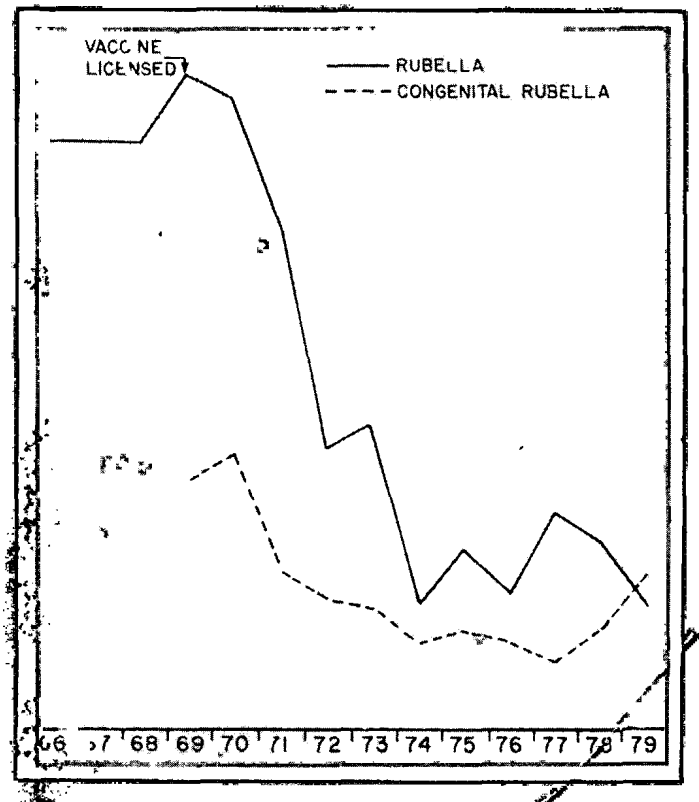
CDC

MONOGRAPH

IMMUNIZATION AGAINST DISEASE

1980



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES • PUBLIC HEALTH SERVICE • CENTER FOR DISEASE CONTROL

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Center for Disease Control

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September 1980

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTER FOR DISEASE CONTROL
ATLANTA, GEORGIA 30333

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FOREWORD

Data in *Immunization Against Disease* are derived from official reports submitted by states and other reporting health jurisdictions. Weekly tallies of the numbers of cases of reportable diseases are sent to the Center for Disease Control (CDC) as part of the established National Morbidity Reporting System and are tabulated in the *Morbidity and Mortality Weekly Report (MMWR)* published by CDC. Official mortality data are provided by the National Center for Health Statistics in the *Monthly Vital Statistics Report (MVSR).*

Collecting information on individual cases of selected diseases, such as poliomyelitis and diphtheria, is a surveillance activity of various programs at CDC. This information comes through epidemiologic and laboratory reporting channels from state and other health jurisdictions. Surveillance data on cases of specific communicable diseases are 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. The reader should remember that the official data (those in *MMWR* and *MVSR)* are the authoritative and archival counts of cases and deaths, but surveillance records provide additional insights into trends and patterns of communicable diseases and therefore merit attention.

Immunization Against Disease represents a collaborative effort of various staff members of CDC. The original version, developed in 1966 in the Office of the Center Director, was 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. Updating *Immunization Against Disease* has been an ongoing project since the original version was published. So many staff members at CDC have been involved in this effort that we cannot acknowledge all contributions on an individual basis; however, we take this opportunity to recognize the people listed below for their contribution to this edition.

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INTRODUCTION

The development and routine use of vaccines has had a dramatic effect on the occurrence of certain infectious diseases, as will become quite apparent in later chapters. For example, 7 vaccines are currently recommended for routine use for children in the United States. Only 6 visits for vaccination are required in order to ensure effective protection before a child enters school.

Vaccinations are given in a variety of settings, including private physicians' offices, local health departments, special school-based clinics, neighborhood health centers, and hospital out-patient clinics. These distributions vary greatly from state to state, but overall it is estimated that private physicians give 50% of the vaccinations received by children and that the other 50% are given in the public sector, primarily in local health department clinics.

Although few visits are required and the vaccines themselves are relatively inexpensive, there is clear evidence that not all children in the United States receive the recommended vaccines. In late 1976, it was estimated that there might be as many as 20 million American preschool and school-age children who needed at least 1 dose of 1 antigen in order to be considered fully protected. To remedy this problem and to counter rising levels of measles morbidity, an intensified immunization effort (the Childhood Immunization Initiative) was undertaken in the period April 1977-October 1979. This Initiative had 2 goals: 1) ensuring that at least 90% of the nation's children had received needed vaccines and 2) developing a permanent system to maintain this percentage in the future.

Various efforts made to achieve these objectives included increased federal support for immunization, increased public information education activities, increased use of volunteers, and improved cooperation among government agencies. Special emphasis was placed on identifying schoolchildren who had not had all needed vaccines. More than 24 million individual school records were reviewed, and the appropriate children were either vaccinated at school or referred for vaccination. It became clear that in order to ensure that a high percentage of the population would be protected by vaccination, requirements for vaccination had to be enforced as a condition of entry into or attendance at school. By October 1979, all 50 states and the District of Columbia had laws requiring that children be vaccinated or have other proof of immunity before they initially entered school. There was good evidence from school entry surveys and record assessments that the goal of having 90% of all school-age children immunized had been reached. Whether this level of success can be maintained in the future will clearly not be known for several years. Several essential factors in this effort include continued emphasis on the need for vaccination, continued enforcement of vaccination requirements and their expansion to include all levels of school, and continued support from federal, state, and local governments for vaccination in the public sector.

This edition of *Immunization Against Disease* is a review of the status of diseases that are important to the United States and for which vaccines are used in an effort to prevent disease—temporarily or permanently. The depth of analysis, scope of coverage, and general level of detail will undoubtedly change with added insights and new sources of information. The discussions primarily cover data summarized through the 1978 calendar year and are addressed to students and practitioners of public health and medicine. The book assesses for this audience not only achievements in control but also the collective obligation to be alert to present and future needs.

The manual is divided into 4 major sections. The first deals with the status of vaccine-preventable diseases. The second contains the 1978 Biologics Surveillance Summary (a collaborative effort of CDC and the major producers of biologics in the United States). The third contains chapters on immunization for hospital employees and for pregnant women and tables showing the recommended schedules for vaccinating infants and children. The fourth contains the current recommendations of the Immunization Practices Advisory Committee (ACIP). Each of the recommendations of the ACIP was printed earlier in the *Morbidity and Moratility Weekly Report.* The compiled recommendations are intended to be a convenient supplement to the reviews of disease status. Each includes an interpretation of the role of immunization and recommendations for practitioners in the areas of public health and preventive medicine in the United States.

SECTION I:
CURRENT REVIEWS

Cholera

Cholera is an acute intestinal infection caused by *Vibrio cholerae* O-group 1. At its worst, cholera deserves its historic reputation; it can produce diarrhea so severe that cardiovascular collapse and death occur in less than a day; however, the infection is usually mild and self-limited or subclinical. Patients with severe cases respond dramatically to simple fluid- and electrolyte-replacement therapy, and cholera deaths are entirely preventable.

V. cholerae O1 is a gram-negative, curved, rod-shaped bacterium that is actively motile and has a single polar flagellum. Symptoms are caused by a heat-labile exotoxin elaborated in vivo. Infection is acquired by ingesting contaminated water or food. Cholera, unlike shigellosis, is not easily transmitted by person-to-person contact. Other hospital patients, physicians, nurses, and ward attendants almost never become clinically ill as a result of contact with cholera patients or their excreta.

The organism is fragile and easily killed by proper chlorination, exposure to sunlight, or drying. Although water plays the major role in transmission, fresh water cannot ordinarily serve as a continuing source of infection. When there are no more cases or carriers in an area, vibrios usually disappear within a few days, even from heavily contaminated water; however, cholera vibrios can survive for weeks and months in salt water.

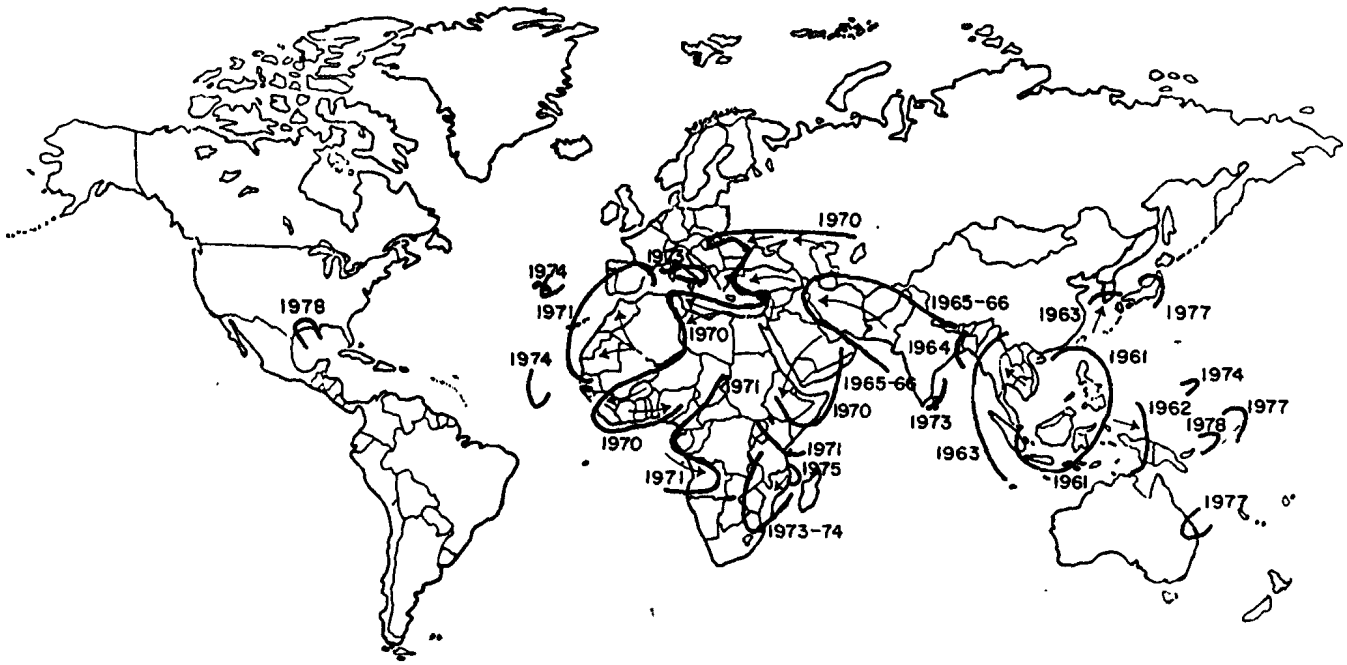
The 2 recognized biotypes of *V. cholerae* O1 are classical and El Tor. Severe cases of illness caused by each biotype are almost identical. The classical biotype is thought to have been responsible for the repeated worldwide pandemics of the 19th century. More recently, this biotype has been found only in a few endemic foci on the subcontinent of Asia. The El Tor biotype has been responsible for the pandemic spread of cholera that began on the island of Celebes in Indonesia in 1961. The pandemic involved the Middle East by 1966 and, beginning in 1970, spread into large portions of Africa and some European countries (Figure 1). The number of countries per year reporting cholera was quite stable from 1970 to 1978, and there were no major changes in the number of reported cases in the period 1972-1978 (Figure 2).

Many more asymptomatic cases are produced by the El Tor biotype than by the classical. Studies have shown that for each diagnosed and reported case, there may be as many as 25 to 100 persons with mild symptoms or asymptomatic infection (Figure 3). With modern transportation, persons with mild or asymptomatic cholera can easily carry the disease long distances and across international borders.

Risk to Travelers

Although literally millions of Americans and Western Europeans have traveled through or lived in cholera-infected areas in the past 15 years, only 7 American travelers have had documented cases of cholera, all nonfatal. Several factors account for this very low risk to Americans and

Figure 1. Extension of El Tor cholera, 1961-1978



SOURCE: World Health Organization, Weekly Epidemiological Record, Second Series.

other Westerners. First, these persons tend to frequent tourist hotels and restaurants that maintain relatively high sanitary standards, and they thereby avoid exposure to questionable water and food supplies. Second, if they plan to travel to areas known to have cholera, they are likely to be vaccinated against cholera shortly before leaving home. Although cholera vaccine affords only partial protection, this protection is greatest for the first 2 months after vaccination.

Travelers in cholera-infected areas should avoid eating uncooked vegetables such as lettuce and celery because farmers are known to "freshen" their products on the way to market with water that may be contaminated. However, fruits peeled by the consumer are safe, and carbonated bottled drinking water and carbonated soft drinks are generally safe. One large outbreak of cholera caused by uncarbonated commercially bottled mineral water has been reported.

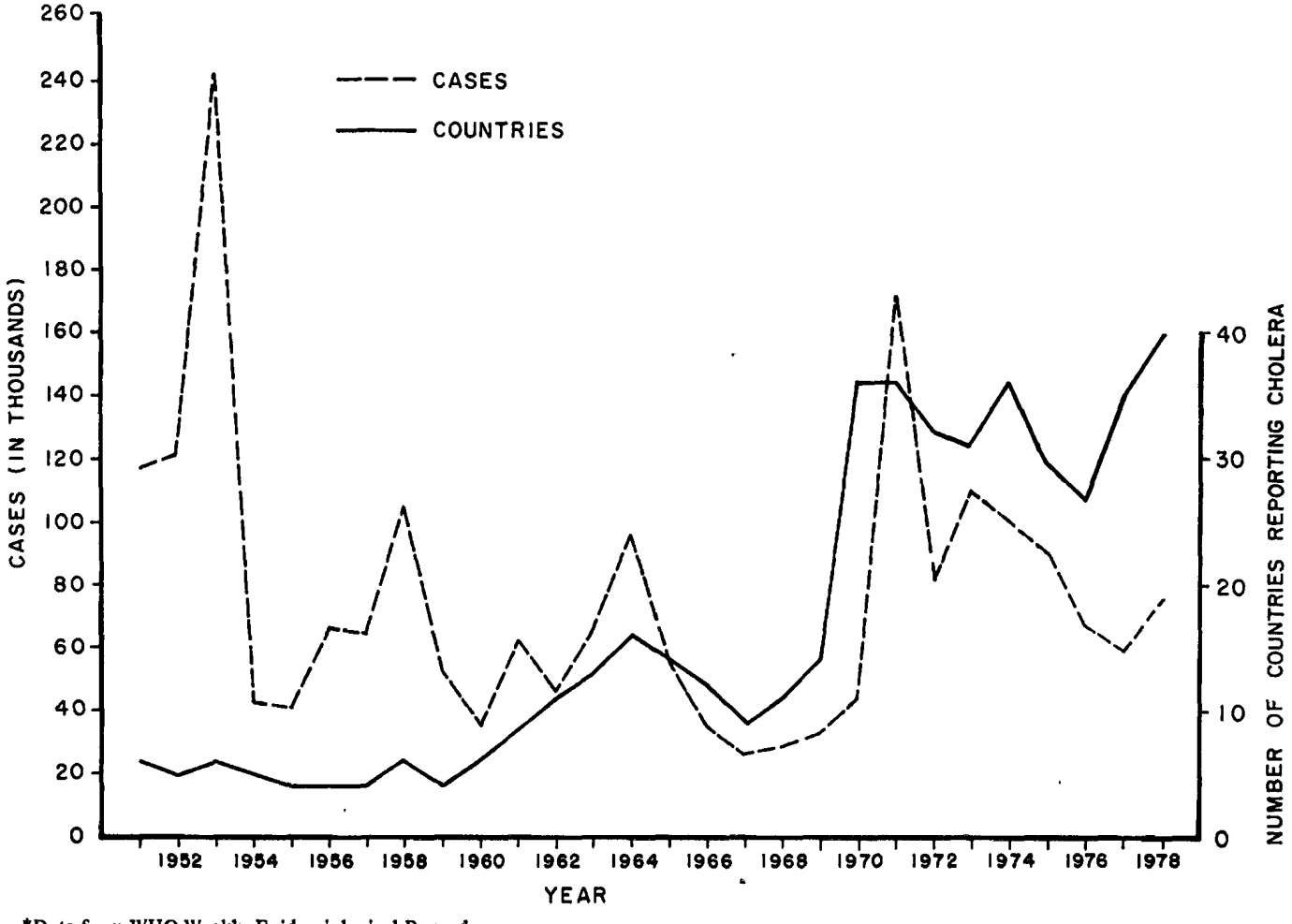
Swimmers should avoid beaches contaminated with human sewage. If in doubt, they should swim only in constructed pools that contain chlorinated water.

