune Globulin, but many children with leukemia and those receiving immunosuppressive drugs respond poorly.

Prior Immunization with Inactivated Measles Vaccine
Atypical measles, sometimes severe, following exposure to natural measles, has occasionally been observed in children previously immunized with inactivated measles virus vaccines. Untoward local reactions such as induration and edema have at times been observed when the live measles virus vaccine was administered to persons who had received inactivated vaccine previously.

Despite these reported instances of unusual associations, children who have been given inactivated measles vaccine should also be given the live vaccine for full and lasting protection against natural infection.

Simultaneous Administration of Live Virus Vaccines
Data on simultaneous administration of live virus vaccines are not sufficient to develop comprehensive recommendations; but there are obvious practical advantages to combining vaccines, and investigations are underway which should help to define optimal practices. When combined administration is indicated, available data do not suggest that undesirable responses will result. The following comment presents current attitudes toward scheduling vaccination with three major live virus vaccines—polio, measles, and smallpox.

It has been generally recommended that immunizations with live virus vaccines be separated by at least one month whenever possible. The rationale for this recommendation is the theory that superimposed reactions and diminished antibody responses might result if two or more live virus vaccines were given simultaneously. Ideally, the initial doses of oral poliovirus vaccine should have been given before a child reaches one year, the age for giving live attentuated measles virus vaccine. Administration of polio and measles antigens should be

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*Inactivated vaccines derived from Edmonston strain measles virus and prepared either in chick embryo or monkey cell cultures are available (Measles Virus Vaccine, Inactivated). These vaccines should be administered in a three-dose schedule at monthly intervals with a subsequent booster 6 months later. Following primary immunization with inactivated measles virus vaccine, the protection achieved in normal children has been satisfactory for the first few months, but has been shown to decline rapidly thereafter. **Inactivated measles virus vaccines should not be used for immunizing normal children.**

separated by at least one month. It is likewise desirable to separate measles and smallpox vaccinations by one or more months because both of these antigens may produce febrile reactions.

When, however, immunization program effectiveness is hindered or when the threat of concurrent exposures exists, the relevant live virus vaccines should be given at the same time. Observations do not indicate that this will cause a significant increase in adverse reactions or depressed antibody responses to either antigen.

Community Immunization Programs

Ongoing Programs
Universal immunization as part of good health care should be accomplished through routine and intensive programs carried out in physicians' offices and public health clinics. Programs aimed at immunizing children against measles at about one year of age should be established by all communities. In addition, all susceptible children entering nursery school, kindergarten, and elementary school should receive vaccine because of their particular role in community spread of natural measles.

Community-wide Mass Programs
Mass immunization programs can be useful supplements to the continuing use of live attenuated measles virus vaccine. Many have been organized as part of community measles eradication campaigns. The following points should be considered in planning mass immunization programs:

1. The active cooperation of private physicians and official health agencies normally concerned with the care of children is important.

2. Because live attenuated measles virus vaccines are administered parenterally, adequate numbers of medical and nursing personnel are required.

3. Despite increased public awareness of measles and its frequent, serious complications, substantial effort may be required to attain complete community support.

4. Although a number of children may have febrile reactions to live attenuated measles virus vaccine, extensive experience in community-wide campaigns and in private medical practice indicates that only a small fraction of these reactions requires medical attention. Parents should be told what reactions to expect, to avoid undue concern after the program gets underway.

Control of Measles Epidemics
Studies have shown that measles epidemics can be curtailed or halted in a community by prompt administration of live attenuated measles virus vaccine to selected groups of children, particularly the susceptibles in nursery school, kindergarten, and the first two or three grades of elementary school. However, once measles is widely disseminated in a community, it may be necessary to immunize susceptible children of all ages to alter the course of the epidemic.

Continued Surveillance
Careful surveillance of measles and its complications is necessary for appraising the effectiveness of national measles immunization programs, particularly measles eradication efforts. Such activities can delineate failures to achieve adequate levels of protection and define groups for which epidemic control programs should be instituted.

Although more than 20 million doses of measles virus vaccine had been administered in the United States by early 1967, continuous and careful review of adverse reactions is still important. All serious reactions should be carefully evaluated and reported in detail to local and State health officials so that collaborative national surveillance can be effective.

Immunization Schedules
Recommended immunization schedules are shown in the table below:

IMMUNIZATION SCHEDULES FOR MEASLES VACCINES

Type of Vaccine	Age	Doses & Administration*
Live attenuated measles virus vaccine (Edmonston Strain)	12** months and older	1
Live attenuated measles virus vaccine (Edmonston Strain) plus Measles Immune Globulin	12** months and older	1 Plus Measles Immune Globulin (0.01 ml per lb. at different site with different syringe)
Live "further attenuated" measles virus vaccine (Schwarz Strain)	12** months and older	1

*Manufacturers' directions regarding administration should be followed.

**May be given to infants between 9 months and 1 year with the expectation of slightly decreased efficacy especially if administered simultaneously with Measles Immune Globulin.

RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

The Public Health Service Advisory Committee on Immunization Practices meeting on May 26, 1967, issued the following recommendation on poliomyelitis vaccines, a revision of the initial recommendation which was released as a supplement to the Poliomyelitis Surveillance Unit Report #285, September 1964. (Reprinted from MMWR, Vol. 16, No. 33, Week Ending August 19, 1967.)

