NCDC

immunization
against infectious disease
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Acknowledgments and Sources of Data

Immunization Against Infectious Disease represents a collaborative effort of various investigators in several Programs and Branches of the National Communicable Disease Center, selected by the editor because of their familiarity with specific diseases. It was originally developed in the Office of the Center Director, based on data collected by the Epidemiology, Smallpox Eradication, Foreign Quarantine, and Ecological Investigations Programs, the Laboratory Division, and the Immunization and Tuberculosis Branches of the State and Community Services Division. Credit is due the staff of Statistical Services Activity of Epidemiology Program for efforts to ensure completeness and accuracy of data. Special credit is due Miss Frances Porcher, chief of Epidemiology Program's editorial-graphics staff, who acted as the managing editor. The diligence of all participants is gratefully acknowledged.

Data in *Immunization Against Infectious 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 insights on trends and patterns of communicable diseases and therefore merit attention.

Foreword

The Public Health Service Advisory Committee on Immunization Practices encouraged the National Communicable Disease Center to undertake the preparation and development of a handbook on Immunization Against Infectious 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 current objectives should be made generally available to the country's public health workers, students of medicine, and physicians in private practice and in academic medicine. And perhaps more importantly, they recommended placing under one cover pertinent material bearing on this subject from several sources.*

This summary covers the basic communicable diseases in which effective vaccines play an important role. In future editions, additional subjects may be covered to provide a more comprehensive background for sound preventive medical practice.

Readers are encouraged to submit comments and suggestions to the editor for improving this handbook, to make it as useful as possible to the professions that find this information helpful.

J. Lyle Conrad, M.D.
Editor

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 in dramatic control of several diseases in the United States.

There has not been one confirmed case of smallpox in this country in 20 years, poliomyelitis is under control, measles incidence is at its lowest point in history, and diphtheria and tetanus are on the wane. In the future, we can expect mumps, rubella, and other common infectious diseases to be controlled or eliminated as public health problems, through the use of vaccines currently available or 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 – "surveillance" – on their performance. The scope of 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, but prevalent elsewhere.

The commitment of a population protected by immunization against infectious 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 for the development of a meaningful immunization pattern.

This edition of *Immunization Against Infectious Disease* is a review of the status of infectious diseases important to the United States and 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 edition, primarily covering data summarized through the 1968 calendar year, is addressed to the students of public health and medicine; it assesses for them not only achievements in control but also their obligations toward maintaining alertness to present and future needs.

The contents of this summary are divided into three major sections: The first deals with the status of major communicable diseases and the effects of vaccines on them. The second section contains summaries of the United States Immunization Survey, which is sponsored by the National Communicable Disease Center and carried out annually by the Bureau of the Census, and the 1968 Biologics Surveillance Summary, a collaborative effort of the major producers of biologics in the United States and the NCDC. The third section contains the Recommendations of the Public Health Service Advisory Committee on Immunization Practices (ACIP).

The first section contains for each disease a brief historical introduction and a current summary with various forms of graphic presentation of data. 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 professionals in public health and preventive medicine in this country.

CURRENT REVIEWS–

SELECTED INFECTIOUS DISEASES

DIPHTHERIA

Clinical diphtheria was first described by Bretonneau, 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.

Over the past 45 years there has been a marked decrease in the total number of cases of diphtheria per year in the United States (Figure 1). Since the early 1940's the decreasing incidence of diphtheria has been associated with general use of toxoid; however, the apparent decrease in rate began prior to mass immunizations with toxoid. The death rate from diphtheria has also decreased dramatically, but the percentage of cases causing death has not changed significantly (Table 1).

DIPHTHERIA IN 1967

In 1967, 219 cases of diphtheria were reported to the National Communicable Disease Center and surveillance information was submitted on 214 cases. The numbers of cases and incidence are presented by state in Figure 2. The highest rate was 1.50 cases per 100,000 population in Louisiana. Alabama and Texas had the next highest rates, 0.62 and 0.60 cases per 100,000 population, respectively. All other states had attack rates of 0.30 per 100,000 population or less, and 24 states had no cases. The incidence in the South was 10 times higher than in the North and West (see Figure 2 for states included in these regions). Seasonal variation was most evident in the South, with the highest prevalence in September, October, and November.

Diphtheria continues to be a disease of children, with 82 percent of the 1967 cases in children under 15 years of age and 61 percent in children under 10. The incidence for other races is about 10 times greater than for whites (0.57 and 0.06 cases per 100,000 population, respectively). In 1967, 55 percent of the cases occurred in persons of other races. Fifty-four percent were in females. Forty-eight percent of the cases were clinically mild, 28 percent moderate, 10 percent severe, and 14 percent fatal. No deaths were reported for persons who had had a complete primary immunization series.

In 1967 mitis type organisms accounted for 76 percent of the typed isolates and gravis type for 13 percent. However, gravis strains were more common in the West.

During the years 1959 through 1967 a total of 187 cases of diphtheria secondary to nontoxigenic *C. diphtheriae* were reported (Table 2). The disease associated with nontoxigenic strains appears to be milder than the disease caused by toxigenic organisms. Otherwise the upper respiratory syndromes are similar. Since nontoxigenic *C. diphtheriae* may play a significant role in the epidemiology of diphtheria, physicians should be aware that the organisms have been associated with a diphtheria-like disease. The role of other etiologic agents is not clear, and cases due to nontoxigenic organisms should also be evaluated for other bacterial as well as viral causative organisms.

FIGURE 1

DIPHTHERIA–REPORTED ANNUAL INCIDENCE AND MORTALITY RATES, AND CASE FATALITY RATIO UNITED STATES, 1920–1968

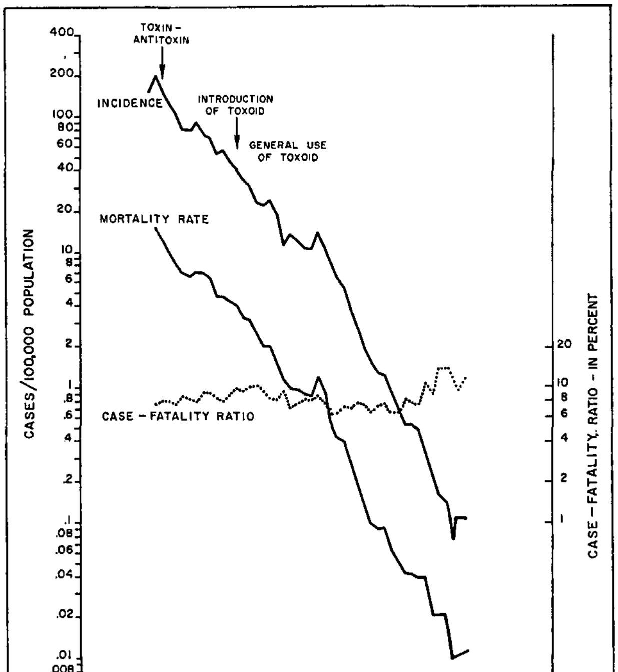


TABLE 1

DIPHTHERIA MORBIDITY AND MORTALITY IN THE UNITED STATES FOR SELECTED YEARS, 1933 - 1967

Year	Cases	Deaths	Rates per 100,000 Population* Incidence	Rates per 100,000 Population* Mortality	Case Fatality Ratio
1933**	50,462	4,937	40.1	3.9	9.8
1940	15,536	1,457	11.8	1.1	9.4
1950	5,796	410	3.8	.3	7.1
1960	918	69	.51	.04	7.5
1961	617	68	.34	.04	11.0
1962	444	41	.24	.02	9.2
1963	314	45	.17	.02	14.3
1964	293	42	.15	.02	14.3
1965	164	18	.08	.01	11.0
1966	209	20	.11	.01	9.6
1967	219	25	.11	.01	11.4

Sources of Data:
1. Cases – Annual Summaries, Notifiable Diseases, National Office of Vital Statistics (NOVS) and NCDC.
2. Deaths – 1933-1961 National Summaries, NOVS; 1962-1966 Vital Statistics of the United States, NCHS; 1967, Preliminary Data, based on surveillance reports to SPS, NCDC.

*Based on population data from the Bureau of Census Population Estimates; 1933 and 1940, Series P-25, No. 139; 1950, Series P-25, No. 165; 1960-1962, Series P-25, No. 259; 1963, Series P-25, No. 273; 1964-1966, Series P-25, No. 369; 1967, Series P-25, No. 380.

**The first year of complete registration, Puerto Rico not included in totals.

FIGURE 2

DIPHTHERIA–REPORTED CASES AND ATTACK RATES PER 100,000 POPULATION, BY STATE AND REGION, UNITED STATES, 1967

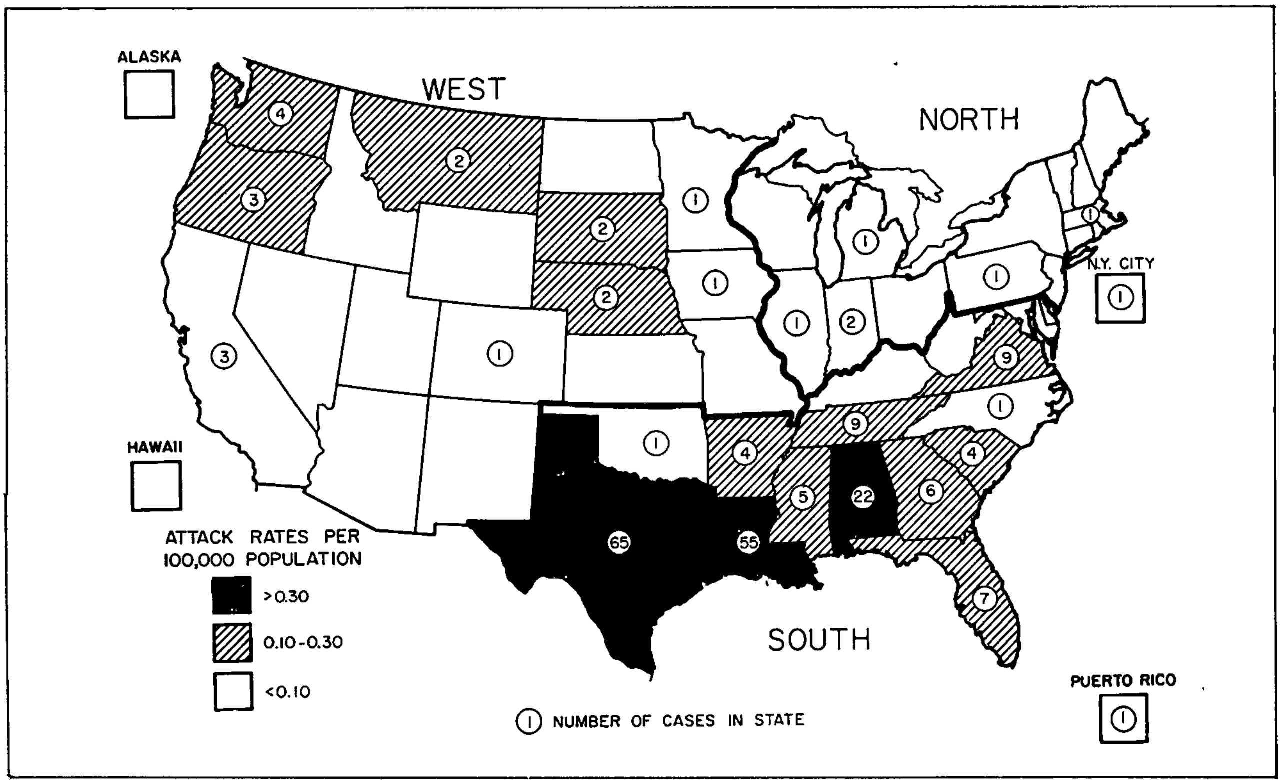


TABLE 2

DIPHTHERIA – CULTURE CONFIRMED CASES BY TYPE
OF *CORYNEBACTERIUM DIPHTHERIAE* AND TOXIGENICITY, USA, 1959-1967

Type	Toxigenic		Nontoxigenic		Total by Type	Percent Nontoxigenic by Type
	Number	Percent	Number	Percent		
Mitis	751	39.3	40	21.4	791	5.1
Gravis	284	14.9	40	21.4	324	12.3
Intermedius	143	7.5	2	1.1	145	1.4
Indeterminate	37	1.9	16	8.6	53	30.2
Unknown	697	36.5	89	47.6	786	11.3
Total	1,912	100.0	187	100.0	2,099	8.9

The definitions of immunization status were recently modified to conform to the recommendations of the United States Public Health Service Advisory Committee on Immunization Practices.

Immunization Status

Full Primary series (three or more injections), or primary series plus booster, completed within 10 years of onset of illness.

Lapsed Primary series, or primary series plus booster, completed more than 10 years prior to onset.

Inadequate Partial primary series at any time prior to onset.

None No diphtheria toxoid ever received prior to onset.

Definitions of cases, carriers, clinical severity, anatomical involvement, and outcome are listed below.

Diphtheria Case Illness in a person with symptoms compatible with diphtheria and for whom the diagnosis is established clinically. Laboratory identification of *C. diphtheriae* is essential for confirmation of a case, but clinically compatible illnesses are accepted as cases when cultures are not done or when cultures are done and no *C. diphtheriae* organisms are isolated or the isolated *C. diphtheriae* organisms are nontoxigenic.

Diphtheria Carrier A person who has no signs or symptoms of infection, but from whom *C. diphtheriae* organisms are cultured.

Clinical Severity

Mild Localized symptoms, no systemic effects.

Moderate Moderate systemic effects.

Severe Symptomatic with marked systemic effects.

Asymptomatic No symptoms attributable to *C. diphtheriae*

Anatomical Involvement

Ant. anterior nares

Nas. nasopharynx

Tons. tonsils (pharyngopalatine tonsils) or tonsillar area

Hard hard palate

Lar. larynx

Conj. conjunctiva

Cut. skin

None

Outcome

Recovered

Died

Unknown

Clinical severity should be assessed at the time of initial diagnosis and evaluated separately from the outcome.

GEORGE F. BROOKS, JR., M.D.

See p. 103 for the Recommendation of the PHS Advisory Committee on Immunization Practices on the use of diphtheria and tetanus toxoids and pertussis vaccine.

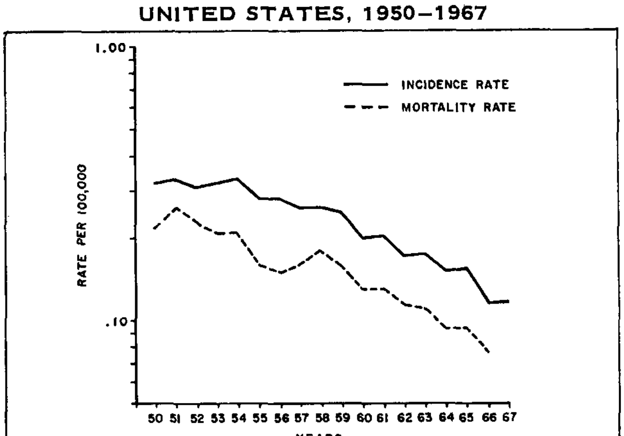
TETANUS

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 animal antitoxin. In 1925 Ramon introduced tetanus toxoid for active immunization. During World War II the incidence of tetanus in immunized American troops declined impressively. There were only eight cases of tetanus in military personnel with unequivocal histories of full immunization. This was in dramatic contrast to the high incidence of tetanus in the armies of other nations during the same conflict.

Since 1945 tetanus toxoid immunization has been used routinely for all age groups from infancy through adulthood. The vaccine has been refined and improved; it is now one of the most effective immunizing agents, with a low incidence of associated reactions. Despite the general availability of this vaccine, there has been only a gradual decline in tetanus morbidity and mortality during the past 18 years (Figure 1). The parallel decline in cases and deaths represents a decrease of only about 50 percent. Over the last 18 years the national tetanus case fatality ratio has not changed significantly, ranging from 60 to 70 percent.

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 in nature. If the exposed individual is personally unprotected he can acquire clinical illness regardless of the general level of protection in the community. Thus, the persistence of the disease is in part explained by the ubiquitousness of the organism, the lack of natural immunity, and the fact that a significant proportion of the population, particularly those over the age of 40, are still not adequately immunized.

FIGURE 1
TETANUS MORBIDITY AND MORTALITY
UNITED STATES, 1950–1967



Source: Morbidity and Mortality Weekly Report, Annual Supplements

TETANUS IN 1967

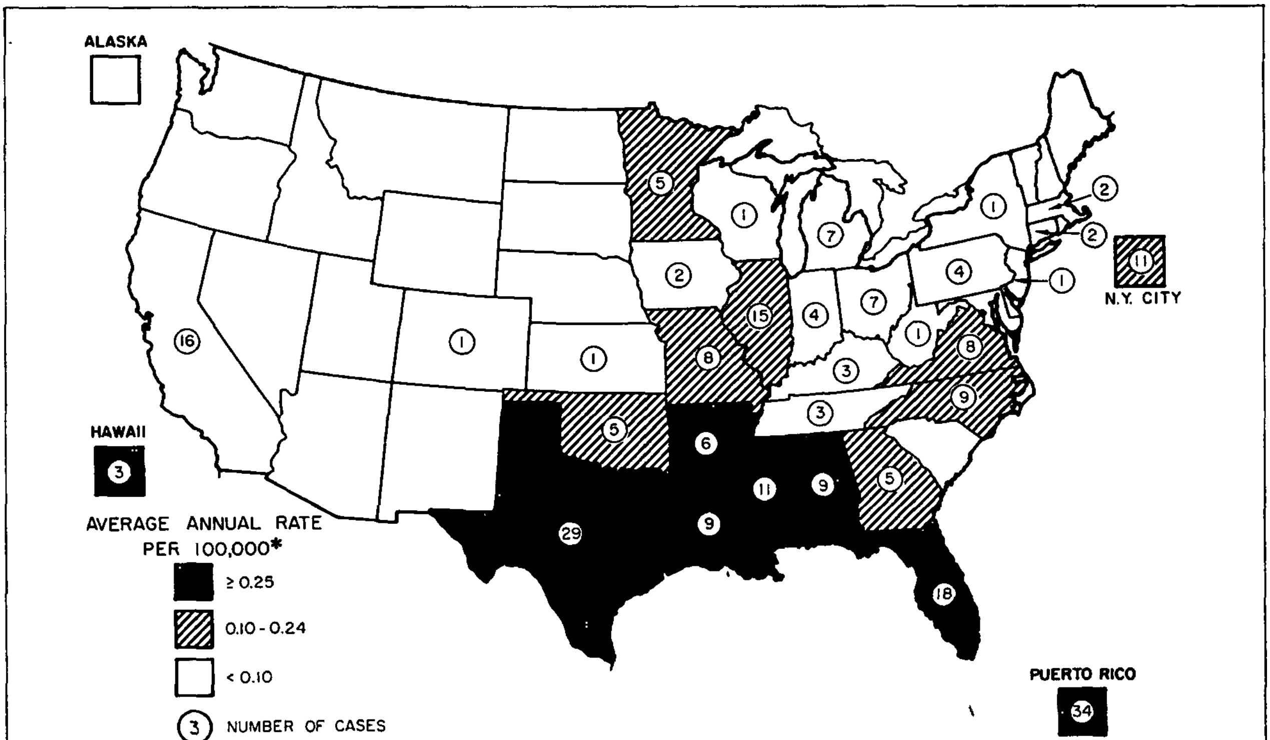
For 1967, 263 cases of tetanus were officially reported from 30 states to the National Communicable Disease Center. An additional 39 cases were reported from the Commonwealth of Puerto Rico.

Various states submitted tetanus surveillance forms for 234 cases, and Puerto Rico submitted 32. The national incidence of the disease was 0.12 per 100,000, essentially unchanged from 1965-1966. Males were affected one and one half times as frequently as females. Disease was some five times more common in other races than in whites, and this relationship persisted when the incidence was considered in terms of race and sex. Peak incidence of the disease occurred at the extremes of age, and the same was true for peaks in the case fatality ratios. Neonatal tetanus comprised approximately 10 percent of all cases in the United States and Puerto Rico. While the national case fatality ratio was 66.7 percent, it was 76 percent for neonates and over 78 percent for those over 50 years of age. The median age of patients, excluding neonates, was 54, which is about 6 years older than the median age of non-neonatal patients in 1965-1966. These data underscore the fact that tetanus is increasingly a disease of the elderly segment of the U.S. population.

Figure 2 shows the number of non-neonatal cases and incidence rates by state. The southern-most tier of states continued to lead the nation in incidence. Almost 80 percent of tetanus cases in 1967 were reported from states either in the Southeast, Southwest, or Mississippi Valley.

The peak incidence occurred in the months from April to October, a finding which is consistent with the interpretation that more cases occur at times of greater outdoor activity and exposure to soil. Lacerations and puncture wounds accounted for almost 60 percent of the total tetanus-predisposing injuries; however, 7.5 percent of the patients had no known wound. Many unusual lesions and some apparently trivial ones were associated with the subsequent development of tetanus. Hands and

FIGURE 2
GEOGRAPHIC DISTRIBUTION OF TETANUS CASES AND INCIDENCE RATES
UNITED STATES AND PUERTO RICO, 1967*



*Excludes neonatal tetanus.

feet were the anatomical sites of injury in over 50 percent of cases. Home and garden associated injuries together accounted for almost 73 percent of all known injuries, and farm associated injuries made up less than 12 percent of the total.

The 1967 neonatal incidence rate was not significantly different from the 1965 rate. Neonatal tetanus is almost always a disease of babies delivered at home to mothers with a history of no immunization or of inadequate immunization. Only one of the neonate patients was born in a hospital with a physician in attendance; in this case of tetanus the incubation period was 22 days, suggesting that contamination of the umbilicus, which was the source of infection, occurred after discharge from the hospital. Most of the other neonates were delivered by midwives. Half the neonatal tetanus cases developed before the seventh day of life.

There was only one case in 1967 in a person who had a verified history of adequate immunization. In 49 cases emergency boosters were given without clearcut history of complete primary immunization. The data strongly suggest that these 49 patients had not had primary vaccination and that a single booster dose in the absence of full immunization cannot be expected to be protective.

Both in terms of number of cases and incidence rates there was a marked downward trend of tetanus in Puerto Rico between 1961 and 1967. Nevertheless this incidence was over 10 times higher than in the United States. With respect to age distribution, incidence, mortality, and case fatality ratios by age and type of injury, the Puerto Rican data closely parallel those of the United States.

The need for universal immunization against tetanus is clear. While routine immunization practices for infants, schoolchildren, and young adults should be maintained, these data emphasize that the elderly and the other than white are the two main subgroups within the U.S. population for whom additional efforts must be made before the national incidence and mortality from tetanus can be substantially reduced.

LOWELL S. YOUNG, M.D.

See p. 103 for the Recommendation of the PHS Advisory Committee on Immunization Practices on the use of diphtheria and tetanus toxoids and pertussis vaccine.

PERTUSSIS - Whooping Cough

EPIDEMIOLOGY

Pertussis has a marked predilection for infants and children. In urban communities where age data are available, 80-90 percent of reported cases occur in preschool children. Approximately 70 percent of all reported deaths occur in the first year of life. In both reported cases and deaths, females are affected with greater frequency than males.

Pertussis is transmitted primarily by direct contact or droplet spread from an infected person. With an incubation period of 5-21 days, most pertussis cases occur within 10 days after exposure. Pertussis is a highly communicable disease with secondary attack rates of 80-90 percent in family susceptibles and 30-80 percent in susceptibles with less intimate exposure. The pertussis patient is most likely to transmit infection during the first week of his disease (the catarrhal stage) with his ability to infect waning as the paroxysmal stage subsides. It is currently felt that the carrier does not play a major role in the transmission of whooping cough.

Cases occur in the United States in all seasons but most prominently in winter and spring. A widespread disease, the incidence of pertussis varies considerably from state to state. This variation undoubtedly reflects differences in actual occurrence as well as in recognition and reporting of the disease.

VACCINE

Although pertussis was described as a clinical entity in 1576, by deBaillau, the causative organism was not isolated until 1906, by Bordet and Gengou. Pertussis vaccines were introduced soon after. Because early vaccines varied in preparation, content, and effectiveness, they had little influence on disease control.

Since the 1940's, pertussis vaccines have been carefully prepared and standardized in this country, and they have been shown to be effective in reducing both the morbidity and mortality of the illness. A gradual loss of vaccine-induced immunity has been documented for all age groups, no matter how many injections of vaccine were received or the age at which the primary course of immunization was begun. While pertussis in adults is rarely a life–threatening illness, cases are now being reported—probably at a rate far below their actual occurrence.

A controversy has developed over the possible relationship of pertussis agglutinogen serotypes and vaccine production, but at this time, there is no laboratory evidence to support claims that vaccine cultures should be selected on the basis of agglutinogen serotype. Finally, note should be made of local reactions in repeat vaccine recipients of current pertussis antigens. It is these possible local reactions, and not an undocumented increasing risk of encephalopathy, which have been the consideration in current recommendations that pertussis vaccine usage be discontinued after age six.

PERTUSSIS TRENDS

Between 1950 and 1967, national pertussis morbidity and mortality rates fell markedly (Figure 1).
The most marked change occurred between 1950 and 1953, followed by a somewhat irregular and more gradual decline. In 1967, 9,718 cases were reported, an increase over the 6,799 cases reported in 1965 and the 7,717 in 1966.

The temporal trend suggests a cyclical pattern with periodic increases in cases every 4 to 5 years. Pertussis case reporting is undoubtedly low because of difficulties both in the clinical diagnosis in some age groups and in laboratory documentation.

Pertussis deaths declined in direct parallel with pertussis cases from 1950 through 1967 (Figure 2). Ages of pertussis patients are not reported nationally. Surveillance data on 1967 deaths, however, provide insight into the prominence of the disease in infancy, where it is particularly severe.

Characteristically, 70 percent or more of the pertussis deaths occur in infants and small children. In 1967 (the most recent year for which mortality data are available) 35 of the 37 who died of pertussis were children less than 2, and 29 (78 percent) were infants less than 1 year old. Of all pertussis deaths in children under age 1, more than half occurred in infants less than 4 months of age.

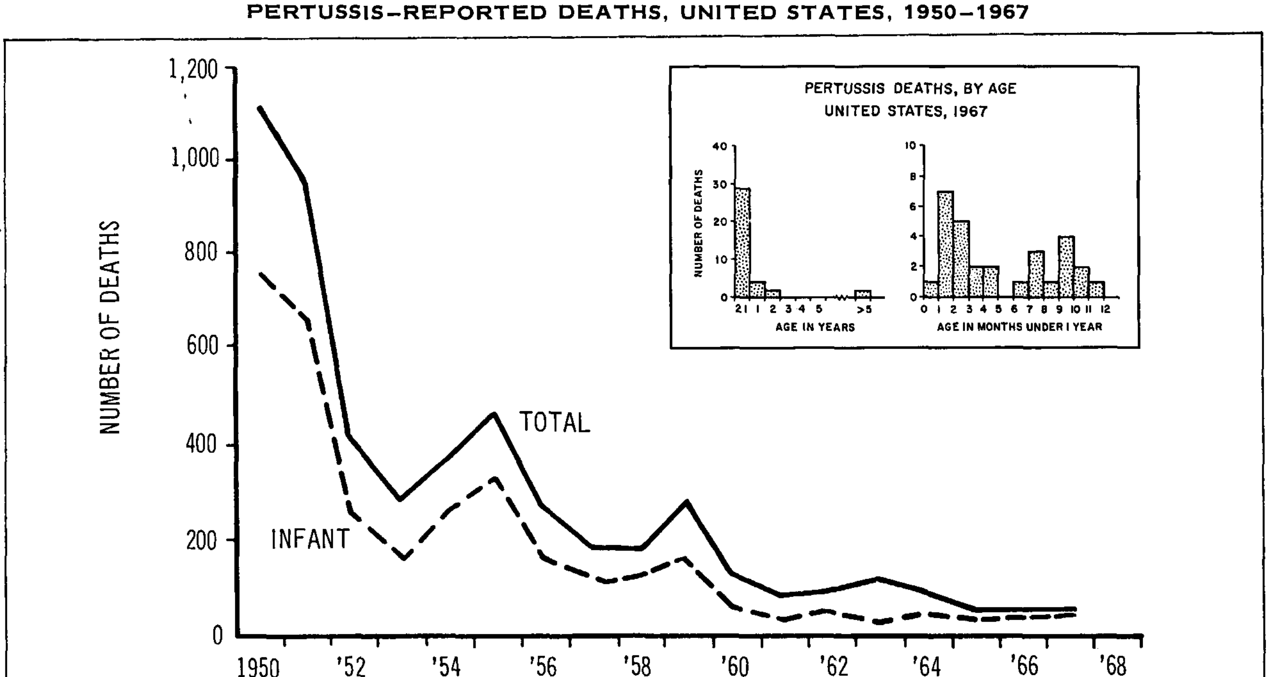
The high death-to-case ratio of pertussis in infants emphasizes the need for early immunization. Importance of the pertussis vaccine component of commonly used DTP is the main justification for beginning primary immunization at 6 to 8 weeks of age.

GEORGE E. HARDY, M.D.

See p. 103 for the Recommendation of the PHS Advisory Committee on Immunization Practices on the use of diphtheria and tetanus toxoids and pertussis vaccine.

FIGURE 1
PERTUSSIS–REPORTED CASES, UNITED STATES, 1950–1967

FIGURE 2
PERTUSSIS–REPORTED DEATHS, UNITED STATES, 1950–1967



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, earlier 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 Faroe Islands; his notes and analysis are an epidemiologic classic. Panum documented a number of the identifying features of measles: characteristic incubation period, high infectivity, respiratory route of spread, higher mortality in infants, and apparently life-long immunity following clinical illness.

In the hundred years after Panum's report was published, few significant advances were made toward a better understanding of measles. In 1954, Enders and Peebles isolated the measles virus in cell culture; it then became possible to develop vaccines that could alter the characteristic pattern of measles in human populations.

Measles has been considered a universal infection. Since reporting began in 1912, mortality rates have been relatively low in the United States and Europe, but measles is still a major cause of death in certain age groups in other parts of the world. Proportionately, measles in the United States does not have a high case-to-death ratio; 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, continued to be relatively common until 1966. Encephalitis developed with approximately one of every 1,000 measles cases; about one-third of the patients with encephalitic complications died, and another one-third suffered permanent central nervous system damage. Deaths due to measles are still reported at the rate of one death for every 1,000 reported cases (Figure 1).

Measles is primarily a disease of infants and young children, with elementary schools serving as the primary focus of community outbreaks in the United States and the reservoir from which disease is transmitted to preschool children and infants. The disease has been so common in the first 7 or 8 years of life that often 95 percent or more of all individuals reaching adolescence have serologic evidence of immunity.

Measles immunization programs since 1963 have already had a marked effect on the characteristic pattern of measles in the United States. A direct relationship is seen between the extent of vaccination and the decline in measles cases (Figure 2).

MEASLES TRENDS

During the latter half of 1966, a major effort was launched in the United States to eradicate measles (Figure 3). This effort resulted not only in accelerated programs of immunization but also in improved reporting of measles cases and outbreaks. As a result of the programs, less than one-third as many cases were recorded in 1967 (62,000) as in 1966 (226,000). By the end of 1968, 23,000 cases had been reported to NCDC, not only an all-time low, but only 5 percent of the average number of cases reported in the 5 prevaccine years, 1958-1962 (Figure 2). The impact of measles vaccine was suggested in 1965, became evident in 1966, and was striking in 1967 and 1968 (Figure 3). The number of cases now being reported is the lowest since measles reporting began early in the century (1912).

FIGURE 1

REPORTED MEASLES CASES AND DEATHS PER 100,000 POPULATION UNITED STATES, 1912–1968

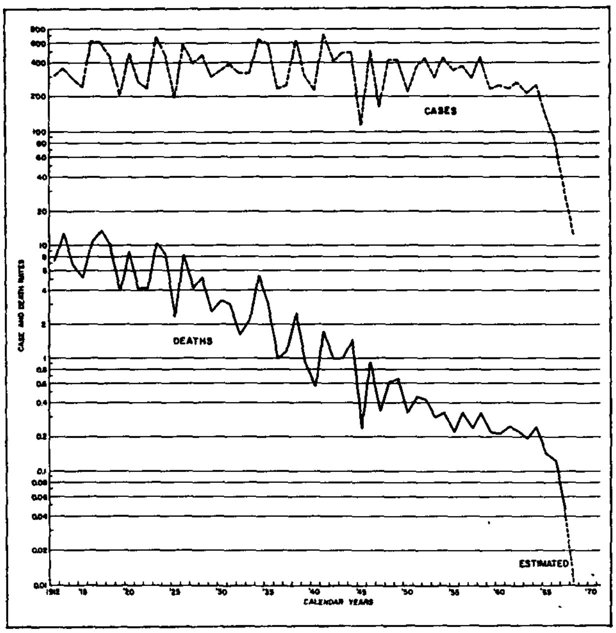


FIGURE 2

MEASLES CASES, UNITED STATES, 1963-1968

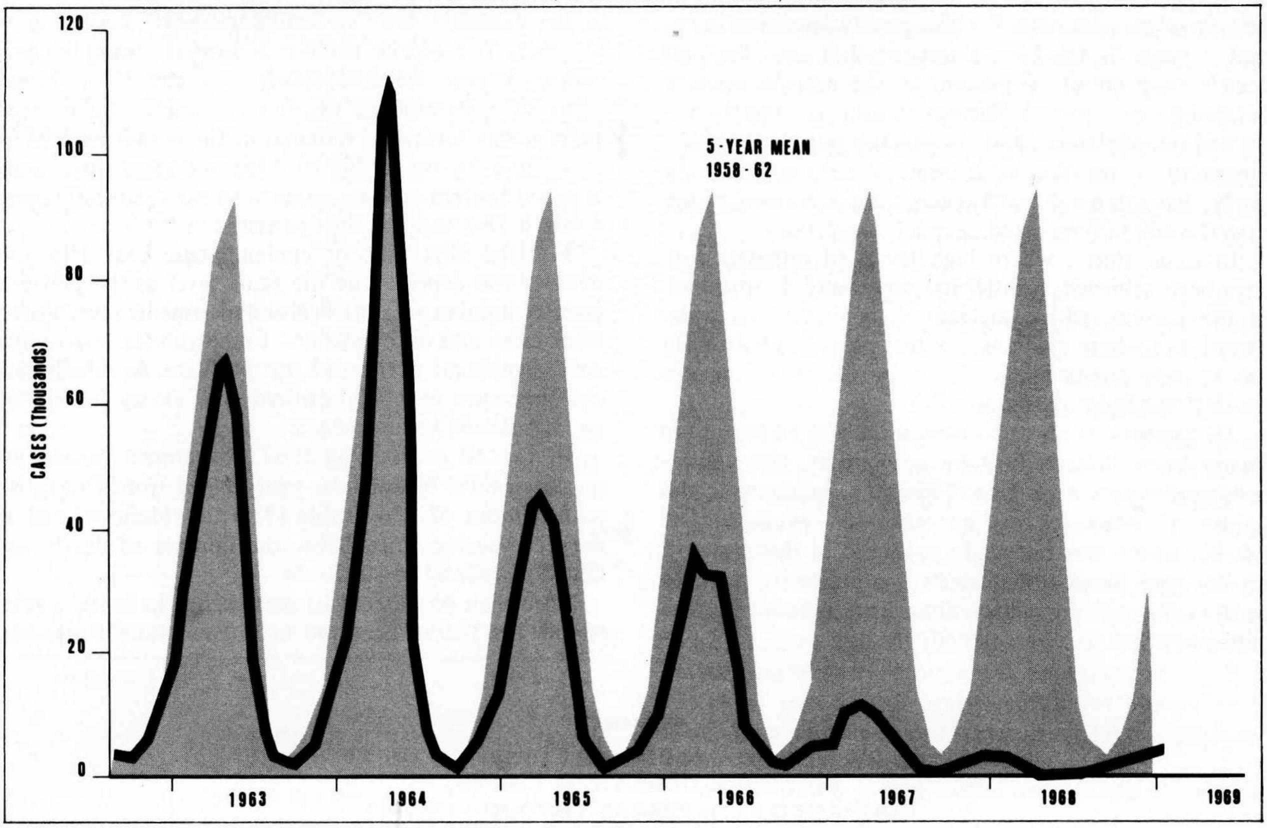
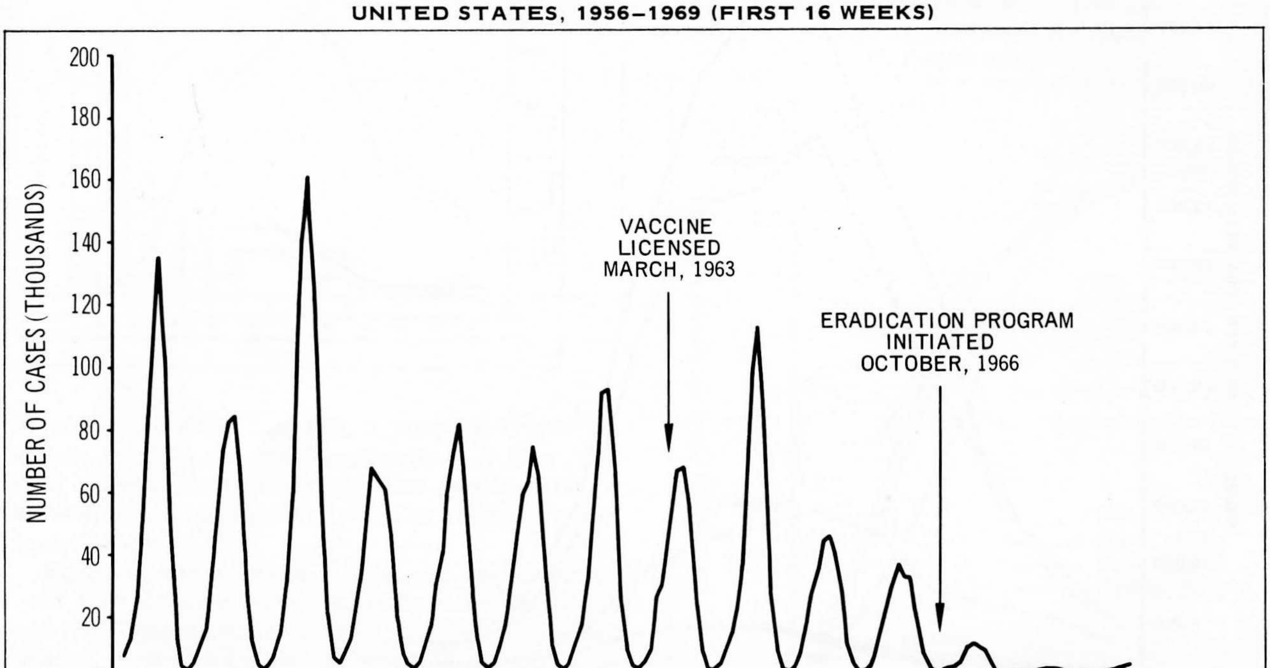


FIGURE 3

REPORTED MEASLES BY FOUR-WEEK PERIODS
UNITED STATES, 1956–1969 (FIRST 16 WEEKS)



The 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 2 years. It has been estimated that over the past decade only about 10 percent of the measles actually occurring was reported. Surveys show that some 90 percent of our adolescent and young-adult populations have immunity to measles; such levels of natural immunity imply that some 4,000,000 cases were occurring, rather than the 400,000 reported, annually until 1965.

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 but not as much.

The pattern of measles cases in the United States has always been characterized by a recurrent late winter-early spring peak each year (Figure 3). 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 2-to-3 year periodicity.

The characteristic winter epidemic of measles is most easily recognized in Figure 4, based on a period relevant to the disease – the "epidemiologic year" beginning in October. The regular decline in measles during the preceding 3 years became dramatic in the 1966-67 and 1967-68 epidemiologic years. Its characteristic seasonal pattern was somewhat damped in the winter months of 1967, and by the spring of 1968 we see a shift in its seasonal pattern to late, rather than early, spring (Figure 4 inset). This seasonal shift persisted in 1969.

For the first half of epidemiologic year 1968-69, measles was reported at the same level as the previous year. A number of state health departments investigated local cases and outbreaks and found rubella responsible for a significant portion of this problem. As rubella vaccine becomes generally utilized, the yearly pattern of measles should become clearer.

In the 10 years 1958-1967, the annual number of measles deaths by calendar year ranged from 552 to 81 with a mean of 356 (Table 1). With widespread use of measles vaccine since 1964, the number of deaths declined to only 81 in 1967.

More than 45 percent of measles deaths in the 5-year period 1962-1966 occurred in infants, and 70 percent

FIGURE 4

REPORTED MEASLES BY FOUR-WEEK PERIODS, UNITED STATES
EPIDEMIOLOGIC YEAR 1968-69,
COMPARED WITH 1964-65 THROUGH 1967-68

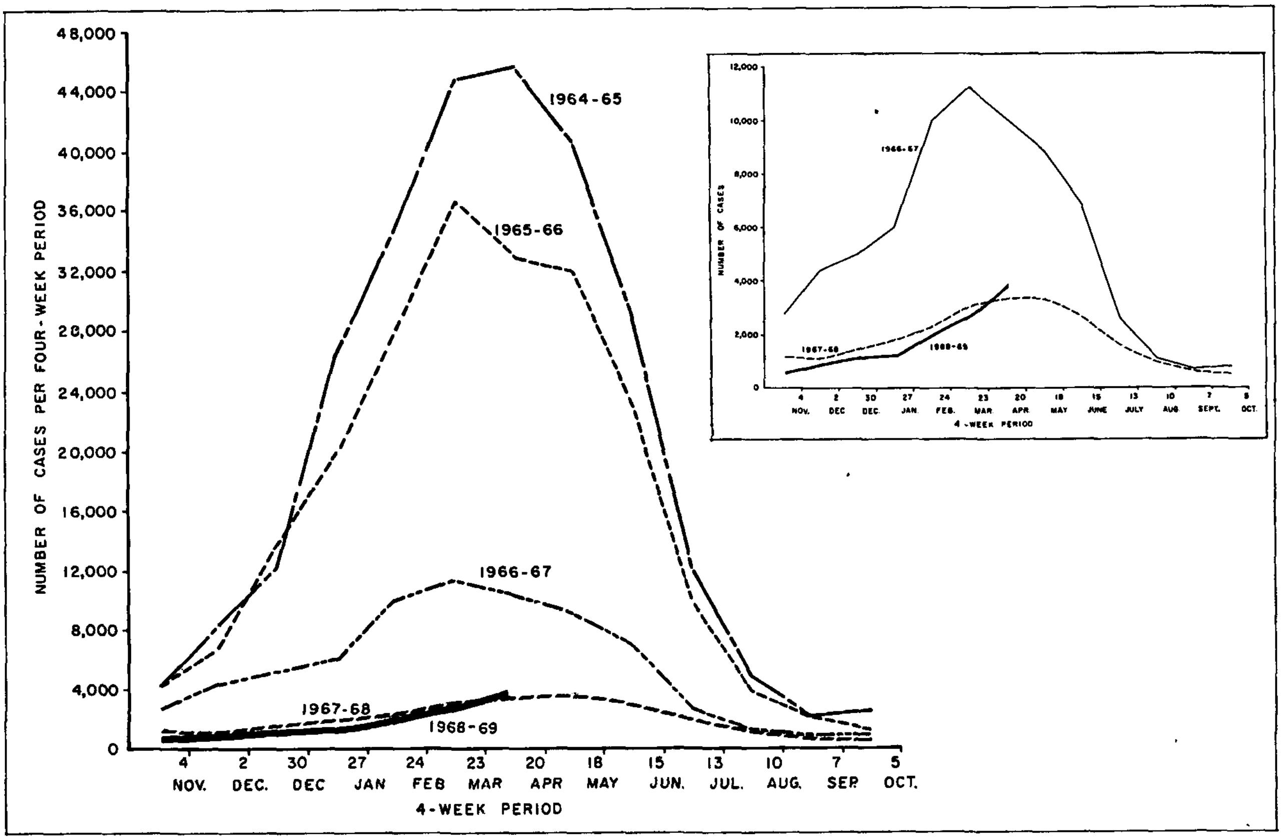


TABLE 1

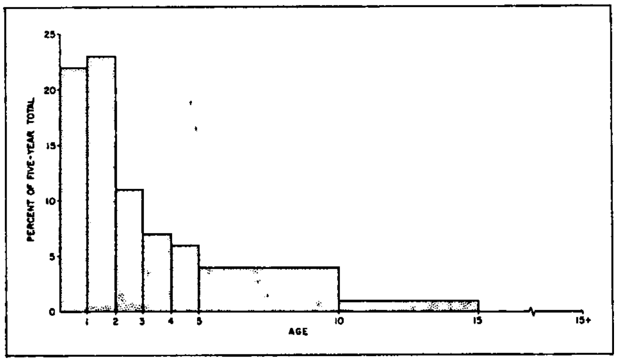
MEASLES–UNITED STATES
CASES AND DEATHS,
1958-1968

Year	Cases (thousands)	Deaths
1958	763	552
1959	406	385
1960	442	380
1961	424	434
1962	482	408
1963	385	364
1964	458	421
1965	262	276
1966	204	261
1967	63	81
1968	23*	Data not available
10 Year Mean 1958-67	388.9	356.2

*Preliminary

FIGURE 5

MEASLES (RUBEOLA) DEATHS IN THE UNITED STATES
PERCENT DISTRIBUTION BY AGE, 1961–1966



occurred in children less than 5 years old (Figure 5). Measles deaths occur almost exclusively in children; rarely is an adult death reported. Most measles fatalities occur from central nervous system or respiratory tract complications.