Risk to the Western Hemisphere

Although *Vibrio cholerae* O1 was introduced into the United States in or before 1973 and apparently persisted through 1978, only 12 cases were reported—in Texas in 1973 and 11 in Louisiana in 1978. The Louisiana cases were all caused by eating contaminated crabs from a coastal Louisiana marsh. Cholera is unlikely to become an important cause of morbidity in the United States because most communities have reasonably modern sewage disposal and safe, chlorinated water supplies. However, conditions in many areas of Latin America favor the transmission of cholera, and rapid air travel makes the eventual introduction of the disease into susceptible environments in the Western Hemisphere likely.

Once *V. cholerae* 01 has been introduced, its spread and the formidable loss of life that formerly accompanied outbreaks can be prevented. The necessary measures consist of maintaining surveillance, conducting epidemiologic investigations to determine the vehicle(s) of transmission, providing sanitary water supplies and waste disposal, and administering modern treatment to individual patients.

Figure 2. Number of reported cholera cases and number of counties reporting, 1951-1978*



*Data from WHO Weekly Epidemiological Record.

Cholera need no longer be considered a dread disease. As mentioned above, persons with severe cases respond well to intravenous fluid and electrolyte replacement therapy. Antibiotics shorten the duration of diarrhea and *Vibrio* excretion. The case-fatality ratio for patients who must be hospitalized and are given proper treatment should not exceed 1%.

Indications for Vaccination

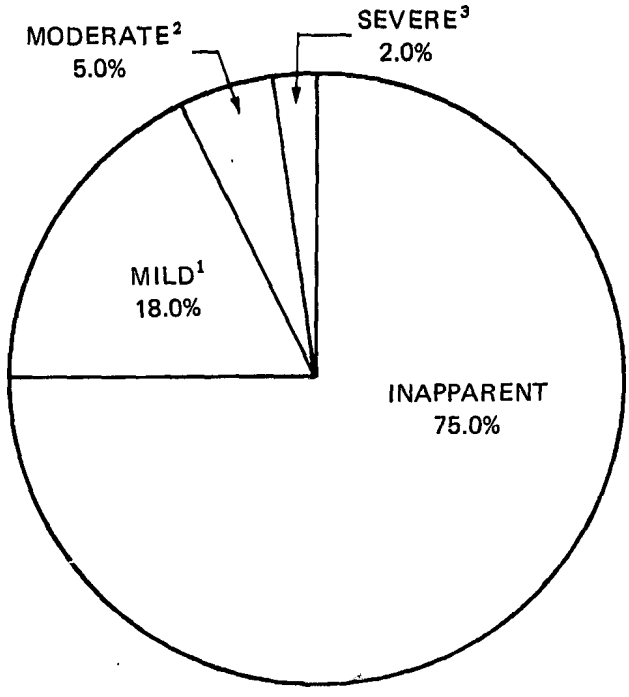
There is no scientific basis for using cholera vaccine in managing imported cases or in combatting outbreaks. Currently available cholera vaccines provide protection for only about 50% of vaccinees and then for only a few months, and they do not prevent transmission of the organism.

Late in 1970, the Surgeon General of the Public Health Service lifted the requirement for vaccination of persons entering the United States from cholera-infected areas, stating:

> There is clear evidence that cholera vaccine is of little use in preventing the spread of cholera across borders. We have, today, excellent treatment for cholera. The only effective method of preventing the spread of the disease is improvement of environmental sanitation. Therefore, in weighing costs and benefits, the United States has decided there is no reason for our Government to require cholera vaccination as a condition of entry to the U.S. for travelers coming from an infected area.

A similar position has been adopted by the World Health Organization. Nevertheless, some countries still require cholera vaccination for travelers who have been in cholera-infected areas. Accordingly, visitors to such countries should be vaccinated to avoid having their travel restricted.

Figure 3. Spectrum of El Tor cholera



[1]Cases detected in bacteriological surveys.
[2]Cases detected in outpatient clinics.
[3]Hospitalized patients with cholera gravis.

Diphtheria

Diphtheria was described as a specific clinical entity in 1826 by Bretonneau, who recognized it as an infectious disorder, but descriptions of illnesses compatible with diphtheria date back as far as the 6th century A.D. It was not until 1883 that Klebs first described the morphology of the diphtheria bacillus (*Corynebacterium diphtheriae*) as seen in smears from the throats of patients with the disease. A year later, Loeffler established that the bacillus caused the disease. Loeffler also postulated the role of a diffusible exotoxin in causing tissue damage in areas remote from the pharynx, and in 1888, Roux and Yersin characterized diphtheria toxin. In 1923, Ramon showed that formalin-treated toxin (now called toxoid) was effective in conveying active immunity. Diphtheria toxoid began being widely used in the United States about 1940 and has been routinely given to children and, to a lesser extent, to adults since that time.

It is now known that diphtheria toxin contributes to the severity of the pharyngeal involvement with diphtheria and is responsible for cardiac and neurologic complications. Nontoxigenic *C. diphtheriae* strains usually cause only mild pharyngitis. Three biotypes of *C. diphtheriae* are recognized: mitis, gravis, and intermedius. However, although biotyping is often useful in epidemiologic studies, the clinical severity of disease caused by the 3 biotypes does not differ markedly.

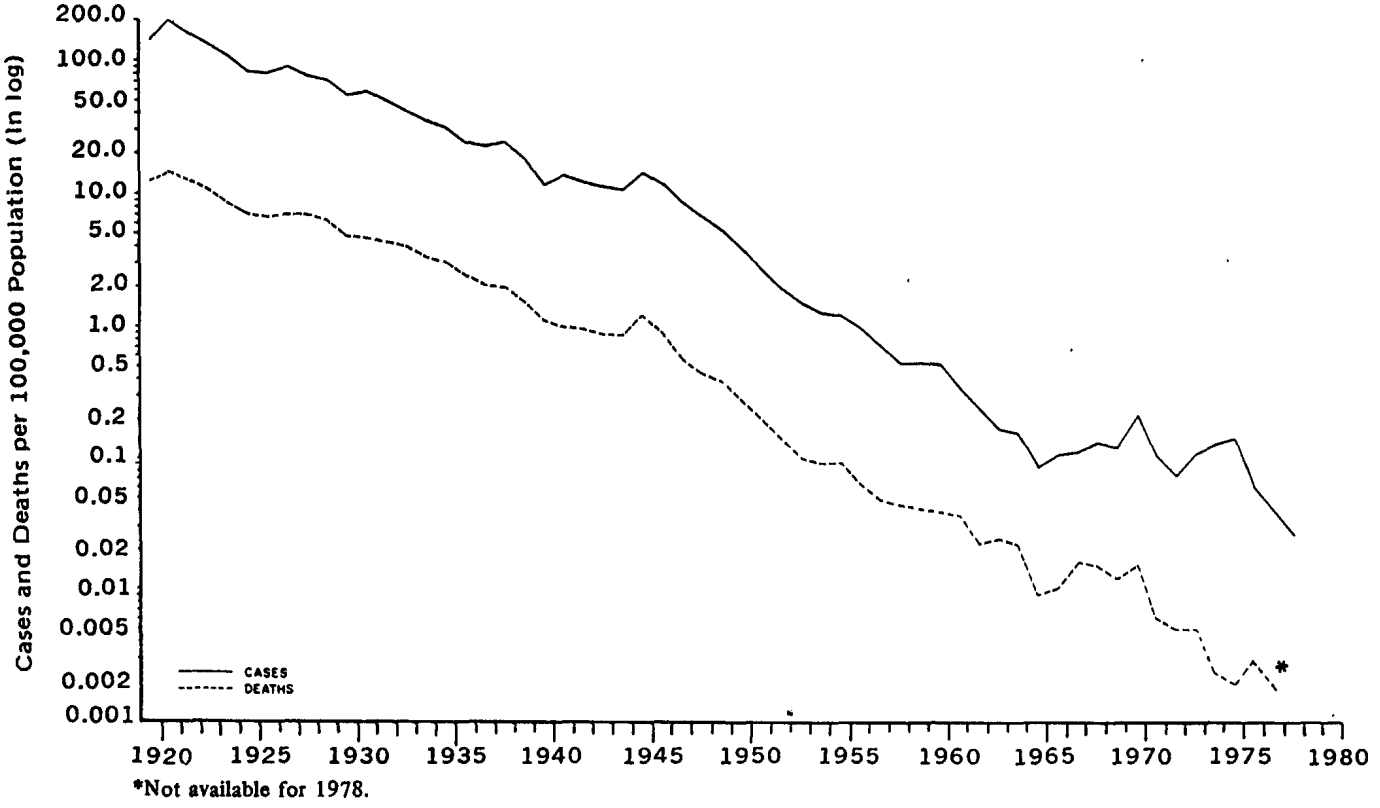
Asymptomatic carriage of *C. diphtheriae* in the nose and throat is far more common than clinical diphtheria. For this reason, carriers appear to be more important than symptomatic persons in the spread of the infection. Skin infection in the form of impetiginous or other types of lesions has been shown to be common in some parts of the United States, and skin carriers appear to spread the organism as effectively as throat carriers.

Recent Trends

Over the 50 years before 1965, there was a progressive 2,000-fold decrease in the incidence of diphtheria in the United States. From 1965 through 1975, a relatively steady 200+ cases were reported each year. After 1975, the incidence declined again, with 76 cases being reported in 1978. From the 1920s into the 1970s, the case-fatality ratio remained constant at about 10%; it has recently decreased to about 5% (Figure 1).

In recent years, diphtheria has become a focal disease; that is, most cases have occurred in a few areas that rather consistently report cases. The number of states reporting cases progressively fell from 43 in 1960 to 9 in 1978. Epidemics in focal areas have contributed a large proportion of cases. For instance, 54% of the cases in 1970 were reported from Texas, where an epidemic was occurring in San Antonio, and 84% of the cases in 1978 were reported

Figure 1. Diphtheria—reported case and death rates by year, United States, 1920-1978

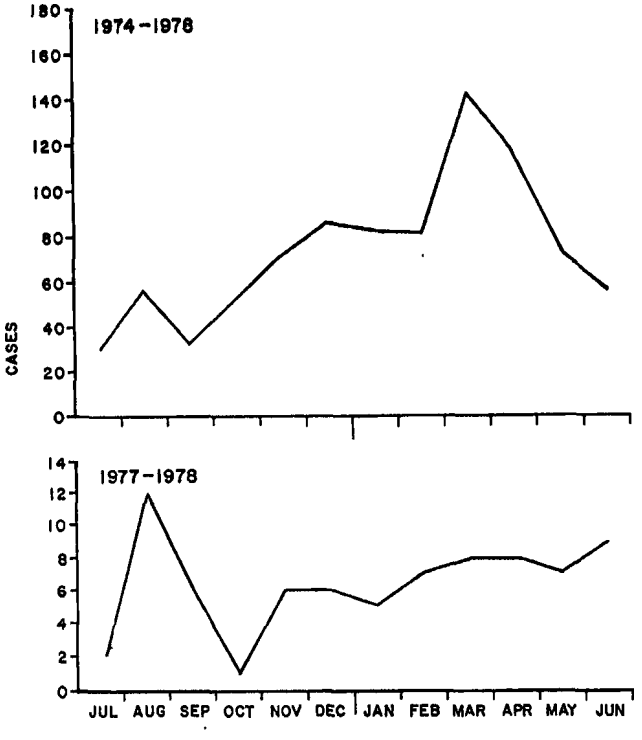


*Not available for 1978.

from Washington, where an epidemic was occurring in Seattle. If cases from those 2 states are excluded, the incidence of diphtheria for the other 48 states has gradually decreased since 1965.

The incidence of diphtheria in the United States has characteristically been higher in the autumn and winter. In the last few years, however, cases have been more evenly distributed throughout the year. This change has occurred primarily because the epidemic in Washington has contributed a large proportion of cases, and these cases have been distributed throughout the year (Figure 2).

Figure 2. Diphtheria cases by month, United States, 1974-1978 and 1977-1978



Although diphtheria affects persons of all ages, it has traditionally been a disease of preschool and school-age children. In recent years, more cases of diphtheria have been reported for older people, a shift primarily reflecting the fact that the epidemic in Washington was among adults. Youngsters and the elderly are most likely to have severe disease, as reflected by case-fatality ratios (Table 1).

American Indians are at significantly higher risk than the general population of acquiring diphtheria. The reported annual incidence in the United States for American Indians from 1971 through 1975, for instance, was 1,209 cases per 100,000 compared with 5.9 for whites, 6.6 for blacks, and <1 for Asian Americans.