POLIOMYELITIS VACCINES

Introduction

Widespread use of poliovirus vaccines has resulted in the virtual elimination of paralytic poliomyelitis in the United States. To insure continued freedom from the disease, it is necessary to pursue regular immunization of all children from early infancy.

Following the introduction of poliovirus vaccine in 1955, paralytic poliomyelitis declined from 18,308 cases in 1954 to a low of 61 cases in 1965. A national survey in September 1966, showed that 70 percent of all children 1-4 years of age had received at least three doses of oral poliovirus vaccine (OPV)*, inactivated poliovirus vaccine (IPV)**, or both. Approximately 90 percent of all children 5 years old and older had been adequately vaccinated.

Nevertheless, low immunization rates can still be found in some population groups, both urban and rural. In 1966, 108 cases of paralytic poliomyelitis were reported in the United States and Puerto Rico, reversing the downward national trend. The majority of the 1966 cases occurred in unimmunized children less than 5 years of age in south Texas. These cases illustrate the possibility of outbreaks where incomplete immunization exists.

With widespread use of poliovirus vaccine, laboratory surveillance of enteroviruses indicates that circulation of wild polioviruses has diminished markedly. It can be assumed that inapparent infections with wild strains will no longer contribute significantly to maintaining immunity in the general population. Therefore, it is essential not only to continue active immunization programs for infants and children but also to make special efforts to raise the low immunization rates existing in certain segments of the population. Identification of population groups requiring special immunization programs should be undertaken through surveys, both of immunization history and serologic status.

Poliovirus Vaccines

From the introduction of IPV in 1955 until the live attenuated vaccines became widely used in 1962, more than 400 million doses of IPV were distributed in the United States. Primary immunization with IPV plus regular booster doses provided a high degree of protection against paralytic disease.

Monovalent OPV types 1, 2, and 3 have been widely used in the United States since 1961-62. Trivalent OPV was introduced in 1963.

OPV is more widely used than IPV in this country because it is easier to administer and produces an immune response which, without regular booster doses, appears to be similar to immunity induced by natural poliovirus infection. Trivalent OPV has largely replaced the monovalent forms because of simplicity of scheduling and record-keeping.

A primary series of trivalent OPV, consisting of three adequately spaced doses, will produce an immune response to all poliovirus types in well over 90 percent of the recipients. Using the immunization schedule recommended in this report, possible interference with immunity produced by wild enteroviruses is minimized. Immunization may, therefore, begin in any season.

For community protection during an epidemic, it is better to immunize against the prevalent poliovirus type. For this purpose, type-specific monovalent OPV is preferable to trivalent OPV.

Very rarely, cases of paralytic poliomyelitis have occurred in recipients of OPV or their close contacts within 30 days of vaccine feeding. Careful analysis indicates a ratio of no more than one case of "vaccine-associated" paralytic disease for every three million doses of OPV administered.

Vaccine Usage

Oral Poliovirus Vaccine (OPV)

Primary Immunization

Trivalent OPV

Infants: The three-dose immunization series should be started at 6 to 12 weeks of age, simultaneously with the first DTP inoculation. The second dose should be given no less than 6 and preferably 8 weeks later. The third dose is an integral part of primary immunization and should be administered 8 to 12 months after the second dose.

Children and Adolescents: In children and adolescents through the level of high school, the primary series should consist of three doses, the first two doses given 6 to 8 weeks apart, and the third, 8 to 12 months after the second. If circumstances do not allow for the optimal interval between the second and third doses, the third may be given as early as 6 weeks after the second.

Adults: Routine poliomyelitis immunization for adults residing in the continental United States is not currently necessary because of the extreme unlikelihood of exposure. However, any unimmunized adult who may be at

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increased risk by virtue of contact with a known case or travel to epidemic or endemic areas should receive trivalent OPV according to the schedule outlined for children and adolescents. Persons employed in hospitals, medical laboratories, and sanitation facilities might also be considered as having an increased risk, especially if poliomyelitis is occurring in the area.

Pregnancy of itself is not an indication for vaccine administration, nor is it a contraindication when immunization is required.

Monovalent OPV

An alternative immunization procedure for infants, children, and adolescents is to give the separate monovalent OPV types at intervals of 6 to 8 weeks. The recommended sequence of types is 2, 1, 3. A fourth OPV dose, but of trivalent vaccine, should be given 8 to 12 months after the third dose of monovalent OPV. The special role of monovalent OPV in epidemic control is discussed below.

Follow-up Doses
School Entrance

On entering elementary school, all children who have completed the primary OPV series should be given a single follow-up dose of trivalent OPV. All others should complete the primary series.

Routine "Boosters"

On the basis of current information, there is no indication for regular or routine "booster" doses of OPV.

Increased Risk

A single dose of trivalent OPV may be administered to anyone who has completed the full primary series described above and has an increased risk of exposure by virtue of contact with a known outbreak, travel to epidemic or endemic areas, or occupation. However, the need for such an additional dose has not been established. If there is uncertainty about the adequacy of previous immunization, a single dose of trivalent OPV should be given.

Inactivated Poliovirus Vaccine (IPV)
Primary Immunization

All Ages: Four parenteral doses should be given, three at approximately monthly intervals and the fourth, a reinforcing dose, 6 to 12 months after the third. This schedule may be integrated with DTP immunization beginning at 6 to 12 weeks of age.