Figure 6, which relates 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 percent 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 percent by early adolescence. There is an almost straight-line increase in the proportion of children between 1 and 8 years old who give a history of measles illness–increasing at a rate of about 10 percent per year.

Table 2, also based on nationwide surveys, compares histories of measles illness with measles vaccination from 1965 through 1968. All age groups showed a moderate rise in the proportion with history of measles vaccination, and all but the infants showed a decline in history of measles illness.

By 1966, 62 percent of the 1-4-year age group and 77 percent of the 5-9-year age group had either had measles or been vaccinated. By 1968 the respective totals were 68.2 percent and 85.1 percent. However, there are still several urban areas in the United States where these high immunity levels have not yet been achieved. For measles to be eradicated in the United States, the total proportion of immune children will need to be increased and maintained at relatively high levels in all socioeconomic segments of our population.

From 1963, when measles virus vaccines became available, through 1968, 1.7 million doses of the inactivated vaccine and 32 million doses of the live, attenuated vaccine were distributed in the United States (Table 3). This reflects the overwhelming preference for the live, attenuated antigen, which gives lasting protection with only a single dose.

Since only one dose of the live, attenuated vaccine is

FIGURE 6

ESTIMATED PROPORTION OF MEASLES IMMUNES BY AGE, IN FOUR STUDIES

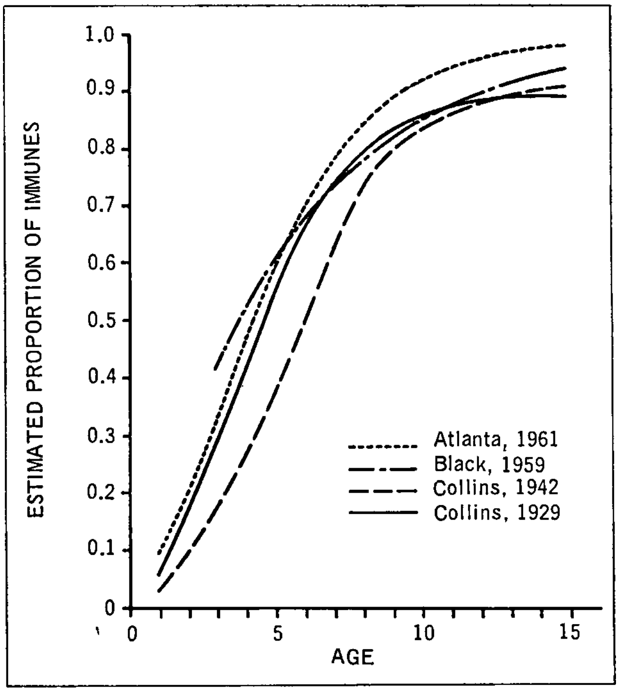


TABLE 2

HISTORIES OF MEASLES ILLNESS AND MEASLES VACCINE

1965-1968

Year	Age	Percent of Group: History of Measles Illness	History of Measles Vaccine	Total Immune
1965	< 1	2.0	6.5	8.5
	1-4	19.7	33.2	52.9
	5-9	54.3	19.3	73.6
1966	< 1	2.0	9.1	11.1
	1-4	16.5	45.5	62.0
	5-9	49.0	28.0	77.0
1967	1	2.8	10.6	13.4
	1-4	12.8	56.4	79.2
	5-9	42.5	40.8	83.3
1968	< 1	2.3	11.5	13.8
	1-4	9.7	58.5	68.2
	5-9	34.7	50.4	85.1

U.S. Immunization Survey

TABLE 3

MEASLES VACCINES – UNITED STATES, 1963-1968

Net Doses (Millions) Distributed Annually

Vaccine	1963*	1964	1965	1966	1967	1968
Measles Virus Vaccine, Inactivated	0.7	0.5	0.3	0.2	0.1	0.0
Measles Virus Vaccine, Live, Attenuated	3.2	3.8	6.0	7.9	6.4	5.3

*Production began during the year

Biologics Surveillance, NCDC

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 percent of the vaccine distributed is not used.

J. LYLE CONRAD, M.D.

See. p. 111 for the Recommendation of the PHS Advisory Committee on Immunization Practices on the use of measles vaccine.

MUMPS

Mumps was one of the first diseases to be described clinically. Hippocrates, in the 5th century B. C., clearly recorded the clinical manifestations of epidemic parotid swelling and noted that testicular swelling was sometimes associated. Not until the beginning of the 20th century, however, did central nervous system involvement, the other major complication, become widely recognized. The biological response to infection with mumps virus ranges from an asymptomatic state (20-30 percent of all infections) to a severe but rarely fatal illness with associated or independent involvement of the nervous system, gonads, pancreas, and other organs. In 1934 Goodpasture demonstrated that this disease was caused by a filterable agent. The mumps virus was more completely characterized by Enders, Habel, and others beginning in 1945.

EPIDEMIOLOGY

Mumps was placed on the list of notifiable diseases in 1922 but was removed in 1950. Many states continued reporting the disease voluntarily, and mumps was reinstated to the list of notifiable diseases as of January 1, 1968, by the Conference of State and Territorial Epidemiologists.

Figure 1 depicts the yearly incidence of reported mumps in the United States between 1922 and 1968. The national annual incidence fluctuates, with no discernible cyclic pattern. Similarly, the incidence of reported cases in smaller areas, such as geographic regions, states, and major cities, rises and falls in no consistent repetitive pattern. There is, however, a seasonal pattern to mumps incidence, with the peak of reported cases occurring in late winter and spring (Figure 2).

FIGURE 1

REPORTED CASES OF MUMPS PER 100,000 POPULATION
UNITED STATES, 1922–1968

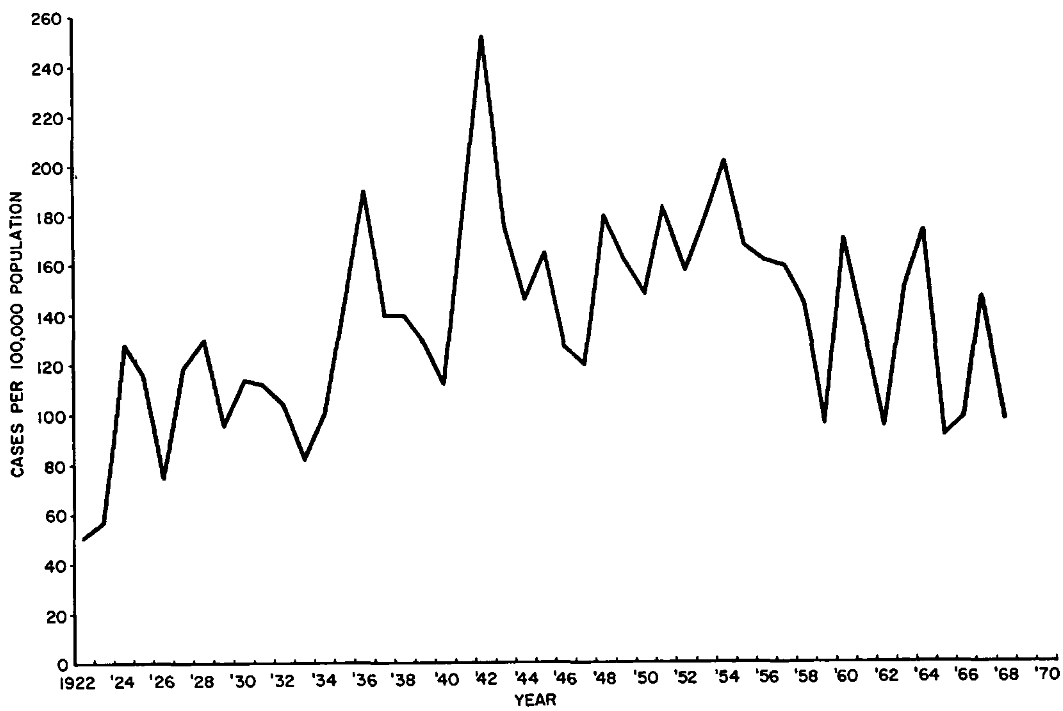


FIGURE 2

REPORTED CASES OF MUMPS BY FOUR-WEEK PERIODS FOR NINETEEN STATES,* 1922–1966

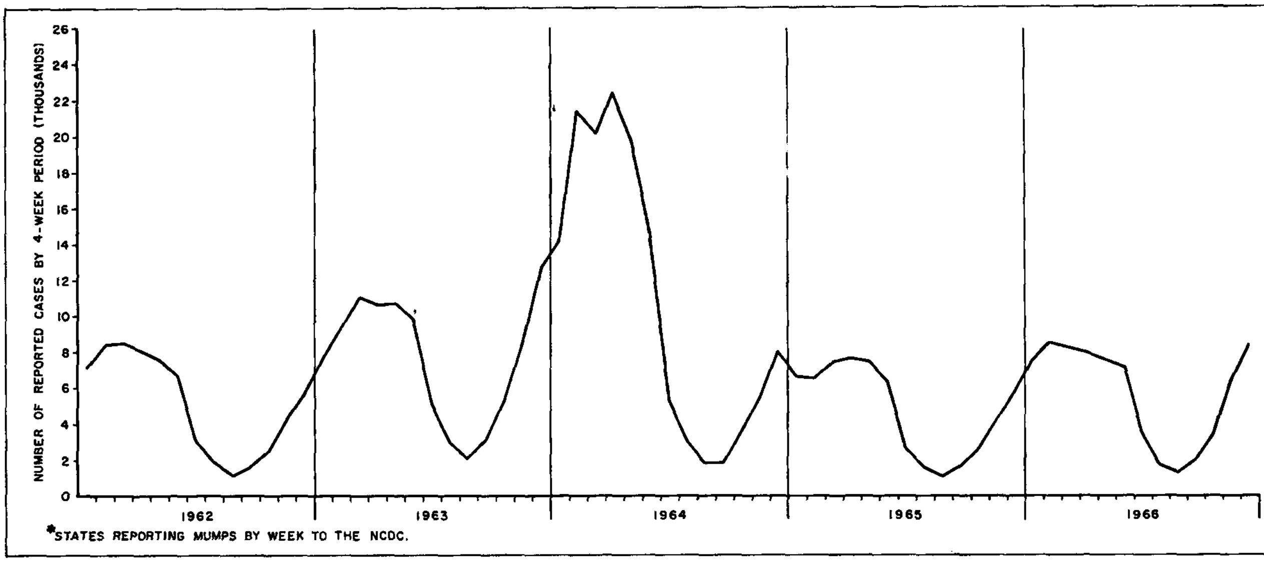


TABLE 1

REPORTED CASES OF MUMPS BY AGE FROM SELECTED AREAS*
1960-1964

Age	Mumps Cases	Percent	Cumulative Percent
0-4	19,427	24.64	24.64
1	793	1.01	1.01
1	2,587	3.28	4.29
2	4,479	5.68	9.97
3	5,332	6.76	16.73
4	6,236	7.91	24.64
5-9	44,328	56.21	80.85
5	11,128	14.11	38.75
6	12,723	16.13	54.88
7	9,314	11.81	66.69
8	6,785	8.60	75.29
9	4,378	5.55	80.85
10-14	8,573	10.87	91.72
15-19	1,825	2.32	94.04
20+	4,703	5.96	100.00
Total	78,856	100.00	

*Los Angeles County (Excluding Los Angeles City), Calif., N. Y. City, and Milwaukee and Madison, Wisc.

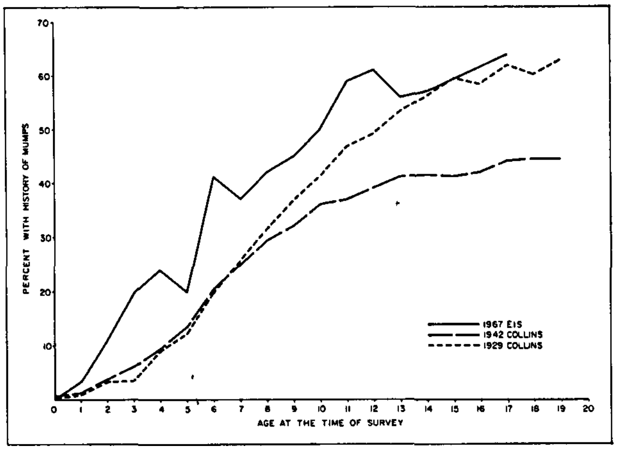
Table 1 shows the age distribution for cases of mumps reported from selected areas between 1960 and 1965. More than 50 percent of the cases occur in children 5-9 years old, with less than 10 percent of the cases occurring after the age of 15. Figure 3 shows the percentage of persons with a history of mumps by age, as determined in three separate surveys. Consistent with Table 1, the curves plateau at about age 15. Thus, mumps virus transmission occurs predominantly among school-age children, although occasional outbreaks have been noted among confined groups of older individuals (military recruits, institutions, etc.)

Reported cases of mumps central nervous system involvement also show a seasonal pattern, with the peak occurring during the spring and early summer. Unlike clinical mumps cases, which occur with nearly equal frequency in males and females, there is a striking male predominance among patients with mumps central nervous system involvement. In addition, 20 percent of mumps central nervous system cases occurred in persons 15 years of age or older, whereas only 6 percent of clinical mumps was reported for this group. In 1960-1966, approximately 2 to 4 cases of mumps central nervous system involvement per 1,000 cases of clinical mumps were reported. However, some studies indicate that up to 30 percent of clinical cases of mumps have some central nervous system involvement, usually of a mild nature consistent with aseptic meningitis.

No national data on the occurrence of mumps orchitis are available. Several studies have indicated that about 20 percent of cases of mumps in post-pubertal males will be complicated by orchitis; however, sterility following this complication is rare.

FIGURE 3

PERCENT OF PERSONS WITH HISTORY OF MUMPS BY AGE, IN THREE SURVEYS



MUMPS PROPHYLAXIS

Formalin inactivated (killed) mumps vaccines have been shown to confer only limited protection against clinical mumps. However, a live, attenuated mumps virus vaccine was developed in 1965 by Hilleman and coworkers and licensed in January 1968. Known as the Jeryl Lynn strain, the virus was isolated from an uncomplicated case of mumps and passed 17 times in chick embryo primary cell culture. Although the live mumps vaccine is effective, control of mumps in the United States is not currently considered to be of high public health priority. The mild nature of mumps infection, in comparison with the severity of other diseases against which vaccines are available, is the basis for this decision. However, the Public Health Service Advisory Committee on Immunization Practices recommends that consideration be given to immunizing with live mumps vaccine any susceptible individual 1 year of age or older.

JOEL P. FRIEDMAN, M.D.
THOMAS C. SHOPE, M.D.

See p. 114 for the Recommendation of the PHS Advisory Committee on Immunization Practices on the use of mumps vaccine.

POLIOMYELITIS

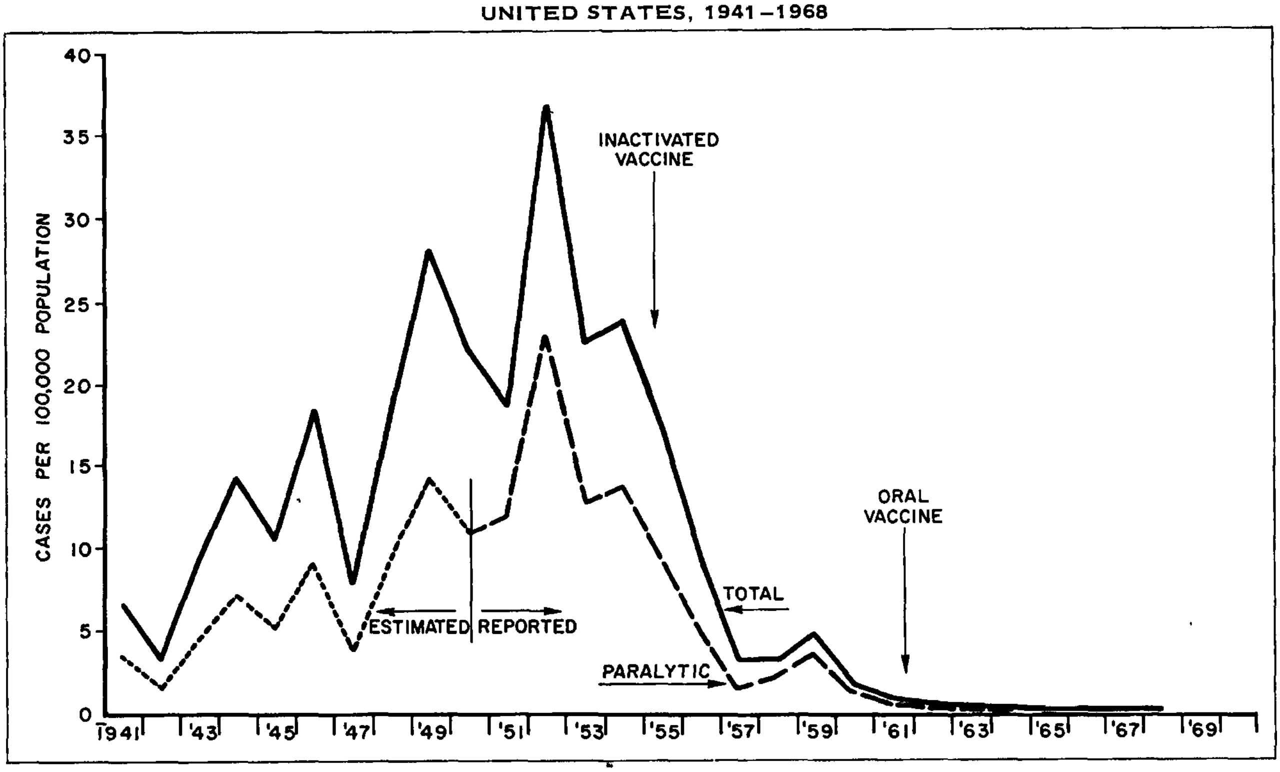
Poliomyelitis (infantile paralysis, Heine-Medin disease) came to be recognized as a distinct entity with wide geographic distribution in the 19th century, although paralytic illness in infants had been known and described earlier. Small outbreaks were reported in both Europe and North America in the mid-19th century, but it was not until the latter part of that century and the early part of the 20th century that the serious epidemic potential of poliomyelitis became manifest. With the emergence of epidemic patterns, poliomyelitis was characterized as an infectious disease, spread through human contact, with both paralytic and non-paralytic expression. In 1909 the viral etiology of poliomyelitis was established. However, only after 40 years of increasingly intensive research were the three serotypes of poliovirus identified and propagated in tissue culture. The foundation was thus laid for the development, first of inactivated poliomyelitis vaccine (IPV), introduced for general use in 1955, and then live, attenuated, oral poliovaccine (OPV), licensed in 1961.

Widespread use of effective vaccines has resulted in virtually complete control of poliomyelitis in the United States. After the large field trials of IPV in 1954, mass use led to the dramatic reduction in the number of paralytic cases from 13,850 in 1955 to 829 in 1961. When live, oral poliovaccines became available, the incidence decreased further (Figure 1), and the long-term immunization status of the population improved. The number of paralytic cases decreased from 762 in 1962 to a record low of 40 cases in 1967.

Over the years the epidemiologic characteristics of poliomyelitis have changed, first with improved hygiene, among other factors, and later with the general availability of effective prophylaxis. From an endemic pattern of high incidence of infection with low paralytic attack rates among infants and young children, the age-specific incidence rates of paralytic poliomyelitis shifted upward during the years of crippling epidemics. Now with the general availability of effective vaccines, a residual incidence of poliomyelitis persists most prominently in pre-

FIGURE 1

ANNUAL POLIOMYELITIS INCIDENCE RATES UNITED STATES, 1941–1968



school children in lower socioeconomic areas that have not been reached by immunization programs.

Reporting practices have also changed, along with improvement of epidemiologic and biologic understanding of poliomyelitis. Prior to 1951, cases of paralytic poliomyelitis were not differentiated from non-paralytic cases in national reporting. The cases were thought to be equally divided between the two classifications. We now know that many of the non-paralytic cases, formerly attributed to poliovirus infection on epidemiologic grounds, were probably caused by ECHO and Coxsackie enteroviruses. These agents also cause paralytic illness occasionally, although the paralysis tends to be transient and less severe. Improvement in the laboratory diagnosis of enteroviral infections is at least partially responsible for the rising ratio of paralytic cases to all cases reported, as evident in Figure 1. In addition, since aseptic meningitis in the summer and fall no longer particularly suggests poliovirus infection to most physicians, cases of aseptic meningitis actually caused by poliovirus usually escape correct diagnosis and reporting.

PARALYTIC POLIOMYELITIS IN 1967 AND 1968

Forty cases of paralytic poliomyelitis were reported in 1967, and in 1968 there were 48 cases. Nevertheless, in most parts of the country the number of cases continued to decrease. In 1967 and 1968, as in 1966, a disproportionate number of cases of paralytic poliomyelitis occurred in states along the U.S.–Mexican border, especially in Texas (Figures 2 and 3). After reporting 66 cases in 1966, Texas reported only nine cases in 1967. In 1968, the Texas total increased to 20, spurring intensified immunization campaigns in a number of affected counties. Virtually all of the cases occurred in unimmunized preschool children from lower socioeconomic areas. They were due almost exclusively to type 1 poliovirus, whereas each of the three poliovirus types was involved in the sporadic cases reported from elsewhere in the country. Three cases reported from California in 1967 were associated with travel in Mexico in the month prior to onset of illness, and another case involved intimate contact with travelers recently returned from Mexico. In 1968 five persons, two from Illinois and one each from Iowa, Michigan, and New York, developed poliomyelitis after travel in Mexico or Texas. Such instances point up the importance of being adequately immunized before going to endemic areas, as recommended by the Public Health Service Advisory Committee on Immunization Practices.

Of the 40 cases of paralytic poliomyelitis reported in 1967, just over 60 percent were in the 0-4-year age group (Figure 4). Six of the patients were under 1 year of age, and four were not more than 6 months old. Of the 40 patients, 28 had never received poliovaccine. Two other patients had each received one dose of monovalent vaccine of a type other than the one implicated in the illness. Thus in only 10 cases, 25 percent, was there any history of vaccination that might have been protective. Only three patients could have received a primary immunization series considered adequate by current PHS recommendations.

In 1967 there were six oral vaccine-associated cases. Two cases of paralytic illness consistent with poliomyelitis occurred in infants who had received oral poliovaccine in the preceding 30 days (recipient vaccine-associated cases). Four cases in close contacts of recent oral vaccinees were reported. Three of these four "contact vaccine-associated" cases were in adults.

Most of the 48 paralytic cases reported in 1968 involved infants and preschool-age children, as in 1967 (Figure 5). Of this total, 31, approximately two-thirds, were under 5 years old, and 12 were under 1 year of age. Six were 6 months old or less. Forty patients had never had any poliovaccine, and another infant had received one dose of a monovalent type different from the one implicated in his paralytic illness. None of the patients had been adequately vaccinated.

In 1968 there were two recipient vaccine-associated cases, both in 3-month-old infants, and four contact vaccine-associated cases, two in infants and two in adults. While the incidence of vaccine-associated cases in 1967 and 1968 remained extremely low in terms of the number of doses distributed, the need for careful surveillance continues.

VACCINE DISTRIBUTION AND VACCINATION STATUS OF THE POPULATION

Two kinds of information indicative of the vaccination status of the U.S. population are available. One is the number of doses of poliovaccines distributed annually in the United States. These data, as summarized for 1962-68 in Table 1, represent not the number of doses administered, but the maximum possible utilization. More importantly, these data show quite clearly certain trends in immunization practice.

After 1963 the distribution of inactivated poliomyelitis vaccine (IPV) (Salk) steadily declined to the low 1968 level of 2.7 million doses. With the introduction of trivalent oral poliovaccine (TOPV) in 1963, use of monovalent oral poliovaccines (MOPV types 1, 2, and 3) diminished to the 1968 level of less than one million doses of each of the three types. It should be noted, of course, that the raw data on doses are not adjusted for the number of doses in each category required for a primary immunization series. Nevertheless, TOPV is now clearly the most widely used vaccine. The overall decrease in total doses of vaccine distributed yearly since 1963 reflects a shift in emphasis from mass immunization campaigns and community-wide programs to routine immunization of infants.

A second approach to estimating immunization levels in the population involves a sample survey of the history of types and doses of vaccine received.* While this ques-

*U.S. Immunization Survey, 1967, 1968, pages 6 and 20.

FIGURE 2

PARALYTIC POLIOMYELITIS, GEOGRAPHIC DISTRIBUTION
UNITED STATES, 1967

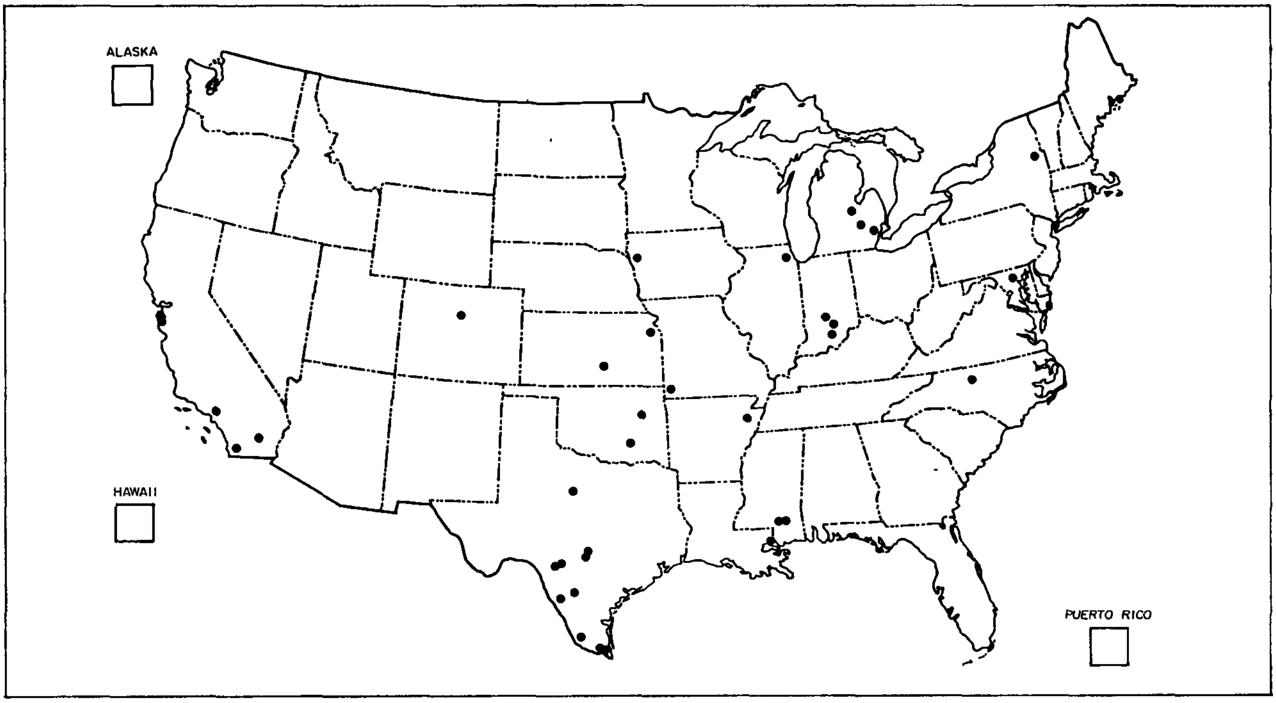


FIGURE 3

PARALYTIC POLIOMYELITIS CASES BY COUNTY
UNITED STATES, 1968

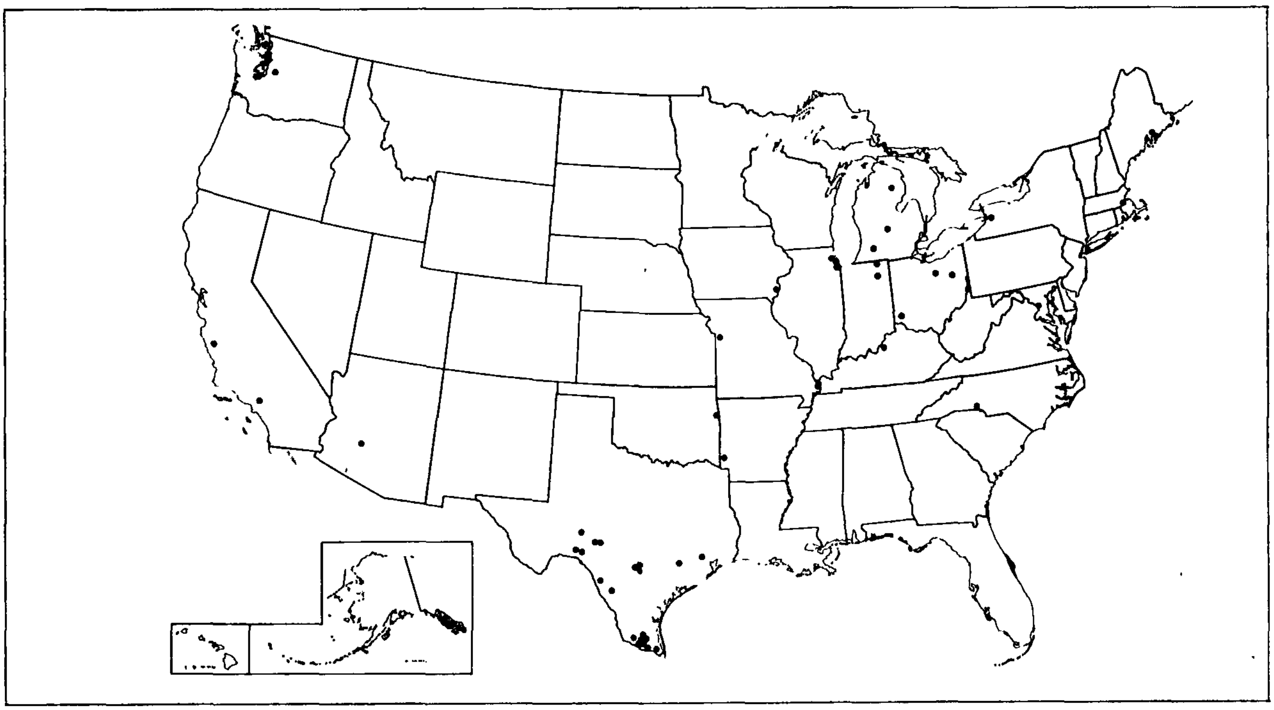


FIGURE 4

PARALYTIC POLIOMYELITIS CASES BY AGE AND VACCINATION STATUS UNITED STATES, 1967

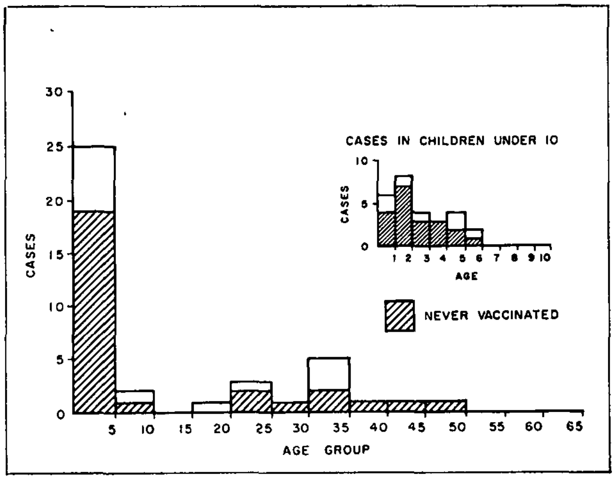


FIGURE 5

PARALYTIC POLIOMYELITIS CASES BY AGE AND VACCINATION STATUS UNITED STATES, 1968

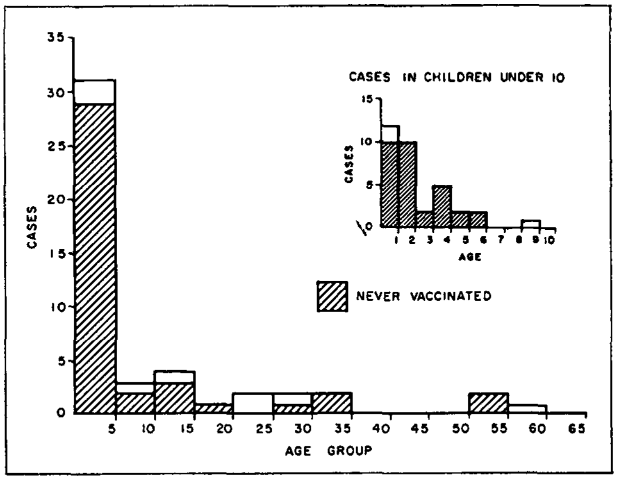


TABLE 1
POLIOMYELITIS VACCINES, NET DOSES (MILLIONS) DISTRIBUTED ANNUALLY, UNITED STATES, 1962-68

	1962*	1963	1964	1965	1966	1967	1968
Poliomyelitis Vaccine (Inactivated) (IPV)	15.3	19.0	8.8	7.5	5.5	4.0	2.7
Poliovirus Vaccine Live, Oral (OPV)							
Monovalent (MOPV)							
Type 1	33.1	38.7	24.9	4.7	1.4	1.3	0.5
Type 2	37.0	34.2	29.8	3.4	1.3	0.9	0.5
Type 3	13.7	54.2	28.4	3.7	1.4	1.0	0.6
Trivalent (TOPV)	---	4.2**	24.0	17.4	24.0	18.0	23.9
Total	99.1	150.3	115.9	36.7	33.6	25.2	28.2

*July-December (Biologics Surveillance Program began July 1962)
**Production began in mid-1962.

Biologics Surveillance, NCDC

tionnaire method is not as accurate as serologic surveillance, it has proved useful in assessing the proportion of the population that can be expected to exhibit immunity to poliovirus infection. For the years 1966-68, Table 2 shows the percentages of the population, by age group, that had received at least three doses of oral poliovaccine (OPV), at least three IPV (but less than three OPV), and no poliovaccine whatsoever. While neither a total of three MOPV doses nor three IPV doses is considered a fully adequate primary series (see Recommendations), percentages based upon three or more doses of IPV or OPV serve as quite a satisfactory index of substantial protection, especially in preschool-age children. It is noteworthy that in 1968 in the 1-4-year age group, only 52.5 percent had received at least three doses of OPV and 16.1 percent at least three of IPV (but less than three OPV doses). In total, only 68.3 percent had been immunized to this extent. In addition to the 10.5 percent never vaccinated, the remaining 21.2 percent represents various degrees of inadequate immunization, by PHS standards. Moreover, there was no substantial improvement over the 1966 level. This situation is reflected in disease incidence. As illustrated in Figures 3 and 4, most cases of poliomyelitis occurred in unvacci-

TABLE 2
PERCENTAGE OF VACCINATED POPULATION 1-19 YEARS OLD, BY AGE GROUP, YEAR, AND VACCINE RECEIVED, USA, 1966-1968

Age Group	At Least 3 OPV			At Least 3 IPV (But Less Than 3 OPV)			Never Vaccinated		
	1966	1967	1968	1966	1967	1968	1966	1967	1968
1-4	48.7	51.6	52.2	21.5	19.3	16.1	11.3	11.7	10.5
5-9	64.8	66.8	65.8	23.3	21.5	19.1	2.9	3.1	3.3
10-14	64.7	67.5	67.4	25.3	22.2	20.4	2.3	2.2	2.2
15-19	58.5	59.3	60.0	27.9	23.2	21.3	4.1	3.1	3.0

TABLE 3
PERCENTAGE OF POPULATION 1-19 YEARS OLD NEVER VACCINATED, BY YEAR AND RACE, USA, AND BY YEAR, RACE, AND SOCIOECONOMIC AREA, CENTRAL CITIES, 1967-1968

	1967	1968
U.S. Total	4.7	4.4
White	4.2	3.7
Other	7.7	8.3
Central Cities (Total), SMAS	4.2	5.0
White	3.6	4.0
Other	6.0	7.4
Central Cities (Pop. 250,000+)		
Poverty Areas	11.8	7.4
Non-Poverty Areas	3.5	4.1

TABLE 4
PERCENTAGE OF POPULATION 1-19 YEARS OLD NEVER VACCINATED, BY AGE GROUP, YEAR, AND RACE, USA, 1966-1968

Age Group	1966		1967		1968	
	White	Other	White	Other	White	Other
1-4	9.5	20.8	10.1	19.5	8.5	20.2
5-9	2.7	4.1	2.7	4.8	2.9	5.9
10-14	2.3	2.4	2.2	2.8	1.9	3.9
15-19	3.9	5.7	2.9	4.5	2.8	4.3

TABLE 5
POLIOVACCINE STATUS – UNITED STATES, 1966-1968
Infants (Less Than 1 Year of Age)
Percent with Doses Specified

	1966		1967		1968	
	1 or more OPV	1 or more IPV	1 or more OPV	1 or more IPV	1 or more OPV	1 or more IPV
U. S. Total	41.6	18.5	45.0	18.0	48.1	16.4
Central Cities						
White	- - -	- - -	49.6	22.5	48.1	20.9
Other	- - -	- - -	32.7	27.5	34.4	24.9

nated preschool children. Reaching the "hard-to-reach" evidently involves this age group. Progress in delivery of preventive medical care will be most evident in statistics on preschool-age children and should result in a decrease in cases of poliomyelitis.

Further data on the group that had received no poliovaccine are presented in Table 3. While percentages are small, they serve as an index of the marked differences in vaccination status among various segments of society; for example, children in selected poverty and non-poverty areas. As indicated above, the percentage of inadequately immunized will be twice as large as of those never vaccinated. Together, these groups constitute a real problem. A similar gap is noted between immunization levels of whites and other races (ages 1-19) in both the United States generally and in the Central Cities.* This is presented in more detail in Table 4, in which the percentages are given by year, race, and age group. The marked difference in preschool versus school-age children can be attributed mainly to vaccine administered at the time of school entrance. The failure to begin immunization early is highlighted in Table 5, in which data for children less than 1 year old are presented. In 1968 only 64.5 percent of all children in this age group had received at least one OPV or one IPV dose, although the PHS recommends that primary immunization begin at 6-12 weeks of age. This percentage represents a maximum, since some infants may be included in the percentages for both IPV and OPV. Comparable 1968 figures for the Central Cities are 59.3 percent for other races and 69.0 percent for whites, representing a slight decrease since 1967. Small improvement may have occurred, however, in the overall level for infants in the United States, although this cannot be determined with certainty from the available data.

While existing immunization programs have gone far toward complete control of poliomyelitis in the Unites States, the job is not finished. The inapparent circulation of wild polioviruses has not been eliminated, and infection can still spread from known endemic areas. Early reporting is the key to effective response once cases begin to occur, but prevention by means of routine immunization of all infants in the first year of life remains the more fundamental public health challenge.

THOMAS H. GLICK, M.D.

*For definition of "Central Cities," see p. 1, U.S. Immunization Survey, 1967, 1968.

See p. 118 for the Recommendation of the PHS Advisory Committee on Immunization Practices on the use of poliomyelitis vaccines.

RUBELLA - German Measles

Rubella was first differentiated from measles (rubeola) and from scarlet fever in Germany in the late 18th century. The illness was called *Rotheln* until Veale, in 1866, proposed the name rubella. During the first half of the 19th century this seemingly mild exanthematous disease of children and young adults was recognized in outbreak form in England and the United States. However, not until Gregg's astute and now classic observations established a relationship between maternal rubella and congenital cataracts and heart disease did the disease achieve importance as a source of significant human morbidity. This relationship, noted in Australia during the 1941 rubella pandemic, clearly defined the current interest in the disease and its public health importance. Although experimental infections in animals and man had suggested a viral etiology for rubella, this was not confirmed until 1962, when two groups, Weller and Neva, and Parkman, Beuscher, and Artenstein, reported the propagation of rubella virus in tissue culture.

In the continental United States postnatal rubella has long been recognized as a mild endemic disease of children and an exceedingly rare cause of death. Temperatures seldom rise above 101°F., and complications are uncommon. Thrombocytopenia and hemorrhage have been noted rarely, and encephalitis is estimated to occur in one of every 6,000 rubella cases. More frequent, but transient and without sequelae, are the frank arthralgias and arthritis noted in some adults, particularly females.

Rapidly improving, although still limited, epidemiologic data suggest that 5-9-year-old children in elementary school are the primary reservoir of disease for communities and that these children propagate outbreaks which spread to older schoolchildren who are still susceptible. Furthermore, infected children in the 5-9-year age group are primarily responsible for the transmission of disease to preschool children and adults. When a susceptible female in early pregnancy is exposed to rubella virus circulating in this pediatric reservoir, prenatal infection of the fetus and resultant congenital rubella deformities become a significant risk.

The 1964 rubella epidemic in the United States resulted in an unusually large group of congenitally deformed children. Although fetal abnormalities previously thought rare among rubella babies were noted frequently, i.e., X-ray detectable abnormalities of long bones, hepatitis and jaundice, and thrombocytopenic purpura, the basic triad of defects remained dominant: congenital heart disease, cataracts, and deafness. In addition, the ability of the prenatally infected child to shed rubella virus during the initial 6-9 months of life and thus become an active part of the chain of infection was first noted after the 1964 epidemic.

RUBELLA IN 1957-1968

Rubella did not become a nationally reportable disease until 1966. However, many reporting areas have maintained surveillance of rubella for decades. Data on reported cases of rubella have been submitted voluntarily to the National Communicable Disease Center by these areas. Although these data are limited by marked under-reporting and variable diagnostic accuracy, the trends of patterns of rubella in the United States can be determined from them. They should, however, be interpreted with relative caution.

The incidence of rubella from 1928 through 1968 in 10 selected areas is shown in Figure 1. Although the annual incidence of rubella varies considerably, major epidemics were obvious in 1935, 1943, and 1964, with high but lower incidence in 1952 and 1958. These periods of increased incidence occur at 6-9-year intervals. This moderately long but slightly variable cyclicity contrasts strikingly with the rather regular 2-year periodicity of measles noted in the United States prior to the extensive use of measles vaccines.

The seasonal distribution of reported rubella is similar to that of other respiratory diseases (Figure 2). Reports of rubella cases begin to increase in the early winter, peak in the spring, and fall to a low point in the late summer and autumn. This seasonal pattern appears to be maintained during periods of relatively low incidence as well as at times of major epidemics, as in 1964.