Prophylaxis

Vaccination with diphtheria toxoid is by far the safest and most effective method of preventing diphtheria. Children should receive a primary series of 3 doses before they are a year old, a booster at 18 months, and another booster when they enter school. After that, every 10 years they should receive a booster containing an adult dose, which is available combined with tetanus toxoid (Td). It has been recommended that previously unvaccinated adults have 2 adult doses, spaced 1 month apart, and a booster 1 year later, although the efficacy of this schedule is unporven. Nonetheless, it is important that diphtheria vaccines be given routinely according to the recommended schedule, because antibodies form over a period of months, and active immunization is not effective in stopping an outbreak quickly.

Adults given the pediatric dose of diphtheria toxoid have frequently had side effects—sometimes severe ones. Relatively few adults given the adult dose have had side effects, and those reported have been milder. The adult dose can be given without Schick testing to adults who have no history of allergic reactions to diphtheria toxoid.

From the 1978 immunization survey, it was estimated that an average of 70.6% of the U.S. population between 0 and 14 years of age had received 3 or more doses of diphtheria-tetanus-pertussis (DTP) vaccine, although the figure was only 52.0% for poor, inner-city dwellers. Thus, many U.S. residents are potentially susceptible to diphtheria, especially those in certain subgroups. Epidemics in recent years have tended to affect groups comprised of relatively low percentages of vaccinated persons.

Table 1. Diphtheria cases and case-fatality ratios by site of infection and age group, United States, 1971-1975

	Cases			Deaths			Case-Fatality Ratio		
Age Group (yr.)	Cutaneous	Non-cutaneous	Total	Cutaneous	Non-cutaneous	Total	Cutaneous	Non-cutaneous	Total
<1	0	5	5	0	0	0	0	0	0
1 – 4	4	94	98	0	10	10	0	10.6	10.2
5 – 9	5	179	184	0	10	10	0	5.6	5.4
10 – 14	4	134	138	0	2	2	0	1.5	1.4
15 – 19	3	66	69	0	1	1	0	1.5	1.4
20 – 29	55	89	144	0	2	2	0	2.2	1.4
30 – 39	105	68	173	0	3	3	0	4.4	1.7
40 – 49	100	50	150	1	4	5	1.0	8.0	3.3
>50	152	75	227	2	15	17	1.3	20.0	7.5
Unknown	3	18	21	0	0	0	0	0	0
TOTAL	431	778	1,209	3	47	50	0.6	6.0	4.1

When an outbreak occurs, immediate preventive measures should combine attempts to vaccinate all susceptible persons and to administer antibiotic treatment to or isolate household and other close contacts at high risk of acquiring the disease. However, because active immunity induced by diphtheria toxoid does not prevent asymptomatic carriage of *C. diphtheriae* or the spread of the organism to others, nasal or pharyngeal specimens from these contacts should be cultured and the contacts treated with penicillin or erythromycin until the laboratory report is available. Alternatively, the contacts can be quarantined until culture results are known. Persons with positive cultures should have second cultures done after having a full course of antibiotics. Those who remain positive should be re-treated until their cultures are negative.

All close contacts should remain under careful daily surveillance in order to detect secondary cases. If susceptible persons cannot be placed under adequate surveillance, they should each receive 20,000 units of diphtheria antitoxin in addition to the appropriate vaccine series and antibiotic treatment.

Hepatitis

Hepatitis dates back at least 2,000 years to the time of Hippocrates. Major epidemics are known to have swept through Europe over 200 years ago and through the United States 100 years ago; yet only in the last 40 years have significant advances been made in understanding the cause, transmission, and control of hepatitis. Progress has been hampered in the past because of the inability to grow the agents in vitro.

In the late 1930s, on the basis of epidemiologic findings, hepatitis was recognized to be of 2 types—infectious hepatitis (what we now call hepatitis A), of short incubation period and primarily of oral-fecal transmission, and serum hepatitis (now called hepatitis B), of long incubation period and primarily of parenteral transmission (Table 1). Differentiating these 2 types clinically is quite difficult, if not impossible.

Table 1. Epidemiologic distinctions of Hepatitis A and B

	Hepatitis A	Hepatitis B
Formerly Called	"Infectious"	"Serum"
Transmission	Fecal-oral	Percutaneous or close personal contact
Incubation Period (days)	Range 15-50 (avg. 25-30)	Range 40-180 (commonly 60-90)
Age Distribution	All ages; primarily young adults	All ages; primarily young adults; infrequently, children
Seasonal Variation in Incidence	Historically more prevalent in spring-fall	None
Animal Model for Infectivity	Marmoset	Chimpanzee
HBsAg	Absent	Present
Anti-HAV IgM	Present	Absent

National reporting of hepatitis began in 1952, and since 1966 hepatitis A and B have been reported separately. Since 1966, the proportion of recorded hepatitis B cases has steadily risen to 28% (Figure 1); however, on the basis of data from epidemiologic investigations, the true proportion of hepatitis B cases is thought to be closer to 50%. As for total incidence, 53,292 cases of hepatitis were reported to the Center for Disease Control (CDC) in 1978, but since only 10%-20% of hepatitis cases are thought to be reported, the true incidence is probably much higher.

The epidemiology of hepatitis A has been better delineated since the discovery of the causative virus. Serologic surveys indicate that nearly 40% of Americans have been infected with hepatitis A virus by the time they are adults. Virus is excreted in stool and spread by the fecal-oral route.

Much of the current work on hepatitis B immunization would not have been possible without the discovery of the associated antigen in the mid-1960s independently by Blumberg and Prince. Formerly called the Australia antigen, serum hepatitis antigen, hepatitis-associated antigen, and hepatitis B antigen, it is now known as the hepatitis B surface antigen (HBsAg). With this marker, the epidemiology of hepatitis B has been elucidated to a large degree. Furthermore, using sensitive tests for this antigen, workers have uncovered a carrier state for hepatitis B. They estimate that 0.3% of the U.S. population carry this antigen asymptomatically.

In the mid-1970s, a third type of hepatitis (now called non-A, non-B hepatitis), with a slightly shorter incubation period than hepatitis B, was recognized. The disease has been associated with transfusions of blood and blood products that have been screened and are known to be free of HBsAg. It appears to be caused by at least 2 distinct viral agents, but we know little about this new type of hepatitis. The efficacy of standard immune serum globulin (ISG) in protecting against this type of hepatitis has yet to be fully established.

ISG for Hepatitis A

Techniques for separating plasma protein components developed in the early 1940s led to the use of the fraction containing antibodies, i.e., ISG, as prophylaxis for hepatitis A. In the United States, plasma pooled from thousands of donors is fractionated by the cold ethanol technique of Cohn to yield a solution that is 16.5% protein, 90% of which is immunoglobulin. Protection against hepatitis A is provided by the antibody to hepatitis A virus contained in ISG. The protection comes from the large IgG fraction, which has a 20-25 day in vivo half-life. In studies done in the period 1968-1971 in England, Israel, and the United States, ISG was shown to be more than 80% effective in suppressing overt hepatitis A for treated vs. untreated populations.

ISG appears to act in 2 ways: it can actually prevent infection, or it can substantially reduce the severity of clinical hepatitis A. Immunity after such infection (passive-active immunity) appears to be long-lasting.

ISG is valuable in protecting not only persons with definite hepatitis exposure but also those with anticipated repeated exposure. A low dose of ISG (0.02 ml/kg body weight) provides protection after any single exposure that carries a high risk of hepatitis A infection, e.g., contact with

an ill household member, exposure to a common-source vehicle, or an accidental puncture with a needle contaminated with blood from a person with hepatitis A. Because most hepatitis A virus is excreted 1-2 weeks before the onset of jaundice, ISG should be given to household contacts of the patient as soon as possible. ISG is efficacious only if given within the first 2 weeks after infection is acquired.

For those who anticipate repeated exposure to hepatitis A—employees of institutions where the disease is endemic, travelers to or residents of developing or tropical areas of the world, and handlers of newly imported nonhuman primates—more long-term protection may be advisable, and therefore a larger dose of ISG (0.05 ml/kg) is Larger doses provide long-lasting, not necessarily greater, protection. When continuous protection is desired, the above dose should be repeated every 4-6 months.

Immunoglobulins for Hepatitis B

Two types of immunoglobulins are available for preexposure or postexposure prophylaxis for hepatitis B. One is regular ISG, of which all lots manufactured after 1972 have lower titers (64 by passive hemagglutination [PHA]) of antibody directed against the surface antigens of the virus (anti-HBs). The other is hepatitis B immune globulin (HBIG), which has PHA titers of at least 100,000. Both are moderately effective treatment preexposure and postexposure. HBIG is currently recommended for persons who have been stuck with needles containing known HBsAg-positive blood or for infants born to HBsAg-positive mothers, although ISG can be substituted in either situation. HBIG may be beneficial in many instances, e.g., for prophylaxis against vertical hepatitis B transmission and the HBsAg carrier state. Clinical trials of HBIG are currently being held to better delineate its protective value and allow the formulation of specific guidelines for its use.

Over the last several years, standard ISG has had steadily rising antibody titers to hepatitis B. Although results of efficacy tests are not clear-cut, evidence suggests that ISG does play a role in preventing hepatitis B under certain circumstances. These circumstances include exposure to a small inoculum of hepatitis B-contaminated blood or other material by ingestion, percutaneous puncture, or splattering onto mucous membranes. In such instances, standard ISG manufactured since 1972 can be given intramuscularly to an adult in a dose of 0.05-0.07 ml/kg body weight. Exposure to a large inoculum, e.g., transfusion of HBsAg-positive blood, is not an appropriate situation in which to use ISG because its efficacy in such a situation has not been demonstrated. Since evidence favoring the use of ISG for family contacts of patients with hepatitis B is equivocal, this practice is not routinely recommended.

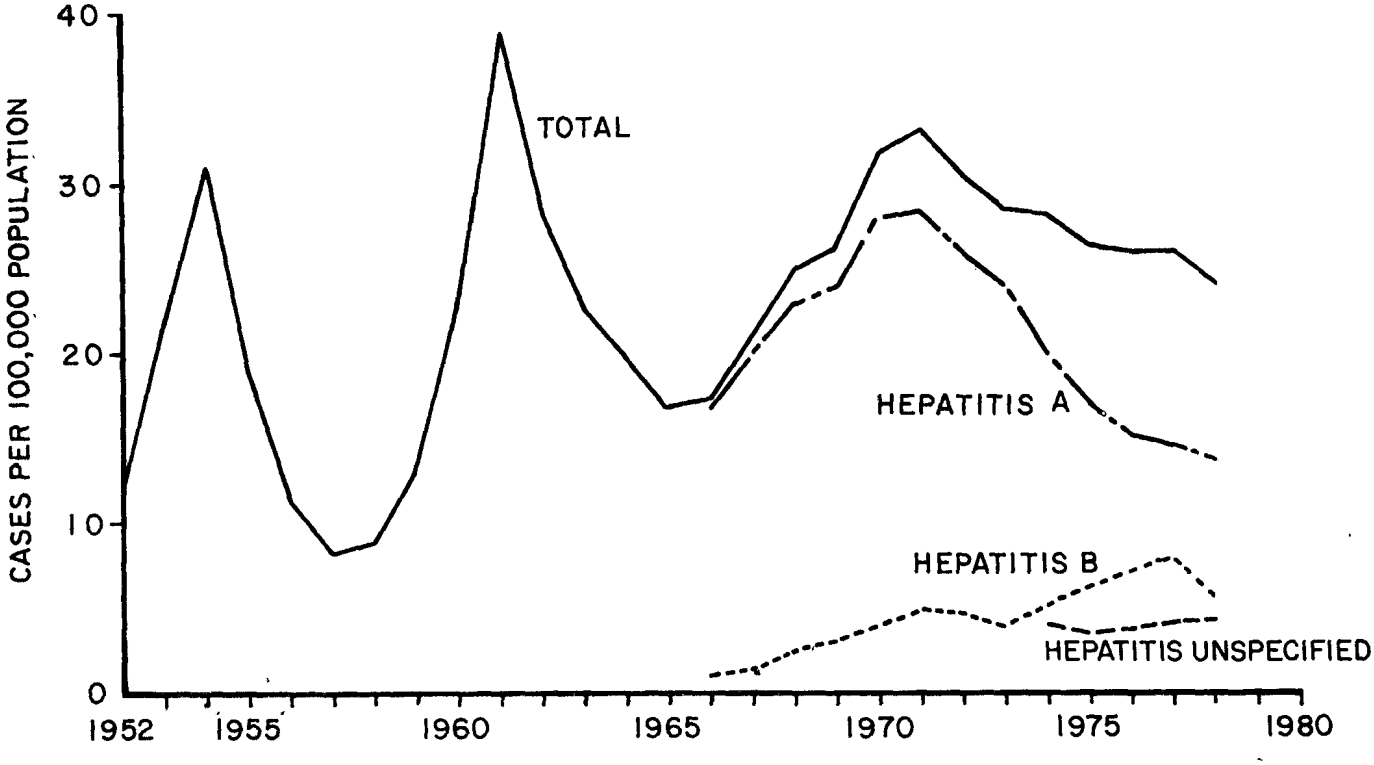
SELECTED BIBLIOGRAPHY

Francis DP, Maynard JE. The transmission and outcome of hepatitis A, B, and non-A, non-B: a review. Epidemiol Reviews 1979;1:17-31.

Maynard JE. Passive immunization against hepatitis B: a review of recent studies and comment on current aspects of control. Am J Epidemiol 1978;107:77-86.

Recommendation of the Public Health Service Advisory Committee on Immunization Practices: Immune globulins for protection against viral hepatitis. December 1977.

Figure 1. Hepatitis—reported case rates by year, United States, 1952-1978



Influenza

The 3 major types of influenza virus are called A, B, and C. Types A and B undergo antigenic variation and can cause epidemics. Over a period of time, the prevalent strains gradually become less like the strain that caused the preceding epidemic and stimulated the production of protective antibodies. Variations in the type A viruses have been observed more frequently and are normally more marked than variations in the type B viruses.

Type A influenza viruses have been further classified into subtypes that can be differentiated by the surface protein antigens hemagglutinin and neuraminidase. Influenza A virus strains are classified by the type of influenza virus, the site and the year of isolation, and the type of hemagglutinin (H) and neuraminidase (N) present, e.g., the Russian influenza virus, first isolated in the Soviet Union in late 1977, is called A/USSR/77 (H1N1).

The periodic major or minor structural changes of the hemagglutinin and neuraminidase surface antigens of influenza viruses influence epidemiologic patterns of the disease and the composition of influenza vaccine. Major changes, or shifts, that have occurred periodically have often been followed by worldwide outbreaks (pandemics) of influenza, because most of the population is not immune to the altered strain of virus. Pandemics occurred in 1918, in 1957 ("Asian flu," H2N2), and in 1968 ("Hong Kong flu," H3N2). Minor changes, or drifts, in the surface antigens occur continually and are often associated with influenza outbreaks or epidemics that may be limited to continents, regions, or even communities.