Booster Immunization

Single booster doses every 2 to 3 years have been recommended to insure adequate levels of antibody. The need for IPV boosters could be obviated by a full course of OPV. For individuals at particular risk as described previously, at least one dose of trivalent OPV, and preferably a full primary series, is recommended.

Epidemic Control*

For operational purposes in the United States, an "epidemic" of poliomyelitis is now defined as two or more cases caused by the same type virus during a 4-week period in a circumscribed population such as that of a city, county, or metropolitan area. An epidemic of poliomyelitis can be controlled by an emergency monovalent OPV immunization program. As soon as possible, the type of poliovirus responsible should be determined and the epidemic area defined. Within the epidemic area, all persons over 6 weeks of age who are not completely immunized or whose immunization status is uncertain should promptly receive one dose of type-specific monovalent OPV.

Simultaneous Administration of Live Virus Vaccines

Data on simultaneous administration of live virus vaccines are not sufficient to develop comprehensive recommendations, but there are obvious practical advantages to combining vaccines, and investigations are underway which should help to define optimal practices. When combined administration is indicated, available data do not suggest that undesirable responses will result. The following comment presents current attitudes toward scheduling vaccination with three major live virus vaccines – polio, measles, and smallpox.

It has been generally recommended that immunizations with live virus vaccines be separated by at least one month whenever possible. The rationale for this recommendation is the theory that superimposed reactions and diminished antibody responses might result if two or more live virus vaccines were given simultaneously. Ideally, the initial doses of oral poliovirus vaccine should have been given before a child reaches one year, the age for giving live attenuated measles virus vaccine. Administration of polio and measles antigens should be separated by at least one month. It is likewise desirable to separate measles and smallpox vaccinations by one or more months because both of these antigens may produce febrile reactions.

When, however, immunization program effectiveness is hindered or when the threat of concurrent exposures exists, the relevant live virus vaccines should be given at the same time. Observations do not indicate that this will cause a significant increase in adverse reactions or depressed antibody responses to either antigen.

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*For epidemic control, monovalent OPV types 1 and 3 are available from the National Communicable Disease Center on request of the State Health Department.

RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

The Public Health Service Advisory Committee on Immunization Practices meeting on February 17, 1967, issued the following recommendations on rabies prophylaxis for the United States. (Reprinted from the MMWR, Vol. 16, No. 19, week ending May 13, 1967.)

RABIES PROPHYLAXIS

Introduction

Although cases of rabies in humans are rare in the United States, thousands of persons receive rabies prophylaxis each year. The following approach to prevention is based on a contemporary interpretation of both the risk of infection and the efficacy of treatment and incorporates the basic concepts of the WHO Expert Committee on Rabies [1].

The problem of whether or not to immunize those bitten or scratched by animals suspected of being rabid is a perplexing one for physicians. All available methods of systemic treatment are complicated by numerous instances of adverse reactions, a few of which have resulted in death or permanent disability. Furthermore, the decision must be made immediately because the likelihood that any prophylactic measure will contribute to the prevention of rabies diminishes rapidly as the interval between exposure and treatment increases.

The acceptable evidence for efficacy of both active and passive immunization following exposure is derived largely from experimental studies in animals. Because rabies on occasion has developed in humans who received antirabies prophylaxis, the value of treatment has been questioned. However, evidence from laboratory and field experience in many areas of the world indicates post-exposure prophylaxis can be highly effective when appropriately used.

Status of Rabies in the United States

The incidence of rabies in humans has declined from an average of 22 cases per year in 1946 through 1950, to 1 case per year in 1963 through 1966. Rabies in domestic animals has diminished similarly. In 1946, there were more than 8,000 cases of rabies in dogs, compared with 412 in 1966. Thus, the likelihood of humans' being exposed to rabies by domestic animals has decreased greatly, although bites by dogs and cats continue to be responsible for the overwhelming majority of antirabies treatments.

In contrast, the disease in wildlife — especially skunks, foxes, and bats — has become increasingly prominent in recent years, accounting for more than 70 percent of all reported cases of animal rabies in 1966. During that year, only four States were reportedly free of wildlife rabies. Wild animals constitute the most important source of infection for both domestic animals and man in the United States today.

Status of Antirabies Treatment in the United States

More than 30,000 people receive post-exposure anti-rabies treatment each year. However, there is no information regarding the number of persons actually exposed to rabid animals.

Nervous tissue origin rabies vaccine of the Semple type (NTV) was used almost exclusively in the United States until 1957, when the duck embryo origin vaccine (DEV) was licensed. More than 75 percent of those who received rabies prophylaxis in the United States in 1965 were given DEV.

There has been remarkable variation in the rate of adverse reactions associated with NTV. In the United States, it is generally accepted that one individual among 4,000 to 8,000 persons receiving NTV antirabies treatment develops neurologic complications. Death has been attributed to NTV in a ratio of one to every 35,000 persons treated.

Neurologic complications associated with DEV have been reported for one of every 25,000 persons treated. One possibly related death has occurred among some 172,000 who have received DEV since its introduction.

Rationale of Treatment

Every exposure to possible rabies infection must be individually evaluated. In the United States, the following factors should be considered before specific antirabies treatment is initiated:

Species of biting animal involved

Carnivorous animals (especially skunks, foxes, coyotes, raccoons, dogs, and cats) and bats are more likely to be infective than other animals. Bites of rodents seldom, if ever, require specific antirabies prophylaxis.