Table 1 shows the age and sex distribution of reported cases of rubella from three selected areas. Approximately two-thirds of the reported cases occurred in the 5-9 and 10-14 year age groups. However, significant numbers of cases are reported among young adults, particularly females. Eighty percent of reported cases have occurred by age 14, 92 percent by age 20.

In stratified random serosurveys conducted in Tampa, Florida, in 1963 and 1968 rapid increases in the percentage of persons with rubella seroimmunity were noted as age increased from the early childhood years to young

FIGURE 1

RUBELLA INCIDENCE, TEN SELECTED AREAS,* UNITED STATES, 1928–1968

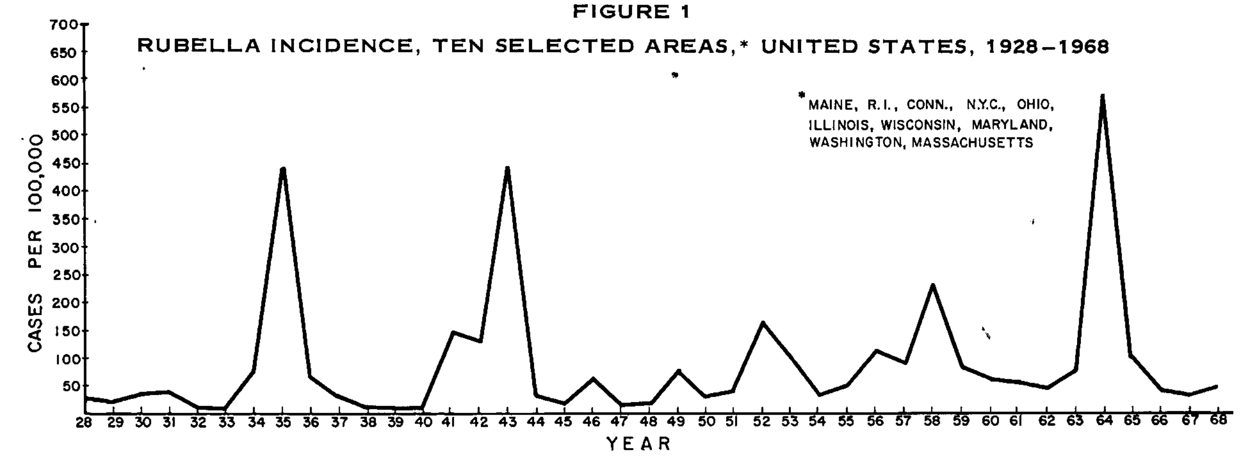


FIGURE 2

REPORTED RUBELLA CASES BY MONTH OF ONSET, TWENTY-FOUR SELECTED STATES, JANUARY 1963–1968

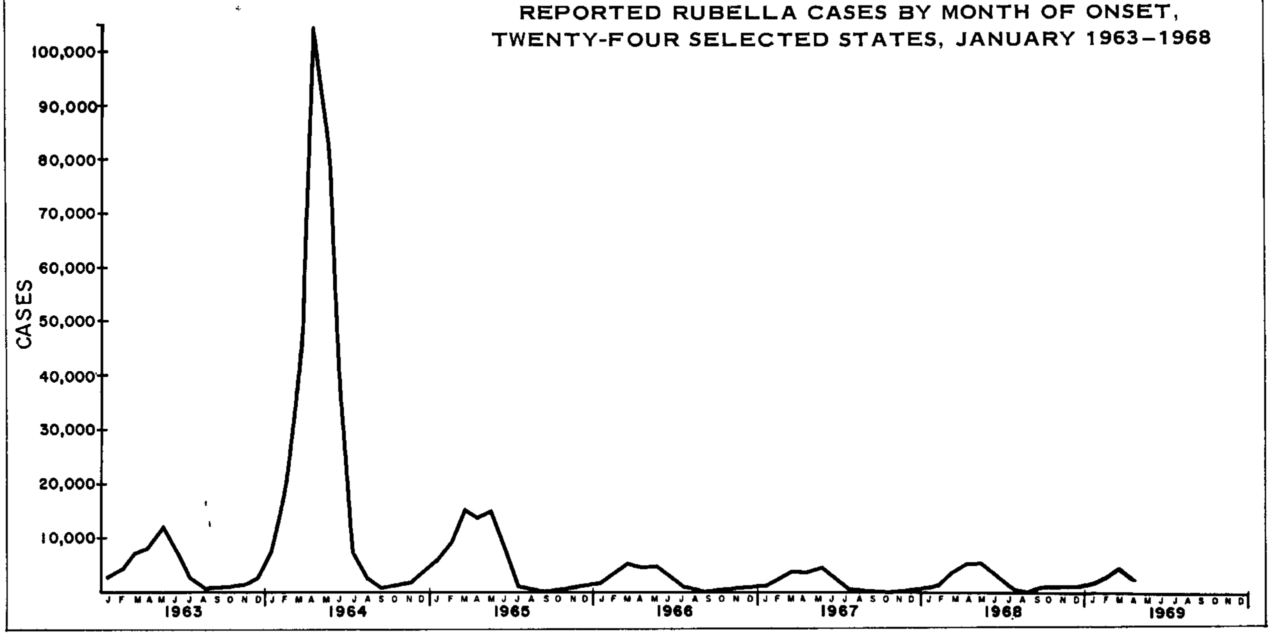


TABLE 1

REPORTED CASES OF RUBELLA BY AGE AND SEX FOR SELECTED AREAS* – 1963-1967

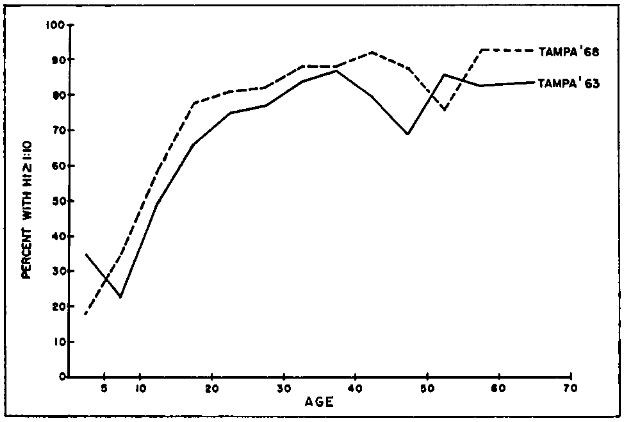
Age	Total			Male			Female		
	Number	Percent	Cum. %	Number	Percent	Cum. %	Number	Percent	Cum. %
0-4	16,373	13.5	13.5	8,218	14.3	14.3	8.155	12.9	12.9
5-9	52,078	43.1	56.6	25,660	44.5	58.8	26,418	41.8	54.7
10-14	28,403	23.5	80.1	13,483	23.4	82.2	14,920	23.6	78.3
15-19	14,527	12.0	92.2	7,446	12.9	95.1	7,081	11.2	89.5
20-39	8,100	6.7	98.9	2,541	4.4	99.5	5,559	8.8	98.3
40+	1,363	1.1	100.0	286	0.5	100.0	1,077	1.7	100.0
Total	120,844			57,634			63,210		

**Massachusetts, Chicago, Ill., Illinois (excluding Chicago), and New York City. New York City reports cases for ages 20-44; therefore, these figures have been adjusted to the 20-39 age group.*

adulthood (Figure 3). A total of 81 percent of persons 20-29 years of age had detectable rubella antibodies in 1968. While the curves depicting percentages of persons with detectable rubella HI antibody by age in 1963 and 1968 have a similar shape, the percentage of persons with rubella antibody was higher for every age group in 1968 than it was in 1963. Similar patterns of detectable

FIGURE 3

RUBELLA HI ANTIBODY BY AGE OF SUBJECT, STRATIFIED RANDOM SURVEYS, TAMPA, FLORIDA MARCH 1963 AND JANUARY 1968



rubella HI antibody by age have been observed in other serosurveys. This pattern of naturally acquired seroimmunity, considered with the age distribution of reported cases of rubella, suggests strongly the important role of the elementary school child in the dissemination of the virus and as a reservoir of rubella.

Approximately 85 to 90 percent of the adult population in the United States is immune to rubella. Such levels of naturally acquired immunity could be achieved only if an average of 3.4 million infections occurred annually. Realizing that the yearly incidence of rubella varies and that extensive subclinical disease occurs, the serology data nevertheless emphasize how under-reported rubella must be for only 100,000 to 400,000 cases to have been reported annually since 1957.

Recommended patterns of vaccine use are based not only upon properties of the vaccine but also upon the epidemiologic characteristics of the disease. Features of rubella noted earlier, i.e., long-term incidence trends, age distribution of reported cases, and seroimmunity patterns, have been important in the framing of current rubella vaccine recommendations. To evaluate vaccine performance adequately and to maintain optimal vaccination levels, surveillance of rubella and congenital rubella syndrome will have to be conducted with vigor.

ADOLF W. KARCHMER, M.D.

See p. 124 for the Recommendation of the PHS Advisory Committee on Immunization Practices on the use of rubella virus vaccine.

CHOLERA

Cholera is an acute intestinal infection caused by *Vibrio cholerae.* The severity of clinical manifestations differs greatly from epidemic to epidemic and from person to person. Asymptomatic infections are common; mild cases may exhibit self-limiting diarrhea; and in the severest form, cholera gravis, the disease is manifested by the sudden onset of profuse watery stools, vomiting, rapid dehydration, and shock, which in untreated cases can cause death within 24 hours.

The etiologic agent, *V. cholerae,* is a gram-negative, curved, rod-shaped bacterium that is actively motile, with a single polar flagellum. Symptoms are caused by a heat labile exotoxin elaborated *in vivo.*

There are two recognized biotypes of *V. cholerae,* the classical and El Tor variants, which cause essentially identical disease. From 1961 through 1966, the El Tor biotype was responsible for a major pandemic that spread from an initial focus in Indonesia as far west as Iraq and as far north as Korea. The classical biotype is responsible for endemic foci on the subcontinent of Asia, although historically, it too has been incriminated in pandemic spread.

Infection is acquired through ingestion of contaminated water or food. It is believed to result from personal contact only in rare instances.

E.J. GANGAROSA, M.D.

See p. 101 for the Recommendation of the PHS Advisory Committee on Immunization Practices on the use of cholera vaccine.

VIRAL HEPATITIS

IMMUNE SERUM GLOBULIN PROPHYLAXIS

In an era when vaccine development has contributed vitally toward eradicating viral diseases such as polio and measles and promises to do the same for mumps and rubella, viral hepatitis is still an important public health problem with no effective active immunologic method of preventing infection. Passive immunization with immune serum globulin (ISG) is the only currently available means of protection against the serious clininal manifestations of hepatitis.

Hepatitis morbidity data have been reported by state health departments to the National Communicable Disease Center since July 1952. Figure 1 shows the incidence of reported cases of hepatitis (infectious and serum) by 4-week periods from July 1952 through May 3, 1969 (18th week 1969). Two peaks in the curve are apparent; the 1953-54 peak was followed by a progressive 5-year decline in incidence, until 1958-59 when the trend took an upward turn. The second peak came 2 years later. The progressive decline in incidence following the 1960-61 peak reversed itself in epidemiologic year* 1966-67, 6 years after the previous peak year. Although this upward trend has continued, its rise is not as marked as the rise that led to the 1960-61 peak. It is not yet possible to predict the occurrence of another peak year in the United States.

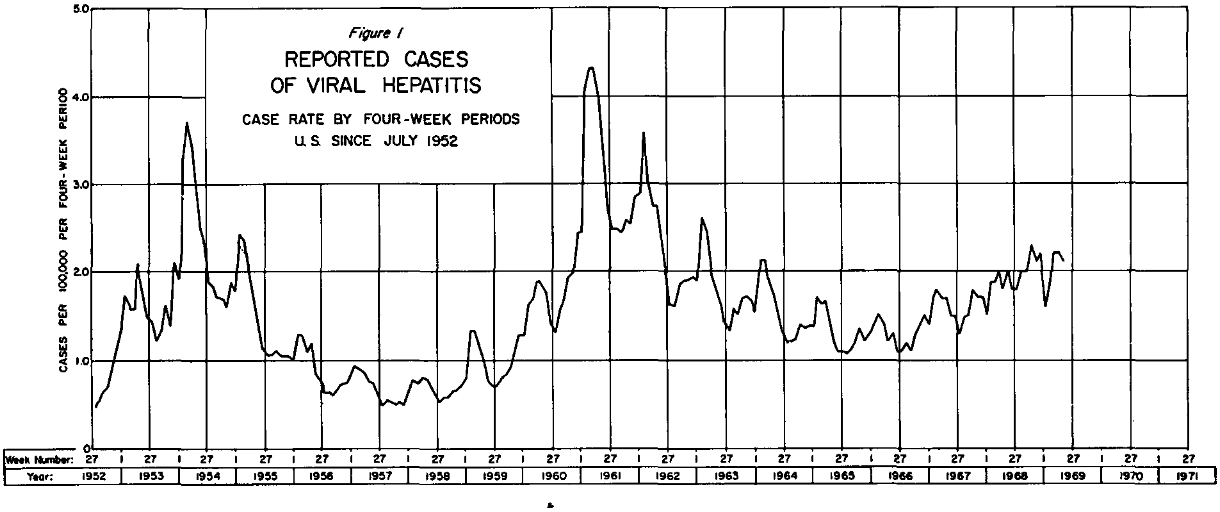
*Hepatitis morbidity data are summarized in terms of an epidemiologic year, which runs from the 27th week of each year through the 26th week of the succeeding year.

INFECTIOUS HEPATITIS

Since 1944, when the first attempt was made to prevent infectious hapatitis by inducing passive immunity, ISG has been recognized as an effective prophylactic agent. ISG produced in the United States is derived from both plasma donations and placental blood. In order to obtain the "immunologic experience" of large populations, manufacturers are required to include plasma or blood from 1,000 or more donors. U.S. preparations are processed by the cold alcohol technique of Cohn and contain 165 ± 1.5 grams of protein per 100 ml, of which at least 90 percent must be gamma globulin. Most of the globulin in commercial ISG is of the IgG type, with small amounts of IgA and IgM also present.

ISG gives passive protection against infectious hepatitis presumably because it contains antibody against the infectious hepatitis virus. Moreover, it appears that only a very small amount of antibody is necessary to afford this protection. Furthermore, ISG derived from a population in one part of the world seems to protect against infectious hepatitis that occurs in other distant areas.

It is not yet possible to measure the infectious hepatitis neutralizing antibody content of ISG. The antibody content of any preparation depends on the immune status of the donor population. Since relatively small doses of commercially prepared ISG confer protection,



it is presumed that the population's experience with hepatitis is general and immunity long lasting. However, not all globulin lots are equivalent in their ability to protect against hepatitis. In one study comparing the protective effect of two different lots of ISG, the lower efficacy of one lot was related to lower levels of measurable antibodies to measles, rubella, and the enteroviruses and a greater amount of fragmentation of the globulin contained in that preparation.

ISG has a modifying rather than a truly prophylactic effect on infectious hepatitis. When ISG is given in adequate doses before exposure, the incidence of infection can be expected to be about the same as among uninoculated controls; however, in those who have been given ISG, cases tend to be mild or subclinical, probably undetectable without specific laboratory tests for liver function. Such infection may produce long active immunity. When globulin is used under these conditions it effects passive-active immunity.

It has been demonstrated that persons with inapparent infection, either with or without the prior protection of ISG, can excrete the virus and thus serve as a source of infection for others. It has been suggested that using ISG to modify what might otherwise be a clinically apparent infection permits infected persons to remain in contact with others in the community and thus promotes the spread of infectious hepatitis. However, a large study in Eastern Europe demonstrated that ISG administered to half a school population lowered the incidence of infectious hepatitis, not only in the recipients, but also in the uninoculated. For this reason it is conceivable that ISG may alter the extent and/or duration of virus excretion.

The sooner ISG is given after known exposure the more likely it is to have a protective effect. It is thought to be effective when given as late as 4 weeks after known exposure. In household contacts, because exposure to the index case is continuous and secondary unrecognized inapparent infections may occur, globulin given as late as 6 weeks after the index case may protect persons not already manifesting the disease.

ISG also has protective value when given to individuals *prior* to exposure to infectious hepatitis. Its use for this purpose, particularly for military personnel and Americans going abroad, has increased greatly in recent years. The duration of protection and time schedule for subsequent doses are a function of the half-life of the globulin preparation. The mean half-life of ISG is approximately 25 days. Increasing the dose of ISG above a certain critical level seems to confer longer, not greater, protection. Epidemiologic evidence indicates that at the dosage levels recommended by the Public Health Service for travelers to highly endemic areas, passive immunity begins to wane after 5-6 months. For this reason persons at constant risk should have their dose repeated at 5-6 month intervals.

It is worth noting that immune serum globulin prepared and recommended for use with certain live measles vaccines is perfectly adequate for use in protecting against infectious hepatitis. The only difference between measles immune globulin and ISG is that the former must have a high titer measles antibody. There is no theoretical reason why this should compromise its ability to confer protection against infectious hepatitis. With increasing use of live measles vaccines that do not require simultaneous administration of measles immune globulin, this globulin preparation can be made available for passive immunization against infectious hepatitis.

SERUM HEPATITIS

While ISG is known to protect against the clinical manifestations of *infectious hepatitis,* its efficacy against *serum hepatitis* is not clear. The increasing use of blood transfusions and their icterogenic products promises to increase the incidence of transfusion-associated hepatitis; however, since the efficacy of ISG in protecting against post-transfusion hepatitis has not been clearly demonstrated, its use for this disease is not recommended.

The use of ISG during the past decade has rapidly increased, and the public, as well as physicians, has become aware of its efficacy, availability, and safety. The indications for the use of ISG and its dosage schedule warrant careful reflections. These considerations have been put forth by the PHS Advisory Committee on Immunization Practices as recommendations for the use of ISG for prevention of viral hepatitis.

KENNETH R. RATZAN, M.D.

See p. 106 for the Recommendation of the PHS Advisory Committee on Immunization Practices on the use of immune serum globulin for prevention of viral hepatitis (infectious hepatitis and transfusion-associated hepatitis).

INFLUENZA

Influenza A and influenza B viruses both cause epidemics. Both virus types have demonstrated antigenic variation; over a period of time the prevalent strains gradually become less like the strain that caused the preceding epidemic and led to the production of protective antibody. The variant strains thus become increasingly more capable of causing new waves of clinical illness. Variations in the type A viruses have been observed more frequently than variations in the type B viruses, and epidemiologists have observed a generally shorter interval between type A epidemics (2 or 3 years) than between type B epidemics (3 to 6 years).

The syndrome produced by influenza viruses consists of fever, malaise, coryza, cough, myalgia, and headache. There are few, if any, gastrointestinal symptoms. Clinically there is nothing to differentiate infections caused by the different influenza types. Influenza-like illness, moreover, may be caused by several other families of viruses, including the adenoviruses, Coxsackie viruses, and ECHO viruses. Thus, an accurate diagnosis of influenza-like illness requires laboratory confirmation.

In contrast to the difficulty in diagnosing individual cases of influenza, it is usually quite easy to recognize epidemics of influenza. They are heralded by abnormal increases in absenteeism in schools and industries, by reports of multiple clinical cases in the same epidemiologic unit (family, school, or industry), or by observation by a single clinician or group of clinicians of an unusally large number of cases of febrile respiratory illness. In general, epidemics caused by type A strains tend to be more widespread and affect a broader age range; epidemics caused by type B strains tend to be more localized and preferentially affect young school-age children.

Although influenza is generally a benign disease, its importance (especially with relation to the A strains) is that it can disrupt community functions by producing illness in many persons in a very short time period. Furthermore, although individual illnesses are usually mild, complications such as pneumonia and even death may occur. The number of deaths in excess of normal that accompany epidemics of influenza is used as a measurement of severity and extensiveness. Numerically, the greatest proportion of the additional or excess deaths occurring in association with an influenza epidemic are of persons who are chronically ill, especially those with cardiovascular or respiratory disease.

In July 1968, a major influenza epidemic was first detected in Hong Kong. Laboratory tests revealed that the type A virus responsible for this epidemic was only distantly related to the previous A2 or Asian strains. The new Hong Kong virus rapidly made its way through the Philippines, Taiwan, and Singapore. Introductions of the Hong Kong strains into the United States were documented in early September, and they occurred throughout the fall with an occasional small outbreak in military populations. Outbreaks in the civilian population began in mid-October, gained momentum in November, were widespread in December, peaked at the first of the year, and then fell off in January and February. All 50 states reported one or more outbreaks of influenza in association with this epidemic.

In 44 states, outbreaks were widespread. In December and January, there was a single sharp wave of excess mortality throughout the entire United States (Figure 1). The excess mortality was as great as that produced by the two waves combined in the pandemic of 1957-58.

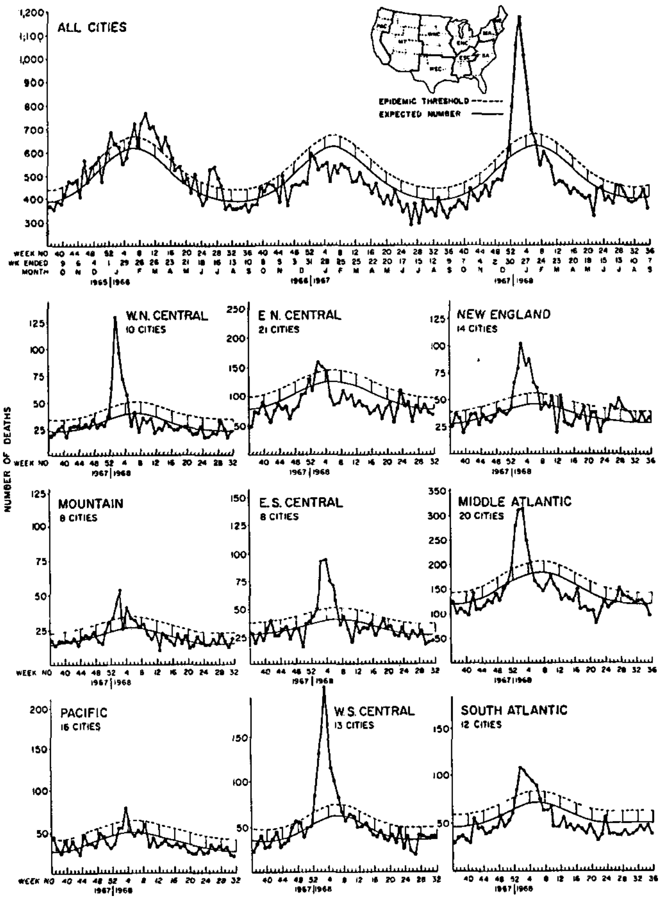
In December 1968, an isolated outbreak of influenza B was reported in the State of Washington. In the last week of January four more states reported outbreaks, and in February many more states reported influenza B activity. In all, 36 states had one or more cases of influenza B, and 21 states had one or more outbreaks. Widespread activity was reported in a band throughout the central United States ranging from Minnesota and Wisconsin down to the northern half of Texas. Notably, virtually no influenza B occurred in New England or New York.

The occurrence of influenza B was well within the established pattern of epidemics every 3 to 6 years. No influenza B outbreaks were recognized in the United States in the 1967-68 season, and there had been only a little influenza B activity in 1966-67. In contrast, the epidemic of A2/Hong Kong influenza occurred only one year after a widespread Asian influenza outbreak in the eastern and central United States: in 1967-68, 45 states reported one or more outbreaks in influenza-like illness. In 1967-68, there was one sharp wave of excess mortality, only about one-third the magnitude of the wave in 1968-69. This is the only documented instance of two major A group epidemics in successive seasons.

Much about the epidemiology of influenza is unexplained. There is no convincing evidence of the location

FIGURE 1

PNEUMONIA-INFLUENZA DEATHS IN 122 UNITED STATES CITIES



The expected number of deaths per week is calculated on the basis of the previous 5 years' reports. They are shown as the regular wavy solid line. The dotted line just above the expected curve is the "epidemic threshold," a statistical measurement which is helpful in determining when epidemic levels of death are occurring.

Each of the 122 cities cooperating in the reporting system tabulates and reports those deaths within their city limits which were listed as due to pneumonia or influenza on the death certificate. In addition, they report the total number of deaths in the city and deaths of persons age 65 and over and of persons less than age 1.

During influenza epidemics, particularly those caused by type A viruses, excess mortality is used as a measure of severity and extensiveness of the disease.

In 1967-68 and 1968-69 major rises in mortality were recorded in the United States. Both peaks were associated with type A influenza epidemics (see text). In 1967-68 all divisions except the Pacific and in 1968-69 all 9 geographic divisions of the United States recorded excess mortality.

or nature of the virus between epidemics, just as there is no explanation of why epidemics should be sharper or more severe in one place than in another. Until more is known about the characteristics of influenza viruses, it will be extremely difficult to devise adequate control measures. Control in this country is based almost exclusively on the use of killed vaccines. It has thus far been impossible to produce them on short notice and in sufficiently large quantities. Moreover, they are only marginally effective in preventing clinical disease.

STEPHEN C. SCHOENBAUM, M.D.

See p. 109 for the Recommendation of the PHS Advisory Committee on Immunization Practices on the use of influenza vaccine—1969-1970.

PLAGUE

Plague, the cause of the Black Death, must be viewed not as a historical phenomenon but as an ever present threat not only in the United States but throughout the world.

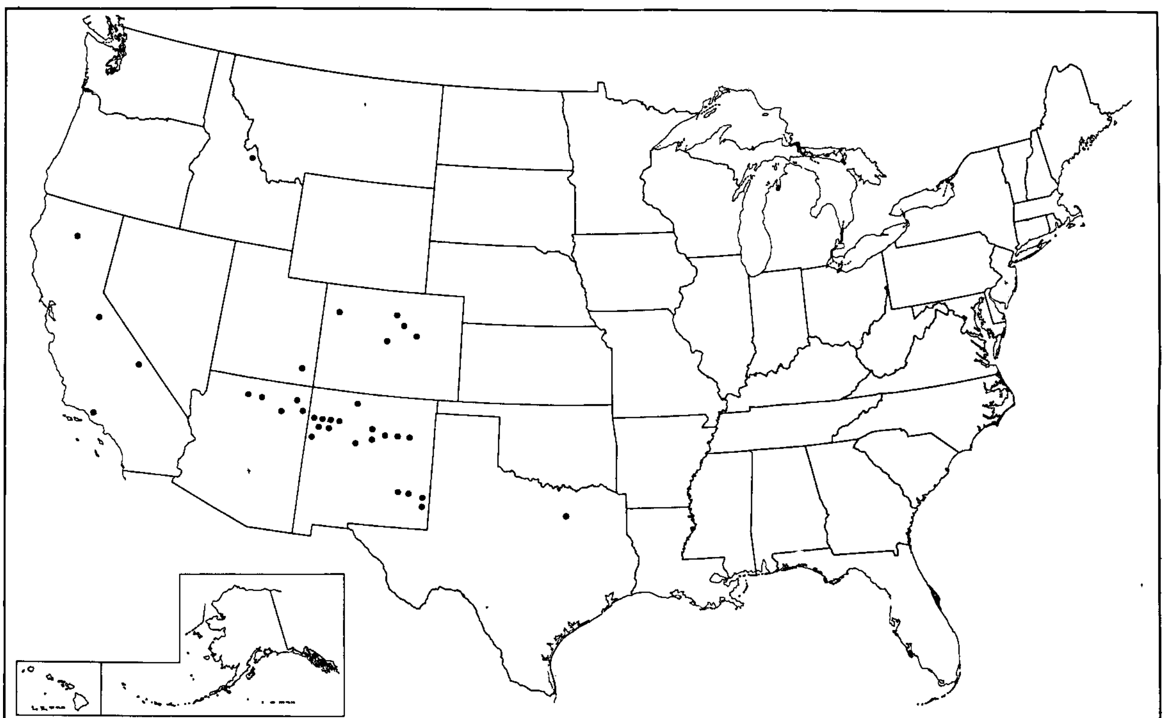
The disease was first recognized in North America in 1900 when a Chinese resident of San Francisco died and was found to be infected with *Pasteurella pestis.* It is believed that the first epidemic of plague in San Francisco began with this case and ended in 1904. The disease was probably introduced by infected rats escaping from a ship originating in the Orient. Between 1900 and 1925 there were more than 400 cases of human plague in the United States during and immediately after urban rat epizootics. Although no human cases have been associated with rat epizootics in the United States since 1925, plague-infected rats have been found in Tacoma, Washington, and San Francisco as recently as 1963. Today, murine plague is a major problem in many countries, particularly those of Southeast Asia; therefore the possibility of importation of plague-infected rodents by ship or airplane has necessitated increased surveillance by quarantine officials at ports of entry into the United States.

Wild rodent plague foci are known to exist on nearly every continent of the world. *P. pestis* has been isolated from at least 18 genera of North American mammals or their fleas in 15 of the western United States. In these wild animals the disease is referred to as sylvatic plague. Four groups of rodents mainly are involved with sylvatic plague in the United States: ground squirrels, woodrats, prairie dogs, and voles.

On the average, two cases of bubonic plague per year have occurred in the United States since 1925. All have been associated with a wild rodent as source of infection, and all but one of the recent cases, in Denver, Colorado, have been contracted in a rural setting (Figure 1). Transfer of the disease from animal to man has occurred directly by the person's handling plague-

FIGURE 1

HUMAN PLAGUE CASES BY COUNTIES, 1950–1968



infected animals or by transfer of the infection through a flea vector from wild rodents to man or to domestic and peridomestic animals and then to man. The last mode of spread is the likely route in the outbreak of plague in Denver in the summer of 1968. Apparent transfer of plague from a wild rodent source to the peridomestic tree squirrel, *Sciurus niger*, resulted in an epizootic of plague in this species of squirrel within the city of Denver. The patient contracted bubonic plague after contact with a dead squirrel near his home.

Plague control is based on the epidemiologic factors involved. When commensal rats and their fleas are involved in a human outbreak, the first control measure is to use insecticides, followed by a program of rat control. When wild rodent plague foci are involved, a combined operation of flea and rodent control is instituted.

Streptomycin and tetracycline are the highly effective antibiotics of choice for both bubonic and pneumonic plague. Other antibacterial agents effective against plague are sulfadiazine and chloramphenicol.

Immunization with plague vaccines, in use since the late 19th century, is known to reduce the incidence and severity of disease, but their effectiveness has never been precisely determined. The plague vaccine licensed for use in the United States is prepared from *P. pestis* grown in artificial media, inactivated with formaldehyde, and preserved in 0.5 percent phenol. The Public Health Service recommends selective immunization of persons traveling to Vietnam, Cambodia, and Laos and all persons whose work brings them into contact with wild rodents in plague-enzootic areas.

BURTON P. GOLUB, M.D.

See p. 116 for the Recommendation of the PHS Advisory Committee on Immunization Practices on the use of plague vaccine.

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 18th and 19th centuries 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 in 1946-1950 to one or two cases per year in 1963-1967.

Rabies in domestic animals has also diminished. In 1946, there were more than 8,000 reported cases of rabies in dogs; in 1967 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. Wild animals now 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 1967

Two human rabies deaths occurred in the United States in 1967, but exposure in both cases occurred in Africa. The first case was in a 58-year-old woman who was bitten on May 31, 1967, by a stray dog in Guinea. Despite a treatment regimen of 21 daily doses of duck embryo vaccine (no hyperimmune serum), she died in New York 56 days after exposure. The second case was in a 9-year-old boy who was bitten by a neighbor's dog in May 1967 while visiting in Cairo, Egypt. He received no specific antirabies treatment and died after arrival in Portland, Oregon, approximately 67 days after exposure.

A total of 4,609 laboratory-confirmed cases of animal rabies were reported in the United States in 1967; this is an approximate 10 percent increase over the number of cases in 1966. The total includes 89 cases from Guam, which had not previously reported any rabies. Tennessee reported the greatest number of cases (559), while Connecticut, Delaware, and Hawaii reported no cases. Wild animals accounted for 70 percent of the rabies in animals, with skunks and foxes being the most frequently infected species.

HUMAN RABIES

Once clinically apparent, essentially all cases of rabies are fatal. In the years 1946 through 1967, 223 persons died of rabies in the United States. The number of human deaths from rabies declined from 34 in 1946 to only one or two per year for the past six years, 1962 through 1967 (Figure 1). This decline probably resulted from reduction – through immunization – of the incidence of rabies in dogs.

Of the 129 persons who died of rabies in the 18-year period from 1950, more than half were less than 15 years of age; 15 percent were less than 5 (Figure 2). Seventy percent of deaths occurred in males, and proportionately, nearly 60 percent of the males who died were boys less than 15 years old. Rabies deaths in females occurred in somewhat older individuals – 63 percent were over 15 years of age. Among adults, death occurred at all ages with a slight predominance between ages 40 and 45.

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.

ANIMAL RABIES

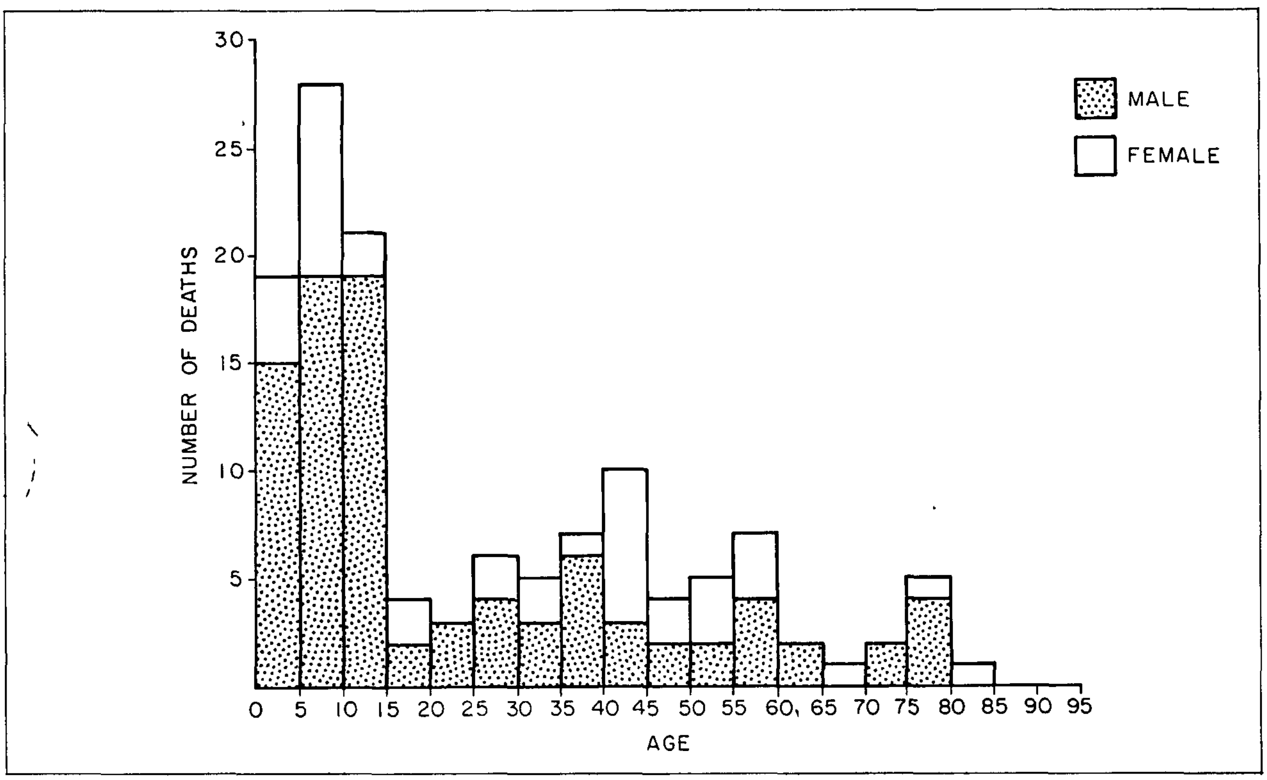
At least one million animal bites occur in the United States each year. Of all animal bites, approximately 3 percent (30,000) are considered possible rabies exposures calling for specific rabies prophylaxis. Approximately one-third of the bites that prompt antirabies treatment are inflicted by wild animals,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

FIGURE 1

NUMBER OF HUMAN RABIES DEATHS, UNITED STATES, 1946–1967

FIGURE 2

HUMAN RABIES DEATHS BY AGE AND SEX, UNITED STATES, 1950–1967



cases of rabies in animals declined from 8,837 in 1953 to 4,609 in 1967 (Figure 3). Since 1960 more cases of rabies have been confirmed in wildlife each year than in domestic animals. The rate of increase of rabies in wildlife has been greatest for skunks and bats.

Rabies in domestic animals diminished from 7,344 cases in 1953 to only 1,396 in 1967, thus accounting heavily for the overall decrease of rabies in animals. The four states along the Mexican Border reported 31 percent of all dog rabies in the United States. Three other states (Kentucky, Missouri, and Tennessee) reported an additional 31 percent of the rabies in dogs (Figure 4).

Thirty-four percent of all the 1967 rabies cases in animals were in skunks. California reported 196 cases, Texas 158 cases, and Illinois 145 cases (Figure 5).

Foxes accounted for 21 percent of all the 1967 rabies cases in animals. Tennessee reported 368 cases of fox rabies, Virginia 147 cases, and Kentucky 113 cases. The presence of livestock rabies generally parallels the existence of wildlife rabies, particularly in foxes and skunks, in the same area.

A rabid bat was identified in the United States for the

FIGURE 3

CASES OF RABIES IN WILD AND DOMESTIC ANIMALS, 1953–1968

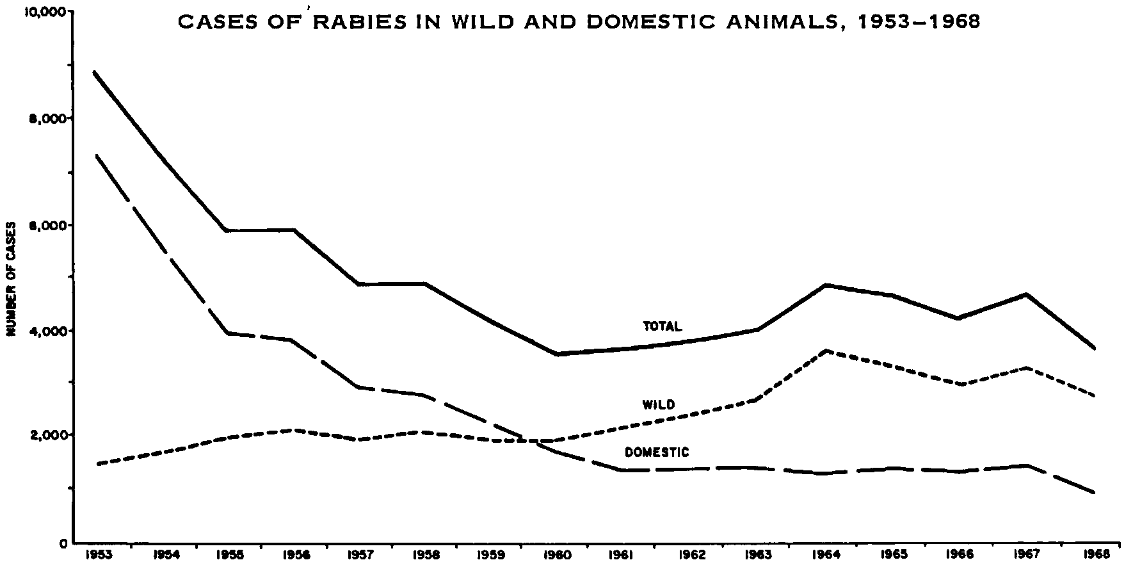


FIGURE 4

COUNTIES REPORTING ANIMAL RABIES–1968

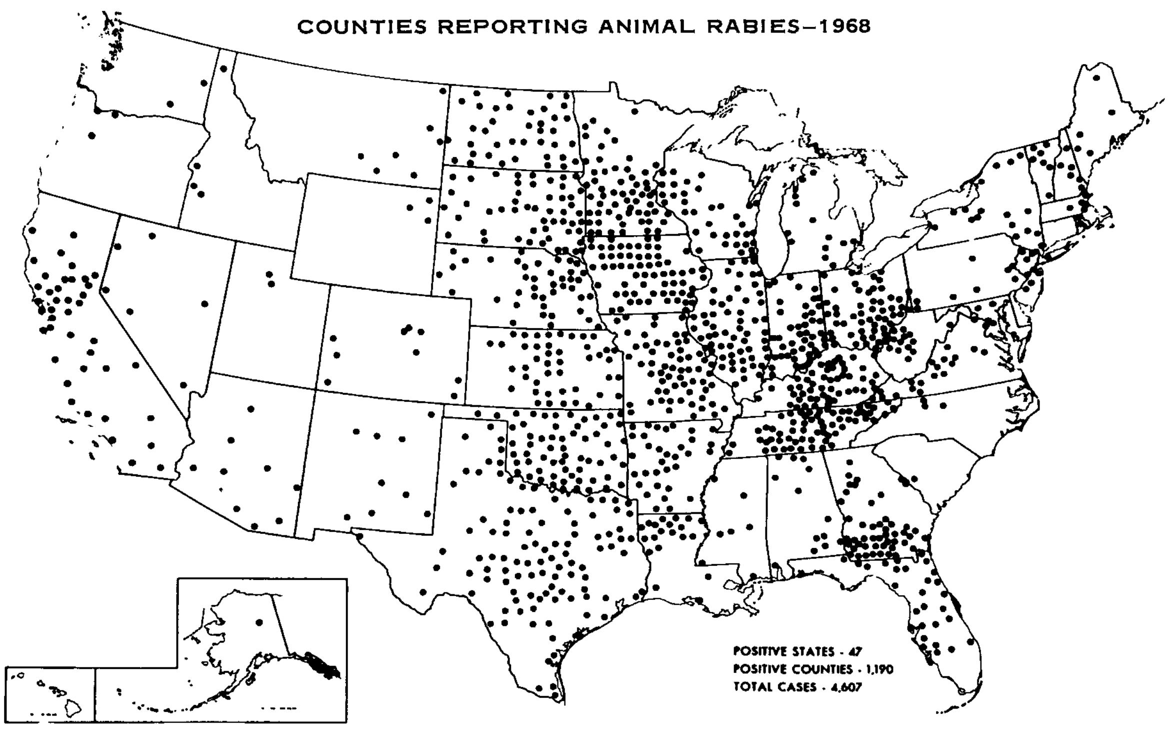


FIGURE 5

CASES OF RABIES IN TRADITIONAL AND EMERGING WILDLIFE HOSTS

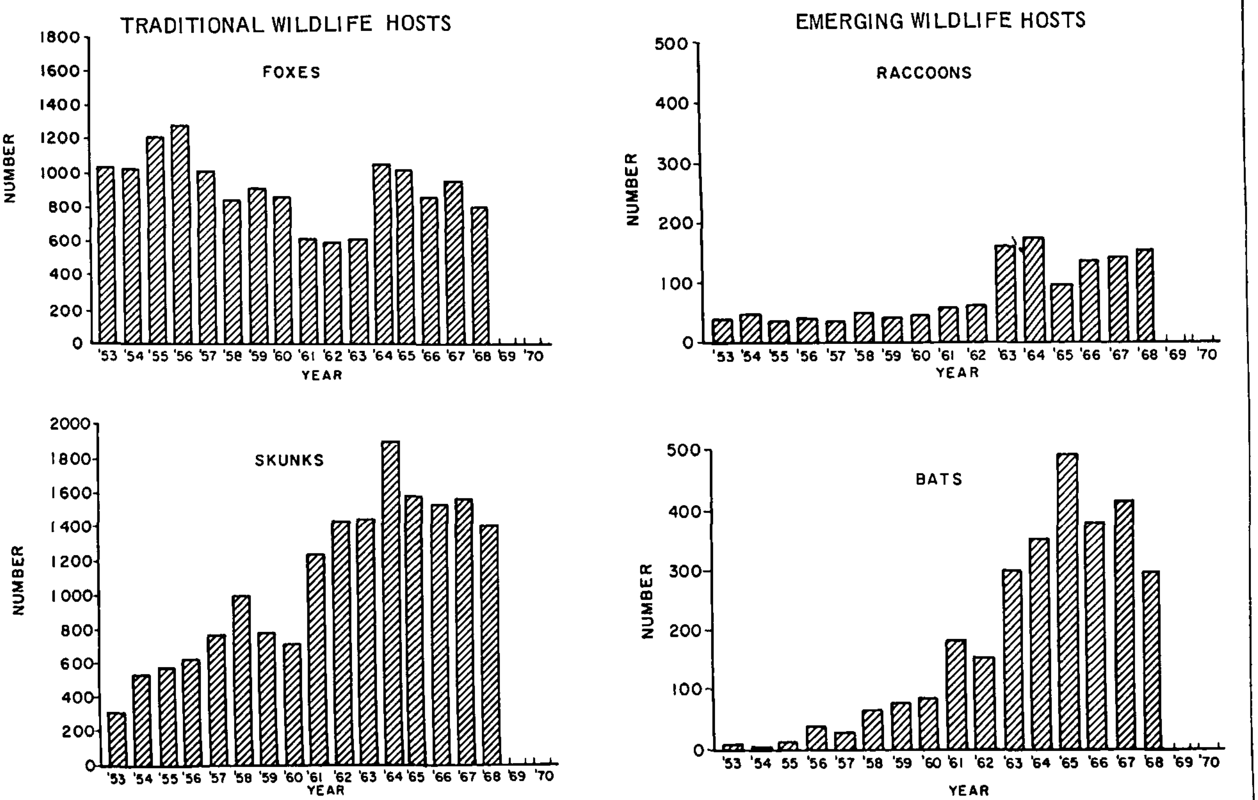


TABLE 1

RABIES VACCINES – UNITED STATES, 1962-1967
Net Doses (Thousands) Distributed Annually

VACCINE	1962*	1963	1964	1965	1966	1967
NTV	41	159	84	83	83	85
DEV	191	343	456	461	887	481

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

Biologics Surveillance, NCDC

first time 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. Only six human rabies deaths have been attributed to exposure to rabid bats in the United States. In 1967, 414 rabid bats were identified. Texas reported 54 and California 41 rabid bats. Rabid bats were reported from all but six of the states.