Influenza viruses cause fever, malaise, coryza, cough, myalgia, and headache. Most adults have few gastrointestinal symptoms. There is no clinical basis for differentiating infections caused by the different influenza virus types, and influenza-like illness may be caused by several other families of viruses, including the adenoviruses, Coxsackie viruses, and echoviruses. Thus individual cases of influenza can only be diagnosed accurately if the virus is isolated from nasal or pharyngeal swabs or if a 4-fold or greater rise in antibody titer is measured with acute- and convalescent-phase serum specimens. However, it is usually 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 an unusually large number of cases of febrile respiratory illness seen by clinicians. 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 to affect school-age children.

Although influenza is usually a self-limited upper respiratory illness lasting only 2-4 days, it can disrupt community functions by attacking many persons in a very short period. Furthermore, some persons may have complications such as pneumonia and even death (Figure 1), especially older persons or those who have chronic underlying illness such as cardiovascular or respiratory disease. Any excess mortality accompanying an epidemic of influenza A is often used as a measurement of the severity and extent of that epidemic. In addition, Reye syndrome is sometimes associated with influenza, as was noted first in influenza B outbreaks in 1973-74 and more recently in outbreaks of influenza A in 1979.

Recent Trends

In 1976, an influenza virus (A/New Jersey/76) isolated from a young military recruit resembled the influenza strain suspected of causing the great 1918 pandemic. The possibility of a recurrence of such a devastating epidemic coupled with the opportunity to prevent its occurrence through vaccination led to the initiation of the National Influenza Immunization Program. In this federal program to vaccinate all Americans against "swine flu," over 40 million doses of vaccine were given; however, the epidemic did not materialize, and only sporadic cases of influenza A/New Jersey were reported.

A new pandemic strain, A/USSR/77 (H1N1), similar to H1N1 strains isolated in the late 1940s, appeared in the United States in January 1978. During that season, 3 distinct influenza A strains—A/Victoria (H3N2), A/Texas (H3N2), and A/USSR (H1N1)—circulated at the same time. This was the first recorded instance when a pandemic strain did not rapidly supplant and replace antecedent strains.

No strains of the subtype H3N2 were isolated in the United States in the 1978-79 influenza season, although other countries reported isolating both H1N1 and H3N2 strains. Sporadic outbreaks of type B influenza also occurred in 1979. The continuing circulation of these 3 strains makes the already difficult task of ascertaining which influenza strain is prevalent in an area even more challenging.

Vaccination and Control Efforts

Efforts to prevent influenza in the United States have been aimed at protecting those at greatest risk of serious illness or death. Usually in influenza epidemics, most of the people who die of influenza-related causes are children, chronically ill adults, and older persons, especially those over age 65. It is therefore recommended that individuals who are considered to be at increased risk of complications be vaccinated each year. Influenza vaccination may also be considered for persons who provide essential community services, such as policemen, or who may be at increased risk of exposure, such as medical care personnel.

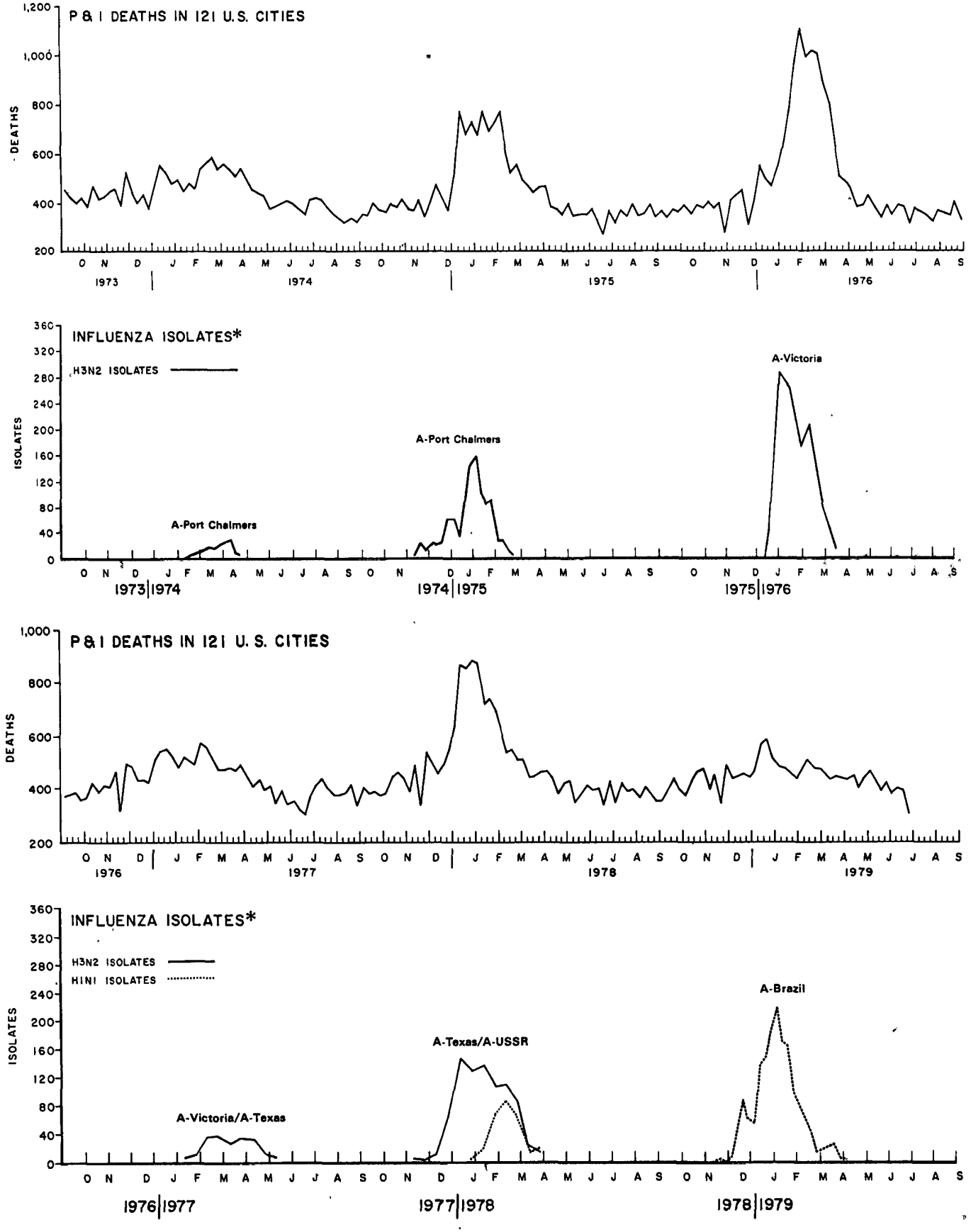
Current inactivated influenza virus vaccines stimulate the production of antibodies in 70%-90% of recipients. However, the effectiveness of influenza vaccine ("vaccine efficacy") is properly measured by the actual degree of protection provided by the vaccine to the recipient who is exposed to the influenza virus. This has been difficult to determine because of unpredictable changes in the antigenicity of influenza virus strains, the similarity of influenza to illness caused by other viruses, and markedly varying attack rates during outbreaks. Because of these difficulties, reported influenza vaccine efficacy has ranged from 0 to 96%. Recent studies have shown vaccine efficacy to be as high as 80% against homologous strains of influenza A.

The level of antibody production stimulated by influenza vaccine declines significantly after 1 year. Also, as has been mentioned, influenza viruses undergo frequent changes in antigenic characteristics. Thus, influenza vaccine is usually reformulated each year, and it is recommended that individuals at high risk be vaccinated against influenza each year.

Recent influenza virus vaccines have been associated with few side effects. During the National Influenza Immunization Program of 1976, however, swine influenza vaccination was associated with the Guillain-Barré syndrome (GBS). GBS is characterized by ascending paralysis that is usually self-limited and reversible, although approximately 5% of cases are fatal. In the 10-week period after the "swine flu" vaccination program began, the incidence of GBS was 5-6 times higher for vaccinees (10 cases per million persons vaccinated) than for persons not given the vaccine. Surveillance of GBS during the 1978-79 influenza season showed no significant association between having GBS and having received the influenza vaccines in use at that time. Even though the risk associated with swine influenza vaccine was extremely low, that risk might also be present with other influenza vaccines, and recipients of influenza vaccine should be aware of it. This possible risk should be balanced against the risk of having influenza and its complications.

Amantadine hydrochloride has been licensed for prophylaxis and treatment for respiratory tract infections caused by all current influenza A viruses. Amantadine can be considered as chemoprophylaxis for unvaccinated, high-risk individuals who are exposed to influenza or as treatment of high-risk individuals with influenza. Prophylaxis must be continued as long as the person is exposed to influenza. As an alternative, amantadine can be started the the time of vaccination and continued for at least 10 days (if the patient has ever had an antigenically related vaccine) to 4-6 weeks (if the patient has never had an antigenically related vaccine) to allow time for serum antibodies to develop.

Figure 1. Pneumonia-influenza (P&I) mortality and laboratory surveillance,* United States



*Of predominant influenza A virus collected from national surveillance laboratories.

Measles (Rubeola)

The first recorded description of measles was by the Persian physician Rhazes (A.D. 865-925). He thought measles was severe, i.e., "more to be dreaded than smallpox"; however, he did not believe that it was contagious and thought it was a necessary part of growing up. The epidemiology of measles was delineated by Panum in 1846 after an investigation of over 5,000 cases in the Faroe Islands, where there had been no known cases of measles for 65 years. He concluded that measles was transmitted solely from person to person. He noted the high degree of infectivity, the 14-day incubation period, the respiratory route of spread, the higher mortality rates for infants, and the life-long immunity produced by a single attack. In 1911, Goldberger and Anderson documented that measles was caused by a virus; they transmitted the disease to monkeys by giving them the filtered respiratory tract secretions of humans with measles. In 1954, Enders and Peebles isolated the measles virus in cell culture. Subsequent attenuation of the virus made it possible to develop vaccines against the disease, and measles vaccine was first licensed for use in the United States in 1963.

Clinical Characteristics

Measles begins with fever (frequently temperatures of ≥101 F), which is soon followed by cough, coryza, and conjunctivitis. After 3-4 days of prodromal symptoms, the rash appears. The rash is a maculopapular eruption, frequently beginning on the face and neck and moving downward. The rash lasts for at least 4 days, although it may begin to fade earlier in regions where it first appeared. Koplik's spots appear about 2 days before the onset of rash and disappear about 2 days after the onset of rash. They are small bluish-white spots on a reddish base and are found on the mucous membranes of the mouth, frequently beginning at the level of the first molar. Koplik's spots are considered pathognomonic for measles, although they may be confused with other oral lesions. Also, persons with measles frequently are not seen by a doctor until after the Koplik's spots have disappeared.

Measles is transmitted in respiratory tract droplets. Direct contact with the droplets is generally required. The patient with measles can transmit the infection from the fifth day of the incubation period through the first few days after rash appears, although the infection is most communicable during the respiratory prodromal phase. The incubation period is 12-14 days, although it may be as long as 20 days with modified measles, which occurs in the presence of passively acquired antibody (maternal antibody or gamma globulin).

Measles is often a severe disease, frequently complicated by middle-ear infection or bronchopneumonia. Encephalitis accompanies approximately 1 of every 1,000 cases; survivors often have permanent brain damage or mental retardation. About 1 of every 1,000 patients reported to have measles dies, predominantly from respiratory and neurologic causes. The risk of encephalitis and death is known to be greater for infants and is suspected to be greater for adults than for children and adolescents.

Another form of the disease, atypical measles, was first reported in 1965. The rash of atypical measles begins on the extremities, usually around the wrists and ankles; it may be vesicular, petechial, or maculopapular, and may involve the palms and soles. Pulmonary involvement, with infiltrates and pulmonary function abnormalities, is common. Atypical measles affects persons who have received killed measles vaccine, either alone or in combination with live measles vaccine; a few cases have been reported to affect persons who had been given only live measles vaccine. Because of the risk of atypical measles and because the vaccine did not provide lasting immunity, production of killed measles vaccine was discontinued in 1967.

Laboratory Detection

Laboratory tests commonly used to detect measles virus include the complement fixation (CF) test and the hemagglutination inhibition (HI) test (Figure 1). A test for measles-specific IgM, a fluorescent antibody test, a neutralization test, and procedures to isolate the virus cannot generally be done except in specialty laboratories. The CF and HI tests require acute- and convalescent-phase blood specimens and consequently cannot be used for rapid diagnosis. However, serologic studies may be of great value in later investigations of patients with index cases or their contacts. This is especially true in the evaluation of sporadic cases of measles, when a clinical diagnosis is difficult to obtain.

Case Investigation

Early reporting of measles cases and rapid case investigation, identification, and vaccination of susceptible contacts are necessary for effective control of measles. Because laboratory methods to diagnose measles rapidly are not readily available and there is no obvious pathognomonic feature of the disease, standard clinical criteria should be used to determine the initial case response. An empirically useful case definition of measles in temperature of ≥101 F, rash of at least 3 days' duration, and cough, conjunctivitis, or coryza. Patients with these symptoms should be considered to have measles unless evidence proves otherwise.

Epidemiologic Trends

Mortality from measles and the death-to-case ratio are highest for children under 1 year of age. Pneumonia is the

most frequent cause of death for members of this age group (Figure 2). Although relatively few persons over 20 years old die as a result of having measles, the death-to-case ratio rises with age. This pattern may be related to a rising rate of measles encephalitis with age.

Before measles vaccine was available, more than 400,000 cases of measles were reported in the United States each year. Seasonal peaks were noted in the winter and spring, with major epidemics every 2-4 years probably resulting from the rising proportion of susceptible children in the population (Figure 3). After the measles vaccine began to be widely used, the reported incidence of measles fell by 90%. Relative increases in the yearly incidence of measles occurred in 1971 and 1977 (Figure 4). The increase in 1971 may have been related to the expiration of federal project grant assistance for measles in 1968-69, and that in 1977 may have been related to a gradual increase in the number of susceptible children. Since 1977, the reported number of cases of measles per year has decreased. In 1978, for example, 26,781 cases were reported, in contrast to the 57,345 cases reported in 1977 (a 53% decrease). The preliminary total for 1979 is 13,448 cases, which is a 49% decrease from the number in 1978 (Figure 5). For 41 of the 52 weeks of 1979, the weekly totals were the lowest ever reported.

As the incidence of measles has declined, the infection has also become more focally distributed. The measles cases reported in 1977 were spread unevenly across the nation (Figure 6). Eight states, the District of Columbia, and 1 territory reported fewer than 10 cases of measles for the entire year. At various times in 1978, 40 states, 3 territories, and the District of Columbia reported no cases of measles for 4 or more consecutive weeks.