Circumstances of the biting incident

An *unprovoked* attack is more likely to mean that the animal is rabid. (Bites during attempts to feed or handle an apparently healthy animal should generally be regarded as *provoked*).

Extent and location of bite wound

The likelihood that rabies will result from a bite varies with its extent and location. For convenience in approaching management, two categories of exposure are widely accepted:

Severe: Multiple or deep puncture wounds, and any bites on the head, face, neck, hands, or fingers.
Mild: Scratches, lacerations, or single bites on areas of the body other than the head, face, neck, hands, or fingers. Open wounds, such as abrasions, which are suspected of being contaminated with saliva also belong in this category.

Vaccination status of the biting animal

An adult animal immunized properly with one or more doses of rabies vaccine has only a minimal chance of developing rabies and transmitting the virus.

Presence of rabies in the region

If adequate laboratory and field records indicate that there is no rabies infection in a domestic species within a given region, local health officials may be justified in taking this into consideration in any recommendations concerning antirabies treatment following a bite by that species.

Management of Biting Animals

A dog or cat that bites a human should be captured, confined, and observed by a veterinarian for at least 5 days, preferably 7 to 10. Any illness in the animal should be reported immediately to the local health department. If the animal dies, the head should be removed and shipped under refrigeration to a qualified laboratory for examination. Because clinical signs of rabies in a wild animal cannot be reliably interpreted, the animal should be killed at once and its brain examined for evidence of rabies.

Local Treatment of Wounds

Immediate and thorough local treatment of all bite wounds and scratches is perhaps the most effective means of preventing rabies. Experimentally, the incidence of rabies in animals can be markedly reduced by local therapy alone.

First-aid treatment to be carried out immediately
Copious flushing with water alone, soap and water, or detergent and water.

Treatment by or under direction of a physician

1. Thorough flushing and cleansing of the wound with soap solution. Quaternary ammonium compounds may also be used.*
2. If antirabies serum is indicated, a portion of the total dose should be thoroughly infiltrated around the wound. As in all instances in which horse serum is used, a careful history should be taken and tests for hypersensitivity performed[2].

3. Tetanus prophylaxis[2] and measures to control bacterial infections as indicated.
4. Suturing of wound or other form of primary closure is *not* advised.

Post-exposure Prophylaxis

Active Immunization

Rabies Vaccine Preparations

Duck Embryo Vaccine (DEV)
Prepared from embryonated duck eggs infected with a fixed virus and inactivated with beta-propiolactone.

Nervous Tissue Vaccine (NTV)
Prepared from rabbit brain infected with a fixed virus and inactivated by phenol at 37°C. (Semple type) or inactivated by ultraviolet irradiation.

Antigenicity of Vaccines

Antigenicity of NTV is often higher than that of DEV when tested in experimental animals. However, all lots of both vaccines must pass minimum potency tests established by the Division of Biologics Standards, National Institutes of Health. There is evidence that the serum antibody response in humans is detectable earlier following DEV vaccination, but the eventual level of response is frequently higher with NTV.

Effectiveness of Vaccines in Humans

In the United States, comparative effectiveness of vaccines can only be judged by frequencies of failure to prevent disease. During the years 1957 through 1967 when both vaccines were available, there were 6 rabies deaths among the 117,700 NTV-treated persons (1:19,600) and 7 deaths among the 172,000 treated with DEV (1:24,500).

Reactions

Erythema, pruritis, pain, and tenderness at the site of inoculation are common with both DEV and NTV. Systemic responses, including low grade fever, or rarely shock, may occasionally occur late in the course of therapy with either vaccine, usually after five to eight doses. In rare instances, serious reactions have occurred after the first dose of DEV or NTV, particularly in persons previously sensitized with vaccines containing avian or rabbit brain tissue.

As described previously, neuroparalytic reactions occur rarely with DEV. They are considerably more frequent following NTV, especially after repeated courses of treatment with this preparation.

Choice of Vaccine

Rates of treatment failures with the two vaccines are not significantly different; therefore, the

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*All traces of soap should be removed before quaternary ammonium compounds are applied because soap neutralizes their activity.

lower frequency of central nervous system re-action with DEV makes it preferable to NTV.

Schedule for Vaccine Use

Primary Course

At least 14 single, daily injections of vaccine in the dose recommended by the manufacturer. These should be given subcutaneously in the abdomen, lower back, or lateral aspect of thighs; rotation of sites is recommended.

For severe exposures, 21 doses of vaccine are recommended. These may be given as 21 daily injections or 14 doses during the first 7 days (either two separate injections or a double dose), the remaining doses given singly during the next 7 days.

Booster Immunization

Two booster doses, one 10 days and the other at least 20 days after completion of the primary course. The two booster doses are particularly important if antirabies serum was used in the initial therapy.

Precautions

When rabies vaccine must be given to a person with a history of hypersensitivity, especially to avian or rabbit tissues, antihistaminic drugs should be used. Epinephrine is helpful in reactions of the anaphylactoid type. If serious allergic manifestations preclude continuation of prophylaxis with one vaccine, the other may be used.

When meningeal or neuroparalytic reactions develop, vaccine treatment should be discontinued altogether. Corticotrophin or corticosteroids are used for such complications.