Rabies in raccoons has been most frequently reported from Georgia and Florida. Rabid raccoons are seldom recognized in other states.

RABIES VACCINE

Nervous tissue antirabies vaccine (NTV) was the only type available in the United States until 1957, at which time duck embryo vaccine (DEV) was licensed. Since then, the preference for DEV has increased annually. In 1967, 85 percent of the commercially produced antirabies vaccine distributed for use in the United States was DEV (Table 1). During the period 1962-1967, approximately 425,000 doses of rabies vaccine were used each year by civilian physicians. Estimating that an average of 14 doses were given to each person treated, approximately 30,000 people received post-exposure antirabies prophylaxis annually.

R.KEITH SIKES, D.V.M.

See p. 120 for the Recommendation of the PHS Advisory Committee on Immunization Practices on the use of rabies prophylaxis.

SMALLPOX

Vaccinia virus was the first agent to be used widely for human immunization, and Jenner's term *Variola vaccinae* (smallpox of the cow) was the basis of the term "vaccination." In 1800, 2 years after Jenner published his initial report, 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 President 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 outbreak of smallpox occurred in 1946, 1947, and 1949. It is probable 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 – WORLDWIDE

The 20-year trend of worldwide smallpox 1950-1969 has been downward (Figure 1). This is particularly meaningful in light of the increase in world population and the probable improvement in disease reporting. Smallpox reports for the first 6 months of 1969 indicate that it will be the lowest year on record. The decline is attributed to a successful program in West and Central Africa plus eradication programs in the majority of smallpox endemic countries. While the general trend of smallpox has been downward, intense surveillance must be maintained in all countries to prevent its reestablishment.

The smallpox reservoir has diminished considerably since 1955 (Figure 2). In South America in 1968, only Brazil remained as an endemic country, compared with eight countries in 1955. Since 1955 Africa has become free of smallpox north of the Sahara, and in 1969 West Africa is becoming smallpox free. Major foci remain in East and South Africa. Since 1955 many countries of the Middle East and Southeast Asia have become free of smallpox, leaving Afghanistan, Pakistan, India, and Indonesia as the only endemic countries in Asia.

In 1968 a total of 73,985 cases of smallpox were reported to the World Health Organization; 59,233 from Asia, 3,812 from South America, 5,527 from East and South Africa, 5,411 from West and Central Africa, and 2 from Europe. The development of many national smallpox eradication programs, the concerted efforts of the World Health Organization, and increase in bilateral aid particularly from Russia and the United States, the use of heat stable lyophilized smallpox vaccine, and innovations in both delivery technique and eradication strategy make the goal of a smallpox-free world attainable in the 1970's.

Until a global smallpox-free state is achieved, increased international travel provides an opportunity for reintroduction of smallpox into smallpox-free areas. A number of European countries, smallpox-free for some years, have experienced limited smallpox epidemics in the last decade. They demonstrated the now recognized pattern of spread from an unsuspected initial case to numerous patients and staff members of the medical facility in which the index patient sought treatment. Important in the transmission of smallpox was the poor immunization status of the most exposed groups in hospitals.

FIGURE 1

WORLDWIDE REPORTED SMALLPOX CASES 1950–1969*

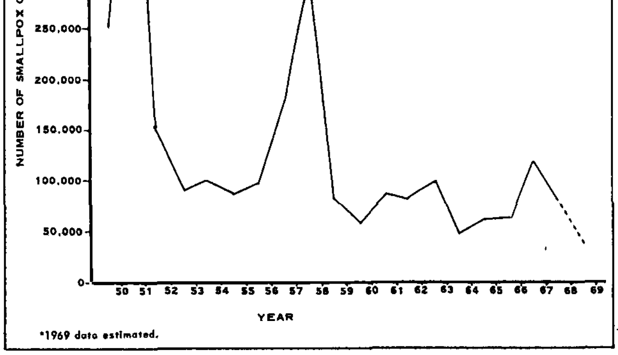
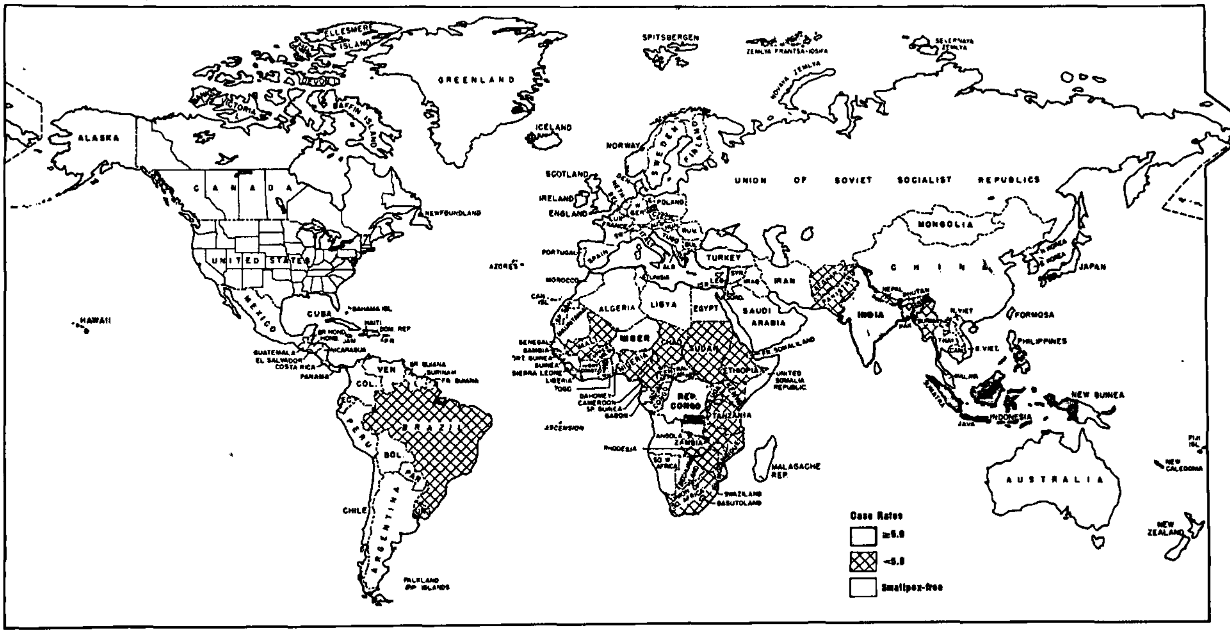


FIGURE 2

SMALLPOX CASE RATES PER 100,000 POPULATION, 1968



SMALLPOX – WEST AND CENTRAL AFRICA

A regional smallpox eradication program involving 19 countries of West and Central Africa began in 1966. Commodities and technical advisors are provided by USAID and the U. S. Public Health Service with local costs and program administration provided by participating countries.

The use of freeze-dried vaccine has eliminated the age-old problem of vaccine's becoming impotent in the tropics. When combined with the use of jet injectors, which have reduced vaccinator variability, take-rates of higher than 99 percent in primary vaccinees are routine. In addition, heavy emphasis has been placed on surveillance, control of smallpox outbreaks, and assessment of program results. Between March 1967 and May 1969, over 81 million people were vaccinated in a total population estimated to be 115 million.

Smallpox reports had fallen to less than 1 percent of the 1960-1967 monthly average by May 1969, and total interruption of transmission is expected in 1969 (Figure 3). Smallpox eradication is not only a feasible concept but achievable in a short period of time. These results provide a stimulus to eradication efforts in other countries.

SMALLPOX – UNITED STATES

Smallpox Patterns

The last year of extensive smallpox outbreaks in the United States was 1930. During the 1920's and 1930's, the case fatality ratio was approximately 1 percent.

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 had not been immunized against the disease.

Small numbers of smallpox cases were officially reported in the late 1940's and early 1950's (Figure 4). 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, 1968*

In 1968, an estimated 4,971,000 of 13,555,000 smallpox vaccinations were primary vaccinations, 8,552,000 were revaccinations, and 32,000 were administered to individuals with unknown prior vaccination history. Although 7.0 percent of the population in 1968 had been vaccinated within the preceding year, many of the vaccinations were given to travelers, military personnel, and others who are revaccinated frequently.

Comparing the 1968 immunization survey data with the 1964 immunization survey data, a slightly higher proportion of preschool children had been vaccinated

*Source: U.S. Immunization Survey, 1967, 1968, Department of Health, Education and Welfare, Public Health Service, HSMHA, NCDC, December 1968

FIGURE 3

REPORTED SMALLPOX CASES BY MONTH, 1960–1967 AVERAGE, 1968 AND 1969, WEST AND CENTRAL AFRICA

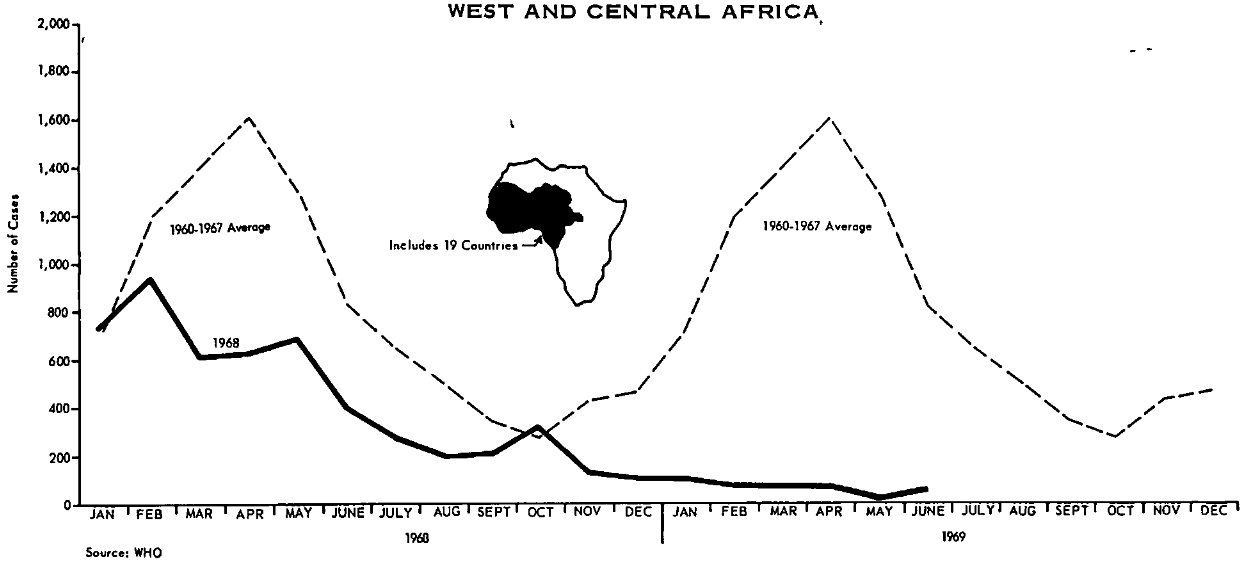
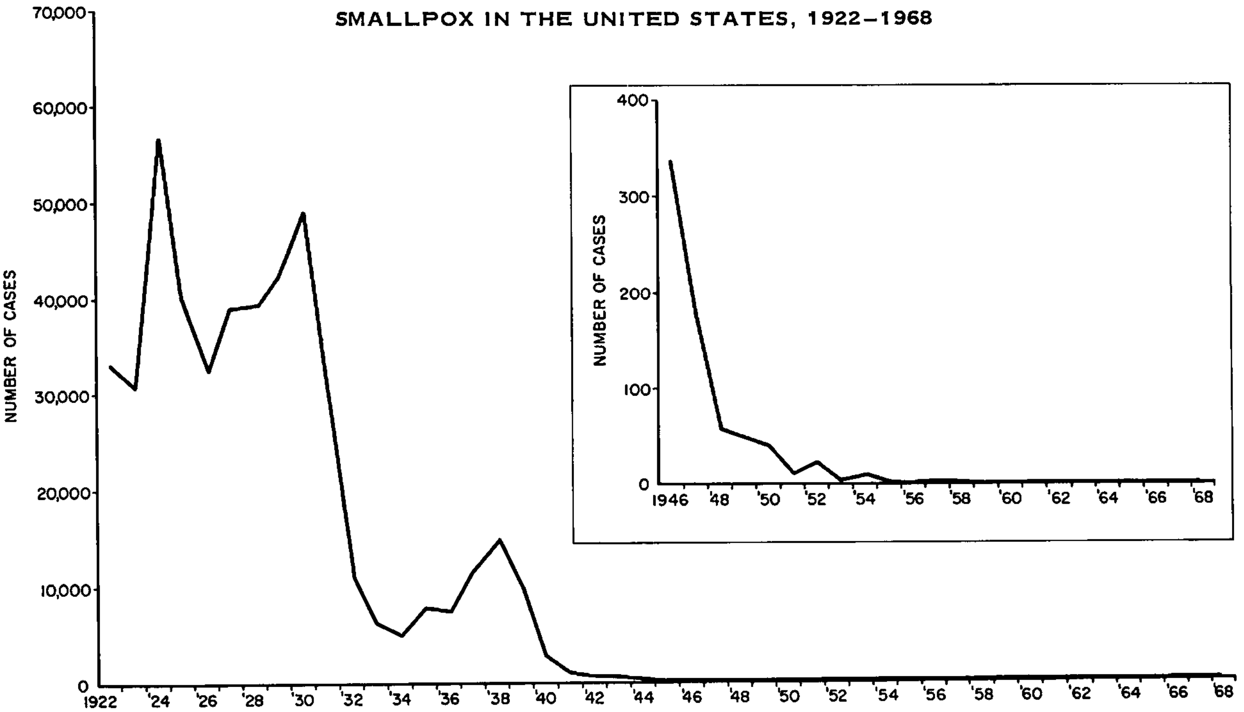


FIGURE 4

SMALLPOX IN THE UNITED STATES, 1922–1968

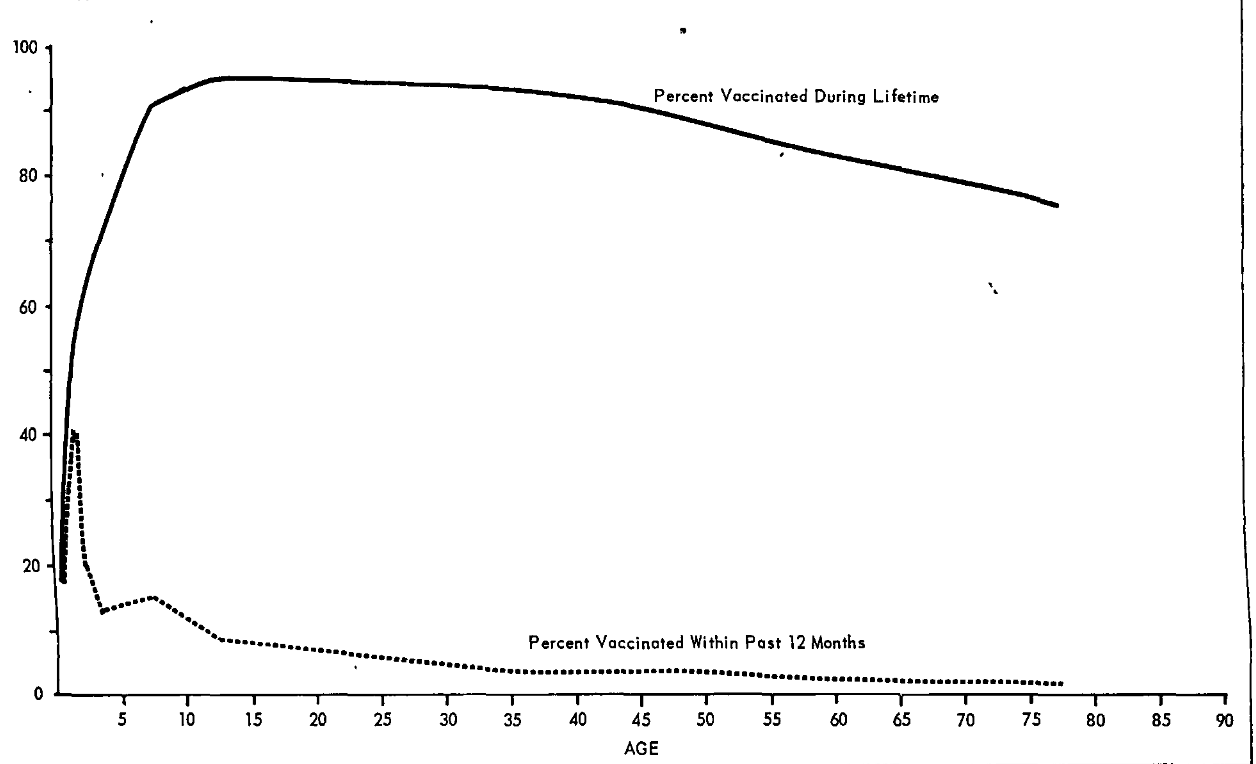


against smallpox in 1968, i.e., 65.9 percent versus 60.9 percent in 1964. The 1968 data were consistently higher for each year of age for these preschool children.

Survey data (1968) indicate geographic differences in vaccination rates. More than 90 percent of the residents of the New England states, the Atlantic states, and the Western states (Mountain and Pacific regions) had been vaccinated, in contrast to approximately 80 percent of those in the West North Central, East South Central, and West South Central states.

Approximately 18 percent of children less than 1 year of age received primary vaccination in 1968. Another 39 percent received primary vaccination in the second year of life. Some 66 percent of children had been vaccinated by the time they reached the age of 5. In the early school years (ages 5-9), vaccination programs brought the proportion vaccinated to 92 percent (Figure 5). Only three percent of those over age 30 are vaccinated annually, largely for international travel.

FIGURE 5
SMALLPOX VACCINATION STATUS, UNITED STATES, 1968



Smallpox Vaccine, United States, 1962-1968

Annual Distribution of Smallpox Vaccine

Year	Millions of Doses
1962*	8.8
1963	14.7
1964	18.1
1965	19.4
1966	17.1
1967	19.8
1968	21.8

*July-December Biologics Surveillance Program began July 1962.

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, particularly during 1967-1968.

The U. S. Immunization Survey estimates of the total numbers of smallpox vaccinations given in 1963 and 1964 correspond with the total number of doses of vaccine distributed in the same years. However, in 1968 the large discrepancy between these two values is a result of increased military use of smallpox vaccine.

Current Smallpox Vaccination Policy

Most medical and public health authorities recommend routine vaccination in the United States of children in the second year of life. Recently this policy has been questioned, and consideration has been given to dropping smallpox vaccination from the list of routine childhood immunizations. This question has not been fully resolved.

Smallpox vaccine has a higher rate of serious complications than any of the other immunizing agents in common use. The death rate may exceed one per million primary vaccinations. Since the United States has not had a documented importation of smallpox since 1949, the necessity for requiring vaccination is questioned. The most potent argument in favor of continuing to vaccinate persons in childhood is the fact that primary vaccination probably carries a higher risk for adults than for children. If smallpox remains endemic in much of the world, and if a high proportion of adults continue to require vaccination for travel, military induction, or occupational requirements, then continued childhood vaccination may be advisable.

Final resolution of the vaccination controversy awaits better data on the risks of vaccination, smallpox importation, and spread of the disease if it is imported, and on the numbers of adult vaccinations that will be necessary in the future.

SMALLPOX ERADICATION PROGRAM

See p. 126 for the Recommendation of the PHS Advisory Committee on Immunization Practices on the use of smallpox vaccine.

TUBERCULOSIS

As far as can be determined, tuberculosis is as old as civilization. *Mycobacterium tuberculosis* infection has been called by many names, among them scrofula, phthisis, and consumption; the last, because it causes in its late stages chronic wasting of the body. Clearer understanding of the disease *tuberculosis* brought the realization that many cases reach far advanced stages without exhibiting consumption or emaciation. Indeed, even in its advanced stages, tuberculosis is often asymptomatic and unsuspected.

Hippocrates was the first to offer a clear description of tuberculosis. Isocrates in the 5th century B.C. believed it to be transmissible from person to person, and the idea became prevalent that an individual could acquire tuberculosis from someone else, or from something that had been in contact with a "consumptive." Stringent laws were passed to isolate patients and to destroy everything that could have been contaminated by them. Since no tangible evidence of a means of transmission could be demonstrated, interest declined.

With Koch's discovery of the tubercle bacillus in 1882, interest in the communicability of tuberculosis was again awakened, but not until the fifth decade of this century, some 70 years later, was the route of transmission by droplet nuclei reasonably well understood. At that time, the tuberculosis case rate in the United States was around 90 per 100,000 population and the death rate, 35 per 100,000.

The steady reduction in tuberculosis morbidity and mortality since the beginning of this century has been attributed to several factors. Probably the most important has been public awareness of the disease and removal of patients with infectious disease from the community in order to provide isolation and sanatorium treatment. Improved social conditions for most (but not all) residents of the United States, development of techniques for radiographic screening of large segments of the population, and public education to accept and demand these services have also been major factors.

Scientific advances during the past decade have provided the means to accelerate the decline of tuberculosis in the United States. Antituberculosis drugs have proven effective for preventing tuberculosis as well as for treating active disease. Tuberculin skin test interpretation has been refined. In addition, the pathogenesis of tuberculosis is better understood, making possible a more rational approach to the infectiousness of the disease.

TUBERCULOSIS IN 1968

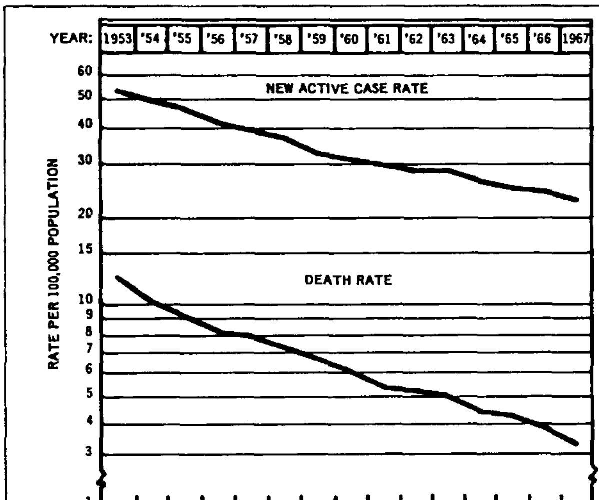
In 1968 state health departments reported 42,758 new active tuberculosis cases (provisional data), a 6.3 percent decline from the 45,647 new cases recorded for the United States in 1967. The new-case rate for the country is provisionally 21.4 per 100,000 population in 1968, compared with a rate of 23.1 in 1967. In each of the last 15 years except 1963, tuberculosis morbidity rates decreased each year; the average annual decrease was 4.2 percent 1953-1967 (Figure 1).

Mortality has been declining more rapidly than morbidity, as is evident in Figure 1 from the steeper slope of the curve for deaths than for cases. This may reflect, in part, the increasing shift of tuberculosis to older segments of the population, who die from other causes; effective chemotherapy has also contributed to the reduced mortality.

Although the case rates for whites (males and females) are substantially lower than for other races, the total number of cases reported for whites is greater than for other races (Figure 2).

FIGURE 1

NEW ACTIVE TUBERCULOSIS CASE RATE AND DEATH RATE UNITED STATES, 1953–1967



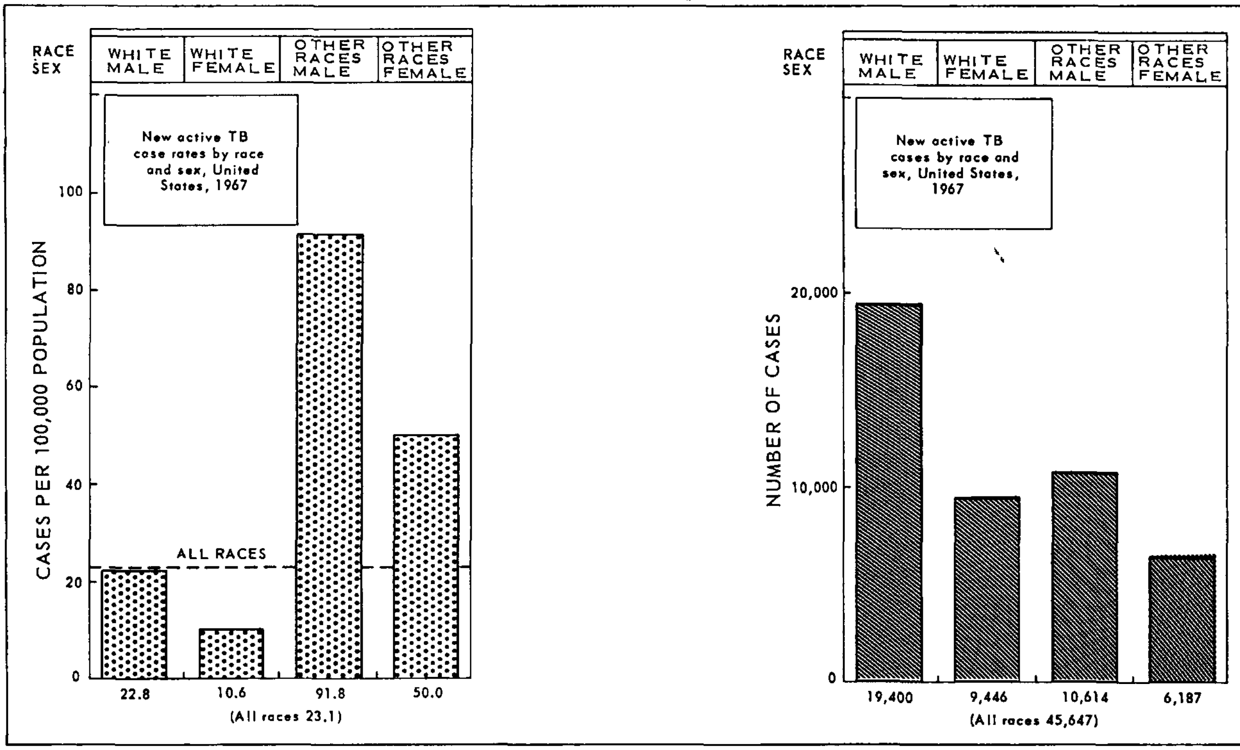
RATES
NEW CASES: 53.0 49.3 46.9 41.6 39.2 36.5 32.5 30.8 29.4 28.7 28.7 26.6 25.3 24.4 23.1
DEATH: 12.4 10.2 9.1 8.4 7.8 7.1 6.5 6.0 5.4 5.1 4.9 4.3 4.1 3.9 3.3*

NOTE: Logarithmic scale

*Provisional death rate based on National Center for Health Statistics ten percent sample

FIGURE 2

NEW ACTIVE TUBERCULOSIS CASES AND CASE RATES BY RACE AND BY SEX UNITED STATES, 1967



Age distribution of cases shows that both the numbers reported and the specific case rates increase with age (Figures 3 and 4).

A third index of tuberculosis is the infection rate, which measures the successful transmission of tubercle bacilli from one person to another. The rate has been high in the past, when nearly everyone had become infected by the time he reached adulthood. The infected child is now becoming a rarity in many parts of the country. Nationwide school testing programs in 1967-1968 reported an average of 0.3 percent tuberculin reactors among children entering school (5 and 6 years old), and less than 2 percent among 13- and 14-year-old schoolchildren.

Figure 5 depicts the distribution of infection among 17- to 21-year-old white male, single-county residents inducted into the U.S. Navy in 1958-1964. It shows that rates of infection are higher along the Mexican Border, throughout Appalachia, and in large metropolitan areas.

The distribution of infected individuals corresponds very closely to the distribution of new active cases reported in the corresponding area, as shown by Figure 6 for the 3-year period 1965-1967.

The decline in tuberculosis infection has been most dramatic in Alaska; the prevalence of infection dropped from 85 percent in 1949 to 1.9 percent in 1967 among 5- and 6-year-old children in the rural Kuskokwim-Bethel area. BCG vaccine was used in children less than 15 years of age during the late 1940's and early 1950's: altogether some 30,000 children were tuberculin tested and around 7,000-8,000 considered uninfected were vaccinated. The use of BCG was discontinued in favor of an aggressive case-finding and treatment program, instituted on a large scale in 1954. Widespread preventive treatment of infected individuals was incorporated into the control program 2 years later.

PREVENTION OF DISEASE

The probability of developing active disease can be reduced by two preventive measures: prophylactic treatment with the drug isoniazid and vaccination with BCG. Preventive treatment (prophylaxis with isoniazid) is preferred in many advanced countries, including the United States, where there is a relatively low incidence of disease and an effective control program. Prevention with BCG vaccine is recommended and widely used in developing countries.

BCG VACCINE

The search for a prophylactic vaccine against tuberculosis began shortly after the discovery of the tubercle bacillus in 1882. It was not until 1922, however, that Weill-Halle first ventured to give a live vaccine to an infant. The vaccine was BCG, prepared from a bovine strain of the tubercle bacillus isolated by Nocard, in 1902, from the udder of a cow. The virulence of the original strain was attenuated through years of serial transfer by Calmette and Guerin at the Pasteur Institute, Paris. No apparent harm resulted from oral vaccination of youngsters with BCG, and its use spread rapidly throughout France despite appeals from some of France's leading clinicians for controlled studies of its effectiveness. Two major setbacks were soon to occur. First, in 1927, Petroff reported from the Trudeau Laboratory at Saranac Lake, N.Y., that he had grown a virulent strain from a BCG culture obtained in Paris; and then in 1930, the tragedy in the Hanseatic city of Lubeck resulted in death from tuberculosis for 73 children who were mistakenly fed a culture of virulent bacilli in place of BCG.

Immediately after World War II, mass vaccination programs were organized as emergency measures in some of the war-devastated countries of Eastern Europe. BCG was given by intracutaneous injection, a technique which became widely accepted as the campaigns spread throughout Europe into the Middle East, Asia, and Latin America. Early support was provided by UNICEF, and by the mid 1950's WHO took over the mass BCG campaigns as part of the tuberculosis control program for developing countries.

Questions again arose as to the effectiveness of BCG vaccination; they led, this time, to the creation by WHO of a Tuberculosis Research Office (1949-1955) and to the two large-scale control trials which began in 1950, one conducted by the U.S. Public Health Service and one by the British Medical Research Council. The work of the WHO/TRO was directed primarily toward answering questions on the nature of BCG vaccine, techniques of administration, and selection of candidates for vaccination. In 1949 little was known about variability in potency of different batches of BCG vaccine, natural evolution of local lesions, cause and course of associated local lymphadenitis, or frequency of other mycobacterial infections which produced tuberculin sensitivity that would interfere with selection of candidates and efficacy of the vaccine. Results of the controlled trials have shown different degrees of effectiveness in comparing the vaccinated and control groups, related possibly to differences in the tuberculosis infection rates (higher in Britain), sources of other mycobacterial infections (higher in the United States), and a variety of other factors, known as well as unknown.

Recommendations for BCG Vaccination

The purpose of BCG vaccination is to modify the course of subsequent infection with virulent tubercle bacilli, and thereby reduce the risk of manifest pulmonary disease and extrapulmonary complications, notably miliary tuberculosis and tuberculous meningitis. Thus, only the uninfected are considered candidates for vaccination, since the infected have already responded to

FIGURE 3

NEW ACTIVE TUBERCULOSIS CASES AND CASE RATES BY AGE GROUP
UNITED STATES, 1967

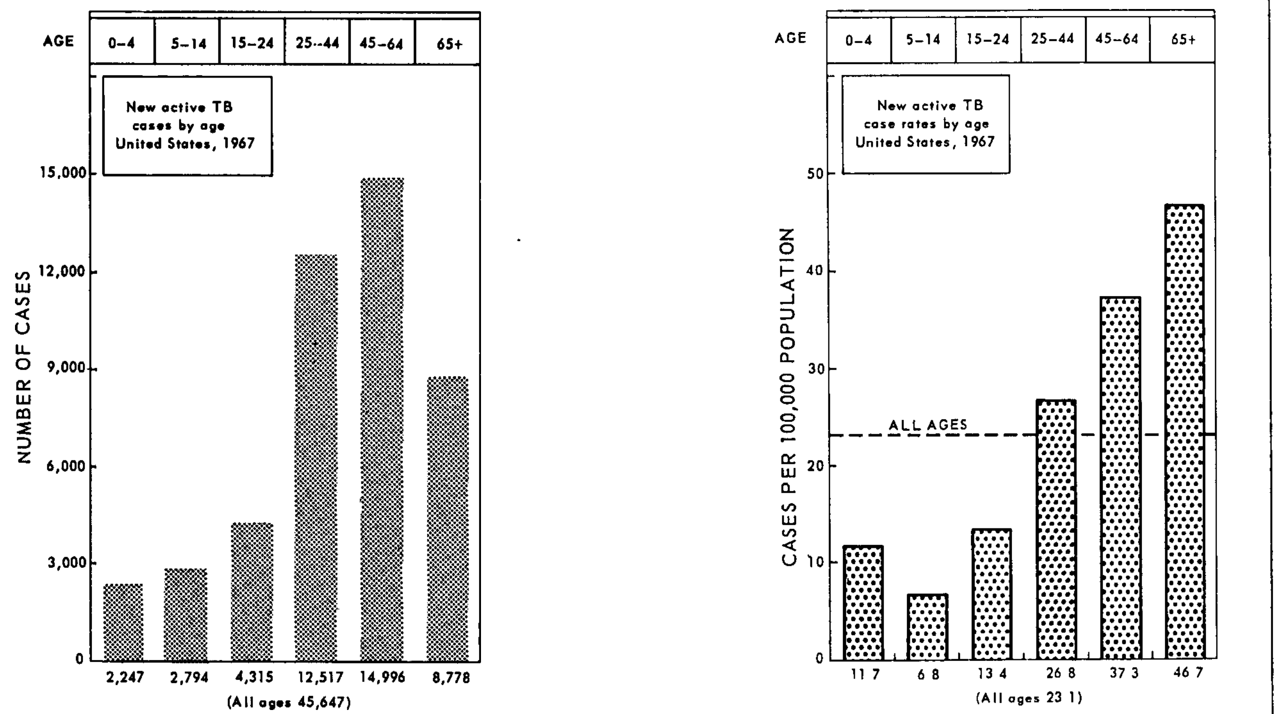


FIGURE 4

NEW ACTIVE TUBERCULOSIS CASE RATES BY AGE, RACE, AND SEX UNITED STATES, 1967

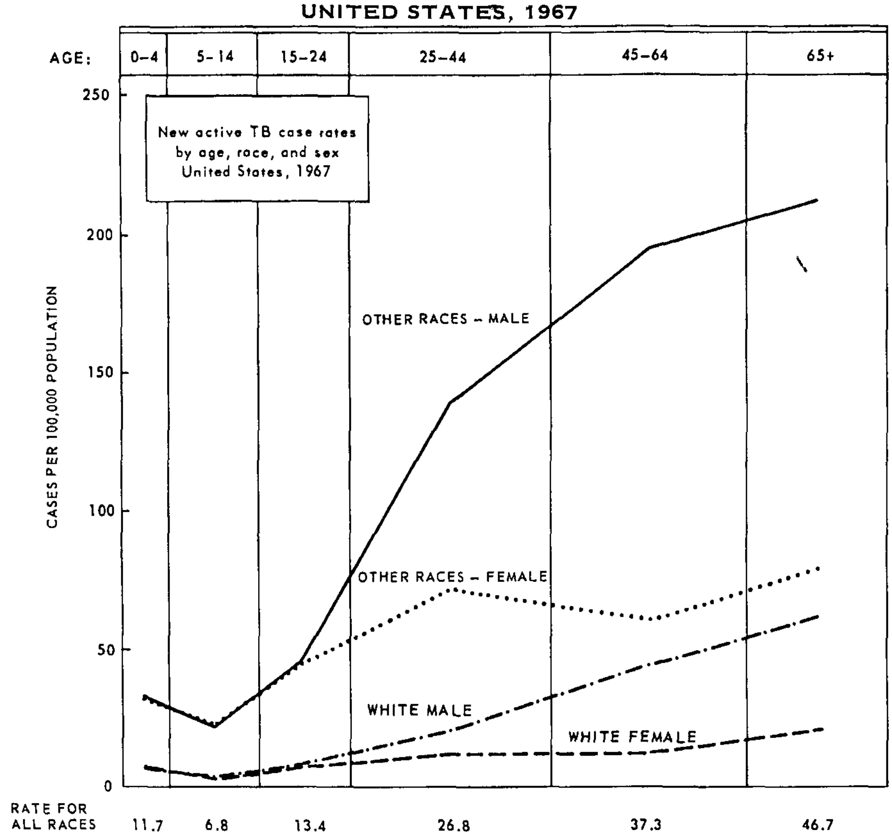


FIGURE 5

TUBERCULIN, PPD-S 0.0001 MG (5TU)

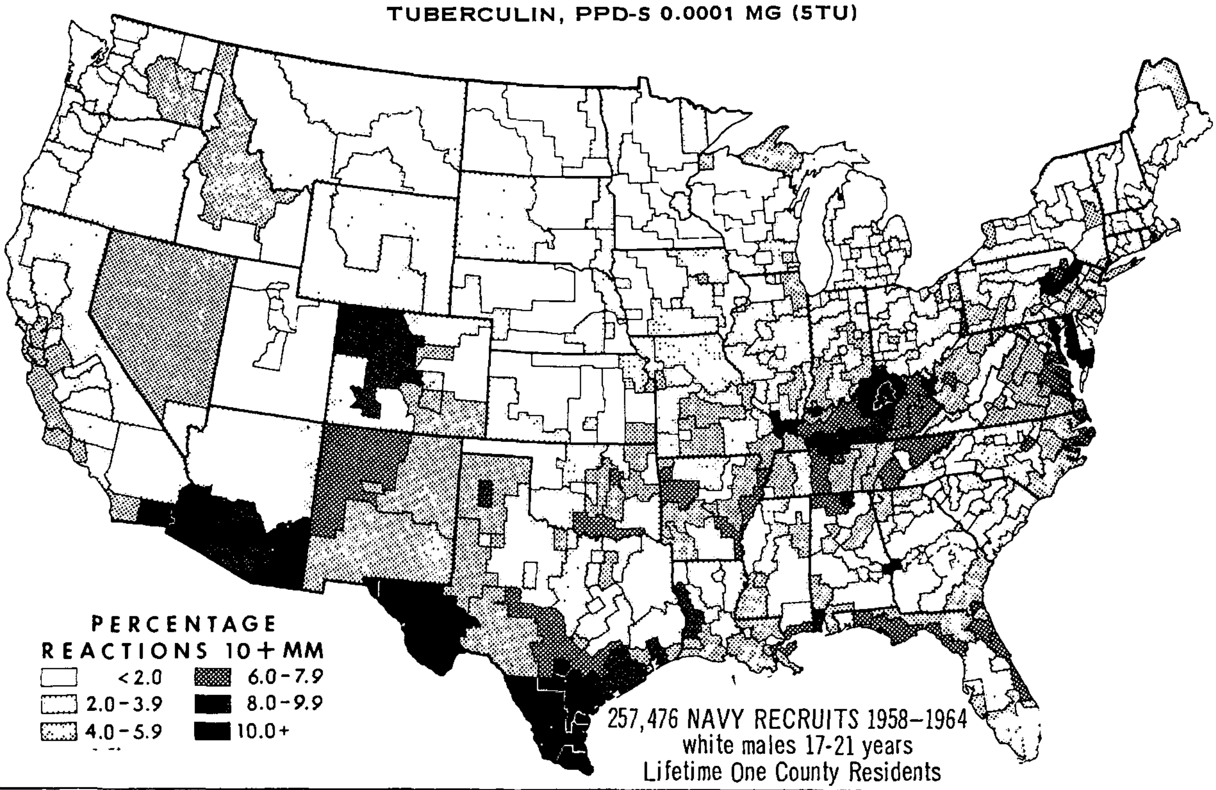
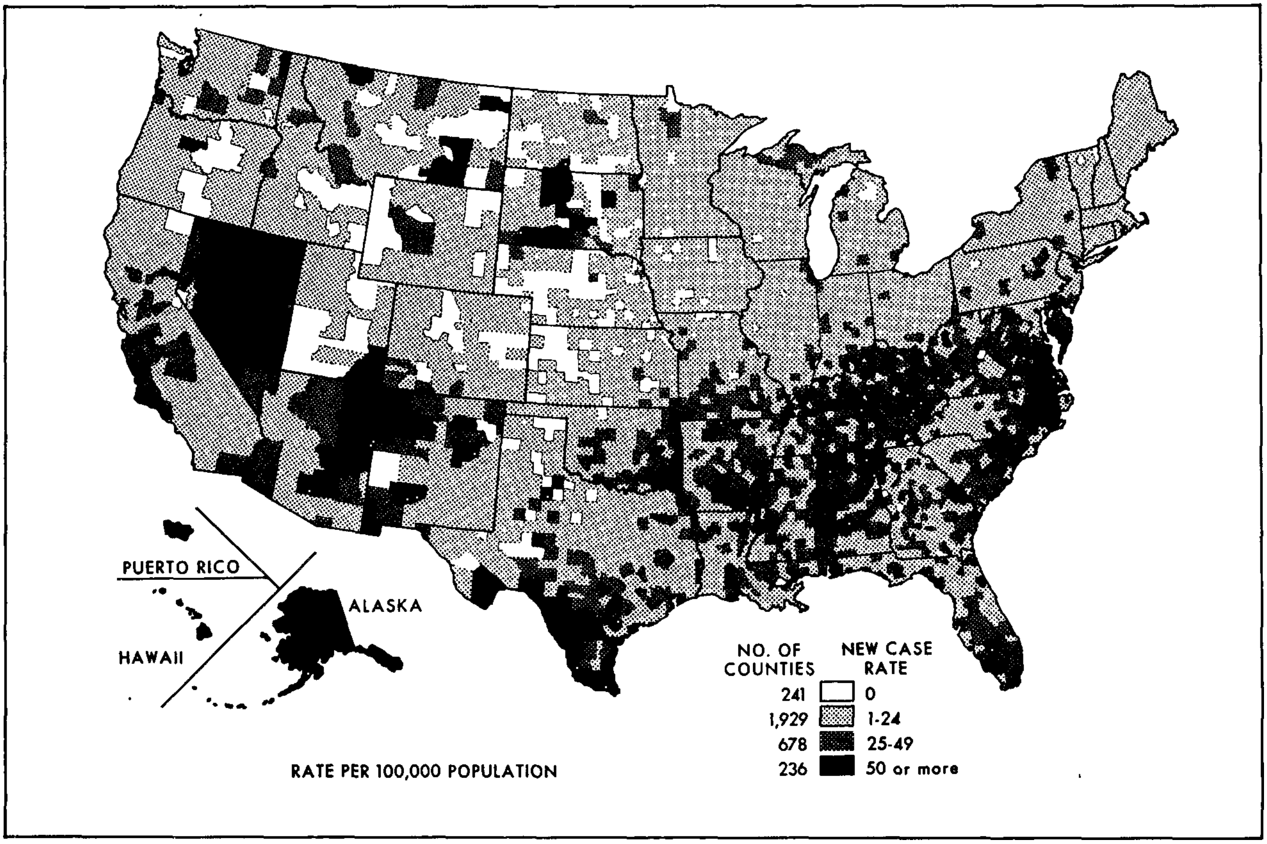


FIGURE 6

NEW ACTIVE TUBERCULOSIS CASE RATES, BY COUNTY, AVERAGE, 1965–1967



a natural challenge with tubercle bacilli. There is no indication that vaccination prevents tuberculous infection or the late consequences of that infection.