Since measles vaccine has been widely used, the age distribution of patients has also changed markedly. In the pre-vaccine era, most persons who had measles were preschool and young school-age children. The decline in the number of cases has been greatest for children 5-9 years old (93.8%), whereas the smallest decrease in incidence has been for children younger than 5 years (88.6%) and for

Figure 1. Schemata of immune response to acute measles infection and to measles vaccine

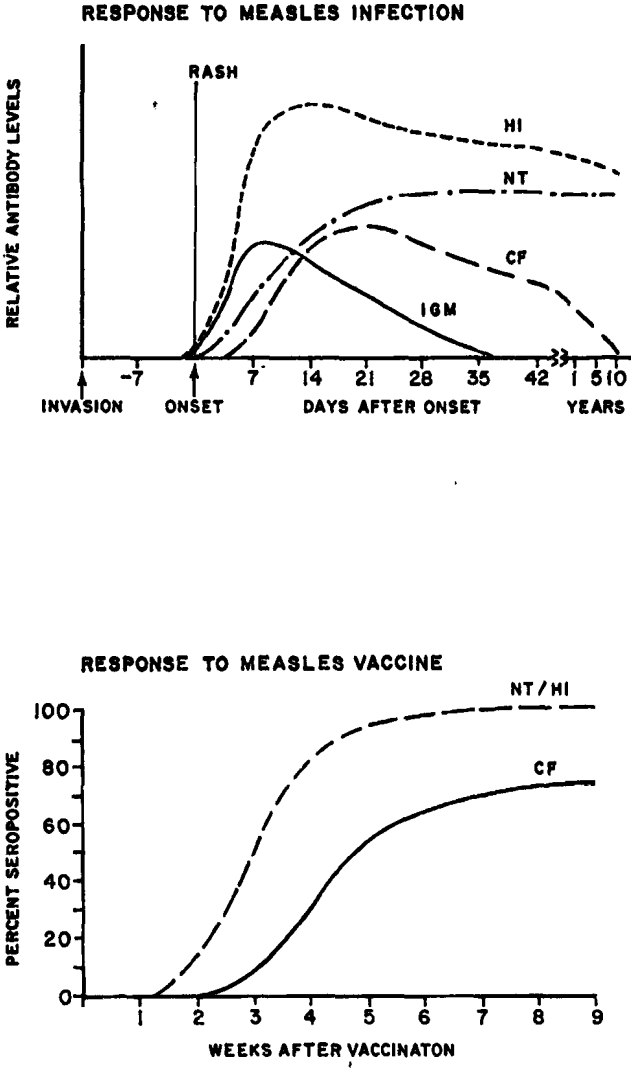


Figure 2. Measles death rates, reported cases, and death-to-case ratio by age group, United States, 1973-1975

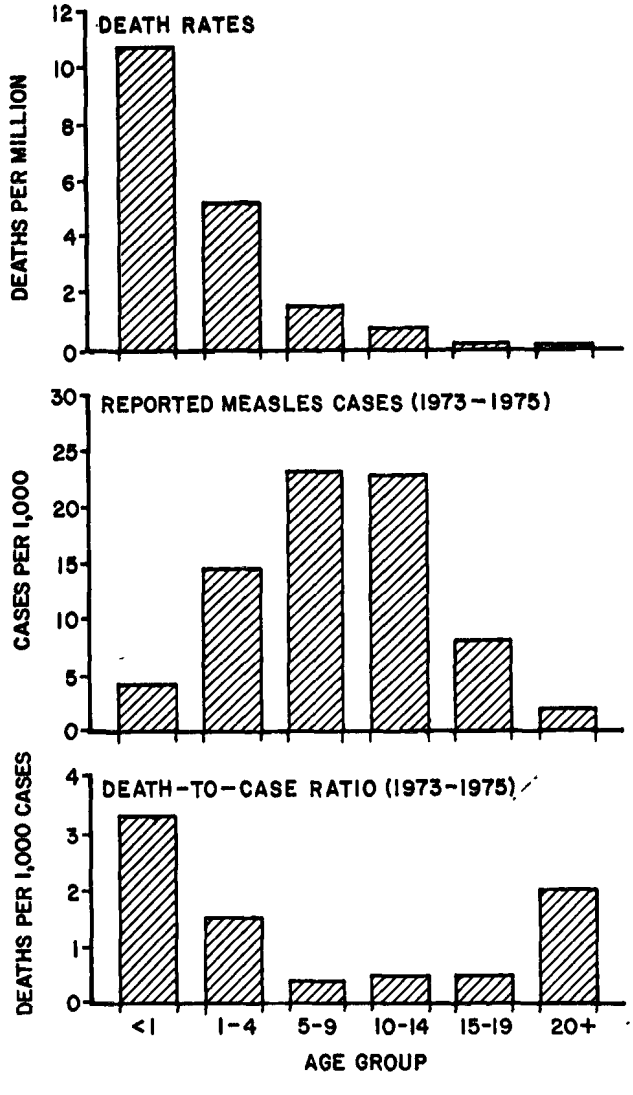


Figure 3. Reported cases of measles by four-week periods, United States, 1956-1978

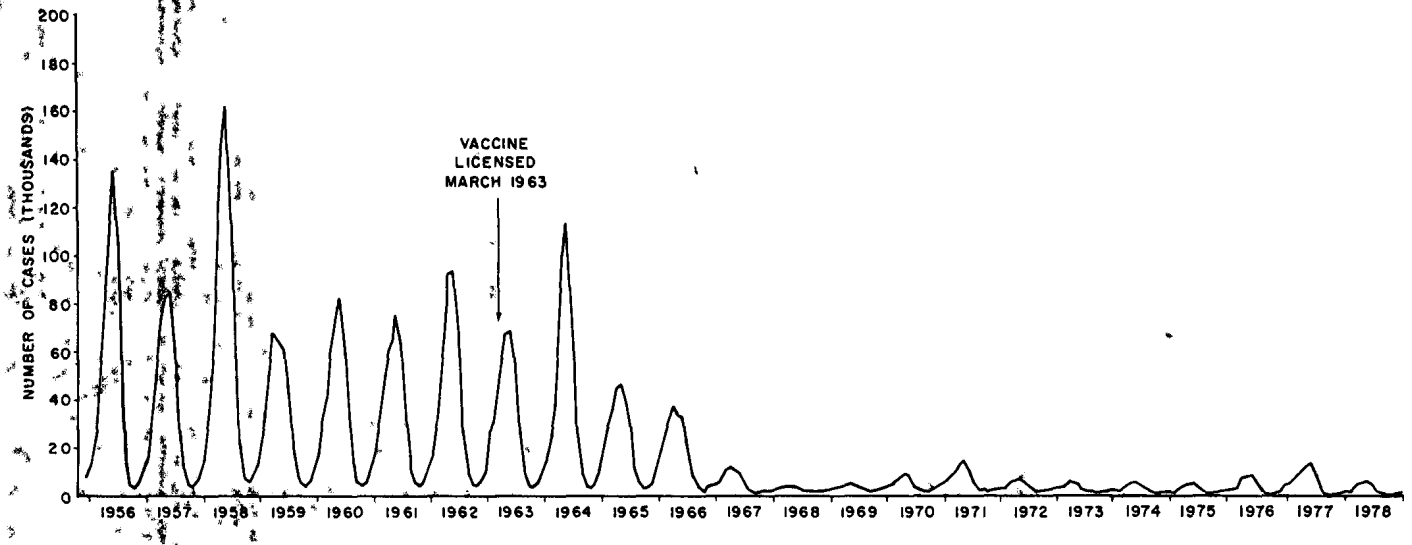
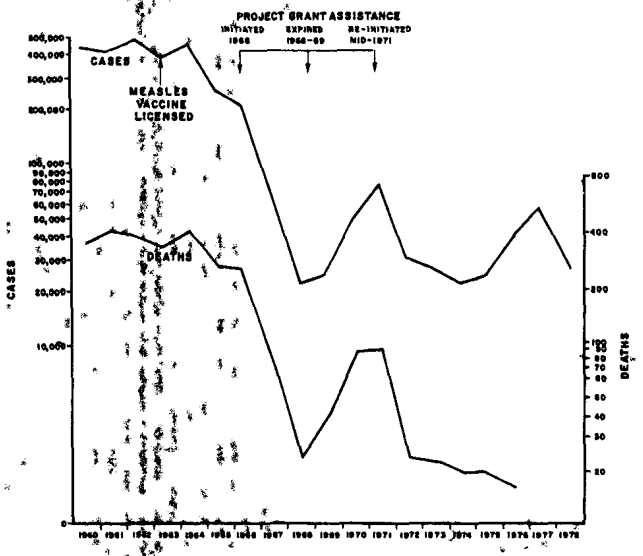


Figure 4. Reported measles cases and deaths, United States, 1960-1978



those 10-14 years old (76.4%). Currently, most of the persons who have measles and whose ages are known are children at least 10 years old (Table 1).

Measles Control Programs

Intensified measles control efforts in 1977 may have reduced the number of susceptible persons in the population and may explain some of the reduction in incidence in 1978; however, other factors contributed significantly to the sharp decline noted in both 1978 and 1979. Several states began enforcing immunization laws and did not allow children to enter school without adequate documentation of measles vaccination. Rigorous school record review and the requirement to vaccinate children without documented immunity have substantially lowered the number of children at risk.

In April 1977, The National Childhood Immunization Initiative was implemented in an attempt to ensure that 90% of all children less than 15 years old would be immune to measles, rubella, poliomyelitis, diphtheria, tetanus, and pertussis. Fifty-four percent more measles vaccine was given in public programs in 1977 than in 1976. This level was essentially maintained in 1978. Data indicate that 90% of the target population now have documented immunity to all of the listed diseases except rubella, although the percentages are lower in some parts of the country.

In October 1978, the Secretary of the Department of Health, Education, and Welfare announced that the United States would try to eliminate indigenous measles from the nation by October 1982. This goal is feasible because of the major progress made through the Immunization Initiative in lowering the incidence of measles in the United States. The availability of an effective vaccine, the absence of a nonhuman host, and the absence of a carrier state indicate that indigenous measles can in fact be eliminated from the United States.

In addition to ensuring that a high percentage of the population continue to have documented immunity, the 4 major thrusts of the measles eradication program are:

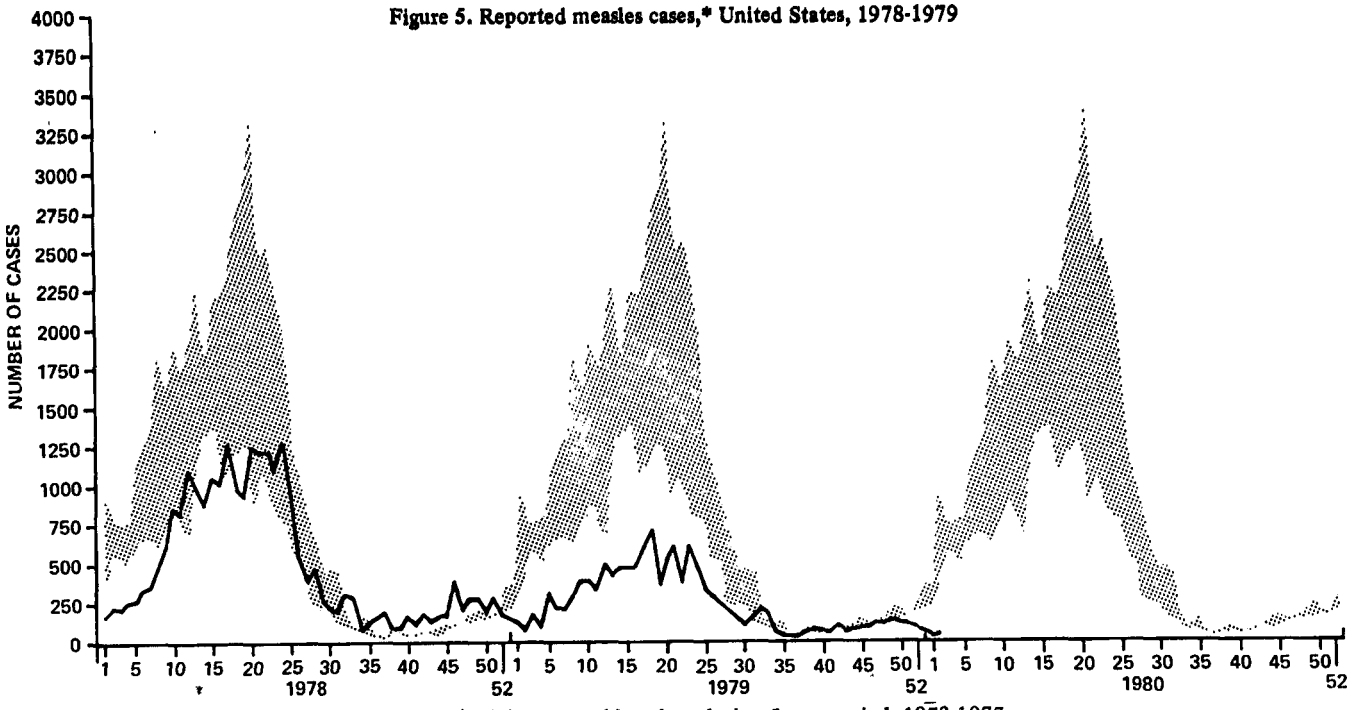
1. Increased emphasis on identifying and vaccinating susceptible adolescents and young adults, who now represent a large segment of the pool of susceptible persons.
2. Increased efforts to broaden school vaccination requirements to cover children in all grades (not just initial entrants) and rigorous enforcement of those requirements.
3. Stronger surveillance systems with the institution of active surveillance systems where they do not now exist. Active surveillance involves aggressive search for cases that would otherwise go unreported.