Passive Immunization

Hyperimmune serum has proved effective in preventing rabies. Its use in combination with vaccine is considered the best post-exposure prophylaxis. However, the only preparation of antirabies serum now available in the United States is of equine origin. Because horse serum induces allergic reaction in at least 20 percent of those receiving it, its use must be limited.

Hyperimmune serum is recommended for most exposures classified as severe, and for *all* bites by rabid animals, wild carnivores, and bats. When indicated, antirabies serum should be used regardless of the interval between exposure and treatment.

The dose recommended is 1000 units (one vial) per 40 pounds of body weight. A portion of the antiserum is used to infiltrate the wound, and the remainder administered intramuscularly. As previously noted, a careful history must be obtained and appropriate tests for hypersensitivity performed.*

Pre-exposure Prophylaxis

The relatively low frequency of reactions to DEV has made it more practical to offer pre-exposure immunization to persons in high-risk groups: veterinarians, animal handlers, certain laboratory workers, and personnel stationed in areas of the world where rabies is a constant threat. Others whose vocational or avocational pursuits result in frequent exposures to dogs, cats, foxes, skunks, or bats should also be considered for pre-exposure prophylaxis.

Two 1.0 ml injections of DEV given subcutaneously in the deltoid area 1 month apart should be followed by a third dose 6 to 7 months after the second dose. This series of three injections can be expected to produce neutralizing antibody in 80 to 90 percent of vaccinees 1 month after the third dose.

If more rapid immunization is desirable, three 1.0 ml injections of DEV may be given at weekly intervals with a fourth dose 3 months later. This schedule elicits an antibody response in about 80 percent of the vaccinees.

All those receiving the pre-exposure vaccination should have their serum tested for neutralizing antibody 3 to 4 weeks after the last injection. Tests for rabies antibody can be arranged with or through state health department laboratories. If no antibody is detectable, booster doses should be given until a response is demonstrated. Persons with continuing exposure should receive 1.0 ml boosters every 2 to 3 years.

When an immunized individual with previously demonstrated antibody is exposed to rabies, it is suggested that for a mild exposure, one booster dose of vaccine be given, and for a severe exposure, five daily doses of vaccine plus a booster dose 20 days later. If it is not known whether an exposed person had antibody, the complete post-exposure antirabies treatment should be given.

References

[1] Technical Report Series No. 321, WHO Expert Committee on Rabies, Fifth Report, 1966.

[2] Recommendation of the Public Health Service Advisory Committee on Immunization Practices: Diphtheria, Tetanus, and Pertussis Vaccines — Tetanus Prophylaxis in Wound Management, *Morbidity and Mortality Weekly Report,* Vol. 15, No. 48, week ending December 3, 1966.

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*A guide for use of animal serum is included in the recommendation for tetanus prophylaxis in wound management prepared by the PHS Advisory Committee on Immunization Practices [2].

CHECKLIST OF TREATMENTS FOR ANIMAL BITES
(See Text for Details)

1. Flush Wound Immediately (First Aid).

2. Thorough Wound Cleansing Under Medical Supervision.

3. Antirabies Serum and/or Vaccine as Indicated.

4. Tetanus Prophylaxis and Antibacterial Treatment when Required.

5. No Sutures or Wound Closure Advised.

GUIDE FOR POST-EXPOSURE ANTIRABIES PROPHYLAXIS

The following recommendations are intended only as a guide. They may be modified according to knowledge of the species of biting animal and circumstances surrounding the biting incident.

Biting Animal		Treatment		
		Exposure		
Species	Status at Time of Attack	No Lesion	Mild*	Severe*
Dog or Cat	healthy	none	none[1]	S[1]
	signs suggestive of rabies	none	V[2]	S+V[2]
	escaped or unknown	none	V	S+V
	rabid	none	S+V	S+V
Skunk, Fox, Raccoon, Coyote, Bat	regard as rabid in unprovoked attack	none	S+V	S+V
Other	consider individually — see Rationale of Treatment in text			

Code: * = See definitions in text.
V = Rabies Vaccine
S = Antirabies Serum
1 = Begin vaccine at first sign of rabies in biting dog or cat during holding period (preferably 7-10 days).
2 = Discontinue vaccine if biting dog or cat is healthy 5 days after exposure, or if acceptable laboratory negativity has been demonstrated in animal killed at time of attack. If observed animal dies after 5 days and brain is positive, resume treatment.

RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY
COMMITTEE ON IMMUNIZATION PRACTICES

The Public Health Service Advisory Committee on Immunization Practices meeting on October 11, 1966, issued the following recommendations on smallpox vaccination practices in the United States. (Reprinted from MMWR, Vol. 15, No. 47, week ending November 26, 1966.)

SMALLPOX VACCINE

Introduction

In the United States, protection of the community against smallpox through routine vaccination of infants and revaccination of older children and adults represents the principal mechanism of defense against the indigenous spread of the disease once introduced. This approach to community protection, as with all practices in preventive medicine, demands continuing reassessment of the potential risk of the disease in comparison to the efficacy and risk associated with preventive procedures.

The Risk of Introduced Smallpox

The risk of introduction and subsequent transmission of smallpox in the United States is difficult to appraise. Although no recognized cases of smallpox have occurred in the United States since 1949, a sizable reservoir of endemic smallpox persists in Asia, Africa and South America. In 1965, over 63,000 cases were reported to the World Health Organization; undoubtedly, many times this number of cases occurred but were not recorded. A substantial proportion of smallpox cases are known to have occurred in urban centers.