BCG vaccination is recommended only for individuals with an expected high probability of becoming infected, i.e., unavoidable and continuous exposure to *M. tuberculosis,* and little likelihood of being kept under surveillance or preventive treatment. In other words, when transmission from an infectious case cannot be blocked and chemoprophylaxis cannot be applied to the individual at risk, BCG vaccination is recommended. In the United States today such conditions are seldom encountered. (See "Public Health Service Recommendations on the Use of BCG Vaccination in the United States," page 49).

BCG vaccine is administered by the intracutaneous technique or the transcutaneous-multiple puncture technique. Specific instructions of the manufacturer should be carefully followed.

Preventive Treatment

Because of the low and falling infection rates in this country, an increasing proportion of the tuberculosis diagnosed each year, estimated at 80 percent of all new cases, arises from the previously infected pool, estimated to comprise about 23 million persons. Preventive treatment (chemoprophylaxis) reduces the incidence of disease in individuals at risk, i.e., those identified as infected. Top priority for chemoprophylaxis is recommended for those at greatest risk: close contacts of infectious persons, old "inactives" and former patients, persons with abnormal chest x-ray findings, recent tuberculin converters, and persons with medical conditions that lower the natural resistance to disease. Isoniazid, 300 mgm by mouth, daily, for a year, is currently recommended preventive treatment for infected adults; for children, 10 mgm/kg, not to exceed 300 mg daily. (See "Preventive Treatment for Tuberculous Infection," page 51).

PHYLLIS Q. EDWARDS, M.D.
VERNON N. HOUK, M.D.

BCG VACCINATION

PUBLIC HEALTH SERVICE RECOMMENDATIONS ON THE USE OF BCG VACCINATION IN THE UNITED STATES

The following recommendations represent the position of the Public Health Service on the use of BCG vaccination in the United States. The statement was drafted by a panel of public health and tuberculosis specialists who met at the Communicable Disease Center in Atlanta on July 21 and 22, 1966. The recommendations have subsequently been approved by the Surgeon General.

Tuberculosis has been and still is the costliest of the communicable diseases in the United States—both in terms of human lives and dollars. It has always been the desire of public health workers in this country to use all the necessary tools to control this disease. Therefore, in 1946 when European countries were adopting mass BCG vaccination as an element of their tuberculosis control programs, the Public Health Service first convened an advisory group to consider the use of BCG in this country. That group recommended against its use since its effectiveness had not been determined. Instead of mass usage, large-scale controlled trials were urged. Subsequent advisory committees have recommended that BCG vaccination be limited to special groups, but emphasized in 1957: "The Committee expressed the opinion that vaccination may lead to a false sense of security which could result in failure to observe precautions that otherwise would be taken," and in 1962: "The Committee wishes to emphasize that BCG vaccination should not be considered a substitute for other control measures, but should be an addition to these, used in special situations." In 1966, this panel recommended an even more limited use of BCG vaccination in the United States.

Vast changes have been seen in tuberculosis control in the past 20 years. In 1945 specific chemotherapy had only recently been discovered and was still in limited use; today excellent drugs are available which cannot only reverse the course of the disease, but will also rapidly eliminate infectiousness. Then, too, in 1946 rates of new infections were thought to be high and most of the disease seen then was thought by many to follow recent infection. Today in this country, accumulated data show that infection rates are very low, and it is recognized that 75 to 80 per cent of new cases of tuberculosis comes from the reservoir of persons infected in the more distant past. Today it is possible and practicable to prevent many of these infected persons from developing disease—namely, with chemoprophylaxis. Finally, and most important, today the resources to combat tuberculosis in the United States are vastly increased and should remain at a high level for the next several years if the 1963 recommendations of the Surgeon General's Task Force are followed.

The panel has reviewed epidemiologic information relating to the status of tuberculosis in this country and is thoroughly familiar with the results of field trials of BCG not only in the United States, but also in Great Britain and other countries. The panel is fully cognizant of the past positions of the Public Health Service as well as the current views in other countries and of the World Health Organization. It is important to recognize that the present epidemiologic situation in the United States is much more favorable than that in developing countries. It is also much more favorable than the situation that existed in many developed countries at the end of World War II when BCG vaccination was widely adopted.

BCG vaccine has been demonstrated to have some effectiveness, particularly where rates of new infections are high. Its impact as a public health measure does, however, diminish progressively as the opportunity to become infected continues to decrease. Because of the favorable epidemiologic, medical, and socioeconomic conditions prevailing in the United States, and in light of the changes described previously, the following recommendations are made for the use of BCG in this country today. The panel recognizes that for regions with different conditions, the recommendations concerning the use of BCG might be quite different.

RECOMMENDED USAGE

For the individual: Since modern methods for detection, isolation, treatment, and chemoprophylaxis, when adequately applied, are highly successful in controlling tuberculosis, BCG should be reserved for situations in which these methods cannot be applied. BCG should be used for the uninfected person or small groups of uninfected people living in unavoidable contact with one or more uncontrolled infectious persons who cannot or will not obtain or accept supervised treatment.

For groups: Based on available data, there is no epidemiologic indication for the use of BCG on a group or community basis in the United States. In particular, BCG is not recommended for medical and paramedical personnel and students, or for employees and inmates of penal and mental institutions, because the knowledge of tuberculin conversion, if it occurs, is essential so that chemoprophylaxis may be instituted and the infectious source identified and treated. Moreover, adequate tuberculosis control programs can be developed in such groups with reasonable assurance of cooperation.

A so-called "micro-epidemic" of infection is another situation in which BCG is not recommended. Today, with low rates of transmission and expanded tuberculin testing, such outbreaks will be more easily recognized than in the past. Their management requires the prompt identification and removal of the source of infection and the identification and treatment of the tuberculin converters.

The recommendations of this panel limiting the use of BCG should not be construed to mean that tuberculosis is no longer a problem. On the contrary, vigorous efforts must be sustained to capitalize on the gains of the past. In addition to the current programs of tuberculosis control, an expanded study of the level of infection, as measured by standardized tuberculin testing, is needed. As the risk of new infection continues to diminish, the need for surveillance will increase to assure that deviations from the norm can be rapidly detected and corrective action instituted.

If, in spite of the above recommendations, an individual health official in the United States believes that the local situation calls for further use of BCG, he should first assure himself that the situation is, in fact, precarious. He should have epidemiologic information on the transmission rate as measured by conversions obtained in repeated tuberculin testing of representative samples of the population; he should identify as precisely as possible the persons who might benefit from BCG vaccination; and he should re-examine his resources to determine if there are not better ways to meet the problem. Under no circumstance should BCG vaccination be an alternative for an adequate tuberculosis control program, nor should other measures be relaxed when BCG is used.

The health official should be aware that the use of BCG does not absolve him or his health jurisdiction from attempting adequate supervision of individuals with tuberculous infection or disease. In addition, he should recognize that the use of BCG will complicate future tuberculosis control programs by adding to the population a group of reactors who cannot be distinguished from those naturally infected.

As the 1957 Report on BCG stated:

"The procedure (BCG vaccination) makes it impossible to use the tuberculin test *(1)* as evidence of recent infection in the individual; *(2)* as an index of infection in population groups; *(3)* for the location of sources of contagion; *(4)* as a preliminary screening device prior to chest roentgenographic examination in the diagnosis of tuberculosis; *(5)* for differential diagnosis in diseases with some similarity to tuberculosis."

Since there will be some continued indication for the use of BCG, according to the recommendations of the panel, the Public Health Service should continue to assure that a safe and potent vaccine is licensed for use in the United States.

SPECIAL PANEL OF PUBLIC HEALTH AND TUBERCULOSIS SPECIALISTS

Dr. Robert J. Anderson
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PREVENTIVE TREATMENT FOR TUBERCULOUS INFECTION

Recommendations of the National Communicable Disease Center

Most active tuberculosis in the United States today occurs among persons who were infected with *Mycobacterium tuberculosis* many years ago.

Because these persons, who are positive tuberculin reactors, comprise the reservoir of future tuberculosis in this country, special priority on preventing this progression from latent to active disease should be an essential element in modern tuberculosis control programs.

Research conducted during the past decade has established that treatment with isoniazid can greatly reduce the risk of active tuberculosis developing among tuberculin reactors.

Today, the U.S. Public Health Service, the American Thoracic Society, and the National Tuberculosis and Respiratory Disease Association, recommend isoniazid for *persons identified as having tuberculous infection.*

Priority Candidates for Preventive Treatment

While all infected persons may benefit from preventive treatment, priority effort should be made to identify and treat individuals in the following groups:

1. Positive tuberculin reactors with "pulmonary fibrosis" or old fibrotic lesions presumably tuberculous in origin, former tuberculosis patients who have never had specific chemotherapy or who have had inadequate drug therapy (e.g., treatment for less than 18 months, no isoniazid, etc.). At particularly high risk are persons with pulmonary lesions of unknown etiology, compatible with tuberculosis, in which active disease has been excluded.

2. Members of the household of a newly diagnosed case of tuberculosis, regardless of tuberculin status. Preventive treatment for these household contacts should continue for a full year, even when exposure to the infectious case has ended and tuberculin tests remain negative. Preventive treatment of negative reactors should also be given other persons who have had close, extended exposure comparable to that of a person living in the same household with an active case.

3. Persons known to have recently become infected, i.e., converted from negative to positive tuberculin reaction.

4. Children who are reactors through the age of adolescence.

5. School personnel and other adult reactors closely associated with children.

6. Tuberculin reactors in certain clinical situations known to lessen their resistance to disease: prolonged corticosteroid treatment, gastrectomy, leukemia, silicosis, Hodgkins' disease, pneumoconiosis, severe or poorly controlled diabetes, pregnancy, and children with measles or whooping cough. In the case of pregnant women, treatment should be started in the *last trimester.*

Isoniazid for Preventive Treatment

A single drug, isoniazid, is generally used for treatment of infection in a dosage of 300 mg. per day for adults and 10 mg. per kilogram body weight for children not to exceed 300 mg. per day, to be administered daily for a period of 12 months.

Effectiveness of Isoniazid

Public Health Service trials that started in 1955 among high risk groups such as infected children, household contacts of an active case, and persons with fibrotic lesions in their lungs, have shown a continued reduction in subsequent cases of tuberculosis ranging from 55 to 85 percent after one year of isoniazid. These reductions tend to minimize the effectiveness of isoniazid since some individuals in the groups studied failed to take the medication daily.

Interpretation of Tuberculin Tests

Positive Reaction = 10 mm or more of induration

A reaction of 10 mm or more induration to the Mantoux test, using 5 TU of PPD, represents infection with *Mycobacterium tuberculosis.* No confirmation test necessary.

"Doubtful" Reaction = 5 mm through 9 mm of induration

Reactions within this range can result from infection with any one of a number of mycobacteria, including *M. tuberculosis.* Clarification may be obtained either by repeating the test with PPD-tuberculin at a different site or by simultaneous testing with PPD-tuberculin and another mycobacterial PPD, if available.

Negative Reaction = 0 mm through 4 mm of induration

No repeat test necessary unless there is other suggestive clinical evidence of tuberculosis.

TYPHOID FEVER

The clinical manifestations of typhoid fever were first clearly described by Willis in 1659. Budd, in 1860, postulated that infective material was excreted in feces and that this material was spread by contaminated milk and water and the hands of those who cared for the sick. The typhoid organism *(Salmonella typhi)* was discovered by Eberth, in 1880, and first cultured, in 1884, by Gaffky.

The first immunizations against typhoid were carried out, in 1896, by Pfeiffer and Kolle and by Wright using a suspension of heat-killed typhoid bacteria. Although some apparent success was noted with the vaccine during the first half of the 20th century, few well controlled studies were carried out. In 1957 and 1958, however, World Health Organization investigators conducted field trials in Yugoslavia and British Guiana (Guyana) and were able to demonstrate the definite, albeit incomplete, protective property of certain typhoid vaccines.

TYPHOID FEVER IN 1967

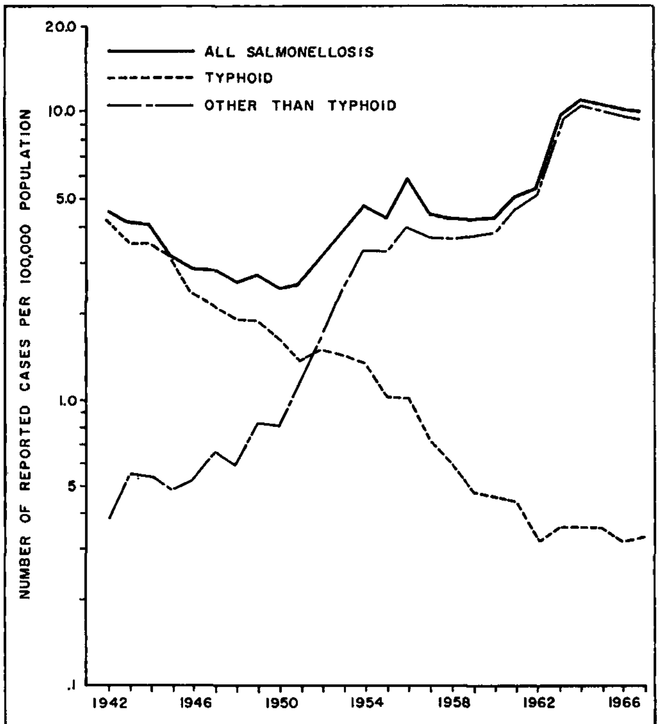
A total of 690 isolations of *S. typhi* were reported to the National Communicable Disease Center in 1967–36 more than in 1966. Of these, 95 were from patients with typhoid fever and 207 were from asymptomatic carriers. No clinical information was reported for the remaining 388.

A marked increase in the reported incidence of salmonellosis has occurred since 1942 (Figure 1) – an increase due at least in part to improved methods of surveillance and reporting. The incidence of typhoid fever, however, dropped from a high of over 4 cases per 100,000 population in 1942 to less than 0.4 case per 100,000 population in 1967. Improved methods of sanitation and hygiene are probably largely responsible for this decrease.

Although still quite common in developing countries, large outbreaks of typhoid fever are becoming infre-

FIGURE 1

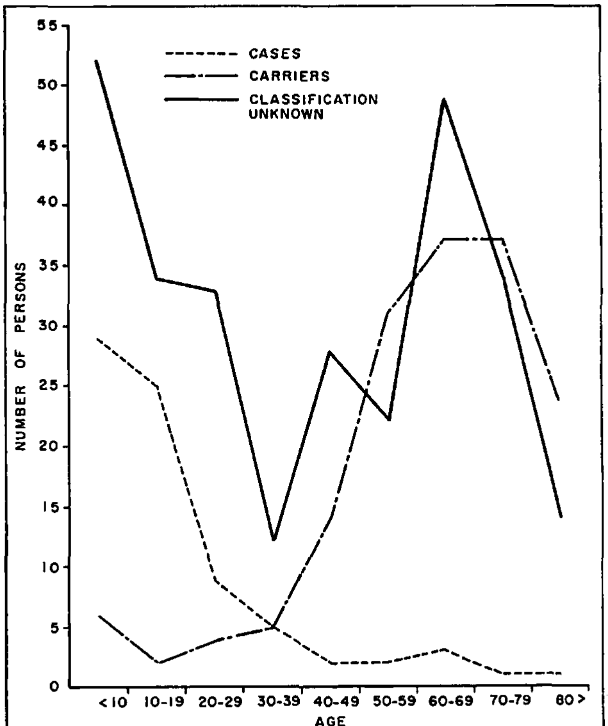
REPORTED INCIDENCE OF HUMAN SALMONELLOSIS UNITED STATES, 1942–1967



NCDC:Salmonella Surveillance Report, Annual Summary 1967

FIGURE 2

TYPHOID FEVER CASES AND CARRIERS UNITED STATES, 1967



NCDC:Salmonella Surveillance Report, Annual Summary 1967 quent in the United States. In 1967, only two large outbreaks originating in this country were reported to the NCDC. The first involved 11 persons attending a luncheon in Colorado. A chronic typhoid carrier who helped prepare the food was probably responsible. The second involved a cook and 30 members of a Stanford University fraternity; the source and vehicle of contamination were never identified.

In most reported series of cases of typhoid fever, the adolescent and young-adult age groups have the highest attack rates (Figure 2). Case-fatality ratios increase progressively with age, however.

Approximately 3 percent of all typhoid patients will continue to excrete the organisms for longer than one year. Women over 40 years of age with gallbladder disease are particularly likely to become excretors. Antibiotic treatment of the acute disease appears ineffective in lowering the tendency. Long-term antibiotic therapy and cholecystectomy have been shown to abolish the carrier state in some cases.

ANDREW MALLORY, M.D.

See p. 131 for the Recommendation of the PHS Advisory Committee on Immunization Practices on the use of typhoid vaccine.

EPIDEMIC TYPHUS FEVER

Epidemic (louse-borne) typhus is caused by *Rickettsia prowazeki* and is transmitted by human body lice. It is a severe disease marked by fever, headache, rash, and stupor or delirium. The word typhus is derived from the Greek *typhos,* meaning smoky or hazy, and was applied to febrile illnesses with clouded sensorium. Gerhard, a Philadelphia physician, differentiated typhus from typhoid fever in 1837. In 1910 Brill described the sporadic cases of milder typhus he was seeing in New York City. Zinsser suggested in 1934 that Brill's disease was recrudescent epidemic typhus, and in 1951 Murray and Snyder proved that it was.

Another kind of typhus is murine (endemic) typhus, which is caused by *R. mooseri* and is transmitted by the rat flea. Clinically a somewhat milder form of typhus, it occurs endemically, especially in sub-tropical and tropical regions, in association with high rat populations. The term typhus is also applied to scrub typhus, or tsutsugamushi disease, another rickettsial infection, which occurs in Asia and neighboring islands of the Southwest Pacific. The term "tick-borne" typhus is sometimes applied to Rocky Mountain spotted fever and certain other typhus-like, tick-transmitted rickettsial diseases that are seen in various parts of the world.

Epidemic typhus fever over the past several centuries, was typically seen as pandemics associated with the social disruption caused by wars and revolutions. The last large epidemic occurred in Eastern Europe and Russia in 1918-1922 and is estimated to have caused 30 million cases and 3 million deaths. In World War II the disease was again seen there and also around the Mediterranean, but it has since largely disappeared from those areas. Recrudescent typhus, or Brill-Zinsser disease, continues to occur in previously infected persons and could initiate epidemics if lousiness were to return.

Today epidemic typhus fever continues to occur in mountainous areas of the tropics where the climate is cool enough for people to wear clothes. In certain areas everyone has been infected by the time he reaches adulthood, yet clinical illness is rarely observed, perhaps because the disease is atypically mild in childhood.

In the United States no epidemics of the disease have occurred in several decades, and the recent cases seen here were infected in other countries. There is now little lousiness, so even when typhus recrudesces, it does not lead to epidemics. Consequently, epidemic typhus vaccine is not indicated for any civilian populations in this country. It is recommended only for military personnel and for civilians whose foreign travel will take them into close association with the populations of mountainous areas of the tropics.

For the purpose of vaccine production, *R. prowazeki* is cultivated in the yolk sacs of embryonated hen eggs. Suspensions of infected yolk sacs are extracted with ether, and the aqueous phase is drawn off for use as vaccine. Potency tests for the vaccine involve immunization of guinea pigs and tests of their sera for antibodies capable of neutralizing the toxic (lethal) effect for mice of suspensions of viable *R. prowazeki* from infected yolk sacs. The protection provided man by the primary course of vaccine is much improved following a booster dose after a sufficiently spaced interval.

CHARLES C. SHEPARD, M.D.

See p. 133 for the Recommendation of the PHS Advisory Committee on Immunization Practices on the use of typhus vaccine.

YELLOW FEVER

Unlike some of the other great epidemic diseases, yellow fever was not recorded in ancient times. Indeed, the first generally acknowledged yellow fever epidemic occurred in Yucatan in 1648. Until early in the 20th century, it was one of the most feared of all epidemic diseases, especially in the seaports of the Americas, Europe, and West Africa, where it took thousands of lives.

Yellow fever is the prototype of arboviral diseases. It is transmitted to man by the bite of an infected mosquito. Five to 10 percent of persons infected with yellow fever die within several days. Illness ranges from the life-threatening disease with jaundice, coma, acute renal failure, and vomiting of blood, to a mild flu-like syndrome, to clinically inapparent infection in infants. Those who recover retain life-long immunity.

Whether yellow fever originated in Africa or in the Americas has long been disputed. The mosquito vector of epidemic yellow fever, *Aedes aegypti*, is generally accepted to be of West African origin and was probably introduced into the Americas early in the 17th century with the beginning of the slave trade. This species, breeding in the water supplies on ships, was readily and rapidly spread to port cities of the Western Hemisphere. The yellow fever virus is thought also to be of African origin and to have shared the route of spread of its vector to the Americas. Part of the dread inspired by yellow fever was due to the mystery surrounding it. Its cause and means of spread were unknown, and thus no control measures were available. In 1881, based on his observations in Havana, Carlos J. Finlay, M.D., proposed the concept of mosquito transmission of yellow fever. This hypothesis was confirmed by Walter Reed, M.D., in Cuba in 1900, and led to the concept of mosquito eradication as the means of control. Mosquito control measures were applied successfully in Havana, in 1901, by Gen. W. C. Gorgas.

Although Reed and his co-workers in 1901 had demonstrated the etiologic agent of yellow fever to be a filterable agent, i.e., a virus, this fact was lost for several years. In 1927, Stokes and co-workers reestablished that yellow fever was caused by a filterable virus; these same investigators achieved the first successful transmission of yellow fever to a non-human subject (*Macaca mulatta* or rhesus monkey). This opened the way for the laboratory study of yellow fever, leading to the immunological proofs that African and American yellow fever are the same disease, and resulting in the subsequent development of the yellow fever vaccine in the 1930's.

In 1932, yellow fever was found to have two forms. The generally known "urban" or "epidemic" man-mosquito-man cycle in which *A. aegypti* transmits the virus from man to man, and "jungle yellow fever." This form of the disease occurs principally in monkeys, away from urban areas, and is generally transmitted from monkey to monkey by mosquitoes other than *A. aegypti.* Man is infected more or less accidentally as he works or travels in forested areas. Jungle yellow fever is felt to be the original, or naturally occurring, cycle of the disease. It persists in enzootic and epizootic form among various wild animals of the African and South American forests. The virus and the disease produced in man by jungle yellow fever are identical to those of the urban or epidemic form.

YELLOW FEVER IN THE AMERICAS

The last outbreak of yellow fever in the United States was in New Orleans in 1905. An estimated 3,402 cases were reported, with 452 deaths before anti-mosquito measures brought the epidemic under control. Epidemics continued to occur sporadically throughout the rest of the Americas; the last large city epidemic was in Rio de Janeiro, Brazil, in 1928-29, with 738 cases and 436 deaths.

Vigorous programs of *A. aegypti* control and eradication, coordinated through the Pan American Health Organization, are generally credited with eradicating epidemic yellow fever. *A. aegypti* formerly ranged throughout most of the Americas, but eradication measures have limited it to the regions shown in Figure 1.

The yellow fever virus itself remains widespread. In the past 20 years, it has been found in Trinidad and all countries in the Americas except Canada, the United States, El Salvador, Chile, and Uruguay. Various monkey species are reservoirs of infection; the virus has also been isolated from marsupials, edentates, and rodents. The virus thus maintains itself in nature, moving through the continually renewed population of susceptible animals in irregular enzootic and epizootic waves. Scattered human cases occurred in 1948-1956 and can occur again whenever the virus and a suitable mosquito are present.

In the past 15 years, human cases of yellow fever in the Americas have been localized (Figure 2). The slight changes in pattern of location within these countries,

FIGURE 1

YELLOW FEVER ENDEMIC ZONE IN THE AMERICAS

Source of Data:
International Sanitary Regulations, Third Edition, World Health Organization, Geneva, 1966.

seen in 5-year periods, are consistent with the known epidemiologic picture. That is, with this moving wave of viral activity, a concurrent shift in location of human cases occurs.

The reported cases and deaths, by major political subdivision, are shown in Table 1 for the years 1953-1968. That the numbers of cases and deaths are similar or identical in most instances is due to the general practice of reporting only autopsy or liver biopsy proven cases. Since approximately 10 survive for every death from yellow fever, these figures can be considered only rough indicators of yellow fever viral activity. In addition, there is probably considerable underreporting. The isolation of many of the areas where jungle yellow fever is contracted makes surveillance difficult, if not impossible.

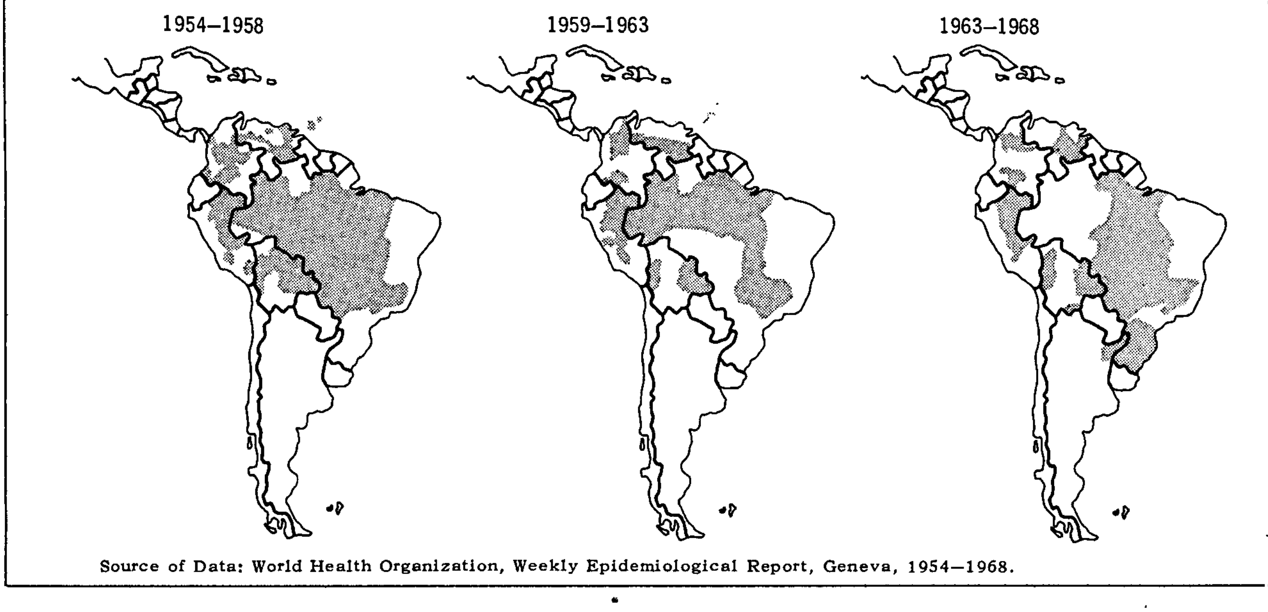
YELLOW FEVER IN AFRICA

Epidemics of yellow fever have been reported from West Africa since the 18th century, but seldom if ever in the native population. The frequency of disease and the high mortality among European settlers and explorers led to the West African coast's being called "the white man's grave." Yellow fever was unknown elsewhere in Africa.

With the establishment of the West Africa Yellow Fever Commission of the Rockefeller Foundation in Nigeria in 1925, the complex epidemiology of yellow fever in Africa began to become known. Serologic studies in human and non-human primates have traced the yellow fever virus over large portions of West, Central, and East Africa. The virus is maintained principally in monkeys, but man and possibly other primates are occasionally involved.

FIGURE 2

YELLOW FEVER IN THE AMERICAS, 1954–1968
MAJOR POLITICAL SUBDIVISIONS WITHIN COUNTRIES REPORTING ONE OR MORE HUMAN CASES



Source of Data: World Health Organization, Weekly Epidemiological Report, Geneva, 1954–1968.

TABLE 1

Yellow Fever in the Americas—1954-1968
Major Political Subdivisions Within Countries Reporting One or More Human Cases

COUNTRY AND STATE	1954	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	15 Yr. Total
TOTAL	59	46	29	77	64	29	49	81	52	141	98	84	304	16	32	1161
ARGENTINA	—	—	—	—	—	—	—	—	—	—	—	2	51	1	—	54
Corrientes	—	—	—	—	—	—	—	—	—	—	—	—	12	—	—	12
Misiones	—	—	—	—	—	—	—	—	—	—	—	2	39	1	—	42
BOLIVIA	—	12	6	19	2	1	30	2	—	81	13	19	69	—	19	273
Beni	—	2	—	—	—	—	—	—	—	—	—	—	—	—	—	2
LaPaz	—	2	5	19	1	1	30	2	—	49	10	16	16	—	17	168
Santa Cruz	—	8	1	—	1	—	—	—	—	32	3	3	52	—	2	102
Tarija	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	1
BRAZIL	—	8	2	10	26	3	1	2	1	—	14	12	167	1	2	249
Para	—	8	1	1	—	—	1	—	—	—	—	—	—	—	2	13
Ron Donia	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	1
Amazonas	—	—	—	1	—	—	—	1	1	—	—	—	—	—	—	3
Goias	—	—	—	2	17	1	—	—	—	—	2	3	—	—	—	25
Mato Grosso	—	—	—	6	4	—	—	—	—	—	12	4	—	—	—	26
Minas Gerais	—	—	—	—	5	2	—	—	—	—	—	5	—	—	—	12
Acre	—	—	—	—	—	—	—	1	—	—	—	—	—	—	—	1
Parana	—	—	—	—	—	—	—	—	—	—	—	—	100	—	—	100
Rio Grand du Sul	—	—	—	—	—	—	—	—	—	—	—	—	22	1	—	23
Santa Catarina	—	—	—	—	—	—	—	—	—	—	—	—	45	—	—	45
BRITISH GUINEA	—	—	—	—	—	—	—	2	—	—	—	—	—	—	—	2
Essequebo	—	—	—	—	—	—	—	2	—	—	—	—	—	—	—	2
COLOMBIA	10	21	17	34	22	21	11	9	30	10	10	2	3	5	7	212
Santander	4	10	5	16	6	—	2	3	5	1	1	2	—	3	3	61
Meta	2	2	2	3	2	—	—	—	—	—	—	—	—	—	—	11
Caqueta	2	4	—	—	3	19	—	—	1	—	4	—	2	—	—	35
Boyaca	1	2	—	2	—	—	3	1	3	—	—	—	—	1	3	16
Antioquia	1	—	2	—	4	—	3	1	3	—	—	—	1	—	—	15
Caldas	—	1	6	8	5	1	—	—	2	3	5	—	—	—	1	32
Putumayo	—	1	—	—	—	—	—	1	—	1	—	—	—	—	—	3
Narino	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Norte deSantander	—	—	2	—	—	—	3	2	7	5	—	—	—	1	—	20
Cundinamarca	—	—	—	5	—	1	—	—	3	—	—	—	—	—	—	9
Tolima	—	—	—	—	1	—	—	—	1	—	—	—	—	—	—	2
Casanare	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—	1
Magdalena	—	—	—	—	—	—	—	1	5	—	—	—	—	—	—	6
GUATEMALA	—	—	—	3	—	—	—	—	—	—	—	—	—	—	—	3
Peten	—	—	—	3	—	—	—	—	—	—	—	—	—	—	—	3
HONDURAS	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Valle de San Pedro Sula	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
PANAMA	—	—	1	2	—	—	—	—	—	—	—	—	—	—	—	3
Panama	—	—	1	—	—	—	—	—	—	—	—	—	—	—	—	1
Colon	—	—	—	2	—	—	—	—	—	—	—	—	—	—	—	2
PERU	7	—	—	3	5	1	5	53	20	49	59	44	9	9	4	268
Junin	6	—	—	—	3	—	—	3	—	15	28	9	—	—	—	64
Loreto	1	—	—	—	1	1	—	—	—	—	—	—	—	1	—	4
Amazonas	—	—	—	3	—	—	—	—	—	—	—	—	—	—	—	3
Puno	—	—	—	—	1	—	—	—	—	—	—	—	—	—	—	1
San Martin	—	—	—	—	—	—	3	3	2	—	2	24	4	4	—	42
Huanuco	—	—	—	—	—	—	2	47	18	31	19	9	5	4	4	139
Ayacucho	—	—	—	—	—	—	—	—	—	3	—	—	—	—	—	3
Huan Caveliva	—	—	—	—	—	—	—	—	—	—	10	1	—	—	—	11
Pasco	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	1
TRINIDAD & TOBAGO	15	—	—	—	—	2	—	—	—	—	—	—	—	—	—	17
Victoria	4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	4
Caroni	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Nariva	4	—	—	—	—	2	—	—	—	—	—	—	—	—	—	6
St. George	4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	4
Naparima	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
St. Andrew	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
VENEZUELA	26	5	3	6.	9	1	2	13	1	1	2	5	5	—	—	79
Monagas	11	—	—	—	—	—	—	—	—	—	—	—	—	—	—	11
Anzoategui	1	—	—	—	—	—	—	—	—	—	—	—	5	—	—	6
Sucre	2	1	—	—	—	—	—	—	—	—	—	—	—	—	—	3
San Cristobal	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Tachira	4	2	1	—	—	1	1	10	—	—	—	—	—	—	—	19
Merida	7	—	—	—	—	—	—	—	—	—	—	—	—	—	—	7
Trujillo	—	1	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Aragua	—	1	1	—	—	—	—	—	—	—	—	—	—	—	—	2
Barinas	—	—	1	4	—	—	—	—	1	—	—	—	—	—	—	6
Bolivar	—	—	—	2	1	—	1	—	—	1	2	4	—	—	—	11
Apure	—	—	—	—	—	—	—	3	—	—	—	—	—	—	—	3
Ter. Delta Amacuro	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	1
Portuguesa	—	—	—	—	8	—	—	—	—	—	—	—	—	—	—	8

Source of Data: World Health Organization, Weekly Epidemiological Report, Geneva, 1954–1968.

Reported cases and deaths are generally low, as shown in Table 2. This is undoubtedly due in part to underreporting, for health care and surveillance systems are just being established in the countries involved.

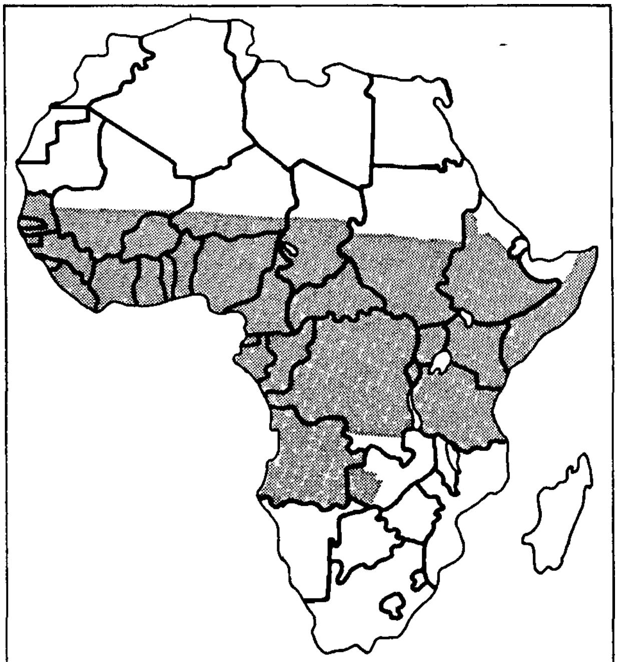
The endemic yellow fever area in Africa as defined by the World Health Organization (Figure 3) is based on immunity surveys. All yellow fever reported from Africa in the past 15 years has been within this area (Figure 4).

In contrast to the situation in the Americas, epidemics of yellow fever still occur in Africa. Sudan had about 15,000 cases and 1,500 deaths in an epidemic in the Nuba Mountains region in 1940. In 1959, 114 cases of yellow fever were reported from the Blue Nile region of the Sudan. The outbreak extended into Ethiopia, where 237 cases were reported that year. This epidemic smoldered in southwestern Ethiopia until 1962. In addition to being the first yellow fever epidemic reported from Ethiopia, it was the largest epidemic ever reported from Africa, with more than 100,000 estimated cases and more than 30,000 deaths. Three thousand deaths were officially reported by Ethiopia to the World Health Organization for 1961. The importance of vectors other than *A. aegypti* in the spread of yellow fever was underscored by this epidemic.

In 1965, an epidemic broke out in Diourbel, Senegal, located near a well known jungle yellow fever focus. Because of previous immunization campaigns, the population at risk consisted largely of the 50,000 children under 10 years of age. There were an estimated 2,000 to

FIGURE 3

YELLOW FEVER ENDEMIC ZONE IN AFRICA



Source of Data:
International Sanitary Regulations, Third Edition, World Health Organization, Geneva, 1966.

TABLE 2
Yellow Fever in Africa
Major Political Subdivisions Within Countries Reporting One or More Human Cases

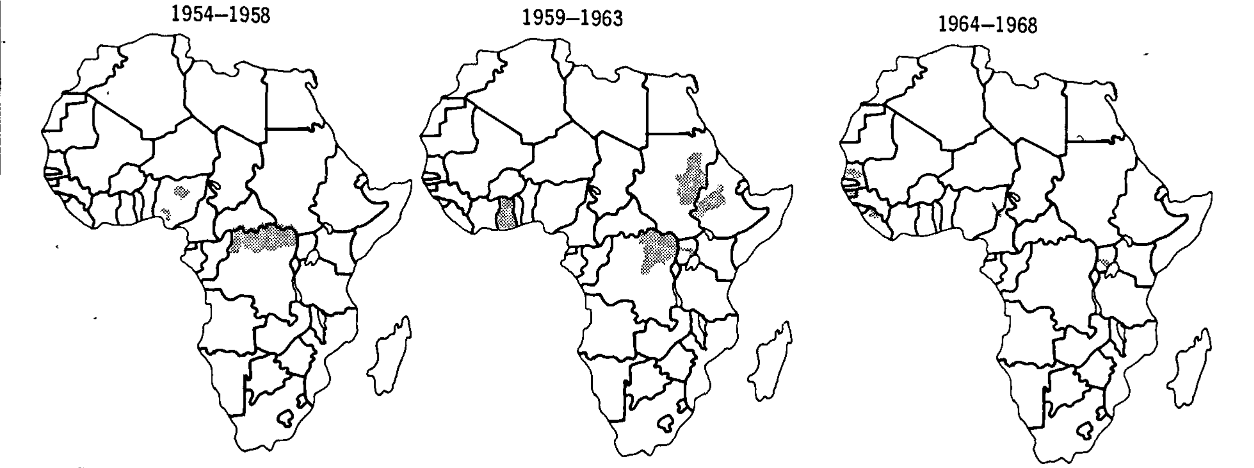
COUNTRY	1954	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	Total
AFRICA	—	—	3	5(2)	60	132	7	3004	10	3	7	238	—	5	—	3474
BELGIAN CONGO	—	—	3	3	60	11	7	4	—	—	—	—	—	—	—	88
Orientale	—	—	3	1	—	11	7	4	—	—	—	—	—	—	—	26
Equateur	—	—	—	2	—	—	—	—	—	—	—	—	—	—	—	2
Province not specified	—	—	—	—	60	—	—	—	—	—	—	—	—	—	—	60
NIGERIA	—	—	—	2*	—	—	—	—	—	—	—	—	—	—	—	2*
Lagos Col.	—	—	—	1*	—	—	—	—	—	—	—	—	—	—	—	1*
Lokoja	—	—	—	1*	—	—	—	—	—	—	—	—	—	—	—	1*
GHANA	—	—	—	—	—	2	—	—	—	3	—	—	—	—	—	5
Acra	—	—	—	—	—	2	—	—	—	—	—	—	—	—	—	2
Ashanti	—	—	—	—	—	—	—	—	—	1	—	—	—	—	—	1
Northern	—	—	—	—	—	—	—	—	—	2	—	—	—	—	—	2
SENEGAL	—	—	—	—	—	—	—	—	—	—	—	238	—	—	—	238
Diourbel Reg.	—	—	—	—	—	—	—	—	—	—	—	238	—	—	—	238
SUDAN	—	—	—	—	—	118	—	—	—	—	—	—	—	—	—	118
Blue Nile	—	—	—	—	—	112	—	—	—	—	—	—	—	—	—	112
Upper Nile	—	—	—	—	—	6	—	—	—	—	—	—	—	—	—	6
ETHIOPIA	—	—	—	—	—	—	—	3000	10	—	—	—	—	—	—	3010
Gamu-Goffa	—	—	—	—	—	—	—	3000	—	—	—	—	—	—	—	3000
Kaffa	—	—	—	—	—	—	—	—	10	—	—	—	—	—	—	10
UGANDA	—	—	—	—	—	1	—	—	—	—	1	—	—	—	—	2
Buganda	—	—	—	—	—	1	—	—	—	—	1	—	—	—	—	2
PORT. GUINEA	—	—	—	—	—	—	—	—	—	—	6	—	—	—	—	6
Catio	—	—	—	—	—	—	—	—	—	—	2	—	—	—	—	2
Farim	—	—	—	—	—	—	—	—	—	—	2	—	—	—	—	2
Gabu	—	—	—	—	—	—	—	—	—	—	2	—	—	—	—	2
LIBERIA	—	—	—	—	—	—	—	—	—	—	—	—	—	5	—	5
Lofa	—	—	—	—	—	—	—	—	—	—	—	—	—	5	—	5

*Not Confirmed

Source of Data: World Health Organization-Weekly Epidemiological Record, Geneva, 1954-1968

FIGURE 4

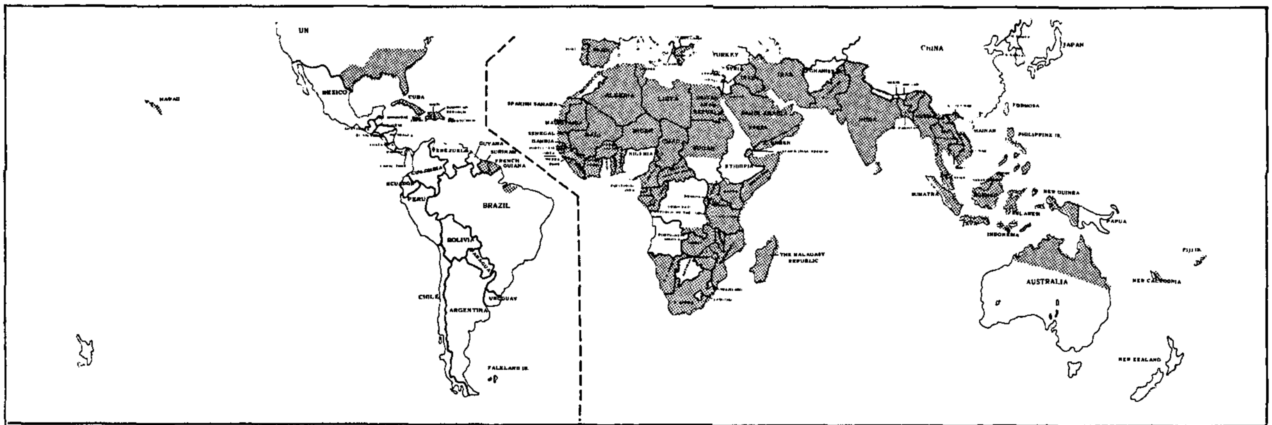
YELLOW FEVER IN AFRICA, 1954–1968
MAJOR POLITICAL SUBDIVISIONS WITHIN COUNTRIES
REPORTING ONE OR MORE HUMAN CASES



Source of Data: World Health Organization, Weekly Epidemiological Record, Geneva, 1954–1968.