Table 1. Reported measles cases, percent distribution and incidence

Age Group, yr	1960-1964		1971-1975		1977	
	% of Total	Cases per 100,000	% of Total	Cases per 100,000	% of Total	Cases per 100,000
0-4	37.2	766	34.6	87	14.0	53
5-9	52.8	1,237	33.8	76	25.2	84
10-14	6.5	169	18.0	40	34.2	102
15+	3.4	179	13.6	4	26.4	64

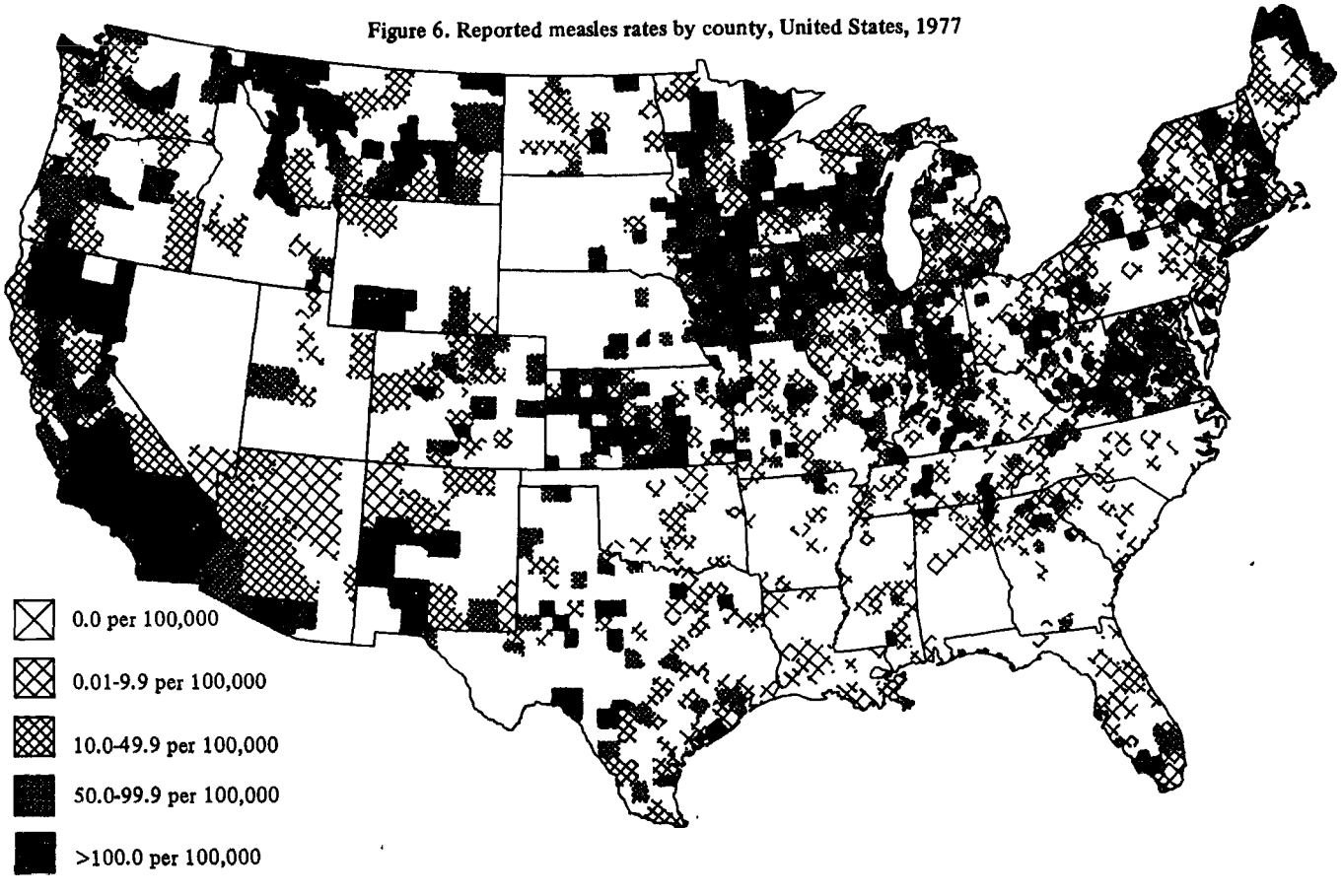
4. Improved efficiency and effectiveness of outbreak-control measures. Whether this goal is achieved will depend primarily on the efforts of local and state health departments and on the support they receive from organized medicine and all levels of government. Once this goal is achieved, it can be maintained only through vigilance and an ability to respond promptly to any imported cases of measles.

Figure 5. Reported measles cases,* United States, 1978-1979



*Shaded area represents maximum and minimum weekly values during 5-year period, 1973-1977.
Source: MMWR weekly reports.

Figure 6. Reported measles rates by county, United States, 1977



Meningococcal Disease

Epidemic "cerebrospinal meningitis" was first recognized as an entity in 1805 in Geneva by Vieusseux. In 1887, Weichselbaum described the causative organism, *Neisseria meningitidis*. In the 20th century in the United States, meningococcal disease occurred in epidemic proportions in each decade until the 1950s. Since then, it has become a sporadic disease with focal outbreaks, and the overall incidence has declined.

In 1909, Dopter found that *N. meningitidis* organisms were serologically classifiable on the basis of specific capsular polysaccharides. Serogroups that have most often been associated with invasive human disease include A, B, C, Y, and W-135. Although members of serogroup A are notorious for causing very large outbreaks, such as those in Brazil and Finland in 1974 and 1975, members of serogroups B and C are currently the major disease producers in the United States. Used primarily as an epidemiologic marker in the past, serogrouping of meningococci has taken on a vastly more important role in disease prevention since licensure of meningococcal polysaccharide vaccines in 1975.

Recent Trends

A yearly average of 1,752 reported cases of meningococcal disease occurred in the United States from 1974 through 1978, for a mean attack rate of 0.81 cases per 100,000 population per year (Figure 1). This incidence is substantially below that of the preceding decade, when the average number of cases per year was between 2,200 and 3,400, for a mean attack rate of more than 1.3 cases per 100,000 population per year.

Attack rates are highest for children <1 year old and next highest for children 1-4; they are substantially lower for persons at least 5 years old. Although organisms from all the most important serogroups in the United States may infect persons in any age group, serogroup B attack rates are significantly higher than C or Y rates for infants.

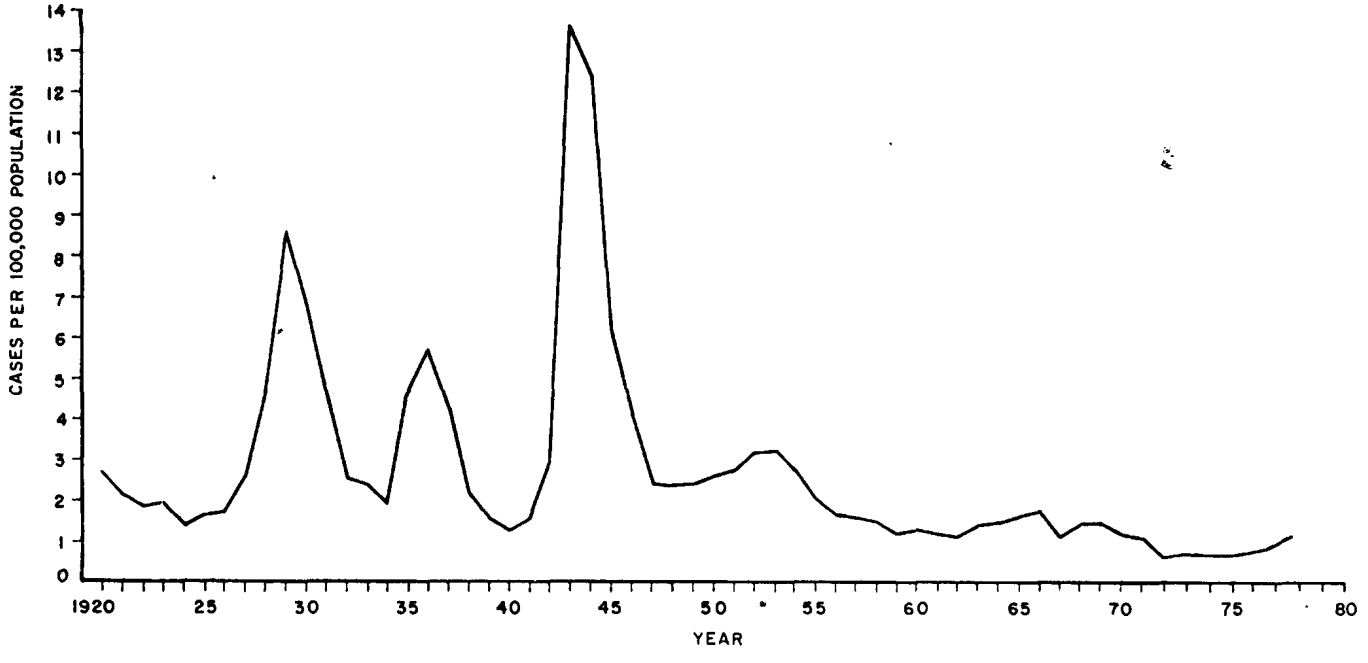
Meningococcal disease has a definite seasonal trend, with most cases occurring in the winter and early spring.

Preventive Measures

Control of outbreaks. A new and powerful tool for preventing epidemic meningococcal disease became available in 1975 with the licensure by the U.S. Food and Drug Administration of polysaccharide vaccines effective against members of serogroups A and C. The vaccines are marketed separately or in combination for controlling epidemic disease caused by members of serogroups A and C, for administering to household contacts of persons with sporadic cases caused by members of serogroups A or C, for administering to travelers to known epidemic areas, and for being routinely used by the military.

The dramatic reduction of epidemics caused by members of serogroup C among U.S. military personnel and the effective control of the epidemics caused by members of serogroup A in Finland and Brazil demonstrate the importance of these 2 vaccines, as well as that of vaccines developed against the other serogroups. In a typical epidemic, one 50-mg dose of the appropriate vaccine should be given to all household contacts of infected persons and to any other persons known to be at high risk. In very large

Figure 1. Reported meningococcal infection rates by year, United States, 1920-1978



epidemics, vaccines must also be made available to groups at lower risk. Serogroup A vaccine seems to be effective at least for persons as young as 1 year old, whereas serogroup C vaccine does not appear to be effective for those <2 years old.

Control of sporadic cases. While the 2 licensed vaccines have proven effective in epidemics, there are not enough data on using them in controlling endemic disease to base recommendations for routine vaccination of civilians. Consequently, chemoprophylaxis for family and other intimate contacts of patients remains an important aspect of disease prevention. The use of chemoprophylaxis for household contacts is based on 2 factors: 1) the secondary attack rate for contacts of persons with sporadic cases (about 4 cases per 1,000 persons exposed in the month after the person with the index case becomes ill) and 2) the availability of antibiotics that can eradicate *N. meningitidis* from the nasopharynx.

To date, 3 drugs are known to kill the organism: sulfonamides, minocycline, and rifampin. However, sulfonamides, among the earliest and most efficacious drugs, have been rendered ineffective in recent years by the continued presence of a high proportion of sulfa-resistant strains (Table 1), and minocycline is not recommended because of its severe side effects. Consequently, only rifampin has proven to be both safe and effective for routine use.

Table 1. Proportion of sulfonamide-resistant isolates of *N. meningitidis* (from civilians) submitted to the Center for Disease Control, 1974-1978

Serogroup	1974	1975	1976	1977	1978
A	1/4[a]	1/3	0/18	0/23	0/7
B	7/196	8/209	7/217	10/326	16/258
C	76/139	51/93	33/71	33/86	31/96
Y	1/72	1/71	0/49	0/53	0/42
W-135	0/3	0/9	0/10	0/34	4/65
Total	85/414 (20.5)	61/385 (15.8)	40/365 (11)	43/522 (82)	51/468 (10.9)

[a]Number of resistant isolates/total number of isolates (% resistant).

The currently recommended dosages of rifampin are: 1) adults—600 mg every 12 hours for 4 doses, 2) children 1 month to 12 years old—10 mg/kg body weight every 12 hours for 4 doses, and 3) children less than 1 month old—5 mg/kg body weight every 12 hours for 4 doses. Because 50% of secondary cases occur within the first 4-5 days after the index case is diagnosed and the patient is hospitalized, this chemoprophylactic regimen should be used for household contacts as soon as possible. In particular, treatment should not be delayed awaiting results of throat culturing. In addition to chemoprophylaxis, the use of serogroup A or C vaccine should be considered for household contacts of persons with sporadic cases caused by either of these organisms.

Mumps

Mumps was first described in the 5th century B.C. by Hippocrates, who described the clinical manifestations of epidemic parotid swelling. However, it was not until the early 20th century that central nervous system (CNS) involvement was first recognized as a complication of mumps.

The clinical manifestations of mumps usually consist of unilateral or bilateral parotid swelling and mild-to-moderate fever; about 30% of infected persons have no symptoms. Epididymo-orchitis is the most common manifestation of mumps infection other than parotitis for postpubertal males. It usually occurs after the parotitis, but about 5% of the time it may precede the parotitis or occur alone. Although mumps epididymo-orchitis is not a reportable disease, studies have indicated that it affects 20%-30% of postpubertal males who have clinical mumps. Most cases are unilateral, but some are bilateral. Sterility rarely follows because testicular tissue usually does not atrophy completely. An important residual complication of mumps is deafness, which may occur with or without meningitis or encephalitis. The incidence is estimated to be 1 case per 15,000 cases of mumps. Mumps infection may involve other organs such as the heart, kidney, liver, pancreas, and thyroid gland. It rarely causes severe illness and is rarely fatal, i.e., between 1 and 3.4 deaths per 10,000 reported cases.

Mumps virus was isolated in 1945 by Habel and Enders, and 20 years later an attenuated live-virus vaccine was developed by Hilleman and co-workers. The live-virus vaccine, licensed in December 1967, has been shown to be effective in conferring long-lasting immunity to mumps.