Travel both by United States citizens and other nationals to and from smallpox endemic areas and this country is increasing annually. As seen recently in Europe, quarantine measures offer, at best, only partial protection against the introduction of smallpox. The traveler who has been vaccinated improperly or vaccinated with impotent vaccine or who bears a spurious vaccination certificate, is fully capable of developing the disease after passing quarantine inspection. Such, in fact, did occur in the United States as recently as 1962: A Canadian boy in apparently good health entered the United States through New York City from Brazil with a seemingly valid vaccination certificate. He developed smallpox after arriving in Canada less than 24 hours later.

In 75 instances during the past 18 years in which smallpox has been introduced into non-endemic areas, nationals of the country involved have been responsible for over three-fourths of the introductions. Should smallpox be introduced into the United States, it is similarly most probable that a United States citizen returning from abroad would serve to introduce the disease.

Smallpox, particularly variola major, remains a highly virulent disease even with excellent medical care. The mortality rate among unvaccinated persons was 40 percent in Sweden and in England during the outbreaks of 1962-63. Since few physicians in practice today are acquainted with clinical smallpox, it is not surprising that in several recent European outbreaks the disease remained unrecognized until the third generation of cases, or even later. During a 1966 outbreak in England, the diagnosis of smallpox was not made until the fourth cycle of transmission and 23 cases had already occurred, more than 10 weeks after the first identifiable case. Should the disease be introduced into the United States, a similar course of events could occur.

Smallpox Vaccination — Efficacy and Risks

The efficacy of smallpox vaccine has never been precisely measured in controlled trials. It is, however, generally agreed that vaccination with fully potent vaccine confers a high level of protection for at least three years and provides substantial but waning immunity for 10 years or more. Protection against a fatal outcome of the disease appears to extend over a longer period, perhaps for decades.

Smallpox vaccination, as with other medical procedures, is associated with a definite, measurable risk of morbidity and, rarely, death. A comprehensive national survey to ascertain the frequency of complications associated with vaccination in the United States during 1963 has recently been completed.[1] Among more than 6,000,000 primary vaccinees and nearly 8,000,000 revaccinees and their contacts, 12 cases of encephalitis following vaccination, 9 cases of vaccinia necrosum, and 108 cases of eczema vaccinatum occurred. Seven persons died. A substantial number of less serious complications, some of which resulted in hospitalization, were also recorded. All deaths and virtually all complications occurred among those vaccinated for the first time.

Furthermore, from these same data, it appeared that over half of the complications could have been prevented had contraindications to vaccination been more closely observed. Additionally, it was noted that complication rates were at least twice as high among children under one year of age as among other children.

If the routine practice of vaccinating infants and young children were to be terminated, consideration would need to be given to the consequence of the later primary vaccination of a large number of adults requiring protection by virtue of military service, travel abroad, or employment in medical or allied health professions. (Over half of all cases occurring following introduction of smallpox to non-endemic areas have been transmitted in the hospital setting.) It is estimated that these three

categories would involve between one and two million primary vaccinations annually.

Available data suggest that if primary vaccination were delayed until adulthood and administered to individuals faced with potential smallpox exposure, the number and seriousness of complications occurring each year would, in fact, be considerably greater than at present.

Other Prophylactic Agents

In recent years, Vaccinia Immune Globulin and certain antiviral compounds have been tested and reported by some to be effective in conferring protection against smallpox when administered shortly after exposure to the disease. At present, however, none appears to be a satisfactory alternative to vaccination. And most important, none confers protection lasting more than a few weeks. Thus, unless the first introduced case can be promptly and correctly diagnosed and all contacts quickly identified and treated, interruption of subsequent transmission of the disease by using these materials is virtually impossible. As previously pointed out, prompt diagnosis of the first introduced case has been the exception rather than the rule in recent European outbreaks.

Of added practical importance are the association of considerable gastrointestinal toxicity with the antiviral compounds and the critically short supply of Vaccinia Immune Globulin. In brief, therefore, none of these prophylactic agents is suitable for mass use at the time of a real or potential outbreak.

Conclusions and Recommendations

In recent years, international travel has increased substantially while the reservoir of endemic smallpox has changed but little. Correspondingly, the potential for the introduction of smallpox into the United States has, if anything, increased.

The 1966 World Health Assembly agreed to embark upon an intensive 10-year smallpox program. Based upon the effectiveness of vaccination campaigns in many of the developing countries, there is every reason to anticipate the success of this program. Eradication of endemic smallpox represents the most direct attack upon the problem and the only sure means for protecting the United States.

Until eradication is achieved or, at least, nears realization, vaccination, although not wholly without risk, clearly represents the only currently practicable approach for community protection in the United States. Considering the comparative risks of smallpox to the United States contrasted with the risks of vaccination, it is therefore important, at this time, to continue the present practice of widespread, routine smallpox vaccination in early childhood with subsequent revaccination.

Recommendations for Smallpox Vaccination

The following smallpox vaccination practices are recommended for the United States: (See Footnote*)

*1. Time of Vaccination

Primary Vaccination

a. During the second year of life (i.e., between 1st. and 2nd. birthdays).

b. At any age under conditions of exposure or foreign travel.