FIGURE 5

YELLOW FEVER RECEPTIVE AREAS



OCEANIA

American Samoa
Australia
Br. Solomon Is. Protectorate
Cook Islands
Fiji
Fr. Polynesia
Gilbert and Ellice Is.
Guam
Nauru
New Caledonia
New Hebrides
Tonga
Trust Terr. of the Pacific
W. Samoa

AMERICAS

Antigua
Bahamas
Barbados
Brazil
Cayman Is.
Cuba
Dominica
Dominican Rep.
El Salvador
Fr. Guiana
Grenada
Guadeloupe
Haiti
Jamaica
Martinique
Montserrat
Neth. Antilles
Puerto Rico
St. Christopher–Nevis-Anguilla
St. Lucia
St. Vincent
Surinam
Trinidad
Turks and Caicos Is.
U. S. A.
Virgin Is. (U.S.)

EUROPE

Albania
Cyprus
Greece
Portugal
Spain (The Canary Is.)

AFRICA

Algeria
Botswana
Burundi
Cameroon
Cape Verde Is.
Cent. African Rep.
Chad
Comoro Is.
Congo (Brazzaville)
Congo, Dem. Rep
Dahomey
Equatorial Guinea
Fr. Territ. of Afars and the Issas
Gabon
Gambia
Ifni
Ivory Coast
Kenya
La Reunion
Liberia
Libya
Madegascar
Malawi
Mali
Mauritania
Mauritius
Mozambique
Namibia
Niger
Port. Guinea
Rwanda
Sao Tome and Principe
Seychelles
Sp. Sahara
Sudan
Togo
Tunisia
Uganda
United Arab Rep.
Tanzania
Upper Volta
Zambia

ASIA

Bahrain
Brunei
Burma
Cambodia
Ceylon
India
Indonesia
Iran
Iraq
Kuwait
Laos
Lebanon
Macao
Malaysia
Pakistan
Philippines
Port. Timor
Qatar
Ryukyu Is.
Saudi Arabia
Senegal
Singapore
Somalia
S. Africa
S. Rhodesia
S. Yemen
Thailand
Trucial States
Viet Nam Rep.
Yemen

Source of Data: World Health Organization, Weekly Epidemiological Record, Geneva, Vol. 44, No. 2.

20,000 cases, with an estimated 15 percent case fatality rate. Ninety percent of the deaths were in children under 10 years of age. The epidemic was rapidly terminated through *A. aegypti* control by spraying, and by mass vaccination of children.

This epidemic emphasized that jungle yellow fever may become epidemic whenever a suitable vector and a susceptible population meet, and that a high vaccination rate must be maintained when jungle yellow fever exists nearby. In addition, it was found that yellow fever in children, like many viral illnesses, is clinically less characteristic and less severe than in adults, and an outbreak in children can be overlooked until it reaches epidemic proportions.

YELLOW FEVER AS A WORLD PROBLEM

Large areas of the world harbor species of mosquitoes that could transmit yellow fever (Figure 5). To date, however, yellow fever has occurred only in Africa, the Americas, and portions of Western Europe, and it is currently limited to Africa and South America. The continued absence of yellow fever from other receptive areas, most notably the Indian subcontinent, Southeast Asia, and the South Pacific results from three conditions. First, in the 16th through 18th centuries when yellow fever was being introduced to the Americas from West Africa, the chain of infection could not be maintained during long sea voyages to the Far East. Whether climatic conditions encountered rounding the tips of South America and Africa or whether the length of the voyage itself was responsible is not known. Second, by the time the Panama Canal had been opened early in this century and more rapid means of travel had become available, yellow fever had been eliminated from most of the port cities of the Americas, thus removing this important source of infection. Third, effective quarantine and immunization measures have been instituted for world travel and commerce, with worldwide surveillance coordinated through the World Health Organization. These measures have helped prevent possible introduction and have allowed rapid attack on threatening epidemic situations. In this time of rapid travel, immunity through vaccination must be maintained if yellow fever is to remain a pestilence of the past.

FOREIGN QUARANTINE PROGRAM

See p. 135 for the Recommendation of the PHS Advisory Committee on Immunization Practices on the use of yellow fever vaccine.

UNITED STATES IMMUNIZATION SURVEY 1967-1968

United States Immunization Survey 1967—1968

These tables present the 1967 and 1968 results of the annual September National Immunization Survey conducted by the Bureau of the Census in cooperation with the National Communicable Disease Center.

Immunization data were collected by the Bureau through a special list of questions attached to the regular monthly questionnaire designed to obtain current population estimates.[1] The sample for estimates of immunization levels of the population of the United States comprised 35,000 households that included about 100,000 persons.

Although the first such survey, conducted in 1957, was for the purpose of collecting information on poliomyelitis immunization status, the scope of the survey was enlarged in 1963 to include information on immunization against other diseases. The format, except for minor changes, has remained the same since that year.

Each year shortly before the immunization survey, an "alert" letter is addressed to households in the sample, advising that questions will be asked on the immunization status of each member of the household. The letter suggests that the respondent "may wish to look up records" on immunizations against specified diseases and to discuss the topic with other members of the family "before the interviewer calls."

In September 1967, information was obtained on poliomyelitis, diphtheria-pertussis-tetanus, measles and smallpox vaccine doses; and on history of measles, rubella and mumps for specified age groups.

After adjusting the immunization sample reports to the current estimates of the population, the data are presented not only for the United States and major geographic divisions, but also for Standard Metropolitan Statistical Areas (SMSA) and for "Poverty Areas" within the largest SMSAs of the United States.

The concept of "Standard Metropolitan Statistical Areas," was developed by the Bureau of the Budget [2] to meet the need for presentation of general-purpose statistics by agencies of the Federal Government, in accordance with specific criteria for defining such areas. A metropolitan area is an integral economic and social unit with a recognized large population nucleus. Thus, each SMSA must contain at least one city of 50,000 population or more. The SMSA will then include the county of such a central city and adjacent counties that are found to be metropolitan in character and closely associated with the central city. (In New England, the requirement with regard to a central city as a nucleus still holds, but the units comprising the area are towns rather than counties.)

The data presented by SMSAs in the tables are based on the 212 Standard Metropolitan Statistical Areas of the United States as of 1960.[3] The coded list below indicates the various geographic categories for which estimates are given in this report on immunization status.

UNITED STATES
STANDARD METROPOLITAN
STATISTICAL AREA (SMSAs)

[Code]

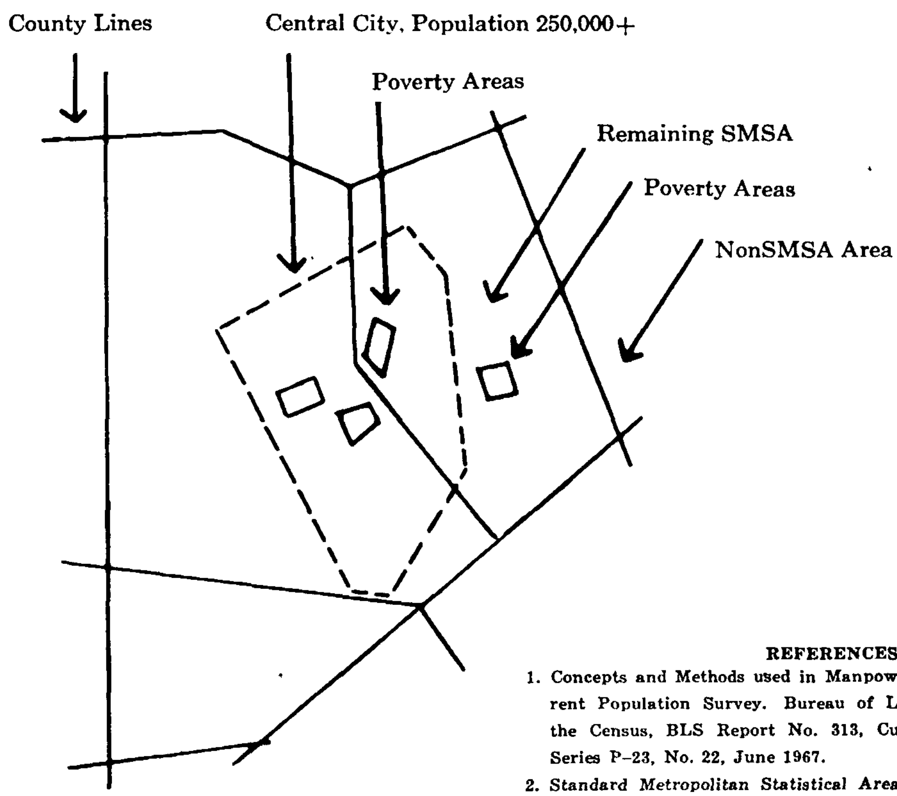
- [*1*] *SMSAs with Central City, Population 250,000+*
  - [*1a*] *Central Cities, population 250,000+*
    - [*1a1*] *Poverty Areas*
    - [*1a2*] *Nonpoverty Areas*
  - [*1b*] *Remaining Areas in SMSAs*
    - [*1b1*] *Poverty Areas*
    - [*1b2*] *Nonpoverty Areas*
- [*2*] *SMSAs with Central City, Population <250,000*
  - [*2a*] *Central Cities*
  - [*2b*] *Remaining areas in SMSAs*
- [*3*] *NonSMSA Areas (Counties not associated with large urban centers)*

"Poverty areas" in the SMSAs of the United States were determined [4] by ranking Census Tracts (divisions within an SMSA comprising a population averaging 6,000 persons) in those SMSAs with a central city of 250,000 population or more, according to the relative presence of each of five equally-weighted poverty-lined characteristics: percent of families with incomes under $3,000; percent of children under 18 years not living with both parents; percent of persons 25 years and over with less than 8 years of school completed; percent of unskilled males in the employed civilian labor force; and percent of housing units dilapidated or lacking some or all plumbing facilities.

The diagram shows the various components of an SMSA for which pooled data for all the SMSAs in the United States (as of 1960) are presented in this report.

—ILS

STANDARD METROPOLITAN STATISTICAL AREA



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1. Concepts and Methods used in Manpower Statistics from the Current Population Survey. Bureau of Labor Statistics, Bureau of the Census, BLS Report No. 313, Current Population Reports, Series P–23, No. 22, June 1967.
2. *Standard Metropolitan Statistical Areas.* Prepared by the Office of Statistical Standards, Bureau of the Budget, Executive Office of the President.
3. County and City Data Book. A Statistical Abstract Supplement. U.S. Department of Commerce, Bureau of the Census, Government Printing Office, Washington, 1962.
4. Current Population Reports, Series P–23, No. 19; and *Poverty Areas in the 100 Largest Metropolitan Areas,* Supplementary Reports to the 1960 Census of Population, PC(51)-54, November 13, 1967. Bureau of the Census.

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December 1968

1967

TABLE 1.

POLIOVACCINE STATUS—ORAL (OPV) AND INACTIVATED (IPV), UNITED STATES, *1967*
Percent of Population with Doses as Specified
Age 1-19

Area	Population in Thousands	3 OPV and 3 or more IPV	3 OPV and less than 3 IPV	3 or more IPV and less than 3 OPV	Total	2 OPV and 0,1,2 IPV	Cumulative Total	All other Combinations Except NEVER Vaccinated	No OPV and No IPV
United States	73,319	33.8	28.2	21.6	83.6	5.2	88.8	6.5	4.7
White	62,516	34.8	27.9	22.4	85.1	4.9	90.0	5.9	4.2
Other Races	10,803	28.5	29.9	17.0	75.4	7.1	82.5	9.8	7.7
All Central Cities, SMSAs Code [1a] + [2a]	20,351	30.4	27.2	23.0	80.6	6.6	87.2	8.6	4.2
White	14,834	32.3	26.6	24.4	83.3	5.4	88.7	7.7	3.6
Other Races	5,517	25.2	28.6	19.4	73.2	9.8	83.0	11.1	6.0
Remaining Areas in SMSAs Code [1b] + [2b]	25,847	34.3	29.3	22.0	85.6	5.2	90.8	5.8	3.3
NonSMSA Area Code [3]	27,121	36.0	27.8	20.2	84.0	4.2	88.2	5.6	6.3
Central Cities, Population 250,000+ Code [1a]									
Poverty Areas Code [1a1]	4,974	25.2	27.6	19.7	72.5	9.4	81.9	6.2	11.8
Nonpoverty Areas Code [1a2]	11,898	33.0	26.0	24.3	83.3	5.5	88.8	7.7	3.5
Remaining Areas in SMSAs Code [1b]									
Poverty Areas Code [1b1]	1,693	35.3	26.4	18.0	79.7	3.5	83.2	10.1	6.8
Nonpoverty Areas Code [1b2]	20,670	34.2	29.0	22.7	85.9	5.4	91.3	5.8	3.0
Central Cities Population <250,000 Code [2a]	3,479	28.9	30.6	23.3	82.8	6.3	89.1	7.0	3.9
Remaining Areas in SMSAs Code [2b]	3,485	34.3	32.7	19.9	86.9	5.2	92.1	4.1	3.8

TABLE 2.

POLIOVACCINE STATUS—UNITED STATES, *1967* BY MAJOR GEOGRAPHIC DIVISIONS
Ages 1-19
Percent of Population with Doses as Specified

Area	Population in Thousands	3 OPV and 3 or more IPV	3 OPV and less than 3 IPV	3 or more IPV and less than 3 OPV	Total	2 OPV and 0,1,2 IPV	Cumulative Total	All other Combinations Except NEVER Vaccinated	No OPV and No IPV
New England States	4,517	42.0	31.3	14.1	87.4	4.1	91.5	5.4	3.1
Middle Atlantic States	12,213	32.6	23.2	27.2	83.0	5.8	88.8	7.7	3.5
East North Central States	15,144	26.2	21.5	33.0	80.7	7.0	87.7	7.3	5.0
West North Central States	5,812	31.1	25.1	26.7	82.9	5.7	88.6	5.8	5.6
South Atlantic States	10,845	37.2	31.9	15.1	84.2	4.9	89.1	5.6	5.3
East South Central States	5,353	42.4	33.2	12.2	87.8	2.6	90.4	3.9	5.7
West South Central States	6,691	35.6	32.2	11.0	78.8	5.0	83.8	8.9	7.3
Mountain States	3,189	38.0	41.1	10.0	89.1	2.9	92.0	4.5	3.4
Pacific States	9,556	34.1	31.2	20.8	86.1	4.7	90.8	6.1	3.1

TABLE 3.

POLIOVACCINE STATUS—UNITED STATES, *1967*
Ages 1-19, by 5-Year Age Groups
Percent of Population with Doses as Specified

Age Groups									
				United States, All Races					
1-4	15,552	11.7	39.9	19.3	70.9	8.7	79.6	8.8	11.7
5-9	20,862	37.1	29.7	21.5	88.3	4.6	92.9	3.9	3.1
10-14	19,827	43.4	24.1	22.2	89.7	4.1	93.8	4.0	2.2
15-19	17,078	39.0	20.3	23.2	82.5	4.1	86.6	10.5	3.1
				White					
1-4	12,995	11.5	41.5	20.1	73.1	8.6	81.7	8.2	10.1
5-9	17,719	38.3	29.2	22.3	89.8	4.2	94.0	3.3	2.7
10-14	17,055	44.6	23.2	22.9	90.7	3.8	94.5	3.5	2.2
15-19	14,747	39.7	19.7	24.1	83.5	3.7	87.2	10.0	2.9
				Other Races					
1-4	2,557	12.9	32.2	15.1	60.2	8.8	69.0	11.6	19.5
5-9	3,144	30.2	32.9	17.4	80.5	7.0	87.5	7.7	4.8
10-14	2,772	36.0	29.4	18.1	83.5	6.5	90.0	7.3	2.8
15-19	2,331	34.5	23.9	17.1	75.5	6.3	81.8	13.7	4.5

TABLE 4.

DIPHTHERIA-PERTUSSIS-TETANUS (DPT) IMMUNIZATION STATUS, UNITED STATES, *1967*
Ages 1-13 years
Number of Injections as Specified

Age	Population (Thousands)	Number of Injections				Unknown		Percent with		
		<4	3	1-2	0	No.	Status	<4	3	0
United States, All Races										
1	3,629	692	1,949	606	372	8	2	19.1	53.7	10.3
2	3,821	1,262	1,716	464	370	2	8	33.0	44.9	9.7
3	4,009	1,630	1,562	427	365	11	15	40.7	39.0	9.1
4	4,093	1,895	1,415	415	334	24	9	46.3	34.6	8.2
1-4	15,552	5,478	6,641	1,912	1,442	45	34	35.2	42.7	9.3
5-9	20,862	13,154	5,126	1,588	818	120	56	63.1	24.6	3.9
10-13	16,022	10,566	3,752	950	597	86	70	65.9	23.4	3.7
White										
1-4	12,995	4,911	5,637	1,431	959	31	27	37.8	43.4	7.4
5-9	17,719	11,778	4,117	1,178	531	67	48	66.5	23.2	3.0
10-13	13,746	9,500	3,014	703	413	65	51	69.1	21.9	3.0
Other Races										
1-4	2,557	567	1,005	481	483	14	7	22.2	39.3	18.9
5-9	3,144	1,376	1,009	410	288	53	8	43.8	32.1	9.2
10-13	2,276	1,066	738	248	184	21	19	46.8	32.4	8.0

TABLE 5.

DIPHTHERIA-PERTUSSIS-TETANUS (DPT) IMMUNIZATION STATUS, UNITED STATES, *1967*

Ages 1-4, 5-9, 10-13, by SMSA Components
Number of Injections as Specified

Age	Population (Thousands)	Number of Injections >4	3	1-2	0	Unknown No.	Status	Percent with >4	3	0
				Central Cities, Population 250,000+						
				Poverty Areas						
				Code [1a1]						
1-4	1,173	237	420	267	225	14	9	20.2	35.8	19.2
5-9	1,409	595	458	211	113	22	9	42.2	32.5	8.0
10-13	1,011	442	342	163	50	10	4	43.7	33.8	4.9
				Nonpoverty Areas						
				Code [1a2]						
1-4	2,501	915	1,037	366	174	5	4	36.6	41.5	7.0
5-9	3,374	2,107	809	328	93	29	8	62.4	24.0	2.8
10-13	2,532	1,583	671	166	80	17	4	62.5	26.5	3.2
				Remaining Areas in SMSAs						
				Poverty Areas						
				Code [1b1]						
1-4	365	113	132	64	56	0	0	31.0	36.2	15.3
5-9	410	243	112	25	27	2	0	59.3	27.3	6.1
10-13	396	225	110	30	30	0	0	56.8	27.8	7.6
				Nonpoverty Areas						
				Code [1b2]						
1-4	4,413	1,676	2,041	499	185	7	4	38.0	46.2	4.2
5-9	5,918	3,969	1,400	413	96	31	10	67.1	23.7	1.6
10-13	4,591	3,195	1,036	222	95	35	9	69.6	22.6	2.1
				Central Cities, Population <250,000						
				Code [2a]						
1-4	741	261	284	118	74	4	0	35.2	38.3	10.0
5-9	968	654	207	69	34	0	4	67.6	21.4	3.5
10-13	760	540	161	35	18	5	2	71.0	21.2	2.4
				Remaining Areas in SMSAs						
				Code [2b]						
1-4	756	313	322	79	41	2	0	41.4	42.6	5.4
5-9	1,066	797	192	47	24	6	0	74.8	18.0	2.3
10-13	719	529	132	35	18	0	5	73.6	18.4	2.5
				NonSMSA Areas						
				Code [3]						
1-4	5,603	1,963	2,405	521	686	12	17	35.0	42.9	12.2
5-9	7,717	4,790	1,948	493	431	28	26	62.1	25.2	5.6
10-13	6,012	4,051	1,300	299	307	19	36	67.4	21.6	5.1

TABLE 6.

DIPHTHERIA-PERTUSSIS-TETANUS (DPT) IMMUNIZATION STATUS, UNITED STATES, *1967*
By Major Geographic Divisions
By Age Groups 1-4, 5-9

Area Age Group	Percent With <4	 3	 0
United States			
1-4	35.2	42.7	9.3
5-9	63.1	24.6	3.9
New England			
1-4	32.7	53.7	5.6
5-9	62.8	28.6	3.6
Middle Atlantic			
1-4	35.8	40.5	8.2
5-9	57.6	29.1	3.2
East North Central			
1-4	31.6	44.9	8.5
5-9	61.0	26.0	3.5
West North Central			
1-4	31.7	47.2	11.6
5-9	68.2	20.0	3.6
South Atlantic			
1-4	35.9	41.8	9.5
5-9	61.5	24.5	5.0
East South Central			
1-4	43.1	34.4	13.3
5-9	70.8	20.2	4.3
West South Central			
1-4	37.4	32.3	17.7
5-9	64.5	20.7	7.6
Mountain			
1-4	37.2	47.7	5.3
5-9	71.5	20.9	1.7
Pacific			
1-4	36.2	45.5	5.4
5-9	63.8	23.8	2.7

TABLE 7.

SMALLPOX VACCINATION STATUS, UNITED STATES, *1967*
All Ages

Age	Population (Thousands)	Total Ever Vaccinated	Vaccinated within Past 12 Mo. Total	Vaccinated within Past 12 Mo. 1st	Vaccinated within Past 12 Mo. Revac.	Vaccinated within Past 12 Mo. Prior Status Unk.	Vac. Status Unk.	Never Vaccinated	Percent Reported Vaccinated Ever	Percent Reported Vaccinated Never	Percent Reported Vaccinated Past 12 Mo.
<1	3,569	632	—	—	—	—	—	—	17.7	—	—
1	3,629	1,964	1,530	1,479	51	0	25	1,640	54.1	45.2	42.2
2	3,821	2,461	770	676	88	6	22	1,339	64.4	35.0	20.2
3	4,009	2,748	525	420	103	2	14	1,247	68.5	31.1	13.1
4	4,093	3,024	573	433	140	0	19	1,050	73.9	25.7	14.0
1-4	15,552	10,195	3,397	3,008	381	8	79	5,277	65.6	33.9	21.8
5-9	20,862	19,131	3,412	1,519	1,882	11	50	1,681	91.7	8.1	16.4
10-14	19,827	18,903	1,834	260	1,570	4	76	849	95.3	4.3	9.3
15-19	17,078	16,024	1,352	106	1,244	2	365	690	93.8	4.0	7.9
20-29	25,306	23,673	1,459	113	1,335	11	430	1,203	93.5	4.8	5.8
30-39	21,762	20,266	810	54	754	2	371	1,125	93.1	5.2	3.7
40-49	23,796	21,605	840	42	798	0	435	1,757	90.8	7.4	3.5
50-64	28,027	23,566	746	50	693	3	639	3,821	84.1	13.6	2.7
65+	18,103	13,520	288	16	272	0	464	4,119	74.7	22.8	1.6
1 & Over	190,313	166,883	14,138	5,162	8,930	41	2,909	20,522	87.7	10.8	7.4
				White							
1-4	12,995	8,617	2,730	2,429	297	4	68	4,314	66.3	33.2	21.0
1 & Over	167,457	147,570	11,676	4,058	7,592	26	2,359	17,531	88.1	10.5	7.0
				Other Races							
1-4	2,557	1,580	667	579	84	4	12	.963	61.8	37.7	26.1
1 & Over	22,857	19,314	2,460	1,109	1,337	14	547	2,991	84.5	13.1	10.7
				Central Cities, Population 250,000+ Poverty Areas Code [1a1]							
1-4	1,173	752	341	286	55	0	9	411	64.1	35.0	29.1
1 & Over	12,487	10,789	1,222	529	690	3	366	1,330	86.4	10.7	9.8
				Nonpoverty Areas Code [1a2]							
1-4	2,501	1,898	673	563	104	6	5	598	75.9	23.9	26.9
1 & Over	34,828	31,895	2,806	868	1,926	12	721	2,212	91.6	6.4	8.1

TABLE 8.

SMALLPOX VACCINATION STATUS BY MAJOR GEOGRAPHIC DIVISIONS,* *1967*

Ages 1-4; 1 and over

Area	Age 1-4 Percent Reported		Age 1 and Over Percent Reported	
	Ever Vaccinated	Never Vaccinated	Ever Vaccinated	Never Vaccinated
United States	65.6	33.9	87.7	10.8
New England	70.8	29.0	92.7	6.2
Middle Atlantic	72.3	27.4	92.6	5.6
East North Central	69.2	30.5	87.5	10.8
West North Central	65.0	34.6	81.8	16.6
South Atlantic	58.8	40.6	87.0	11.7
East South Central	52.2	47.6	80.5	18.7
West South Central	44.4	54.7	82.0	16.3
Mountain	77.1	21.5	89.9	8.9
Pacific	74.7	24.7	90.3	8.0

TABLE 9.

PERCENT OF PERSONS BY SINGLE YEAR OF LIFE REPORTED WITH HISTORY OF MEASLES, MEASLES VACCINE, RUBELLA, MUMPS, *1967*

Ages 0-13

Age Group	History of Measles (8-Day) Infection	Percent of Population of Specified Age Who Received Measles Vaccine	History of Rubella (3-Day Measles) Infection	History of Mumps Infection
<1	2.8	10.6	5.6	1.9
1	6.1	54.1	13.8	5.6
2	10.5	60.0	16.4	9.8
3	15.6	57.0	21.8	14.9
4	18.3	54.5	28.0	20.2
5	25.2	54.7	34.7	28.7
6	35.8	47.8	41.1	35.9
7	41.8	40.1	46.3	45.4
8	51.9	33.3	53.6	47.5
9	57.9	27.6	58.4	51.7
10	63.4	21.6	63.0	56.9
11	66.1	18.8	63.9	58.0
12	66.9	15.4	66.1	60.4
13	69.5	13.7	68.3	60.8
	SUMMARY—by Age Groups, 1-4, 5-9, 10-13			
1-4	12.8	56.4	20.2	12.9
5-9	42.5	40.8	46.8	41.8
10-13	66.4	17.4	65.3	59.0

TABLE 10.

PERCENT OF PERSONS WITH REPORTED HISTORY OF MEASLES, MEASLES VACCINE, RUBELLA, MUMPS, *1967*
By Age Groups and Selected Population Groups

Age Group	History of Measles (8-Day) Infection	Percent of Population of Specified Age Who Received Measles Vaccine	History of Rubella (3-Day Measles) Infection	History of Mumps Infection
		Central Cities, Population 250,000+ Code [1a]		
		White		
1-4	11.9	62.7	19.5	10.7
5-9	41.5	45.4	45.4	39.5
10-13	68.0	19.5	62.9	54.9
		Other Races		
1-4	20.3	39.9	18.6	11.7
5-9	50.2	35.7	39.6	34.6
10-13	56.3	28.0	48.3	47.2
		Poverty Areas Code [1a1]		
1-4	17.8	37.0	19.3	12.4
5-9	50.2	33.9	40.0	37.2
10-13	58.3	28.5	50.4	44.3
		Nonpoverty Areas Code [1a2]		
1-4	13.3	64.3	19.1	11.2
5-9	42.5	46.6	43.4	38.2
10-13	65.8	21.1	59.5	55.6
		Remaining Areas in SMSAs Code [1b]		
1-4	10.6	63.3	18.5	13.5
5-9	40.4	44.7	46.0	43.7
10-13	65.7	17.5	65.2	60.7

TABLE 11.

PERCENT OF PERSONS REPORTING HISTORY OF MEASLES VACCINE AND SOURCE OF VACCINE, *1967*
Ages 1-4, 5-9, 10-13
By Selected Population Groups

Age Group	Population (Thousands)	Percent Reporting History of Measles Vaccine			Percent Receiving Vaccine Since 1/1/67
		Ever	From Priv. Phy.	Other Sources	
		United States			
1-4	15,552	56.4	42.2	14.2	19.2
5-9	20,861	40.8	29.3	11.5	7.6
10-13	16,023	17.4	11.1	6.3	2.6
		Central Cities Code [1a] + [2a] White			
1-4	3,043	62.7	48.6	14.1	20.2
5-9	4,104	45.4	33.8	11.6	8.2
10-13	3,176	19.5	14.7	4.8	2.1
		Other Races			
1-4	1,373	39.9	12.3	27.6	18.9
5-9	1,647	35.7	9.8	25.9	12.5
10-13	1,127	28.0	5.5	22.5	5.9

TABLE 12.

PERCENT OF PERSONS REPORTING HISTORY OF MEASLES VACCINE AND SOURCE OF VACCINE, *1967*

Ages 1-4, 5-9, 10-13 by SMSA Components

Age Group	Population (Thousands)	Percent Reporting History of Measles Vaccine			Percent Receiving Vaccine Since 1/1/67
		Ever	From Priv. Phy.	Other Sources	
		Central Cities, Population 250,000+ Poverty Areas Code [1a1]			
1-4	1,173	37.0	11.6	25.4	16.2
5-9	1,409	33.9	10.1	23.8	9.2
10-13	1,011	28.5	6.7	21.8	5.6
		Nonpoverty Areas Code [1a2]			
1-4	2,502	64.3	48.0	16.3	21.9
5-9	3,373	46.6	33.2	13.4	9.5
10-13	2,531	21.1	15.4	5.7	2.5
		Remaining Areas in SMSAs Poverty Areas Code [1b1]			
1-4	366	40.2	24.3	15.9	14.8
5-9	411	24.8	14.8	10.0	6.3
10-13	396	15.9	7.3	8.6	6.8
		Nonpoverty Areas Code [1b2]			
1-4	4,413	65.7	54.2	11.5	20.4
5-9	5,918	46.9	37.6	9.3	7.0
10-13	4,591	18.0	13.5	4.5	2.5
		Central Cities, Population <250,000 Code [2a]			
1-4	740	55.9	42.3	13.6	18.1
5-9	968	41.4	29.8	11.6	9.3
10-13	760	14.5	9.5	5.0	1.6
		Remaining Areas in SMSAs Code [2b]			
1-4	756	60.2	47.6	12.6	22.6
5-9	1,067	39.6	32.9	6.7	5.7
10-13	719	15.2	12.5	2.7	1.7
		NonSMSA Areas Code [3]			
1-4	5,604	50.1	36.9	13.2	17.6
5-9	7,718	35.7	24.9	10.8	7.2
10-13	6,013	14.3	8.5	5.8	2.3

TABLE 13.

IMMUNIZATIONS AMONG INFANTS (CHILDREN UNDER 1 YEAR—PERCENT WITH *ONE* DOSE OR MORE: DPT, OPV, IPV, MEASLES VACCINE, SMALLPOX VACCINATION, *1967*

Population (Thousands)	Diphtheria-Pertussis-Tetanus	Poliovaccine Oral	Poliovaccine Inactivated	Measles Vaccine	Smallpox Vaccination
		United States			
3,569	66.6	45.0	18.0	10.6	17.7
		Central Cities Code [1a] + [2a]			
1,053	66.1	44.3	24.1	10.2	21.2
		White			
711	70.6	49.6	22.5	10.5	20.3
		Other Races			
342	56.4	32.7	27.5	9.1	23.1
		Remaining Areas in SMSAs Code [1b] + [2b]			
1,267	69.1	45.1	17.5	10.7	17.4
		NonSMSA Areas Code [3]			
1,249	64.4	45.6	13.1	10.8	15.0

TABLE 14.

IMMUNIZATIONS AMONG INFANTS: DPT, MEASLES VACCINE, SMALLPOX VACCINATION IN POVERTY AND NONPOVERTY AREAS, *1967*

Population (Thousands)	Diphtheria-Pertussis-Tetanus	Measles Vaccine	Smallpox Vaccination
	Central Cities, Population 250,000 + Code [1a]		
889	65.0	10.5	21.9
	Poverty Areas Code [1a1]		
308	54.5	7.8	17.5
	Nonpoverty Areas Code [1a2]		
581	70.6	11.9	24.3
	Remaining Areas in SMSAs Code [1b]		
1,083	69.3	11.8	18.3
	Poverty Areas Code [1b1]		
89	71.9	12.4	14.6
	Nonpoverty Areas Code [1b2]		
994	69.1	11.8	18.6

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TABLE 1.

POLIOVACCINE STATUS—ORAL (OPV) AND INACTIVATED (IPV), UNITED STATES, *1968*

Percent of Population with Doses as Specified
Age 1-19

Area	Population in Thousands	3 OPV and 3 or more IPV	3 OPV and less than 3 IPV	3 or more IPV and less than 3 OPV	Total	2 OPV and 0,1,2 IPV	Cumulative Total	All other Combinations Except NEVER Vaccinated	No OPV and No IPV
United States	73,653	30.0	32.1	19.4	81.5	6.6	88.1	7.6	4.4
White	62,679	31.0	32.3	19.9	83.2	6.2	89.4	6.9	3.7
Other Races	10,974	24.5	30.9	16.3	71.7	8.9	80.6	11.2	8.3
All Central Cities, SMSAs Code [1a] + [2a]	20,118	27.6	30.4	19.9	77.9	7.8	85.7	9.4	5.0
White	14,369	29.3	30.2	21.2	80.7	7.2	87.9	8.1	4.0
Other Races	5,749	23.3	30.8	16.7	70.8	9.3	80.1	12.4	7.4
Remaining Areas in SMSAs Code [1b] + [2b]	26,950	31.7	34.2	18.5	84.4	6.4	90.8	6.7	2.5
NonSMSA Area Code [3]	26,585	30.2	31.3	19.8	81.3	5.8	87.1	7.1	5.9
Central Cities, Population 250,000+ Code [1a]									
Poverty Areas Code [1a1]	4,953	25.0	29.1	16.6	70.7	9.0	79.7	13.0	7.4
Nonpoverty Areas Code [1a2]	11,748	28.2	31.1	21.3	80.6	7.2	87.8	8.1	4.1
Remaining Areas in SMSAs Code [1b]									
Poverty Areas Code [1b1]	1,757	30.1	34.0	16.3	80.4	5.9	86.3	8.8	5.0
Nonpoverty Areas Code [1b2]	21,396	31.4	34.1	19.1	84.6	6.4	91.0	6.7	2.4
Central Cities Population <250,000 Code [2a]	3,417	29.2	29.7	20.1	79.0	8.3	87.3	8.3	4.4
Remaining Areas in SMSAs Code [2b]	3,797	34.1	34.9	16.2	85.2	6.3	91.5	6.0	2.3

TABLE 2.

POLIOVACCINE STATUS—UNITED STATES, *1968* BY MAJOR GEOGRAPHIC DIVISIONS

Ages 1-19

Percent of Population with Doses as Specified

Area	Population in Thousands	3 OPV and 3 or more IPV	3 OPV and less than 3 IPV	3 or more IPV and less than 3 OPV	Total	2 OPV and 0,1,2 IPV	Cumulative Total	All other Combinations Except NEVER Vaccinated	No OPV and No IPV
New England States	4,470	33.1	36.8	14.8	84.7	6.9	91.6	6.2	2.1
Middle Atlantic States	11,966	30.4	29.7	23.6	83.7	6.0	89.7	7.4	3.0
East North Central States	15,499	24.7	25.9	27.8	78.4	8.2	86.6	8.5	4.9
West North Central States	5,404	26.6	26.8	26.3	79.7	7.2	86.9	8.3	4.9
South Atlantic States	11,241	31.9	33.6	14.4	79.9	6.9	86.8	7.6	5.6
East South Central States	5,126	38.2	35.9	11.1	85.2	5.0	90.2	5.2	4.6
West South Central States	7,095	29.9	36.4	12.1	78.4	6.2	84.6	8.7	6.7
Mountain States	3,368	34.0	43.4	8.5	85.9	3.6	89.5	6.9	3.6
Pacific States	9,483	30.8	34.8	17.9	83.5	6.0	89.5	7.2	3.4

TABLE 3.

POLIOVACCINE STATUS—UNITED STATES, *1968*

Ages 1-19, by 5-Year Age Groups

Percent of Population with Doses as Specified

Age Groups	Population in Thousands	3 OPV and 3 or more IPV	3 OPV and less than 3 IPV	3 or more IPV and less than 3 OPV	Total	2 OPV and 0,1,2 IPV	Cumulative Total	All other Combinations Except NEVER Vaccinated	No OPV and No IPV
				United States, All Races					
1-4	14,994	9.3	42.9	16.1	68.3	10.4	78.7	10.8	10.5
5-9	20,856	30.3	35.5	19.1	84.9	6.5	91.4	5.2	3.3
10-14	20,223	39.4	28.0	20.4	87.8	5.2	93.0	4.8	2.2
15-19	17,580	36.5	23.5	21.3	81.3	4.9	86.2	10.8	3.0
				White					
1-4	12,488	9.2	45.0	16.8	71.0	10.3	81.3	10.1	8.5
5-9	17,649	30.9	35.9	19.5	86.3	6.1	92.4	4.6	2.9
10-14	17,356	40.8	27.6	20.8	89.2	4.7	93.9	4.2	1.9
15-19	15,185	37.8	23.0	21.7	82.5	4.4	86.9	10.2	2.8
				Other Races					
1-4	2,506	9.7	32.3	12.5	54.5	10.7	65.2	14.7	20.2
5-9	3,207	27.0	33.4	16.6	77.0	8.8	85.8	8.4	5.9
10-14	2,867	31.2	30.5	17.6	79.3	8.6	87.9	8.2	3.9
15-19	2,394	28.5	26.4	18.3	73.2	7.7	80.9	14.8	4.3

TABLE 4.

DIPHTHERIA-PERTUSSIS-TETANUS (DPT) IMMUNIZATION STATUS, UNITED STATES, *1968*

Ages 1-13 years
Number of Injections as Specified

Age	Population (Thousands)	Number of Injections						Percent With		
						Unknown				
		>4	3	1-2	0	No.	Status	>4	3	0
				United States, All Races						
1	3,519	574	1,905	642	378	15	6	16.3	54.1	10.7
2	3,633	1,227	1,563	494	337	12	0	33.8	43.0	9.3
3	3,828	1,463	1,501	527	303	26	8	38.2	39.2	7.9
4	4,014	1,858	1,367	493	265	16	14	46.3	34.1	6.6
1-4	14,994	5,123	6,336	2,156	1,283	70	27	34.2	42.3	8.6
5-9	20,856	12,954	4,853	2,009	846	108	86	62.1	23.3	4.1
10-13	16,266	11,042	3,238	1,178	633	112	62	67.9	19.9	3.9
				White						
1-4	12,488	4,531	5,453	1,571	857	51	23	36.3	43.7	6.9
5-9	17,649	11,585	3,872	1,493	566	73	61	65.6	21.9	3.2
10-13	13,947	9,962	2,607	821	428	80	49	71.4	18.7	3.1
				Other Races						
1-4	2,506	591	882	585	425	18	4	23.6	35.2	17.0
5-9	3,207	1,370	981	516	280	35	25	42.7	30.6	8.7
10-13	2,319	1,080	631	358	204	32	13	46.6	27.2	8.8

TABLE 5.

DIPHTHERIA-PERTUSSIS-TETANUS (DPT) IMMUNIZATION STATUS, UNITED STATES, *1968*

Ages 1-4, 5-9, 10-13, by SMSA Components
Number of Injections as Specified

Age	Population (Thousands)	Number of Injections						Percent With		
						Unknown				
		>4	3	1-2	0	No.	Status	>4	3	0
				Central Cities, Population 250,000+ Poverty Areas Code [1a1]						
1-4	1,087	312	337	245	183	12	0	28.7	31.0	16.8
5-9	1,455	720	357	230	120	13	14	49.5	24.5	8.2
10-13	1,038	563	239	150	61	16	9	54.2	23.0	5.9
				Nonpoverty Areas Code [1a2]						
1-4	2,457	830	994	454	160	12	6	33.8	40.5	6.5
5-9	3,311	1,919	841	424	89	21	17	58.0	25.4	2.7
10-13	2,544	1,540	657	265	46	22	13	60.5	25.8	1.8
				Remaining Areas in SMSAs Poverty Areas Code [1b1]						
1-4	350	94	149	62	41	3	0	26.9	42.6	11.7
5-9	491	306	112	46	25	2	0	62.3	22.8	5.1
10-13	381	239	77	45	18	4	0	62.7	20.2	4.7
				Nonpoverty Areas Code [1b2]						
1-4	4,303	1,611	1,957	521	185	16	14	37.4	45.5	4.3
5-9	6,236	4,129	1,376	524	159	24	23	66.2	22.1	2.5
10-13	4,784	3,485	859	281	117	19	22	72.8	18.0	2.4
				Central Cities, Population <250,000 Code [2a]						
1-4	702	239	290	108	61	4	0	34.0	41.3	8.7
5-9	887	589	190	63	40	4	2	66.4	21.4	4.5
10-13	788	573	127	54	25	8	2	72.7	16.1	3.2
				Remaining Areas in SMSAs Code [2b]						
1-4	747	283	358	76	26	3	0	37.9	47.9	3.5
5-9	1,084	750	240	65	23	7	0	69.2	22.1	2.1
10-13	864	636	163	45	18	1	0	73.6	18.9	2.1
				NonSMSA Areas Code [3]						
1-4	5,348	1,753	2,251	690	627	19	7	32.8	42.1	11.7
5-9	7,392	4,541	1,737	657	391	37	29	61.4	23.5	5.3
10-13	5,867	4,007	1,116	338	348	43	15	68.3	19.0	5.9

TABLE 6.

DIPHTHERIA-PERTUSSIS-TETANUS (DPT) IMMUNIZATION STATUS, UNITED STATES, *1968*

By Major Geographic Divisions
By Age Groups 1-4, 5-9

Area Age Group	Percent With		
	<4	3	0
United States			
1-4	34.2	42.3	8.6
5-9	62.1	23.3	4.1
New England			
1-4	42.2	44.0	3.5
5-9	67.0	24.9	1.3
Middle Atlantic			
1-4	32.9	43.7	7.3
5-9	58.4	26.8	3.2
East North Central			
1-4	33.1	41.1	9.4
5-9	61.8	21.1	3.6
West North Central			
1-4	29.4	49.6	9.9
5-9	66.1	21.6	3.9
South Atlantic			
1-4	31.4	41.6	9.3
5-9	59.3	23.5	5.0
East South Central			
1-4	38.7	38.2	9.6
5-9	63.2	24.4	5.1
West South Central			
1-4	34.4	34.1	14.6
5-9	63.3	21.1	6.9
Mountain			
1-4	29.1	53.7	5.8
5-9	64.9	25.2	3.0
Pacific			
1-4	38.7	42.2	5.8
5-9	63.7	22.3	4.0

TABLE 7.