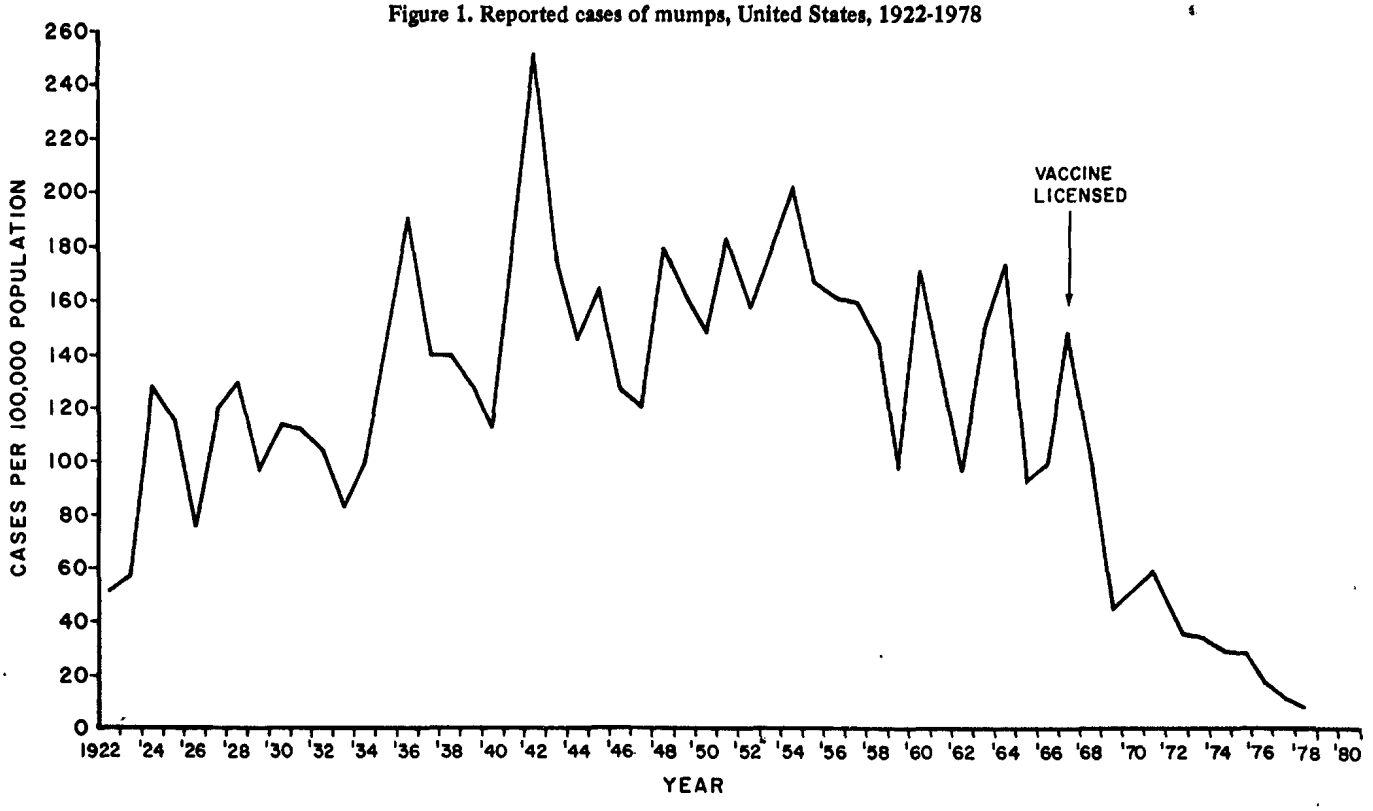
Epidemiology

Mumps was placed on the list of nationally reportable diseases in the United States in 1922 but was removed in 1950. Many states continued reporting the disease voluntarily, and mumps was again placed on the list on January 1, 1968.

In the period 1922-1971, the national annual incidence of reported mumps cases showed no discernible cyclic pattern; however, since 1971 there has been a continuous decline (Figure 1). In 1978 (final total of 16,817 cases of mumps), the incidence reached the lowest point in the history of mumps surveillance. The seasonal pattern of mumps cases, with a peak incidence in the winter and spring, has remained unchanged (Figure 2).

Mumps remains predominantly a disease of young children. By age 15, approximately 60% of all U.S. children have a history of mumps infection. Over the past decade the incidence in 3 selected areas—California, Massachusetts, and New York City—has been highest for the 5- to 9-year-old group, which has more than 50% of all reported cases, followed by the incidences for the 0-4, 10-14, and 15+ age groups (Table 1). As the mumps vaccine began to be more widely used, reported mumps incidence in these same 3

Figure 1. Reported cases of mumps, United States, 1922-1978



locations declined dramatically for all age groups. The most marked decrease (68.6%) has been for 5- to 9-year-old children. Age data from at least 32 reporting areas in the United States indicate that mumps continues to be a disease primarily of elementary school children (Table 2). Children 10-14 years of age now have a higher incidence than in prevaccine years and have the second highest incidence for any age group. These changes in the age-specific epidemiology of mumps undoubtedly reflect current vaccination practices and are similar to changes observed with measles and rubella.

Aseptic meningitis and encephalitis, or more properly "meningo-encephalitis," are the only complications of mumps officially reported to the Center for Disease Control. The continuing decrease in the number of mumps cases is paralleled by the reported number of both of these mumps-associated central nervous system (CNS) complications (Figure 3). The overall incidence of CNS involvement is approximately 3.5 cases per 1,000 cases of mumps reported. This figure may not reflect the true incidence because of underreporting and the arbitrary distinction between aseptic meningitis and encephalitis. The seasonal

Figure 2. Mumps—reported cases by month, United States, 1976-1978

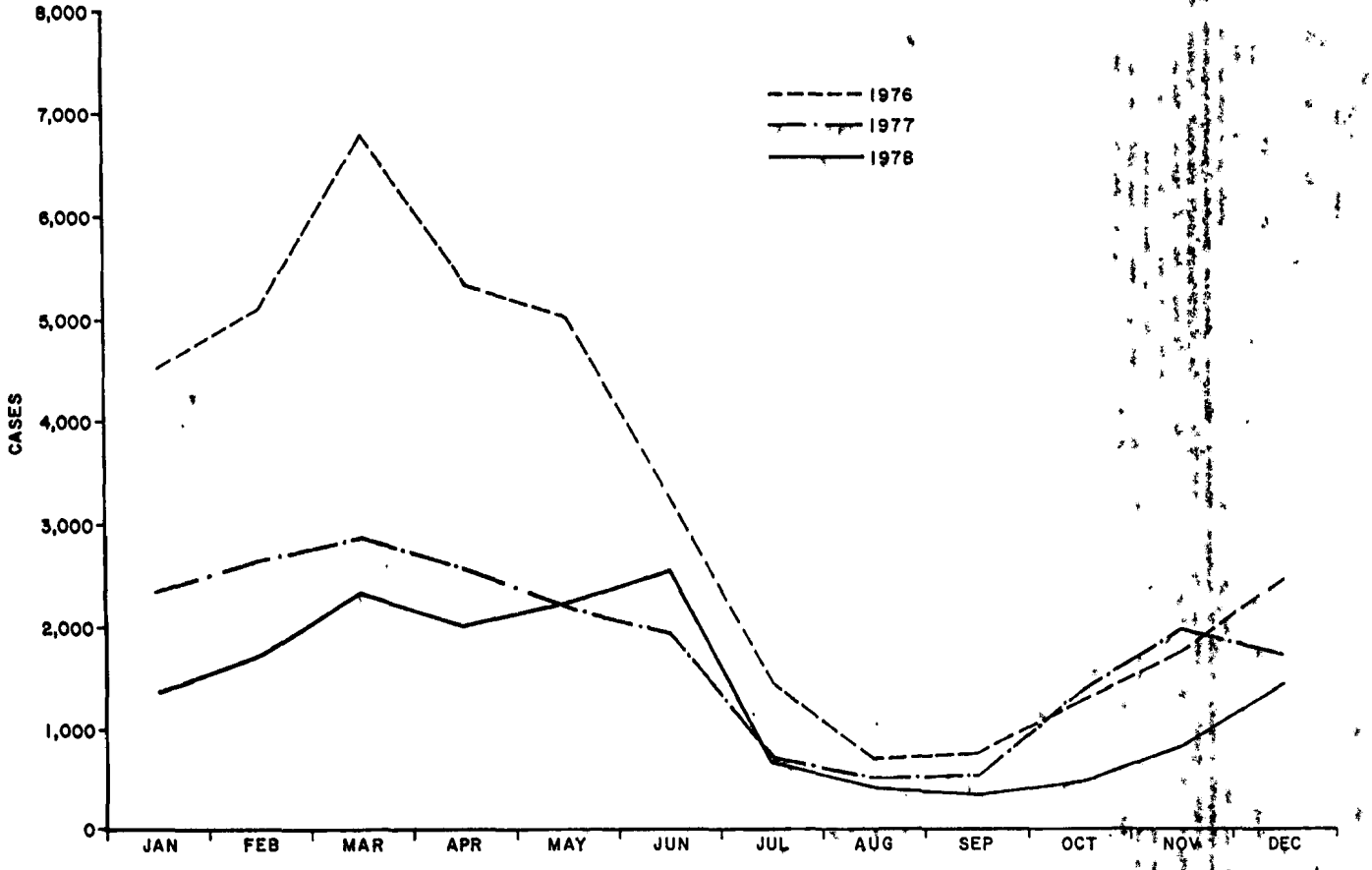


Table 1. Reported cases of mumps affecting persons of known age, by 5-year age group, for California, Massachusetts, and New York City, 1967-1971 and 1972-1976

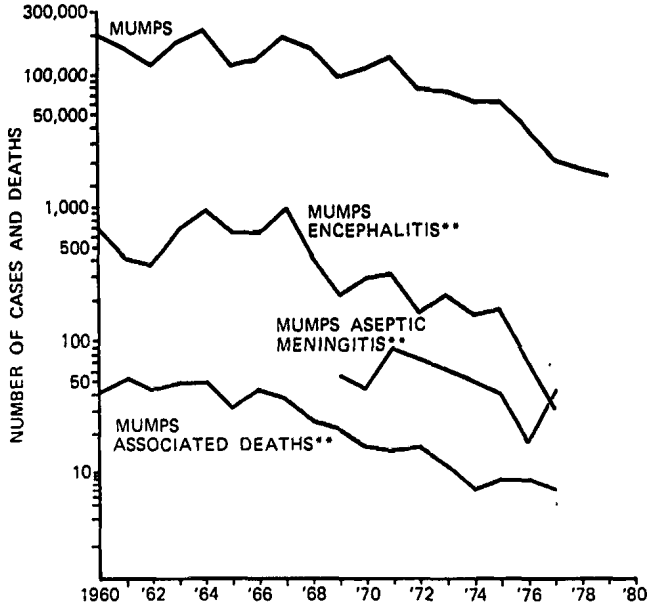
Age Group Years	1967-1971			1972-1976			% Decrease In 1972-1976 from 1967-1971
	Average Annual No. Cases	%	Average Annual Incidence Per 100,000 Pop.	Average Annual No. Cases	%	Average Annual Incidence Per 100,000 Pop.	
0-4	2,932	17.1	102.5	1,125	18.7	41.2	61.6
5-9	10,413	60.8	336.8	3,272	54.3	105.8	68.6
10-14	2,372	13.8	75.5	992	16.5	31.6	58.1
	1,418	8.3	5.8	633	10.5	2.6	55.3
TOTAL	17,125	100.0	51.1	6,022	100.0	18.0	64.9

Table 2. Percentage distribution of reported mumps cases and incidence rate,[a] by age group, United States, 1977-1978

Age Group Years	1977			1978			Percentage Change 1977-1978	
	No.	%	Rate	No.	%	Rate	%	Rate
<5	1,041	15.1	21.2	774	12.5	13.8	−17.2	−34.9
5–9	3,318	48.1	60.1	3,092	50.1	49.1	+ 4.2	−18.3
10-14	1,709	24.8	27.7	1,526	24.9	21.8	+ 0.4	−21.3
15–19	510	7.4	7.5	400	6.5	5.2	−12.2	−30.7
20+	319	4.6	0.7	381	6.2	0.7	+34.8	0.0
Total with Known Age	6,897	32.2	–	6,173	36.7	–	–	–
Unknown Age	14,539	67.8	–	10,644	63.3	–	–	–
TOTAL	21,436	100.0	9.9	16,817	100.0	7.8	–	−21.2

[a]Incidence = cases per 100,000 population (1977 census) extrapolated from the age distribution of persons with documented cases from 32 (1977) and 33 (1978) reporting areas.

Figure 3. Reported cases of mumps, mumps aseptic meningitis, and mumps-associated deaths by year, United States, 1960-1979*



*1979 provisional data.
**Mumps encephalitis data through 1977,
Mumps deaths data through 1977,
Mumps aseptic meningitis data through 1977.

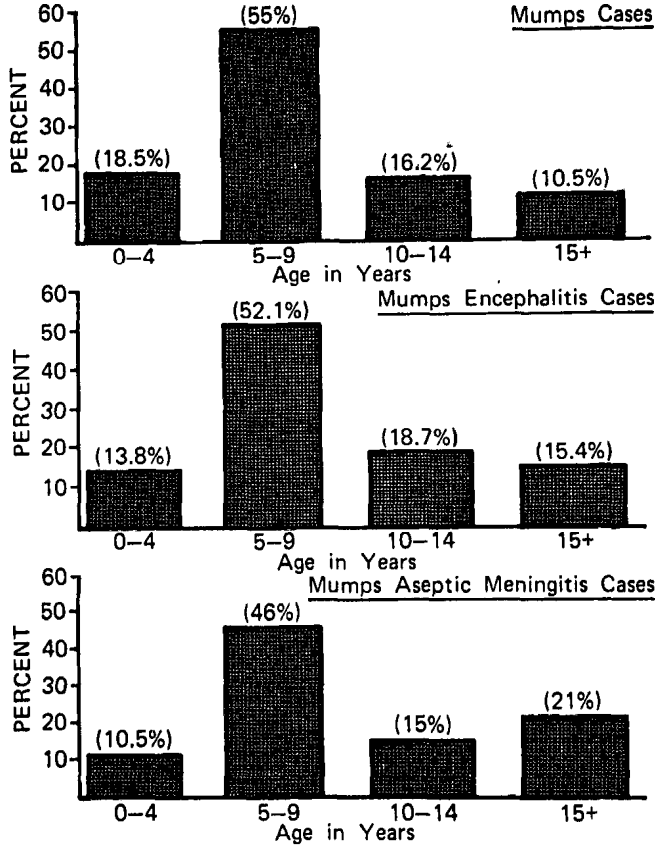
pattern of mumps-associated meningo-encephalitis is similar to that of uncomplicated mumps.

Although uncomplicated mumps affects males and females with equal frequency, 3 times more males than females are reported to have mumps meningo-encephalitis. Furthermore, older persons are more likely to be affected than young children. For example, reports for the period 1973-1975 show that although only 10.5% of all patients with mumps were over 15 years old, 15.4% of those who had encephalitis and 22.1% of those who had aseptic meningitis were in that age group (Figure 4).

Prophylaxis

The mumps virus was isolated in 1945, and formalin-inactivated (killed) virus vaccines were developed in 1948. Although these vaccines stimulated antibody development and protected against clinical illness, immunity waned in less than a year, making frequent boosters necessary. The first live-attenuated mumps virus vaccine, reported from Russia in 1958, also failed to provide lasting immunity. In 1963, the Jeryl Lynn strain of mumps was isolated from the buccal mucosa of a person with an uncomplicated case of mumps and was attenuated in chick-embryo cell culture. After extensive clinical testing, this live-attenuated mumps

Figure 4. Mumps,* mumps-associated encephalitis,** and aseptic meningitis** by age group, United States, 1973-1975



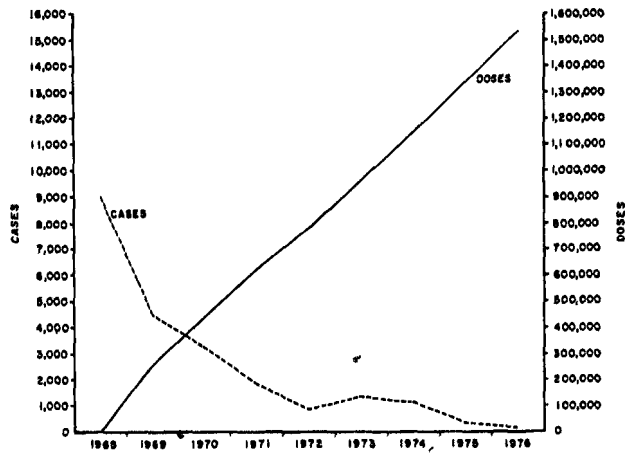
*California, Illinois (except Chicago), Massachusetts, New York City, Texas, and Virginia.
**Using U.S. totals.

vaccine was licensed in December 1967. From 1968 through 1978, over 40 million doses of this mumps vaccine were distributed in the United States.