Revaccination

a. At time of entry into elementary school.

b. At three-year intervals for:

1) Persons who conceivably might be exposed in endemic or potentially endemic areas by virtue of international travel.

2) Persons likely to be exposed by newly introduced infection into the United States, particularly:

a) Hospital personnel, including physicians, nurses, attendants, laboratory and laundry workers.

b) Other medical, public health, and allied professions.

c) Morticians and other mortuary workers.

c. At approximately 10-year intervals for all others.

2. Site of Vaccination

On the skin over the insertion of the deltoid muscle or on the posterior aspect of the arm over the triceps muscle.

3. Methods of Vaccination

Multiple Pressure Method[2]

A small drop of vaccine is placed on the *dry*, cleansed skin and a series of pressures is made within an area about 1/8" in diameter with the side of a sharp, sterile needle held tangentially to the skin. The pressures are made with the side of the needle. For primary vaccination, 10 pressures are adequate; for revaccination, 30 pressures should be made. The remaining vaccine should be wiped off with dry, sterile gauze. Preferably, no dressing should be applied to the site.

Other Vaccination Techniques

Vaccination may be performed with other devices shown to be equally effective in assuring takes.

Jet Injection Method

Using vaccine specifically manufactured for this purpose, the recommended dose is inoculated intradermally with a jet injection apparatus. Excess vaccine should be wiped off with dry, sterile gauze. Preferably, no dressing should be applied to the site.

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*All persons, regardless of age, entering the United States from *non-exempt areas are required to be vaccinated or revaccinated within three years unless vaccination is medically contraindicated. The International Sanitary Regulations provide that "If a vaccinator is of the opinion that vaccination is contraindicated on medical grounds, he should provide the persons with written reasons underlying that opinion, which health authorities may take into account."[3]

4. Interpretation of Responses*

The vaccination site should be inspected 6 to 8 days after vaccination. The response should be interpreted as follows:.

Primary Vaccination

A primary vaccination which is successful should show a typical Jennerian vesicle. If none is observed, vaccination procedures should be checked and vaccination repeated with another lot of vaccine until a successful result is obtained.

Revaccination

Following revaccination, two responses are defined by the WHO Expert Committee on Smallpox eliminating use of older terms such as "accelerated" and "immune":[2]

a. "Major reaction"

A vesicular or pustular lesion or an area of definite palpable induration or congestion surrounding a central lesion which may be a crust or ulcer. This reaction indicates that virus multiplication has most likely taken place and that the revaccination is successful.

b. "Equivocal reaction"

Any other reaction should be regarded as equivocal. These responses may be the consequence of immunity adequate to suppress virus multiplication or may represent only allergic reactions to an inactive vaccine. If an equivocal reaction is observed, revaccination procedures should be checked and revaccination repeated with another lot of vaccine.

5. Types of Vaccine

Smallpox vaccine is presently available both in the glycerinated and the lyophilized form. Both forms, when properly preserved, afford excellent protection. The glycerinated form requires constant refrigeration at all stages in its transport and storage at temperatures recommended by the manufacturer. Comparatively minor storage difficulties may reduce its potency sufficiently to decrease efficacy in vaccination and particularly in revaccination. Even in excellent medical facilities, the glycerinated vaccine is often stored under improper conditions. Use of the much more stable lyophilized vaccine would insure more consistently effective vaccination. Due care must be exercised to provide proper handling of the lyophilized vaccine after reconstitution as described by the manufacturer.

6. Contraindications to Vaccination

a. Eczema and other forms of chronic dermatitis in the individual to be vaccinated or in a household contact. If vaccination is required for an individual with dermatitis because of potential exposure in an endemic area. Vaccinia Immune Globulin should be administered to the affected individual at the same time as the vaccine. If there is real need to vaccinate an individual who may create a hazard for a household contact with dermatitis, consideration should be given to separation of the vaccinee and his contact until a crust has developed.

b. Pregnancy. Vaccinia virus may, on occasion, cross the placental barrier during any stage of pregnancy and infect the fetus. Virtually all cases of fetal vaccinia have followed primary vaccination. If vaccination is indicated because of potential exposure in an endemic area, Vaccinia Immune Globulin should generally be given simultaneously with the vaccine, particularly if she is undergoing primary vaccination.

c. Patients with leukemia, lymphoma, and other reticuloendothelial malignancies or dysgamma globulinemia or those under therapy with immunosuppressive drugs such as steroid and antimetabolites or receiving ionizing radiation. If exposure should, by chance, occur, or if vaccination is absolutely essential, Vaccinia Immune Globulin should be administered.

7. Vaccinia Immune Globulin (VIG) (See Appendix)

a. Prophylaxis — 0.3 ml./kg. by the intramuscular route.

b. Treatment — 0.6 ml/.kg. by the intramuscular route:

1) In eczema vaccinatum, vaccinia necrosum or auto-inoculation vaccinia of the eye, VIG may be effective.

2) For severe cases of generalized vaccinia, VIG may be helpful in treatment. Such cases, however, almost invariably have a favorable outcome.

Note: For postvaccinal encephalitis, VIG is of no value.

8. Thiosemicarbazones

Certain of the thiosemicarbazone derivatives are reported by some to show a short-term protective effect against smallpox and possibly a therapeutic effect in individuals with severe vaccinal complications. These are experimental drugs and are not available for general use; their potential usefulness remains to be established.