SMALLPOX VACCINATION STATUS, UNITED STATES, *1968*

All Ages

Age	Population (Thousands)	Total Ever Vaccinated	Vaccinated within Past 12 Mo. Total	1st	Revac	Prior Status Unk.	Vac. Status Unk.	Never Vaccinated	Percent Reported Vaccinated Ever	Never	Past 12 Mo.
<1	3,491	614	—	—	—	—	—	—	17.6	—	—
1	3,519	1,867	1,433	1,372	59	2	39	1,616	53.1	45.9	40.7
2	3,633	2,386	741	638	99	4	22	1,225	65.7	33.7	20.4
3	3,828	2,669	499	377	122	0	21	1,139	69.7	29.8	13.0
4	4,014	2,967	540	341	199	0	29	1,019	73.9	25.4	13.5
1-4	14,994	9,887	3,211	2,727	478	6	109	4,998	65.9	33.3	21.4
5-9	20,856	19,162	3,196	1,549	1,638	9	68	1,626	91.9	7.8	15.3
10-14	20,223	19,357	1,735	290	1,440	5	115	752	95.7	3.7	8.6
15-19	17,580	16,576	1,328	105	1,217	6	405	597	94.3	3.4	7.6
20-29	26,266	24,843	1,571	121	1,448	2	447	975	94.6	3.7	6.0
30-39	21,672	20,309	700	36	661	3	344	1,019	93.7	4.7	3.2
40-49	23,858	21,830	706	49	657	0	443	1,584	91.5	6.6	3.0
50-64	28,410	24,314	778	69	707	2	518	3,579	85.6	12.6	2.7
65+	18,412	14,047	329	24	305	0	420	3,946	76.3	21.4	1.8
1 & Over	192,272	170,326	13,555	4,971	8,552	32	2,870	19,077	88.6	9.9	7.0
White											
1-4	12,488	8,359	2,566	2,187	373	6	101	4,029	66.9	32.3	20.5
1 & Over	169,057	150,393	11,155	3,851	7,281	23	2,489	16,174	89.0	9.6	6.6
Other Races											
1-4	2,506	1,528	645	540	105	0	9	970	61.0	38.7	25.7
1 & Over	23,215	19,931	2,399	1,119	1,270	10	381	2,902	85.9	12.5	10.3
Central Cities, Population 250,000+ Poverty Areas Code [1a1]											
1-4	1,087	729	302	239	63	0	4	355	67.1	32.7	27.8
1 & Over	12,173	10,743	1,108	431	664	13	267	1,162	88.3	9.5	9.1
Nonpoverty Areas Code [1a2]											
1-4	2,457	1,825	574	468	106	0	6	626	74.3	25.5	23.4
1 & Over	34,679	32,042	2,686	804	1,882	0	589	2,049	92.4	5.9	7.7

TABLE 8.

SMALLPOX VACCINATION STATUS BY MAJOR GEOGRAPHIC DIVISIONS, *1968*

Ages 1-4, 1 and Over

Area	Age 1-4 Percent Reported: Ever Vaccinated	Age 1-4 Percent Reported: Never Vaccinated	Age 1 and Over Percent Reported: Ever Vaccinated	Age 1 and Over Percent Reported: Never Vaccinated
United States	65.9	33.3	88.6	9.9
New England	72.1	26.9	92.3	5.4
Middle Atlantic	73.3	26.1	94.1	4.3
East North Central	70.2	29.1	88.5	10.2
West North Central	62.6	37.5	81.9	16.5
South Atlantic	58.3	41.0	88.2	10.7
East South Central	50.8	48.2	81.5	17.6
West South Central	48.4	50.4	83.9	14.7
Mountain	74.5	25.5	90.3	8.6
Pacific	75.1	24.1	90.3	7.5

TABLE 9.

PERCENT OF PERSONS BY SINGLE YEAR OF LIFE REPORTED WITH HISTORY OF MEASLES, MEASLES VACCINE, RUBELLA, MUMPS, *1968*

Ages 0-13

Age	History of Measles (8-Day) Infection	Percent of Population of Specified Age Who Received Measles Vaccine	History of Rubella (3-Day Measles) Infection	History of Mumps Infection
<1	2.3	11.5	5.0	1.5
1	5.7	52.4	13.6	3.8
2	6.4	61.5	14.1	8.4
3	11.6	61.5	19.1	13.4
4	14.3	59.6	26.2	18.5
5	18.9	60.9	31.8	25.0
6	26.4	60.1	37.9	35.0
7	34.4	51.2	44.4	41.3
8	44.2	42.7	49.7	47.9
9	49.4	37.1	57.0	51.9
10	58.2	29.7	58.7	56.1
11	62.3	24.3	63.6	59.3
12	64.7	20.6	65.4	60.1
13	68.3	18.1	68.3	59.1
		SUMMARY—by Age Groups, 1-4, 5-9, 10-13		
1-4	9.7	58.8	18.5	11.3
5-9	34.7	50.4	44.2	40.3
10-13	63.3	23.2	64.0	58.7

TABLE 10.

PERCENT OF PERSONS WITH REPORTED HISTORY OF MEASLES, MEASLES VACCINE, RUBELLA, MUMPS, *1968*
By Age Groups and Selected Population Groups

Age Group	History of Measles (8-Day) Infection	Percent of Population of Specified Age Who Received Measles Vaccine	History of Rubella (3-Day Measles) Infection	History of Mumps Infection
		Central Cities, Population 250,000+ Code [1a]		
		White		
1-4	10.2	61.3	16.9	7.6
5-9	33.1	54.6	41.3	36.5
10-13	64.7	24.7	64.6	53.6
		Other Races		
1-4	15.6	46.8	15.0	10.1
5-9	37.7	42.8	37.8	33.2
10-13	55.1	32.7	47.3	47.7
		Poverty Areas Code [1a1]		
1-4	13.2	43.8	15.6	7.9
5-9	41.3	38.5	36.9	31.2
10-13	61.3	32.6	51.6	49.6
		Nonpoverty Areas Code [1a2]		
1-4	12.2	61.8	15.8	8.5
5-9	32.7	56.2	40.8	38.1
10-13	61.1	26.1	61.0	52.9
		Remaining Areas in SMSAs Code [1b]		
1-4	7.2	66.0	17.1	12.8
5-9	32.7	54.8	43.5	43.8
10-13	62.1	23.9	64.2	61.8

TABLE 11.

PERCENT OF PERSONS REPORTING HISTORY OF MEASLES VACCINE AND SOURCE OF VACCINE, *1968*
Ages 1-4, 5-9, 10-13
By Selected Population Groups

Age Group	Population (Thousands)	Percent Reporting History of Measles Vaccine: Ever	From Priv. Phy.	Other Sources	Percent Receiving Vaccine Since 1/1/68
		United States			
1-4	14,994	58.8	42.9	15.9	16.9
5-9	20,857	50.4	34.3	16.1	6.7
10-13	16,267	23.2	14.5	8.7	2.6
		Central Cities Code [1a] + [2a] White			
1-4	2,911	61.3	48.4	12.9	16.8
5-9	3,964	54.6	40.8	13.8	6.4
10-13	3,134	24.7	16.7	8.0	3.0
		Other Races			
1-4	1,336	46.8	15.9	30.9	18.1
5-9	1,689	42.8	12.3	30.5	8.8
10-13	1,236	32.7	7.2	25.5	4.8

TABLE 12.

PERCENT OF PERSONS REPORTING HISTORY OF MEASLES VACCINE AND SOURCE OF VACCINE, *1968*
Ages 1-4, 5-9, 10-13
By SMSA Components

Age Group	Population (Thousands)	Percent Reporting History of Measles Vaccine: Ever	From Priv. Phy.	Other Sources	Percent Receiving Vaccine Since 1/1/68
		Central Cities, Population 250,000+ Poverty Areas Code [1a1]			
1-4	1,087	43.8	14.0	29.8	15.9
5-9	1,454	38.5	11.7	26.8	7.3
10-13	1,038	32.6	7.1	25.5	4.5
		Nonpoverty Areas Code [1a2]			
1-4	2,457	61.8	47.6	14.2	17.4
5-9	3,312	56.2	40.1	16.1	6.9
10-13	2,543	26.1	16.6	9.5	3.2
		Remaining Areas in SMSAs Poverty Areas Code [1b1]			
1-4	351	48.7	25.9	22.8	17.4
5-9	491	43.8	20.4	23.4	12.6
10-13	381	14.7	4.7	10.0	3.4
		Nonpoverty Areas Code [1b2]			
1-4	4,303	68.7	56.5	12.2	17.9
5-9	6,236	56.6	44.2	12.4	5.8
10-13	4,783	25.7	19.7	6.0	1.9
		Central Cities, Population <250,000 Code [2a]			
1-4	701	58.9	42.9	16.0	18.3
5-9	887	52.4	36.4	16.0	7.3
10-13	788	22.3	14.6	7.7	2.7
		Remaining Areas in SMSAs Code [2b]			
1-4	748	58.3	41.7	16.6	16.8
5-9	1,084	49.7	35.2	14.5	6.8
10-13	864	17.7	13.8	3.9	0.7
		NonSMSA Areas Code [3]			
1-4	5,348	53.3	37.0	16.3	15.9
5-9	7,391	45.1	28.3	16.8	6.7
10-13	5,867	19.8	11.4	8.4	2.8

TABLE 13.

IMMUNIZATIONS AMONG INFANTS (CHILDREN UNDER 1 YEAR)—PERCENT WITH *ONE* DOSE OR MORE: DPT, OPV, IPV, MEASLES VACCINE, SMALLPOX VACCINATION, *1968*

Population (Thousands)	Diphtheria-Pertussis-Tetanus	Poliovaccine		Measles Vaccine	Smallpox Vaccination
		Oral	Inactivated		
		United States			
3,491	66.8	48.1	16.4	11.5	17.6
		Central Cities Code [1a] + [2a]			
1,005	66.3	43.6	22.1	15.0	21.9
		White			
671	70.9	48.1	20.9	11.9	21.2
		Other Races			
334	56.9	34.4	24.9	21.0	23.4
		Remaining Areas in SMSAs Code [1b] + [2b]			
1,211	70.5	53.3	16.4	12.2	18.6
		NonSMSA Areas Code [3]			
1,275	63.7	46.7	11.9	8.2	13.5

TABLE 14.

IMMUNIZATIONS AMONG INFANTS: DPT, MEASLES VACCINE, SMALLPOX VACCINATION IN POVERTY AND NONPOVERTY AREAS, *1968*

Population (Thousands)	Diphtheria-Pertussis-Tetanus	Measles Vaccine	Smallpox Vaccination
	Central Cities, Population 250,000+ Code [1a]		
856	65.3	15.2	22.8
	Poverty Areas Code [1a1]		
269	56.1	16.4	27.9
	Nonpoverty Areas Code [1a2]		
587	69.5	14.7	20.4
	Remaining Areas in SMSAs Code [1b]		
1,069	70.3	13.1	19.5
	Poverty Areas Code [1b1]		
119	70.6	17.6	21.8
	Nonpoverty Areas Code [1b2]		
950	70.2	12.5	19.2

BIOLOGICS SURVEILLANCE

1965-1968 SUMMARY

Biologics Surveillance Program 1965—1968 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 year-to-year trends in vaccine utilization.

Each major antigen is represented by a line showing the net distribution in 1965-1968; these amounts represent 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, the 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 patterns of vaccine utilization.

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

BIOLOGICS SURVEILLANCE PROGRAM PARTICIPANTS

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

BIOLOGICS – UNITED STATES, 1965-1968

Net Doses Distributed Annually

Biologics	Net Total Doses (Thousands)			
	1965	1966	1967	1968
Influenza Virus Vaccine (Polyvalent)	10,548**	20,895**	8,810	6,345
Influenza Virus Vaccine (Bivalent)	–	–	10,944	19,212
Diphtheria Toxoid	28,987	34,459**	65	39
Pertussis Vaccine	20,886 **	22,501**	135	156
Tetanus Toxiod	47,353**	53,722**	22,208	21,871
Poliomyelitis Vaccine*	7,462	5,548	3,532	2,573
Poliovirus Vaccine, Live, Oral, Type I	4,651	1,425	1,259	514
Poliovirus Vaccine, Live, Oral, Type 2	3,353	1,315	936	535
Poliovirus Vaccine, Live, Oral, Type 3	3,708	1,374	962	563
Poliovirus Vaccine, Live, Oral, Trivalent	17,379	24,000	18,017	23,894
Measles Virus Vaccine, Inactivated	336	167	82	(-12)
Measles Virus Vaccine, Live, Attenuated	5,732	7,929	6,364	5,269
Smallpox Vaccine	19,371	17,050	19,794	21,783
Rabies Vaccine	544	970	567	864
Immune Serum Globulin (Human), cc.	9,438	9,612	5,196	7,150
Poliomyelitis Immune Globulin (Human), cc.	–	1,957	1,032	836

*Inactivated (Salk Type)
**Combined Biologics Included

COMBINED BIOLOGICS – UNITED STATES, 1965-1968

Net Doses Distributed Annually

Biologics	Net Total Doses (Thousands)			
	1965	1966	1967	1968
Diphtheria and Tetanus Toxoids	3,121	3,560	4,453	3,830
Diphtheria and Tetanus Toxoids and Pertussis Vaccine	19,942	21,726	23,655	22,541
Diphtheria Toxoid and Pertussis Vaccine	**	**	**	**
Tetanus and Diphtheria Toxoids (For Adult Use)	5,064	8,472	7,187	8,074
Diphtheria and Tetanus Toxoids and Poliomyelitis Vaccine; Diphtheria and Tetanus Toxoids and Pertussis and Poliomyelitis Vaccines	260	411	432	127

**Not shown since fewer than three producers reported

MORRIS T. SUGGS, D.P.H.

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. This policy has continued, and 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 Epidemiology Program of the National Communicable Disease Center.

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.

ACIP membership as of July 1969:

Chairman
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National Communicable Disease Center

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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

CHOLERA VACCINE

INTRODUCTION

Cholera generally occurs in endemic and epidemic form only in South and Southeast Asia. In recent years, however, it has also been epidemic in certain areas of the Middle East.

Infection is acquired from contaminated water or food. It is believed to result from personal contact only in rare instances.

CHOLERA VACCINE

Various cholera vaccines have been widely used, but until recently their efficacy was unproved. Carefully controlled field studies have now clearly demonstrated the effectiveness of current vaccines against both the classical and El Tor strains of cholera vibrios. However, severe cases of cholera have occurred in vaccinated persons.

The duration of immunity induced by vaccine is relatively brief. Antibody titers reach a peak within 4 weeks of vaccination and are maintained for about 3 months. Protection against disease seems to last no more than 6 months after the primary series or a booster dose.

Vaccine available in the United States is prepared from a combination of inactivated suspensions of classical Inaba and Ogawa strains of cholera vibrios grown on agar or in broth and preserved with phenol.

VACCINE USAGE

Vaccination for International Travel

A primary vaccination or a booster dose within the previous 6 months is generally required for persons traveling to or from countries with cholera.* Vaccination requirements are published annually by the World Health Organization and summarized by the Public Health Service in its booklet *Immunization Information for International Travel* (PHS Publication No. 384). Because cholera sometimes reappears in countries free of the disease for several years, travelers should seek up-to-date information to determine the need for a valid International Certificate of Vaccination.

Physicians administering vaccine to travelers should emphasize that an International Certificate of Vaccination must be validated for it to be acceptable to quarantine authorities. Validation can be obtained at most city, county, and State health departments. Failure to secure validation can cause travelers to be revaccinated or quarantined during the course of travel. The Certificate remains valid for 6 months.

The traveler's best protection against cholera, as well as against many other enteric diseases, is to avoid potentially contaminated food and water. Persons following the usual tourist itinerary through countries reporting cholera and using standard accommodations run virtually no risk of acquiring cholera.

Primary Immunization

Injections may be given subcutaneously or intramuscularly.

For travelers vaccinated in the United States, a single 0.5 ml dose of cholera vaccine is considered adequate to satisfy the International Sanitary Regulations. The single dose for children is proportionately smaller (see table below).

Two doses of cholera vaccine, 0.5 ml and 1.0 ml, preferably given a month or more apart, are recommended for adults traveling or working in areas where cholera is epidemic or known to be endemic and living under conditions in which sanitation is less than adequate. The doses for children are suggested in the summary table. A two-dose schedule of vaccination is also advisable for persons working with cholera vibrios in the laboratory.

Booster Doses

Booster injections should be given every 6 months as long as the likelihood of exposure exists. In areas where cholera only occurs in a 2 to 3 month "season," protection is optimal when the booster dose is given at the beginning of the season. The primary series need never be repeated for booster doses to be effective.

Summary

The following table summarizes the recommended doses for primary and booster vaccination:

Dose Number	Age (Years) Under 5	5–10	Over 10
1	0.1 ml	0.3 ml	0.5 ml
2 & Boosters	0.3 ml	0.5 ml	1.0 ml

Reactions

Vaccination often results in discomfort at the site of injection for one or more days. The local reaction may be accompanied by fever, malaise, and headache.

*For a current listing, consult the most recent issue of the World Health Organization's Weekly Epidemiological Record.

Contraindication

Rarely, severe reactions of various kinds follow administration of cholera vaccine. If one experiences such a reaction, revaccination is not advisable. Most governments will permit such an individual to proceed provided he carries a physician's statement of the medical contraindication. However, any inadequately vaccinated traveler coming from an infected area may be quarantined or placed under surveillance for 5 days.

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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

DIPHTHERIA AND TETANUS TOXOIDS AND PERTUSSIS VACCINE

INTRODUCTION

Routine immunization against diphtheria, tetanus, and pertussis during infancy and childhood has been widely advocated and generally practiced in the United States in the past 25 years. Its effectiveness is reflected in decreasing incidence of and mortality from these three diseases.

Diphtheria

There has been continuing decline in the annual incidence of diphtheria since World War II, and diphtheria is now a rare disease in many parts of the United States. However, localized outbreaks continue to appear with some severe cases and a case-fatality ratio often greater than 10 percent. In 1968, 260 cases were reported.

Although most diphtheria cases occur in children, cases and deaths are reported in all age groups. Nearly all cases occur in inadequately immunized individuals. Diphtheria toxoid, when administered according to recommended schedules, prevents diphtheria mortality and greatly reduces clinical illness and complications. Following adequate immunization, protective levels of antitoxin appear to persist for 10 years or more.

Tetanus

Although its incidence in the United States has declined in recent years, tetanus remains a public health problem which can only be prevented by universal active immunization. In 1968, 163 cases of tetanus were reported, the majority in unimmunized adults; the median age was 48, excluding neonates. The national death-to-case ratio was more than 65 percent. Thus, primary immunization and periodic boosters must be emphasized not only for children but also for all adults. Adequate immunization with tetanus toxoid provides effective and durable protection against disease and eliminates the need for passive immunization at the time of injury. Universal active immunization will ensure protection against the significant proportion of tetanus infections which follow trivial injury or through unrecognized portals of entry.

Tetanus toxoid is an almost ideal immunizing agent. It is highly effective, has almost no side effects, and provides long-lasting protection. Because there is no natural immunity to the ubiquitous tetanus organism and no general contraindications to tetanus toxoid, the importance of immunization is universal.

Pertussis

The high mortality from pertussis in infancy is the major rationale for immunization early in life. The disease is highly communicable, and attack rates up to 90 percent are reported among unimmunized household contacts. Most cases occur in infants and young children. In 1967, nearly three-fourths of pertussis deaths occurred in infants less than a year old – some 40 percent of the total occurred in infants 3 months of age or less.

Pertussis immunization is effective in reducing both cases and deaths. Mortality from pertussis has declined dramatically with increasingly widespread use of standardized pertussis vaccines beginning in the mid 1940's. Because the incidence of and mortality from pertussis decrease with age, pertussis immunization is not generally required past age 6 years or after entry to elementary school.

Severe central nervous system reactions, occasionally with permanent sequelae or death, occur very rarely after administration of pertussis vaccine. Their incidence, however, is much lower than the incidence of similar serious reactions following the disease itself.

PREPARATIONS USED FOR IMMUNIZATION

Diphtheria and tetanus toxoids are prepared by formaldehyde treatment of the respective toxins. Pertussis vaccine is made from a killed suspension of bacteria or a bacterial fraction.

The toxoids and pertussis vaccine are available in both fluid and adsorbed forms. Comparative tests have shown that the adsorbed toxoids are clearly superior in stimulating high antibody titers and achieving durable protection. The promptness of antibody responses to booster doses of either fluid or adsorbed toxoids is not sufficiently different to be of clinical importance. Therefore, adsorbed toxoids are the agents of choice for both primary and booster immunization.

These three antigens are available in various combinations and concentrations for specific purposes. Three preparations 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 15 to 20 percent of that contained in the standard DTP preparation used in infants and young children.

VACCINE USAGE

Schedule and Dose

Recommendations are based upon immunologic and epidemiologic considerations, taking into account the possibly increased risks of exposure at school entrance. Since the concentration of antigens varies in different manufacturers' products, the labeling provides specific information on the proper volume of a single dose.

Primary Immunization

Children 2 months through 6 years: The recommended dose of **DTP** given intramuscularly on **three** occasions at 4 to 6 week intervals with a reinforcing dose approximately 1 year after the third injection. Ideally, immunization is begun at age 2 to 3 months or at the time of a 6-week "check-up" if such timing is an established routine.

Schoolchildren and adults: The recommended dose of **Td*** given intramuscularly or subcutaneously on **two** occasions at 4 to 6 week intervals with a reinforcing dose approximately 1 year after the second.

Booster Doses

Children 3 through 6 years (Preferably at time of school entrance – kindergarten or elementary school): The recommended dose of **DTP** intramuscularly.

Thereafter and for all other persons: The recommended dose of **Td** intramuscularly or subcutaneously every 10 years. (If a dose is administered sooner as part of wound management – see specific recommendations – the next booster is not needed for another 10 years.) More frequent booster doses are not indicated and may be associated with increased frequency and severity of reactions.

TETANUS PROPHYLAXIS IN WOUND MANAGEMENT

An important part of the management of wounds is prevention of tetanus. The physician is then often faced with questions of using tetanus toxoid for active protection and Tetanus Immune Globulin (Human) (TIG) or tetanus antitoxin of animal origin for passive protection. Available evidence demonstrates that complete primary immunization with tetanus toxoid (initial doses plus reinforcing dose) provides a very long-lasting basis for active protection against tetanus. Therefore, passive protection need be considered **only** when the patient has **no** valid history of **any** previous tetanus toxoid. This liberal interpretation is justifiable in view of evidence that persons who have previously received even one dose of tetanus toxoid will respond adequately to a single booster, even after an interval of many years.

The following outline is a conservative guide to active and passive tetanus immunization in wound management. It presumes a **reliable** knowledge of the patient's immunization history. (Considerable evidence indicates that immunity often persists very much longer than the specified 1 year interval; but until this observation is established conclusively, the 1 year interval is reasonable for general purposes.)

1. **Primary immunization or last booster dose less than 1 year before injury:** No tetanus prophylaxis required.
2. **Primary immunization or last booster dose more than 1 year before injury:** The recommended single dose of Td† intramuscularly or subcutaneously.
3. **Incompletely immunized:** Complete primary immunization.
4. ***Unimmunized or immunization history uncertain:*** Initiate primary immunization.

The decision to administer concomitant passive prophylaxis in this case will depend upon medical judgment after evaluating such factors as location of wound, its type and severity, the degree and kind of contamination, and the time elapsed since injury. If passive therapy is to be used, TIG is preferable. It offers the advantages of a longer period of protection and freedom from undesirable reactions. The currently recommended prophylactic dose of TIG is 250 units for wounds of average severity. When used concurrently, tetanus toxoid and globulin should be given in separate syringes at separate sites.

Should TIG be unavailable, equine or bovine antitoxin may be used, bearing in mind the risk that serious reactions may follow injections of animal serum. The usual dose is 3,000 to 5,000 units. Its administration should always be preceded by careful screening for sensitivity in accordance with instructions furnished with the antitoxin by the manufacturer.

*Td is considered the agent of choice for immunization of school-age children on the basis of data regarding its adequacy in primary immunization of older children and adults and because of increasing reactions to full doses of diphtheria toxoid with age. Such reactions are not uncommon from about age 6 in the southern United States, to 10 or 12 in the northern portions of the country. The use of Td 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).

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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

IMMUNE SERUM GLOBULIN FOR PREVENTION OF VIRAL HEPATITIS (Infectious Hepatitis and Transfusion-Associated Hepatitis)

INFECTIOUS HEPATITIS

The agent that causes human infectious hepatitis has not yet been identified but is presumed to be a virus. No vaccine is available. Administration of Immune Serum Globulin (ISG)* to exposed persons can, however, afford a high degree of protection against infectious hepatitis. ISG substantially reduces the frequency of overt clinical disease, although inapparent infection may occur. Following such infection, lifelong active immunity is thought to develop.

Patients with infectious hepatitis have been shown to excrete virus in stool as much as 2 to 3 weeks before and 2 weeks after onset of jaundice. Viremia has been demonstrated approximately 2 weeks before and less than 1 week after onset of jaundice.

Transmission of the disease is principally by the fecal-oral route and is most likely to occur under conditions of inadequate sanitation or close contact with infected individuals. Direct person-to-person spread of infection otherwise is unusual. Transmission is also possible by the parenteral route. The incubation period of infectious hepatitis is relatively long, in most cases between 15 and 50 days (average 25 to 30 days).

IMMUNE SERUM GLOBULIN

ISG is prepared for intramuscular injection from large pools of plasma (1,000 or more donors) obtained from venous and/or placental blood. The product is a 16.5 percent solution of globulin prepared by cold alcohol fractionation. Serum hepatitis has not been transmitted by ISG of this type.

ISG FOR PREVENTING INFECTIOUS HEPATITIS

The decision to administer ISG should be based on assessment of the epidemiologic circumstances – specifically, whether the exposure could result in infection. The administration of ISG is relevant when there is: 1) definite exposure to a known case or source of infection, or 2) anticipated continuous or intermittent exposure.

ISG given after known exposure should be given as soon as possible. Its prophylactic value decreases as time increases after exposure. The use of ISG more than 5 to 6 weeks after exposure is not indicated.

*Official name: Immune Serum Globulin (Human). Poliomyelitis Immune Globulin (Human) is an equivalent product and may also be used; other immune globulin products are not suitable.

Dosage

The dosage patterns of ISG in common use have been derived primarily from field and clinical observations. Data from these observations provide operational guidelines on which to base recommendations.

Under most conditions of exposure, protection has been afforded by giving 0.01 ml of ISG per pound of body weight (0.01 ml/lb or approximately 0.02 ml/kg). This dosage may be conveniently simplified (Table 1):

Table 1
Guidelines for ISG Prophylaxis of Infectious Hepatitis for General Use

Person's Weight (lb)	ISG Dose (ml)*
up to 50	0.5
50-100	1.0
over 100	2.0

*Within limits, larger doses of ISG provide longer-lasting but not necessarily more protection. Higher doses are, therefore, used under certain circumstances (See Institutional Contacts and Travelers to Foreign Countries).

Individual Recommendations

Household contacts: There is good evidence that close personal contact, such as occurs among permanent or even temporary household residents, is important in spreading infectious hepatitis. Secondary attack rates are high for household contacts, particularly children and teenagers. Although secondary attack rates are somewhat lower for adults, their illnesses tend to be more severe. For these reasons, ISG is recommended for all household contacts who have not already had infectious hepatitis.

School contacts: Although the highest incidence of hepatitis is among school-age children, contact at school is usually not an important means of transmitting this disease. Therefore, routine administration of ISG is not indicated for pupil or teacher contacts of a case. However, when epidemiologic study has clearly shown that school or classroom contact is responsible for continued transmission of disease, it is reasonable to administer ISG to individuals at risk.

Institutional contacts: In contrast to schools, conditions favoring transmission of infectious hepatitis exist in institutions such as prisons and facilities for the mentally retarded. Sporadic cases as well as epidemics have frequently been reported in such institutions. ISG administered to patient and staff contacts of cases in the doses shown in Table 1 effectively limited the spread of disease in these circumstances.

Where infectious hepatitis exists endemically, particularly in very large institutions with high rates of admission and discharge, residents and staff personnel may be subject to frequent and continuing exposure. Under these conditions, use of ISG has not resulted in eradication of hepatitis. However, it has been shown to provide temporary protection when administered in doses of 0.02 to 0.05 ml/lb at the time of admission or employment. It may be necessary to readminister ISG in the same dose after 6 months if the risk is felt to persist.

Hospital contacts: Routine prophylactic administration of ISG to hospital personnel is not indicated. Emphasis should be placed on sound hygienic practices. Intensive, continued education programs pointing out the risks of exposure to infectious hepatitis and the recommended precautions should be directed toward hospital personnel who have close contact with patients or infectious materials.

For those accidentally inoculated with blood or serum of patients with hepatitis, the appropriate prophylactic dose of ISG is that recommended in Table 1. There is no reason to give a larger dose because ISG appears to be effective in preventing only infectious hepatitis, not transfusion-associated (serum) hepatitis (See Transfusion-Associated Hepatitis).

Office and factory contacts: Routine administration of ISG is not indicated for persons in the usual office or factory situation exposed to a fellow worker with hepatitis.

Common source exposures: When a vehicle, such as food or water, is identified as a common source of infection of multiple hepatitis cases, administration of ISG should be considered for all those exposed to the source.

Pregnancy: Current information does not indicate that pregnancy in itself should alter the recommendations for ISG prophylaxis.

Travelers to foreign countries: The risk of infectious hepatitis for U.S. residents traveling abroad varies with living conditions and the prevalence of hepatitis in the areas to be visited. Travelers may be at no greater risk than in the United States when their travel involves ordinary tourist activities and little exposure to uncooked foods or water of uncertain quality. For these travelers, ISG is not recommended.

For travelers visiting areas where hepatitis is a major health problem who may be exposed to infected persons and to contaminated food and water, there is increased risk of acquiring hepatitis. A single dose of ISG is recommended for them as shown in Table 2, which gives guidelines for U.S. residents traveling in foreign countries. (Large geographic areas have been defined for ease of interpretation and because information is inadequate to permit developing more precise boundaries.)

For individuals who reside abroad in areas where hepatitis is common, the risk of hepatitis is greatly increased and appears to continue so for years. Experience has shown that regular administration of ISG offers at least partial protection against hepatitis. It is recommended that prophylactic ISG be repeated every 6 months at doses indicated in Table 2.*

Table 2
Guidelines for ISG Prophylaxis of Infectious Hepatitis for U.S. Residents Traveling or Living in Foreign Countries*
(See text for additional details)

Area	Person's Weight (lb)	Short-Term Travel (1-2 months) ISG Dose (ml)	Extended Travel or Residence (3-6 months)** ISG Dose (ml)
Africa Asia North America Central America Mexico (Rural) Pacific Region Philippine Islands South Pacific Islands South America	up to 50 50-100 over 100	0.5 1.0 2.0	1.0 2.5 5.0
Europe North America Canada Caribbean Islands Mexico (Urban) Pacific Region Australia Japan New Zealand	Routine ISG prophylaxis is not indicated		

*In all travel, care should be exercised in consuming uncooked foods and water of uncertain quality.
**Repeat every 6 months of travel or residence.

Reactions

Intramuscular administration of ISG rarely is followed by adverse reactions. Discomfort may occur at the site of injection, especially when larger volumes are used. A few instances of hypersensitivity have been reported, but in view of the very large number of persons who have received ISG, the risk is exceedingly small.

ISG should not be administered intravenously because of the danger of severe reactions.

Antibody against gamma globulin may appear following administration of ISG although its clinical significance is unknown. When ISG is indicated for prophylaxis of infectious hepatitis, this theoretical consideration should not preclude its administration.

*Some agencies have used up to 0.05 ml/lb each 5 to 6 months rather than the 5 ml for adults recommended here.

TRANSFUSION-ASSOCIATED HEPATITIS

The risk of transmitting viral hepatitis by blood transfusion is a serious and continuing problem. Several 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. Furthermore, the case-fatality rate of transfusion-associated hepatitis increases with advancing age.

Evidence has been advanced both for and against the effectiveness of ISG as prophylaxis of transfusion-associated hepatitis. Although some investigators have reported that 10 ml of ISG at the time of transfusion and again 1 month later reduced the number of cases, other equally careful studies have not substantiated this claim. Existing evidence provides no adequate basis for recommending that ISG be given routinely to recipients of blood transfusions.

Among the means of effectively lowering the incidence of transfusion-associated hepatitis are: careful selection of donors, development of central registries of known or suspect carriers, and use of blood and potentially icterogenic blood products only when necessary.

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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

INFLUENZA VACCINE–1969-70

INTRODUCTION

The nationwide epidemic of A2 influenza in the United States in the fall and winter of 1968-69 showed the impact of a major antigenic change in the prevalent influenza viruses. The Hong Kong strain responsible for the epidemic was the most distinctive variant among A2 influenza viruses identified since initial appearance of the A2 sub-type in 1957. The 1968-69 epidemic highlighted again the problems that are encountered in rapidly developing and producing sufficient quantities of vaccine incorporating a new antigen.

Forty-four States reported widespread outbreaks of Hong Kong strain influenza; in six, involvement was less extensive. In all nine geographic divisions of the country, excess pneumonia and influenza mortality peaked sharply in early January 1969.

In December 1968, Washington State reported an outbreak of type B influenza concurrent with Hong Kong strain A2. In January and February 1969, 18 additional States reported type B influenza; it was widespread only in States in the central part of the country. Unlike Hong Kong strain A2 influenza, which affected all age groups, type B influenza illness occurred primarily in school-age children.

INFLUENZA VIRUS VACCINES

The Division of Biologics Standards, National Institutes of Health, regularly reviews influenza vaccine formulation, and, when indicated, recommends revision to include contemporary antigens. After characterization of the A2 Hong Kong virus in September 1968, a monovalent vaccine incorporating the new strain was recommended.

While some influenza vaccines have achieved 60 percent or greater effectiveness in protection against the same or closely related virus strains, vaccines in general civilian use often have not been this effective. Final data on vaccine field trials conducted in the 1968-69 influenza season are being compiled. Preliminary data indicate the monovalent Hong Kong strain vaccine was considerably less effective than would have been desirable.

For 1969-70, both standard and highly purified bivalent influenza vaccines will be available. The recommended adult dose will contain 400 chick cell agglutinating (CCA) units of Hong Kong strain antigen (A2/Aichi/2/68) and 300 CCA units of type B antigen (B/Mass/3/66). The highly purified vaccine is equivalent in potency to the standard vaccine but contains less non-viral protein.

VACCINE USAGE

General Recommendations

It is unlikely that there will be more than sporadic cases of influenza due to A2 strains in the 1969-70 season. Type B influenza may appear in areas where it did not occur in 1968-69.

Until good protection is provided consistently by influenza vaccine, it is not recommended for healthy adults and children.

Acknowledging its limited effectiveness, vaccine should be considered only for persons of any age with certain chronic debilitating conditions: 1) rheumatic heart disease, especially mitral stenosis; 2) such cardiovascular disorders as arteriosclerotic heart disease and hypertension, particularly with evidence of cardiac insufficiency; 3) chronic bronchopulmonary diseases, such as asthma, chronic bronchitis, cystic fibrosis, bronchiectasis, pulmonary fibrosis, pulmonary emphysema, and advanced pulmonary tuberculosis; or 4) diabetes mellitus or Addison's disease.

Although the indications of vaccination are less clear, older persons, who may have incipient or potential chronic disease, particularly cardiovascular and bronchopulmonary, should also be considered candidates for vaccination.

Schedule

The primary series consists of two doses administered subcutaneously, preferably 6 to 8 weeks apart. (Dose volume for adults and children is specified in the manufacturers' labeling.) Persons at high risk who regularly receive influenza vaccines and had one or more doses of the monovalent vaccine containing Hong Kong strain antigen in the 1968-69 season require only a single full dose booster of bivalent vaccine. Immunization should be scheduled for completion by early December.

Local or mild systemic reactions to standard influenza vaccines are common. They occur in up to 50 percent of adults and appear to be related primarily to the non-viral components of the vaccine.

Individuals who should receive influenza vaccine but have had severe local or systemic reactions to the standard vaccine might be given a highly purified vaccine subcutaneously.

Precautions

Influenza vaccine should not be administered to anyone who is clearly hypersensitive to eggs because the vaccine viruses are grown in embryonated chicken eggs.

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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

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 in vaccination programs have brought a 95 percent reduction in the incidence of measles, but a continuing effort to immunize all susceptibles in the childhood population is necessary if the goal of measles eradication is to be realized.

Measles is often a severe disease, frequently accompanied by complications such as bronchopneumonia, middle ear infection, and encephalitis. Encephalitis, which follows measles in approximately one of every 1,000 cases, often causes permanent brain damage and mental retardation. One in every 10,000 measles cases is fatal.

MEASLES VIRUS VACCINES

Live, attenuated measles virus vaccines*, the original Edmonston B and the further attenuated strains (Schwarz and Moraten), are widely used in the United States. Edmonston B strains are prepared in either chick embryo or canine renal cell culture; the further attenuated strains are prepared only in chick embryo cell culture.

These measles virus vaccines produce a mild or inapparent, non-communicable infection. Fifteen percent of children receiving either the Edmonston B strain with Measles Immune Globulin (MIG) or the further attenuated strains experience fever, with temperatures of 103°F. (rectal) or higher, beginning about the sixth day after vaccination and lasting up to 5 days. About twice as many (30 percent) of those receiving Edmonston B without MIG have similar febrile responses. The great majority of reports indicate that even children with high fevers experience relatively little discomfort and minimal toxicity. As a result, febrile reactions often go unnoticed by the parents.

An antibody response develops in virtually all susceptible children given live measles virus vaccine. Edmonston B vaccine administered without MIG induces antibody at about the level of natural measles infection. Antibody titers in response to Edmonston B with MIG or to further attenuated vaccine are slightly lower. However, all of these vaccines appear to confer durable protection in most individuals.

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

Experience with more than 35 million vaccinations in the United States by mid-1969 indicates that live measles virus vaccines are among the safest immunizing agents available. Reports of reactions to measles vaccination have been rare, and in no case has it been shown that the reaction was actually vaccine induced and not merely temporally associated.

VACCINE USAGE

General Recommendations

All susceptible children – those who have not had natural measles or measles vaccine – should be vaccinated. It is particularly important to vaccinate susceptibles entering nursery school, kindergarten, or elementary school. They are often responsible for transmitting measles to other children in the community. In order to achieve adequate measles protection, communities should encourage ongoing programs to vaccinate all children at about 1 year of age.

The risk of acquiring measles in the United States has been greatly reduced by extensive vaccination, and susceptible children are therefore unlikely to be infected. The risk in other countries may be considerably greater; therefore, it would be wise to immunize susceptible children before they travel abroad.

Dose: The single dose of live measles vaccine should be given subcutaneously. No booster dose is needed.

Administration of the Edmonston B strain should ordinarily be accompanied by MIG 0.01 ml/lb, given with a different syringe at a different site. MIG should not be given with further attenuated measles vaccine.

Age: For maximum efficacy, measles virus vaccine should be administered when children are at least 12 months old. It may be given to infants at 9 to 12 months of age recognizing that the proportion of seroconversions may be slightly reduced. The proportion is further decreased if MIG is administered with vaccine.

Vaccination of adults at the present time is rarely necessary, because nearly all Americans over 15 years old now are immune. 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, for malnourished children, and for those in institutions.

Use of Vaccine Following Exposure

Live, attenuated measles virus vaccine can usually prevent disease if administered **before or on the day of exposure** to natural measles; study findings indicate that protection is not conferred when vaccine is administered after the day of exposure. No untoward effects have been observed when vaccination followed exposure to natural measles.

Precautions

Severe febrile illnesses: Vaccination should be postponed until the patient has recovered.

Tuberculosis: Exacerbations of tuberculosis known to follow natural measles infection might, by analogy, be associated with the live, attenuated measles virus. Therefore, an 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 value of protection against natural measles outweighs the theoretical hazard of possible exacerbation of an unsuspected tuberculosis infection by vaccination.

Recent Immune Serum Globulin administration: After administration of Immune Serum Globulin, vaccination should be deferred for 3 months. Persistence of measles antibody from the globulin might interfere with suitable response to the vaccine.

Marked hypersensitivity to vaccine components: Measles vaccine produced in chick embryo cell culture should theoretically not be given to children clearly hypersensitive to chicken eggs. Similarly, vaccine produced in canine renal cell culture should not be administered to children highly sensitive to dog hair or dander. To date, however, there have been no documented reports of serious or anaphylactic hypersensitivity reactions to measles vaccine in the United States.

Contraindications

Altered immune states: Administration of measles virus vaccine to children with leukemia has occasionally been followed by such serious complications as fatal giant cell pneumonia. Theoretically, attenuated measles virus infection might be potentiated by severe underlying diseases, such as lymphomas and generalized malignancies, or by lowered resistance, such as from therapy with steroids, alkylating drugs, antimetabolites, or radiation; therefore, vaccination of such patients should be avoided.

Pregnancy: On theoretical grounds, it would be reasonable to avoid vaccinating pregnant women with live, attenuated measles virus vaccine.

Management of Patients with Contraindications

If immediate protection against measles is required for persons for whom live, attenuated measles virus vaccine is contraindicated, passive immunization with MIG (dose approximately 0.1 ml/lb or 0.25 ml/kg) should be given as soon as possible after a known exposure. It is important to note, however, that this dose of MIG which is effective in preventing measles in normal children may not be equally effective in children with acute leukemia. To decrease the risk of measles infection for such children, all their close contacts who are susceptible to measles should be immunized.

Prior Immunization with Inactivated Measles Virus Vaccine

Atypical measles, sometimes severe, has occasionally followed exposure to natural measles in children previously inoculated with inactivated measles virus vaccines.

Untoward local reactions such as induration and edema have at times been observed when live measles virus vaccine was administered to persons who had previously received inactivated vaccine. Despite the risk of local reaction, children who have previously been given inactivated vaccine should also be given the live vaccine for full and lasting protection against natural infection.

SIMULTANEOUS ADMINISTRATION OF LIVE VIRUS VACCINES

There are obvious practical advantages to administering two or more live virus vaccines simultaneously. Data from specific investigations are not yet sufficient to develop comprehensive recommendations on simultaneous use, but a summary of current experience, attitudes, and practices provides useful guidance.

It has been generally recommended that live virus vaccines be given at least a month apart whenever possible – the rationale for this being that more frequent and severe adverse reactions as well as lower antibody responses otherwise might result. Field observations indicate, however, that with simultaneous administration of certain live virus vaccines, results of this kind have been minimal or absent. (For example, the third dose of trivalent oral polio-virus vaccine, which is recommended during the second year of life, is commonly given at the same time as smallpox vaccination without evident disadvantage.)

If the theoretically desirable 1-month interval is not feasible, as with the threat of concurrent exposures or disruption of immunization programs, the vaccines should preferably be given on the same day – at different sites for parenteral products. An interval of about 2 days to 2 weeks should be avoided because interference between the vaccine viruses is most likely then.

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 at about 1 year of age against measles should be established by all communities. In addition, all susceptible children entering nursery school, kindergarten, and elementary school should receive vaccine because of their role in community spread of natural measles.

Special Intensive Programs

Community-wide immunization programs have been useful in the rapid distribution of live measles virus vaccine. Attention should now be directed toward systematic programs for groups of susceptible children remaining in both urban and rural areas.

Control of Measles Epidemics

Studies have shown that community-wide measles epidemics can be controlled by prompt administration of measles vaccine to **selected** groups of children, particularly the susceptibles in nursery schools, kindergartens, 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

Continued careful surveillance of measles and its complications is necessary to appraise nationally and locally the effectiveness of measles immunization programs, particularly efforts at measles eradication. Surveillance can delineate failures to achieve adequate levels of protection and define groups in need of control programs.

Although more than 35 million doses of measles virus vaccine have now been administered in the United States, continuous and careful review of any adverse reaction remains important. All serious reactions or suspected measles illnesses in vaccinated children should be carefully evaluated and reported in detail to local and State health officials.

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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

MUMPS VACCINE

INTRODUCTION

Mumps, one of the common communicable diseases, is observed with greatest frequency in young school-age children. However, approximately 15 percent of reported cases occur after the onset of puberty.

Overt evidence of central nervous system disease with sequelae is rare in mumps, although meningeal involvement appears to be common. Orchitis has been reported in up to 20 percent of clinical cases occurring in postpubertal males. Symptomatic involvement of other glands and organs is observed less frequently. Nerve deafness is a very rare, but serious, complication of mumps.

All naturally acquired mumps infections, including the estimated 30 percent which are subclinical, confer durable immunity.

LIVE MUMPS VIRUS VACCINE*

Live mumps vaccine is prepared in chick embryo cell culture. It produces an inapparent, non-communicable infection following administration. Since its introduction approximately 1 year ago, mumps vaccine has been given to more than 1 million persons without report of significant side reactions clearly attributable to vaccination.

More than 95 percent of susceptible vaccinees develop detectable antibodies after vaccination. Although titers are lower than those induced by natural infection, the pattern of antibody persistence parallels that seen following clinical mumps. The long-term duration of vaccine-induced immunity is unknown, but 3-year observations show continuing protection against natural infections and, in two small groups of children, antibody levels which are persisting without decline.

VACCINE USAGE

General Recommendations

Age: Live mumps vaccine may be used at any age from 12 months. It should not be administered to children less than 12 months old because of possible persistence of interfering maternal antibody. The vaccine is of particular value in children approaching puberty, adolescents, and adults, especially males, who have not had mumps parotitis, either unilateral or bilateral.**

Since the Committee's initial statement on live, attenuated mumps vaccine in 1967, further experience with the vaccine has been accumulated. In view of evidence showing continued vaccine efficacy and safety, the Committee has modified its recommendation for limited vaccination of young children and now suggests that consideration be given to immunizing all susceptible children over 1 year of age. The Committee reaffirms its position, however, that mumps vaccination programs should not be allowed to take priority over essential ongoing health activities.

Dose: A single dose of vaccine should be administered subcutaneously in the volume specified by the manufacturer.

Use of Vaccine Following Exposure

It is not known whether live mumps vaccine will provide protection when administered after exposure. There is, however, no contraindication to its use at that time.†

Precautions

Severe febrile illnesses: Vaccination should be postponed until the patient is completely recovered.

Marked hypersensitivity to vaccine components: Mumps vaccine is produced in chick embryo cell culture and should not be given to persons hypersensitive to ingested egg proteins. Also, the vaccine contains small amounts of neomycin, so it should not be given to individuals known to be sensitive to this antibiotic.

Altered immune states: Mumps vaccine virus infection might be potentiated by severe underlying diseases, such as leukemia, lymphoma, or generalized malignancy, and by lowered resistance, such as from therapy with steroids, alkylating drugs, antimetabolites, or radiation; therefore, vaccination of such patients should be avoided.

Pregnancy: On theoretical grounds, it is reasonable to avoid using live mumps vaccine during pregnancy.

Simultaneous Administration of Live Mumps Virus Vaccine with Other Live Virus Vaccines

In order to evaluate the live mumps vaccine adequately, its simultaneous administration with other vaccines should be deferred until results of controlled clinical investigations are available. Until then, it is recom-

*Official name: Mumps Virus Vaccine, Live

**The mumps skin test with currently available antigens is an unreliable indicator of immunity.

†Inactivated mumps vaccine and Mumps Immune Globulin (Human) are of questionable effectiveness under these circumstances.

mended that mumps vaccination be separated from other immunization procedures by about one month whenever possible.

SURVEILLANCE

Careful surveillance of mumps is important. There is need to improve reporting of mumps cases and their complications, to demonstrate continuing vaccine effectiveness, and to document patterns of vaccine use.

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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

PLAGUE VACCINE

INTRODUCTION

Plague is a sylvatic infection of rodents and their ectoparasites in many parts of the world. In the western United States, a few human cases occur each year following exposure to infected wild rodents. In some countries of Asia, Africa, and South America, epidemic plague results when the domestic rat population becomes infected. Currently the area of most intensive epidemic and epizootic infection is Vietnam.

PLAGUE VACCINE

Plague vaccines have been used since the late nineteenth century, but it has never been possible to measure their effectiveness precisely. Immunization with plague vaccine, however, is known to reduce the incidence and severity of disease.

The plague vaccine licensed for use in the United States is prepared from *Pasteurella pestis* grown in artificial media, inactivated with formaldehyde, and preserved in 0.5 percent phenol.

VACCINE USAGE

General Recommendations

Routine vaccination is **not** indicated for persons simply living in plague enzootic areas of the western United States or for travelers going to most of the countries reporting cases.* Selective immunization is advisable for the following:

1. All persons traveling to Vietnam, Cambodia, and Laos.
2. All persons whose vocations or field work brings them into frequent and regular contact with wild rodents in plague enzootic areas of the western United States, South America, Africa, or Asia.
3. All laboratory personnel working with the *P. pestis* organism or with plague-infected rodents.

Primary Immunization

All injections should be given intramuscularly.

Adults and children over 10 years old: The primary series consists of three doses of vaccine. The first two doses, 0.5 ml each, should be administered 4 or more weeks apart, followed by a third dose, 0.2 ml, 4 to 12 weeks after the second injection. When less time is available, satisfactory but less than optimal results can be obtained with two 0.5 ml injections administered at least 3 weeks apart.

*For a current listing, consult the most recent issue of the World Health Organization's *Weekly Epidemiological Record*

Children less than 10 years old: The primary series also is three doses of vaccine, but the doses are smaller. The manufacturer's guide to proportions of the adult dose for children is: Infants under 1 year – one-fifth adult dose; 1-4 years – two-fifths adult dose; 5-10 years – three-fifths adult dose. The intervals between injections are the same as for adults.

Booster Doses

Boosters should be given every 6 to 12 months while individuals remain in an area where the risk of exposure persists. Satisfactory doses for children and adults are the same volumes suggested for the third dose in the primary series. The primary series need never be repeated for booster doses to be effective.

Summary

The following table summarizes the recommended doses for primary and booster vaccination:

Dose Number	Age (Years) Under 1	1–4	5–10	Over 10
1 & 2	0.1 ml	0.2 ml	0.3 ml	0.5 ml
3 & Boosters	0.04 ml	0.08 ml	0.12 ml	0.2 ml

Reactions

Mild reactions consisting of pain, reddening, and swelling at the injection site are frequently recognized. With repeated doses, systemic reactions of fever, headache, and malaise occur more often and tend to become more pronounced. Sterile abscesses are reported to occur rarely. No fatal or disabling complications have been observed.

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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

POLIOMYELITIS VACCINES

INTRODUCTION

Widespread use of poliovirus vaccines since 1955 has resulted in the virtual elimination of paralytic poliomyelitis in the United States. To ensure continued freedom from the disease, it is necessary to pursue regular immunization of all children from early infancy.

Paralytic poliomyelitis declined from 18,308 cases in 1954 to 40 cases in 1967 and 48 cases in 1968. A national survey in 1968 showed that 82 percent of individuals 1-19 years old had received at least three doses of oral poliovirus vaccine (OPV)*, inactivated poliovirus vaccine (IPV)**, or both.

Nevertheless, low immunization rates still prevail in certain disadvantaged urban and rural groups, particularly for infants and young children born since the mass immunization campaigns conducted between 1958 and 1962. Most of the cases of paralytic poliomyelitis in recent years occurred in these populations.

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; 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 other segments of the population. Population groups requiring immunization can be identified by immunization history and serologic survey.

POLIOVIRUS VACCINES

Between 1955, when IPV was introduced, and 1962, when live, attenuated vaccines became widely used, 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.

OPV has largely replaced IPV in this country because it is easier to administer, requires no boosters, and produces an immune response like that induced by natural poliovirus infection.

Monovalent OPV types 1, 2, and 3 were widely used in the United States beginning in 1961, but they have generally been supplanted by trivalent OPV because of greater simplicity in scheduling and recordkeeping.

A primary series of three adequately spaced doses of trivalent OPV will produce an immune response to the three poliovirus types in well over 90 percent of recipients.

Very rarely, paralysis has occurred in recipients of OPV or in their close contacts within 2 months of vaccine administration. Currently, for each 9 million doses of OPV given, no more than one case of "vaccine associated" paralysis in recipients and two in recipient contacts are reported.

VACCINE USAGE

Trivalent OPV—Primary Immunization

Infants: The three-dose immunization series should be started at 6 to 12 weeks of age, commonly with the first dose of DTP. The second dose should be given not 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: For unimmunized children and adolescents through high school age, the primary series is three doses: The first two should be given 6 to 8 weeks apart, and the third, 8 to 12 months after the second. If circumstances do not permit 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 necessary because of the extreme unlikelihood of exposure. However, an unimmunized adult at increased risk through contact with a known case or travel to areas where polio is epidemic or occurs regularly should receive trivalent OPV as indicated for children and adolescents. Persons employed in hospitals, medical laboratories, and sanitation facilities might also be at increased risk, especially if poliomyelitis is occurring in the area.

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

Monovalent OPV—Primary Immunization

An alternative primary immunization is one dose of each of the three types of **monovalent** OPV given at 6 to 8 week intervals, with a dose of **trivalent** OPV given 8 to 12 months after the third dose of monovalent OPV to ensure adequate responses.

* Official names of the products in use: (1) Poliovirus Vaccine, Live Oral, Type 1, (2) Poliovirus Vaccine, Live, Oral, Type 2, (3) Poliovirus Vaccine, Live Oral, Type 3, (4) Poliovirus Vaccine, Live, Oral Trivalent.

** Official name: Poliomyelitis Vaccine.

OPV—Booster Doses

Entering school: On entering kindergarten or first grade, all children who have completed the primary series of OPV should be given a single dose of trivalent OPV; others should complete the primary series.

There is no indication for routine booster doses of OPV beyond that given at the time of entering school.

Increased risk: A single dose of trivalent OPV can be administered to anyone who has completed the full primary series because of travel or occupational hazard as described above. The need for such an additional dose has not been established, but if there is uncertainty about the adequacy of existing protection, a single dose of trivalent OPV should be given.

Contraindications

Altered immune states: Infection with live, attenuated polioviruses might be potentiated by severe underlying diseases, such as leukemia, lymphoma, or generalized malignancy, or by lowered resistance, such as from therapy with steroids, alkylating drugs, antimetabolites, or radiation; therefore, vaccination of such patients should be avoided.

IPV—Primary Immunization

All ages: Four parenteral doses should be given, three at approximately 1-month intervals and the fourth 6 to 12 months after the third. This schedule can be integrated with DTP immunization beginning at 6 to 12 weeks of age.

IPV—Booster Doses

A booster dose every 2 to 3 years is generally recommended to ensure 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, but preferably a full primary series, is recommended.

EPIDEMIC CONTROL

For operational purposes in the United States, an "epidemic" of poliomyelitis is defined as two or more cases caused by the same poliovirus type and occurring within a 4-week period in a circumscribed population, such as that of a city, county, or a metropolitan area. An epidemic can be controlled with either trivalent OPV, or, after identification of the responsible type of poliovirus, homotypic monovalent OPV. Within the epidemic area, all persons over 6 weeks of age who have not been completely immunized or whose immunization status is unknown should promptly receive OPV.

SIMULTANEOUS ADMINISTRATION OF LIVE VIRUS VACCINES

There are obvious practical advantages to administering two or more live virus vaccines simultaneously. Data from specific investigations are not yet sufficient to develop comprehensive recommendations on simultaneous use, but a summary of current experience, attitudes, and practices provides useful guidance.

It has been generally recommended that live virus vaccines be given at least 1 month apart whenever possible – the rationale for this being that more frequent and severe adverse reactions as well as diminished antibody responses otherwise might result. Field observations indicate, however, that with simultaneous administration of certain live virus vaccines, results of this type have been minimal or absent. (For example, the third dose of trivalent oral poliovirus vaccine, which is recommended during the second year of life, is commonly given at the same time as smallpox vaccination without evident disadvantage.)

If the theoretically desirable 1-month interval is not feasible, as with the threat of concurrent exposures or disruption of immunization programs, the vaccines should preferably be given on the same day – at different sites for parenteral products. An interval of about 2 days to 2 weeks should be avoided because interference between the vaccine viruses is most likely then.

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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

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.

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 longer treatment is postponed, the less likely it is to be effective.

Accepted evidence of the efficacy of active and of passive immunization after exposure was derived largely from experimental studies in animals. Because rabies has on occasion developed in humans who had received antirabies prophylaxis, its value has been questioned. Evidence from laboratory and field experience in many areas of the world, however, indicates that post-exposure prophylaxis is usually effective when appropriately used.

Rabies in the United States

Rabies in humans has decreased from an average of 22 cases per year in 1946-1950, to only one or two cases per year since 1963. Rabies in domestic animals has diminished similarly. In 1946, for example, there were more than 8,000 cases of rabies in dogs, compared with 296 in 1968. 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 1968. Wild animals constitute the most important source of infection for man and domestic animals in the United States today. In 1968, only three States reported no wildlife rabies.

Antirabies Treatment in the United States

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

In the United States, nervous tissue origin rabies vaccine of the Semple type (NTV) was used almost exclusively until 1957, when duck embryo origin vaccine (DEV) was licensed. More than 90 percent of those who received rabies prophylaxis in the United States in 1968 were given DEV.

RABIES VACCINES

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 with phenol (Semple type) or inactivated with ultraviolet irradiation.

Antigenicity of Vaccines

The 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 sooner with DEV, 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 be judged only by reported failures. During the years 1957 through 1968 when both vaccines were available, there were six rabies deaths among the 125,000 NTV-treated persons (1:20,800) and eight among the 225,000 treated with DEV (1:28,100).

Reactions

Erythema, pruritus, 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 much more frequently follow NTV, especially after repeated courses of treatment with this preparation.

Choice of Vaccine

Treatment-failure rates for the two vaccines are not significantly different; therefore, the lower incidence of central nervous system reaction with DEV makes it preferable to NTV.

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

Carnivorous animals (especially skunks, foxes, coyotes, raccoons, dogs, and cats) and bats are more likely to be infective than other animals. Bites of rodents, including squirrels, chipmunks, rats, and mice, seldom, if ever, call for specific rabies prophylaxis.

Circumstances of 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, or 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, suspected of being contaminated with saliva also belong in this category.

Vaccination Status of 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 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 making recommendations on antirabies treatment following a bite by that species.

MANAGEMENT OF BITING ANIMALS

A dog or cat that bites a person 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. Clinical signs of rabies in wild animals cannot be interpreted reliably; therefore, any wild animal that bites or scratches a person should be killed at once (without unnecessary damage to the head) and the 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, soap and water, or detergent and water.

Treatment by or Under Direction of Physician

1. Thorough flushing and cleansing into the wound with soap solution. Quaternary ammonium compounds may also be used.*

2. If antirabies serum is indicated, (See Passive Immunization), some of the total dose should be thoroughly infiltrated around the wound. As in all instances when horse serum is to be used, a careful history should be taken and prior tests for hypersensitivity performed.

3. Tetanus prophylaxis and measures to control bacterial infection, as indicated.

POST-EXPOSURE PROPHYLAXIS

Active Immunization

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

For severe exposure, 21 doses of vaccine are recommended. These may be given as 21 daily doses or 14 doses in the first 7 days (either as two separate injections or a double dose), and then seven daily doses.

Booster doses: 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 given. 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.

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

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 has induced serum sickness in at least 20 percent of those who have received it, it should be used only when indicated.

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

The dose recommended is 1,000 units (one vial) per 40 pounds of body weight. A portion of the antiserum should be used to infiltrate the wound, and the rest 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 individuals, especially children, living in areas of the world where rabies is a constant threat. Others whose vocational or avocational pursuits result in frequent contact with 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 have produced neutralizing antibody in 80 to 90 percent of vaccinees by 1 month after the third dose.

For more rapid immunization, three 1.0 ml injections of DEV should 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.

*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.

All who receive 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 detected, 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.

ACCIDENTAL INOCULATION WITH LIVE RABIES VIRUS VACCINE

Persons inadvertently inoculated with attenuated rabies vaccines for use in animals, such as the Flury strain vaccine, are not considered at risk, and antirabies prophylaxis is not indicated.

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ANIMAL BITE TREATMENT CHECKLIST

(See text for Details)

1	2	3	4
FLUSH WOUND IMMEDIATELY (FIRST AID)	CLEANSE WOUND THOROUGHLY UNDER MEDICAL SUPERVISION	ANTIRABIES SERUM and/or VACCINE AS INDICATED	TETANUS PROPHYLAXIS & ANTIBACTERIAL WHEN REQUIRED

POST-EXPOSURE ANTIRABIES PROPHYLAXIS GUIDE

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. (See text for details.)

ANIMAL BITE		TREATMENT		
		EXPOSURE		
SPECIES	STATUS AT TIME OF ATTACK	NO LESION	MILD*	SEVERE*
DOG 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

RUBELLA VIRUS VACCINE PRELICENSING STATEMENT†

INTRODUCTION

The live, attenuated rubella virus vaccine* soon to become available appears to be a highly effective immunizing agent and the first suitable method of controlling rubella.

Rubella is generally a mild illness, but if the infection is acquired by a woman in the early months of pregnancy, it poses a direct hazard to the fetus. Preventing infection of the fetus is the principal objective of rubella control. This can best be achieved by eliminating the transmission of virus among children, who are the major source of infection for susceptible pregnant women. Furthermore, the live, attenuated rubella virus vaccine is safe and protective for children, but not for pregnant women because of an undetermined risk of the vaccine virus for the fetus.

Rubella

Rubella is one of the common childhood exanthems. Most cases occur in school-age children particularly during the winter and spring. By early adulthood, approximately 80 to 90 percent of individuals in the United States have serological evidence of immunity.

Rubella is clinically variable, and its common features, such as post-auricular and sub-occipital lymphadenopathy and transient erythematous rash, are often overlooked or misdiagnosed. A mild febrile illness may not be recognizable as rubella, and moreover, subclinical infection occurs, which further decreases the reliability of clinical history.

Complications of rubella are rare in children, but in adults, particularly women, the illness is commonly accompanied by transient polyarthritis. Far more important is the frequent occurrence of fetal abnormalities when a woman acquires rubella in the first trimester of pregnancy.

Rubella Immunity

Immunity following rubella appears to be long lasting, even after mild illness or clinically inapparent infection. The only reliable evidence of immunity is a positive serological test. However, because of the variation among reagents and technical procedures, results of serological tests should be accepted only from laboratories of recognized competency that regularly perform these tests.

At the present time, the hemagglutination-inhibition (HI) antibody determination is particularly useful for evaluating immunity. It is a rapid and sensitive procedure. The complement fixation (CF) and other serological tests are less useful.

LIVE RUBELLA VIRUS VACCINE

Live rubella virus vaccine is prepared in cell culture of avian or mammalian tissues. It is administered as a single subcutaneous injection. Although vaccinees shed virus from the pharynx at times for 2 or more weeks after vaccination, there is no clear evidence of communicability. Approximately 95 percent of susceptible vaccinees develop antibodies, but titers are lower than those observed following natural rubella infection. Recent investigations have shown that vaccination affords protection against illness following either natural exposure or artificial challenge.

Antibody levels have declined very little during the 3-year period of observation of children who were among the first to be immunized with rubella vaccine. Long-term protection is likely, but its exact duration can be established only by continued observation.

More than 30,000 susceptible children have received live rubella virus vaccine in field investigations, with almost no untoward reactions. Only rarely has transient arthralgia or evanescent rash been reported in children.

Many susceptible women have had lymphadenopathy, arthralgia, and transient arthritis beginning 2 to 4 weeks after vaccination; however, fever, rash, and other features of naturally acquired rubella have occurred less commonly. Not enough susceptible men have been vaccinated to show whether they experience comparable reactions as frequently as women.

VACCINE USAGE

General Recommendations

Live rubella virus vaccine is recommended for boys and girls between the age of 1 year and puberty. Vaccine should not be administered to infants less than 1 year old because of possible interference from persisting maternal rubella antibody.

Children in kindergarten and the early grades of elementary school deserve initial priority for vaccination because they are commonly the major source of virus dissemination in the community. A history of rubella

†Rubella vaccine was licensed on June 9, 1969, for distribution in the U.S.A. Revision of the ACIP recommendation awaits accumulation of data based on experience.

*Official name: Rubella Virus Vaccine, Live.

illness is usually not reliable enough to exclude children from immunization.

Vaccination of adolescent or adult males is of much lower priority because so few are susceptible. However, the vaccine may be useful in preventing or controlling outbreaks of rubella in circumscribed population groups.

Pregnant women should not be given live rubella virus vaccine. It is not known to what extent infection of the fetus with attenuated virus might take place following vaccination, or whether damage to the fetus could result. Therefore, **routine** immunization of adolescent girls and adult women should **not** be undertaken because of the danger of inadvertently administering vaccine before pregnancy becomes evident.

Women of childbearing age may be considered for vaccination only when the possibility of pregnancy in the following 2 months is essentially nil; each case must be considered individually. This cautious approach to vaccinating postpubertal females is indicated for two reasons: First, because of the theoretical risk of vaccination in pregnancy; and second, because significant congenital anomalies occur regularly in approximately 3 percent of all births, and their fortuitous appearance after vaccine had been given during pregnancy could lead to serious misinterpretation.

If vaccination of a woman of childbearing age is contemplated, the following steps are indicated:

Optimally, the woman should be tested by the HI test for susceptibility to rubella (See Rubella Immunity).

If **immune**, she should be assured that vaccination is unnecessary.

If **susceptible**, she may be vaccinated only if she understands that it is imperative for her to avoid becoming pregnant for the following 2 months. (To ensure this, a medically acceptable method for pregnancy prevention should be followed. This precaution also applies to women in the immediate postpartum period.) Additionally, she should be informed of the frequent occurrence of self-limited arthralgia and possible arthritis beginning 2 to 4 weeks after vaccination.

Use of Vaccine Following Exposure

There is no evidence that live rubella virus vaccine given after exposure will prevent illness. There is, however, no contraindication to vaccinating children already exposed to natural rubella. For women exposed to rubella, the concepts listed previously apply.

Precautions and Contraindications

Pregnancy: Live rubella virus vaccine is contraindicated. (See General Recommendations)

Altered immune states: Attenuated rubella virus infection might be potentiated by severe underlying diseases, such as leukemia, lymphoma, or generalized malignancy, and when resistance has been lowered by therapy with steroids, alkylating drugs, antimetabolites, or radiation. Vaccination of such patients should be avoided.

Severe febrile illnesses: Vaccination should be postponed until the patient has recovered.

Hypersensitivity to vaccine components: Rubella vaccine is produced in cell culture. Care should be exercised in administering vaccine to persons with known hypersensitivity to the species from which the cells were derived (indicated in the labeling). The vaccine contains a small amount of neomycin and should not be given to individuals known to be sensitive to this antibiotic.

Simultaneous Administration of Live Rubella Virus Vaccine and Other Live Virus Vaccines

Simultaneous administration of live rubella virus vaccine and other live virus vaccines should be deferred until results of controlled clinical investigations are available. Until then, it is recommended that rubella vaccination be separated by at least 1 month from administration of other live virus vaccines.

SURVEILLANCE

Careful surveillance of rubella infection is particularly important with an effective vaccine in use. Emphasis should be placed upon improved diagnosis and reporting of rubella, of the congenital rubella syndrome, and of complications of the disease. Competent laboratory investigation of all infants with birth defects suspected of being due to rubella is essential. It will likewise be important to observe patterns of vaccine use and determine their effectiveness.

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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

SMALLPOX VACCINE

INTRODUCTION

In the United States, protection of the population 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 with the efficacy and risk associated with preventive procedures.

THE RISK OF INTRODUCING SMALLPOX

While the current risk of introduction and subsequent transmission of smallpox in the United States is difficult to define, not one confirmed case of smallpox has occurred since 1949 despite increased travel by United States citizens and other nationals to and from smallpox endemic areas. The reservoirs of endemic smallpox in Asia, Africa, and South America are shrinking, and in these areas many of the smallpox cases are now occurring away from urban centers. Furthermore, recent evidence suggests that the communicability of smallpox through casual contact, as on common carriers, is quite small.

It must be recognized, however, that quarantine measures at ports of entry offer at best only partial protection against the introduction of smallpox. In almost half of the 39 instances since 1950, when smallpox was introduced into Western Europe, nationals of the country involved were responsible. Should smallpox be introduced into the United States, it is similarly quite possible that a United States citizen returning from abroad would introduce the disease.

Smallpox, particularly variola major, is a highly virulent disease even with excellent medical care. The mortality rate for unvaccinated persons was 40 percent in Sweden and England in the outbreaks of 1962-63.

Because few physicians in practice today have seen clinical smallpox, it is not surprising that in several recent European outbreaks the disease went unrecognized until the third generation of cases, or even later. During a 1966 outbreak of variola minor in England, the diagnosis of smallpox was not made until the fourth cycle of transmission, when 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 VACCINE

Effectiveness

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 3 years. Vaccination provides substantial but waning immunity for 10 years or more, but appears to protect against a fatal outcome of disease for an even longer period, perhaps for decades.

Complications and Risks

It is recognized that with smallpox vaccination, as with other medical procedures, there is a definite, measurable risk of untoward reaction and rarely death. Comprehensive national surveys to determine the frequency of smallpox vaccine complications in the United States were made in 1963 and 1968. In 1968, among more than 5.6 million primary vaccinees and nearly 8.6 million revaccinees and their contacts, 16 cases of encephalitis, 11 cases of vaccinia necrosum, and 126 cases of eczema vaccinatum occurred in association with vaccination. Nine persons died. A substantial number of less serious complications, some of which necessitated hospitalization, were also recorded. All deaths and virtually all complications occurred in primary vaccinees.

Survey data show clearly that more than half of the complications from smallpox vaccination would not have occurred if acknowledged contraindications to vaccination had been closely observed. Furthermore, complication rates appear to be at least twice as high for children under one year of age as for slightly older children. Also primary vaccination of adolescents and adults appears to carry a higher risk of adverse reactions than vaccination of younger children.

Thus, with no introductions of smallpox into the United States in 20 years and with a small but definite risk of adverse reactions to smallpox vaccine, the justification for its routine use must be examined regularly. In weighing the relative risks, the consequences of having to vaccinate persons for the first time as adults needing protection against smallpox when entering military service, traveling overseas, working in medical or allied health professions, or being exposed in local outbreaks must be considered.

OTHER PROPHYLACTIC AGENTS

In recent years, Vaccinia Immune Globulin (VIG) and certain antiviral compounds have been found to be effective in conferring protection against smallpox when administered shortly after exposure to the disease. At present, none appears to be a satisfactory alternative to vaccination, and more importantly, none confers more than temporary protection. Thus, unless the first introduced smallpox case could be promptly and correctly diagnosed and all contacts quickly identified and treated, interruption of subsequent transmission of the disease by using these materials would be virtually impossible.

It is of added practical importance that antiviral compounds have considerable gastrointestinal toxicity and the supply of VIG is limited. Therefore, none of these prophylactic agents is suitable for mass use as a substitute for vaccination at the time of an actual or potential outbreak.

CONCLUSIONS AND RATIONALE FOR VACCINATION

In recent years, international travel has increased dramatically, and while the reservoir of endemic smallpox has decreased, the potential for introduction of smallpox into the United States continues.

The 1966 World Health Assembly agreed to embark on an intensive 10-year smallpox eradication program. Vaccination campaigns in many of the developing countries have been very effective, so there is every reason to anticipate success with this program. Eradication of endemic smallpox represents the most direct attack on the problem and the surest means of protecting the United States.

Until eradication is achieved or, at least, nears realization, vaccination, although not wholly without risk, now represents the only suitable approach for community protection in the United States. Comparing the risks of smallpox spread in the United States and the risk of primary vaccination complications for adults with the risks of complications of vaccination of children, it seems prudent for the present to continue the practice of regular smallpox vaccination in early childhood and subsequent periodic revaccination.

VACCINE USAGE

The following smallpox vaccination practices are recommended for the United States:*

Primary Vaccination

Age: Within the second year of life (i.e., between first and second birthdays) or at any age under conditions of exposure or foreign travel.

*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."

Revaccination

School entrance: On entering kindergarten or elementary school.

Potential exposure: At 3-year intervals for persons who conceivably might be exposed in endemic or potentially endemic areas by virtue of international travel or likely to be exposed by newly introduced infection into the United States, in particular: hospital personnel, including physicians, nurses, attendants, and laboratory and laundry workers; other medical, public health, and allied professions; and morticians and other mortuary workers.

Routine vaccination: At approximately 10-year intervals for all others.

Site of Vaccination

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

Methods of Vaccination

Multiple pressure: A small drop of vaccine is placed on the dry, cleansed skin, and a series of pressures is made in an area about 1/8-inch in diameter with the side of a sharp, single pointed, 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. (Proportionately fewer pressures are required with a "bifurcated" needle.) The remaining vaccine should be wiped off with dry, sterile gauze. Preferably, no dressing should be applied to the site.

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

Other techniques: Vaccination may be performed with other devices and techniques shown to be equally effective in assuring takes.

Interpretation of Responses†

Time of inspection: The vaccination site should be inspected 6 to 8 days after vaccination. The response at this time should be interpreted.

Primary vaccination: A "successful" primary vaccination shows a typical Jennerian vesicle. If none is observed, vaccination procedures should be checked and vaccination repeated with vaccine from another lot until a successful result is obtained.

Revaccination: Two types of revaccination response are defined by the WHO Expert Committee on Smallpox, eliminating use of older terms such as "accelerated" and "immune." They are:

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 an

†For purposes of validating an International Certificate of Vaccination, primary vaccination must be inspected. Although desirable, inspection of revaccination is not mandatory.

ulcer. This reaction indicates that virus multiplication has taken place and that the revaccination is successful.

Equivocal reaction – All reactions other than "major reactions." They may be the consequences 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 vaccine from another lot.

Types of Smallpox Vaccine

Smallpox vaccine is available both in the glycerinated and the lyophilized form. Both forms, when properly preserved and administered, afford excellent protection. The glycerinated form requires constant refrigeration in all stages of transport and storage at temperatures recommended by the manufacturer. Comparatively minor storage difficulties may reduce its potency enough 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 ensure more consistently effective vaccination. Due care must be exercised to provide proper handling of the lyophilized vaccine after reconstitution as directed by the manufacturer.

Contraindications

Skin disorders: 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, VIG should be administered to the vaccinee. If there is real need to vaccinate an individual who may thus create a hazard for a household contact with dermatitis, consideration should be given to separating the vaccinee from his contact until a crust has developed.

Pregnancy: Vaccinia virus rarely may cross the placental barrier at 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 in cases of primary vaccination. VIG will not prevent a take.

Altered immune states: Leukemia, lymphoma, and other reticuloendothelial malignancies; dysgammaglobulinemia; therapy with immunosuppressive drugs, such as steroids and antimetabolites; or radiation. If exposure should by chance occur, or if vaccination is absolutely essential, persons with any of the above conditions should be given Vaccinia Immune Globulin.

VACCINIA IMMUNE GLOBULIN

Prophylactic Use

Dose: 0.3 ml/kg by the intramuscular route.

Therapeutic Use

Dose and indications: 0.6 ml/kg by the intramuscular route. For eczema vaccinatum, vaccinia (progressive vaccinia), or autoinoculation vaccinia of the eye, VIG may be effective. For severe cases of generalized vaccinia, VIG may be helpful in treatment, but such cases almost invariably have a favorable outcome anyway. For mild cases of generalized vaccinia or autoinoculation **not** involving the eye, VIG is generally considered unnecessary. For postvaccinial encephalitis, VIG is of no proved value.

THIOSEMICARBAZONES

Certain of the thiosemicarbazone derivatives reportedly have a short-term protective effect against smallpox and possibly a therapeutic effect on individuals with severe vaccinial complications These are still experimental drugs and are not available for general use.

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VOLUNTEER CONSULTANTS FOR THE DISTRIBUTION OF VACCINIA IMMUNE GLOBULIN

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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

TYPHOID VACCINE

INTRODUCTION

The incidence of typhoid fever has declined steadily in the United States in the last half century, and in the recent years fewer than 400 cases have been reported annually. The continuing downward trend is due largely to better sanitation and other control measures; vaccine is not deemed to have played a significant role.

TYPHOID VACCINES

Although typhoid vaccines have been used for many decades, only recently has definitive evidence of their effectiveness been observed in well controlled field investigations. Several different preparations of typhoid vaccine have been shown to protect 70 to 90 percent of recipients, depending in part on the degree of their subsequent exposure.

VACCINE USAGE

Routine typhoid vaccination is **no longer** recommended for persons 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.

Typhoid vaccination should not be interpreted as permitting relaxation in careful selection of foods and water in areas where typhoid infections are occurring.

Although typhoid vaccine was at one time suggested for persons going to summer camps and those in areas where flooding has occurred, there are no data to support the continuation of these practices.

Primary Immunization

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

Adults and children over 10 years old: 0.5 ml subcutaneously on two occasions, separated by 4 or more weeks.

Children less than 10 years old*: 0.25 ml subcutaneously on two occasions, separated by 4 or more weeks.

*Since febrile reactions to typhoid vaccine are common, an antipyretic may be indicated.

In instances where there is not sufficient time for two doses to be administered at the interval specified, it has been common practice to give three doses of the same volumes listed above at weekly intervals recognizing that this schedule may be less effective. When vaccine is to be administered for travel overseas under constraint of time, a second dose may be administered en route at a more suitable interval.

Booster Doses

Under conditions of continued or repeated exposure, a booster dose should be given at least every 3 years. Even when more than 3 years have elapsed since the prior immunization, a single booster injection is sufficient.

The following alternative routes and dosages of booster immunization can be expected to produce comparable antibody responses; generally less reaction follows vaccination by the intradermal route (except when acetone killed and dried vaccine is used. This vaccine should not be given intradermally).

Adults and children over 10 years old: 0.5 ml subcutaneously or 0.1 ml intradermally.

Children 6 months to 10 years*: 0.25 ml subcutaneously or 0.1 ml intradermally.

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 are not effective, in the usually small amounts contained in "TAB" vaccines. Knowing this and recognizing that combining paratyphoid A and B antigens with typhoid vaccine increases the risk of vaccine reaction, paratyphoid A and B vaccines should **not** be used.

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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

TYPHUS VACCINE

INTRODUCTION

The United States has not experienced an outbreak of louse-borne (epidemic) typhus since 1922. The last reported case, 1950, did not result from an indigenous source of infection.

Louse-borne typhus was widespread in many countries affected by World War II. Since 1945, reported cases have declined steadily. Effective insecticides and generally improved standards of living have permitted many populations to free themselves of louse infestation. A human reservoir of latent infections persists in many parts of the world, and resurgence of the disease might occur under conditions of war or disaster. Vaccination of any civilian population in the United States, however, is unwarranted.

TYPHUS VACCINE

Typhus vaccines of the type available today were first used widely in World War II. There were no deaths from typhus among vaccinated persons during the North African campaign, and incidence of disease in the vaccinated was reportedly lower than in the unvaccinated. In unvaccinated adults, the case-fatality ratio is reported to be 20 percent or higher.

Although no controlled studies of typhus vaccine have been carried out in human populations, experience from the field and the laboratory suggests that the incidence and severity of typhus cases is diminished among the vaccinated, especially if booster doses have been received.

Typhus vaccine is prepared from formaldehyde inactivated *Rickettsia prowazekii* grown in embryonated eggs. This vaccine provides protection against only louse-borne (epidemic) typhus; it does not protect against murine or scrub typhus.

VACCINATION USAGE

Vaccination for International Travel

The rarity of epidemic typhus minimizes the need for vaccination. Typhus is at present no threat to United States residents visiting most other countries. This is true even in places still reporting large numbers of cases if travel is limited to urban areas with modern hotel accommodations. It is only in mountainous, highland, or areas where a cold climate and other local conditions favor louse infestation that a potential threat exists.

Vaccination may be indicated for travelers to rural or remote highland areas of Ethiopia, Rwanda, Burundi, Mexico, Ecuador, Bolivia, or Peru, and mountainous areas of Asia. Even there, however, the risk of typhus for U.S. travelers is extremely low. No typhus case in an American traveler is known to have occurred in recent years. Vaccination against typhus is not required by any country as a condition for entry.

Typhus vaccination is suggested only for the following special-risk groups:

1. Such persons as scientific investigators (e.g., anthropologists, archaeologists, or geologists), oil-field and construction workers, missionaries, and some government workers who live in or visit areas where the disease actually occurs and who will be in close contact with the indigenous population in such areas.
2. Medical personnel, including nurses and attendants, providing care for patients in areas in which louse-borne (epidemic) typhus occurs.
3. Laboratory personnel working with *Rickettsia prowazekii.*

Primary Immunization

Two subcutaneous injections of vaccine 4 or more weeks apart using the dose volume indicated by the manufacturer for adults or for children.

Booster Doses

A single subcutaneous injection of vaccine at intervals of 6 to 12 months for as long as opportunity for exposure exists using the dose volume indicated by the manufacturer for adults or for children. The primary series need never be repeated for booster doses to be effective.

Reactions

Pain and tenderness at the injection site should be expected. A few individuals have reportedly experienced exaggerated local reactions and fever, presumably a manifestation of hypersensitivity.

Contraindications

As is the case for all vaccines propagated in eggs, typhus vaccine should not be administered to anyone who is hypersensitive to eggs.

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RECOMMENDATION OF THE PUBLIC HEALTH SERVICE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

YELLOW FEVER VACCINE

INTRODUCTION

At present, cases of yellow fever are reported from only Africa and South America. Two forms of yellow fever – urban and jungle – are distinguishable epidemiologically. Clinically and etiologically, they are identical.

Urban yellow fever is an epidemic viral disease of man transmitted from infected to susceptible persons by a vector, the *Aedes aegypti* mosquito. With the elimination of *A. aegypti*, urban yellow fever has disappeared from previously epidemic foci.

Jungle yellow fever is an enzootic viral disease transmitted among non-human hosts by a variety of mosquito vectors. It is currently observed only in the jungles of South America and Africa, but in the past it extended into parts of Central America as well. Human cases occur by chance. The disease can ostensibly disappear from an area for years and then reappear. Delineation of areas affected depends upon accurate diagnosis and prompt reporting of all cases.

Urban yellow fever can be prevented by eradicating *A. aegypti* mosquitoes. Jungle yellow fever can be prevented in humans only by immunization. Because infection is from a non-human reservoir, prevention of human cases requires vaccination of all persons at risk.

YELLOW FEVER VACCINE

Yellow fever vaccine is a live, attenuated virus preparation made from one of two strains of virus: 17D and Dakar (French neurotropic). The Dakar strain has been associated with a significant (0.5 percent) incidence of meningoencephalitic reactions and is not recommended. The 17D strain has caused no significant complications.

Licensed vaccine available in the United States is prepared from the 17D strain, which is grown in chick embryo inoculated with a fixed passage level seed virus. The vaccine is freeze-dried supernate of centrifuged embryo homogenate.

Vaccine should be stored at the temperature recommended by the manufacturer until it is reconstituted by the addition of sterile physiologic saline. Unused vaccine should be discarded within approximately 1 hour of reconstitution.

VACCINE USAGE

General Recommendations

Age: Persons 6 months of age or older traveling or living in areas where yellow fever infection exists (currently Africa and South America. (See Vaccination for International Travel).

Special risk: Laboratory personnel who might be exposed to virulent yellow fever virus.

Vaccination for International Travel

To be acceptable for purposes of international travel, yellow fever vaccines must be approved by the World Health Organization and administered at a Yellow Fever Vaccination Center listed with WHO. Vaccinees should have an International Certificate of Vaccination filled in, signed, and validated with the stamp of the Center where the vaccination is administered. (Yellow Fever Vaccination Centers in the United States are designated by the Foreign Quarantine Program of the Public Health Service.*)

Vaccination for international travel may be required under circumstances other than those included in these recommendations. A number of countries in Africa and South America require evidence of vaccination from all entering travelers; some may waive the requirements for travelers coming from non-infected areas and staying less than 2 weeks. These requirements may change, so all travelers should seek current information from health departments and travel agencies.

Some countries require an individual, even if only in transit, to have a valid International Certificate of Vaccination if he has been in countries either known or thought to harbor yellow fever virus. This applies particularly to travelers to South and Southeast Asia by way of the Atlantic.

Primary Vaccination

A single subcutaneous injection of 0.5 ml of reconstituted vaccine for both adults and children.

Revaccination

Yellow fever immunity following vaccination with 17D strain virus has been shown to persist for more than 10 years; the International Sanitary Regulations do not require revaccination more frequently than every 10 years.

Reactions

The few reactions to 17D yellow fever vaccine that occur are generally mild. Five to 10 percent of vaccinees

*For a list of such centers, see *Immunization Information for International Travel*, PHS Publication No. 384, available from the Supt. of Documents, U.S. Government Printing Office, Washington, D.C. 20402 at 40 cents.

have mild headache, myalgia, low-grade fever, or other minor symptoms 5 to 10 days after vaccination. Symptoms cause less than 0.2 percent to curtail regular activities. Only two cases of encephalitis have been reported in the United States, for more than 34 million doses of vaccine distributed.

Because yellow fever vaccine is prepared from chick embryos, it may induce reactions of varying degrees of severity in individuals hypersensitive to eggs. Experience in the Armed Forces suggests that allergy severe enough to preclude vaccination is very uncommon and occurs only in those who are actually unable to eat eggs.

Precautions and Contraindications

Pregnancy: Although specific information is not available concerning adverse effects of yellow fever vaccine on the developing fetus, it is prudent on theoretical grounds to avoid vaccinating pregnant women.

Altered immune states: Yellow fever vaccine virus infection might be potentiated by severe underlying diseases, such as leukemia, lymphoma, or generalized malignancy, and by lowered resistance, such as from therapy with steroids, alkylating drugs, antimetabolites, or radiation; therefore, vaccination of such patients should be avoided.

Allergy: Documented hypersensitivity to eggs can be contraindication to vaccination. In making the decision to vaccinate despite a history of egg allergy, a physician must weigh three factors: 1) the nature of the history and of the reported hypersensitivity, 2) the relative risk of exposure to yellow fever, and 3), in the case of international travel, the possible inconvenience from disrupted travel plans.

If international quarantine regulations are the only reason to vaccinate a patient hypersensitive to eggs, efforts should first be made to obtain a waiver. A physician's letter which clearly states the contraindication to vaccination has been acceptable to some governments. (Ideally, it should be written under his letterhead and bear the authenicating stamp used by health departments and official immunization centers to validate International Certificates of Vaccination.) Because this is not uniformly true, however, it is prudent for the traveler to obtain specific and authoritative advice from the country or countries he plans to visit. Their embassies or consulates may be contacted. Subsequent waiver of requirements should be documented by appropriate letters.

SIMULTANEOUS ADMINISTRATION OF LIVE VIRUS VACCINES

There are obvious practical advantages to administering two or more live virus vaccines simultaneously. Data from specific investigations are not yet sufficient to develop comprehensive recommendations on simultaneous use, but a summary of current experience, attitudes, and practices provides useful guidance.

It has been generally recommended that live virus vaccines be given at least 1 month apart whenever possible – the rationale for this being that more frequent and severe adverse reactions as well as diminished antibody responses otherwise might result. Field observations indicate, however, that with simultaneous administration of certain live virus vaccines, results of this type have been minimal or absent. (For example, the third dose of trivalent oral poliovirus vaccine, which is recommended during the second year of life, is commonly given at the same time as smallpox vaccination without evident disadvantage.)

If the theoretically desirable 1-month interval is not feasible, as with the threat of concurrent exposures or disruption of immunization programs, the vaccines should preferably be given on the same day – at different sites for parenteral products. An interval of about 2 days to 2 weeks should be avoided because interference between the vaccine viruses is most likely then.

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