REFERENCES

[1] Neff, John M., et al. Smallpox Vaccination Complications — United States — 1963. I. National Survey. II. Results Obtained by Four Statewide Surveys. To be published — New England Journal of Medicine.

[2] WHO Technical Report Series No. 283, WHO Expert Committee on Smallpox, 1964.

[3] International Sanitary Regulations, Article 98 (Footnote 9), World Health Organization, Geneva, 1966.

*For purposes of validating certificates for international travel, primary vaccinations must be inspected. Although desirable, inspection of revaccinations is not mandatory.

COMMITTEE OF AMERICAN RED CROSS VOLUNTEER
CONSULTANTS FOR THE DISTRIBUTION OF VACCINIA IMMUNE GLOBULIN

VIG may be obtained within a few hours from any of the listed Regional
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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

The Public Health Service Advisory Committee on Immunization Practices meeting on February 18, 1966, issued the following recommendation dealing with the current status of methodology in the prevention of transfusion-associated hepatitis. (Reprinted from MMWR, Vol. 15, No. 16, week ending April 23, 1966.)

TRANSFUSION-ASSOCIATED HEPATITIS

The risk of viral hepatitis following blood transfusion represents a serious and continuing problem. A number of reports indicate that the incidence of clinical hepatitis is greater among recipients of blood obtained from certain categories of donors. The risk also becomes greater as the number of transfusions increases. In addition, the case-fatality rate of transfusion-associated hepatitis increases with advancing age.

Evidence has been advanced both for and against the effectiveness of immune globulin in the prophylaxis of transfusion-associated hepatitis. Although the administration of immune globulin in a dose of 10 ml at the time of the transfusion and again one month later has been reported by some investigators to be effective in reducing the number of cases, evidence of the efficacy of this procedure is lacking in other carefully conducted trials. In view of these uncertainties, existing data do not provide a basis for allocating supplies of immune globulin for its routine administration to recipients of blood transfusions.

Several methods for lowering the incidence of transfusion-associated hepatitis are available. More attention should be directed toward enforcement of adequate standards of donor quality, development of central registries for the identification of known or suspect carriers, and encouraging the practice of using blood and potentially icterogenic blood products only when necessary.

RECOMMENDATIONS OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

The Public Health Service Advisory Committee on Immunization Practices meeting on May 16, 1966, issued the following recommendations on typhoid and paratyphoid A and B vaccines. (Reprinted from MMWR, Vol. 15, No. 29, July 23, 1966)

TYPHOID VACCINE

The incidence of typhoid fever in the United States has declined steadily for many years. At the present time, less than 500 cases are reported annually, and a continuing downward trend can be expected. Cases are sporadic and are primarily related to contact with carriers rather than to common source exposure. Recognizing this epidemiologic pattern of typhoid fever, re-definition of the role and use of typhoid vaccine is indicated.

Current Status of Typhoid Vaccine

Although typhoid vaccines have been employed for many decades, definitive evidence of their effectiveness has been accumulated only recently from well controlled field investigations. Several different preparations of typhoid vaccine have been shown to afford protection in approximately 70 to 90 percent of individuals immunized, depending in part on the degree of their subsequent exposure[1].

Recommendations for Vaccine Use

Routine typhoid immunization is not recommended in the United States. Selective immunization is, however, indicated in the following situations:

1) Intimate exposure to a known typhoid carrier as would occur with continued household contact.
2) Community or institutional outbreaks of typhoid fever.
3) Foreign travel to areas where typhoid fever is endemic.

Although typhoid vaccine has been suggested for individuals attending summer camps and those in areas where flooding has occurred, there are no data to support the continuation of these practices.

Reference:

[1]Cvjetanovic, B. and Uemura, K., The present status of field and laboratory studies of typhoid and paratyphoid vaccine. Bull WHO *32*:29-36, 1965.

Dosage and Schedule

On the basis of the field trials referred to above, the following dosages are recommended, employing the vaccines available in the USA:

Primary Immunization

Adults and children over 10 years

0.5 ml. subcutaneously on two occasions, separated by four or more weeks

Children 6 months to 10 years*

0.25 ml. subcutaneously on two occasions, separated by four or more weeks

In instances where there is insufficient time for the two doses to be administered at the time intervals specified, three doses of the same volume listed above may be given at weekly intervals.

Booster Immunization

Under conditions of continued or repeated exposure, a booster dose should be given at least every three years. Even if an interval greater than three years has elapsed since the prior immunization, a single booster injection should be sufficient.

The following alternative routes and dosages of booster immunization can be expected to give comparable antibody responses; generally less reaction follows the intradermal route.

Adults and Children over 10 years

0.5 ml. subcutaneously or 0.1 ml. intradermally

Children 6 months to 10 years*

0.25 ml. subcutaneously or 0.1 ml. intradermally

*Since febrile reaction in this age group are common following typhoid vaccination, an antipyretic may be indicated.

PARATYPHOID A AND B VACCINES

The effectiveness of paratyphoid A vaccine has never been established, and recent field trials have shown that available paratyphoid B vaccines were ineffective. In view of these data and recognizing that the paratyphoid A and B antigens when combined with typhoid vaccine may increase the occurrence of vaccine reactions, use of paratyphoid A and B vaccines is not recommended.