The Jeryl Lynn vaccine elicits an antibody response in over 90% of recipients and in 1 study was 95%-97% effective in providing protection after exposure to wild virus. The subclinical infection induced by this vaccine is noncommunicable. Mumps vaccine has been combined successfully with live-attenuated measles and rubella virus vaccines in antigen preparations that provide comparable protection.

Neutralizing antibody titers after vaccination are lower than those induced by naturally acquired mumps; however, vaccine-induced antibody levels decline more slowly than those induced by natural infection, a phenomenon that may reflect antibody boosts associated with subclinical reinfection of vaccinees. Finally, both neutralizing antibody and protection against clinical mumps have been shown to persist for at least 8 years after vaccination.

Figure 5. Reported cases of mumps and cumulative doses of mumps vaccine* administered, Massachusetts, 1968-1976



*All products containing this antigen.

Vaccination

Mumps vaccination can practically be included in routine vaccination programs. Major public health programs to control mumps through vaccination can substantially decrease the number of mumps cases (Figure 5) and reduce costs associated with this infection. The Immunization Practices Advisory Committee and the American Academy of Pediatrics recommend vaccinating all children older than 12 months. In particular, vaccination for mumps should be considered for all children approaching puberty and for adolescents and adults, especially males, who have not had mumps.

Limited experimental, clinical, and epidemiologic data are consistent with the hypothesis that pancreatic damage may result from gradual auto-immune response to pancreatic tissue injured by early, direct invasion by the virus; however, further research is indicated to determine whether mumps infection contributes to the pathogenesis of diabetes mellitus for certain individuals. Even if such an association exists, it would seem prudent to prevent mumps infection by giving the mumps vaccine.

Since specific tests for establishing susceptibility are misleading (hemagglutination inhibition and complement fixation tests), expensive and not generally available (neutralization and radial hemolysis tests and enzyme-linked immunosorbent assay), or unreliable (mumps skin test), any individual suspected on clinical grounds of being susceptible should be given the vaccine. There is no contraindication to receiving mumps vaccine antigen more than once or after having had naturally acquired mumps infection. Finally, although mumps vaccine given after exposure may not provide protection, there is no contraindication to its use, and if the exposure does not result in infection, the vaccine should induce protection against any later exposures.

Pertussis (Whooping Cough)

The clinical aspects of whooping cough were first described in 1576, but not until 1906 was the disease related to infection with the bacillus *Bordetella pertussis.*

We now know that whooping cough can be caused by at least 3 different *Bordetella* species. Over 95% of cases studied in the United States are caused by infection with *B. pertussis,* and the others are caused by *B. parapertussis* and *B. bronchiseptica.* Some have suggested that adenovirus can cause whooping cough, although the issue is disputed. In any case, unless *B. pertussis* is isolated in cultures, the diagnosis of pertussis (i.e., whooping cough caused by *B. pertussis)* is uncertain.

It has been known since the early 1950s that isolates of *B. pertussis* can be grouped according to the degree to which they agglutinate with specifically absorbed serum. Differences among strains can be detected by the presence or absence of various combinations of 7 agglutinins. However, while the agglutinin patterns are of some epidemiologic significance, they do not apparently play an important role in conferring immunity.

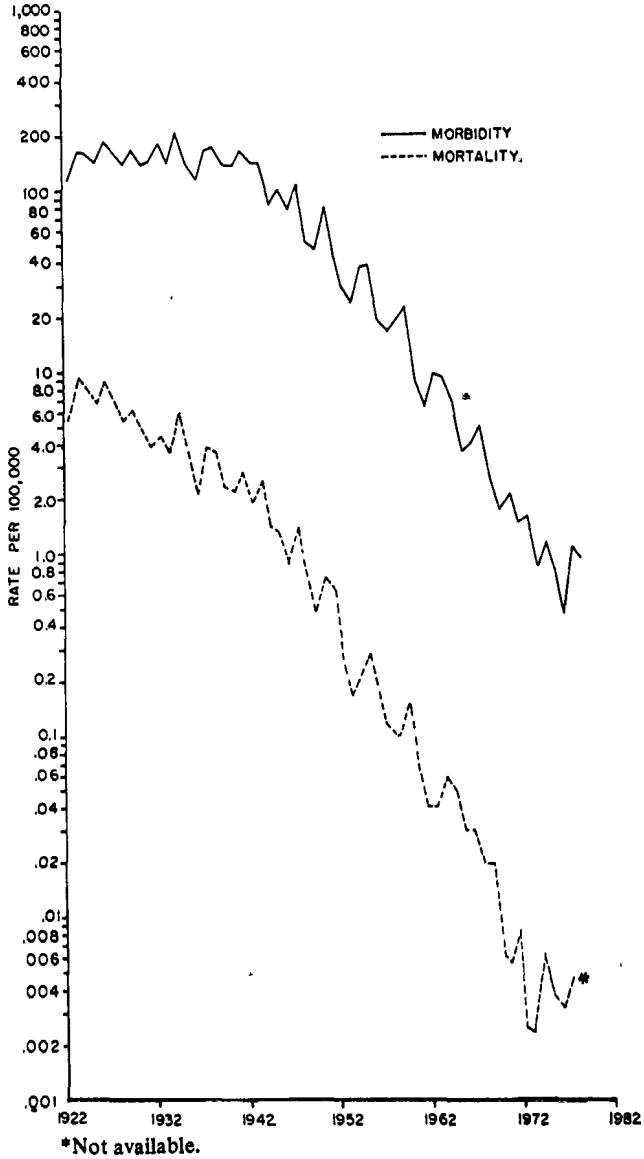
B. pertussis is transmitted primarily by droplets from a person with clinical illness; asymptomatic carriers have not been shown to transmit the disease. The incubation period is 5-21 days, although most cases occur within 10 days after exposure. Pertussis is highly communicable, with susceptible family members having the highest secondary attack rates—80% to 90%. The patient with pertussis is most likely to transmit infection during the first week of the disease, because the number of organisms shed wanes as the paroxysmal stage subsides.

After *B. pertussis* was isolated in 1906, many attempts were made to produce a vaccine from various field strains; however, results were variable, suggesting that the vaccines were not uniform in potency. In 1949, minimum requirements for *B. pertussis* vaccines were established for the United States on the basis of the concentration of killed bacteria in the vaccine and on results of a mouse potency test. In 1953, these requirements were modified, and 12 units were specified as the total human dose (THD) for primary vaccination of children. Calculations for some early trials showed that a THD of 12-15 units was 86%-91% effective in preventing disease for family contacts, whereas a THD of 7 units was only 29% effective. Pertussis vaccines usually contain 1 of 3 aluminum adsorbents. Although there are not enough data to evaluate the adsorbents' relative merits, it is known that the potency of an adsorbed product is greater and the toxicity less than those of unadsorbed (fluid) vaccines.

Vaccines are effective in reducing both morbidity and mortality from pertussis; however, gradual loss of vaccine-induced immunity has been documented for persons in all age groups, regardless of the age at which they received the primary series or the number of doses they were given.

The national incidence of pertussis was relatively stable from 1922, when nationwide reporting was instituted, until the 1940s, when pertussis vaccines were introduced (Figure 1). However, the mortality and case-fatality ratios fell in the early 1900s before the vaccine was widely used. Since pertussis vaccine was introduced, these rates have continued to fall, and the incidence has decreased as well. Giving erythromycin to susceptible infants in contact with persons with pertussis has been recommended, but no scientifically reliable studies support the antibiotic's efficacy in this context.

Figure 1. Pertussis, United States, 1922-1978



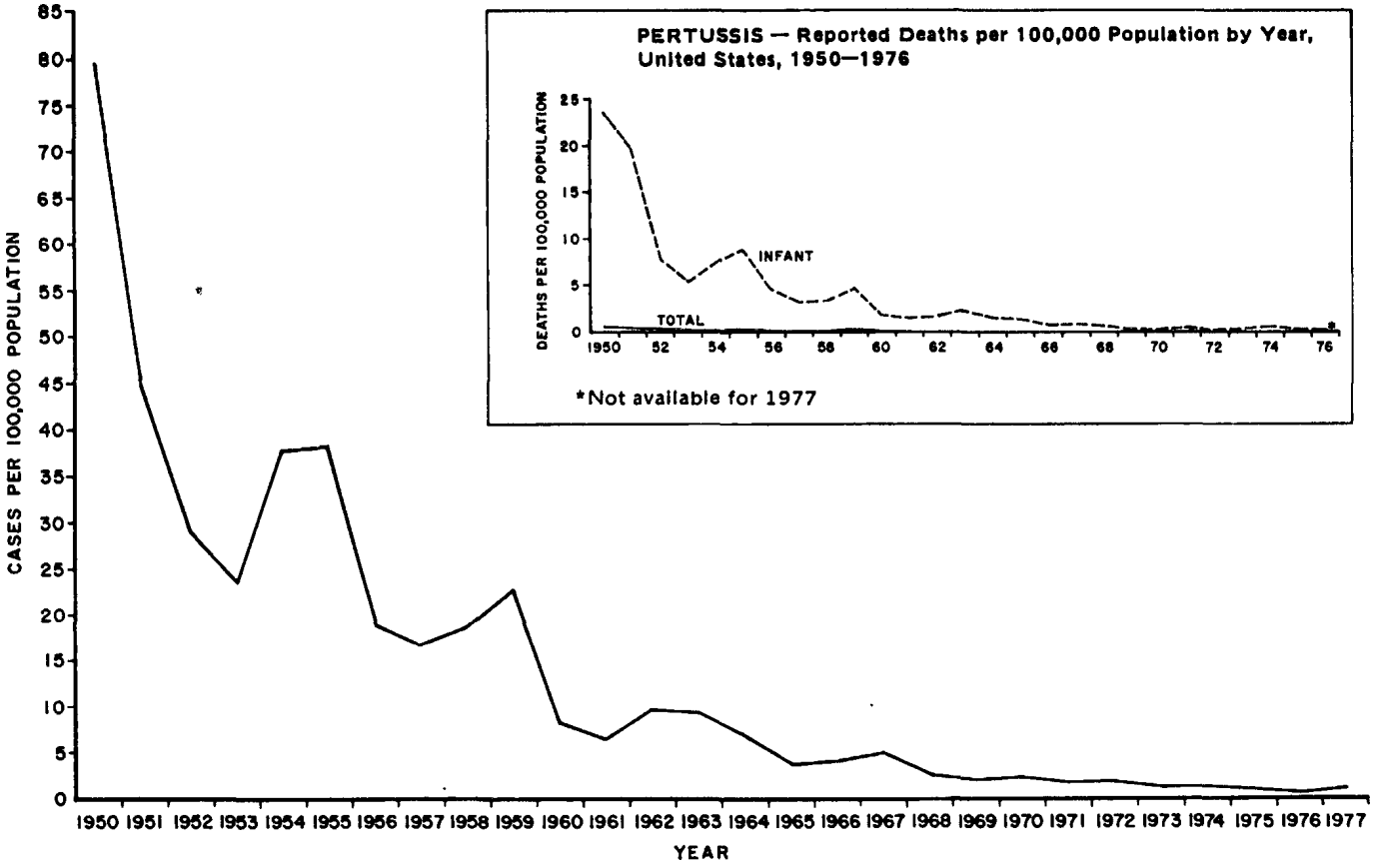
*Not available.

Pertussis is widespread in the United States, but the reported incidence varies considerably from state to state. This variation undoubtedly reflects differences in actual occurrence as well as in recognizing and reporting the disease. Pertussis is underreported because of difficulties both in the clinical diagnosis for some age groups and in laboratory documentation. Wider use of diagnostic techniques including examining nasopharyngeal swabs with direct fluorescence and examining cultures made from swabs and grown on Bordet-Gengou medium supplemented with methicillin would permit more precise application of control techniques.

Most of those who die from pertussis are infants (Figure 2). In a 12-year period, 1960-1971, 72% (508 of 704) of all reported pertussis deaths were of children in their first year of life, with most being 2- and 3-month olds. In contrast, only 3.4% (24 of 704) of the persons who died from pertussis were at least 5 years old. The fact that most patients who die are infants emphasizes the need for early vaccination.

In the last few years, outbreaks of pertussis involving vaccinated hospital staff members have been recognized. Consideration has been given to revaccinating hospital workers to prevent nosocomial infection of patients, but the frequency with which adults have local and systemic reactions indicates that they should not generally be given the vaccine.

Figure 2. Pertussis (whooping cough)—reported cases and deaths by year, United States, 1950-1977



Plague

At least 3 plague pandemics have been recorded, the most infamous being the "Black Death" that decimated Europe in the Middle Ages. The causative agent, *Yersinia pestis*, was first described in Hong Kong by Yersin and Kitasato in 1894. The first human reported to have plague in the continental United States was a crew member aboard a ship that docked in San Francisco in June 1899. Between 1900 and 1924, the disease spread, and outbreaks of urban, rat-associated human plague occurred in San Francisco, Oakland, Los Angeles, New Orleans, and other coastal cities. Since 1925, however, almost all the human plague cases reported in the United States have been sporadic and associated with infected wild mammals or their fleas, i.e., so-called sylvatic plague. Plague associated with wild rodents has been documented in a wide area encompassing much of the western United States, with natually acquired human cases reported from Arizona, California, Colorado, Hawaii, Idaho, Nevada, New Mexico, Oregon, and Utah.

Enzootic plague and associated human infections have also occurred in many other areas of the world. In the past decade, human plague has been reported in Africa (Angola, Equatorial Guinea, Lesotho, Libya, Mozambique, Madagascar, South-West Africa, Zimbabwe-Rhodesia, South Africa, Tanzania, and Zaire), South America (Bolivia, Brazil, Ecuador, and Peru), and Asia (Burma, Kampuchea, Indonesia, Nepal, and Vietnam). Enzootic plague, however, is probably more extensive than this list of countries suggests.

Most human cases result from the bites of fleas that have fed on plague-infected animals or, less commonly, from contact with the tissue of infected animals. It is not unusual, however, for patients to have no recollection of flea bites or animal contact before becoming ill. Person-to-person spread may also occur through droplet transmission from patients with either primary pneumonic plague or plague pneumonia, a complication of bubonic or septicemic plague.

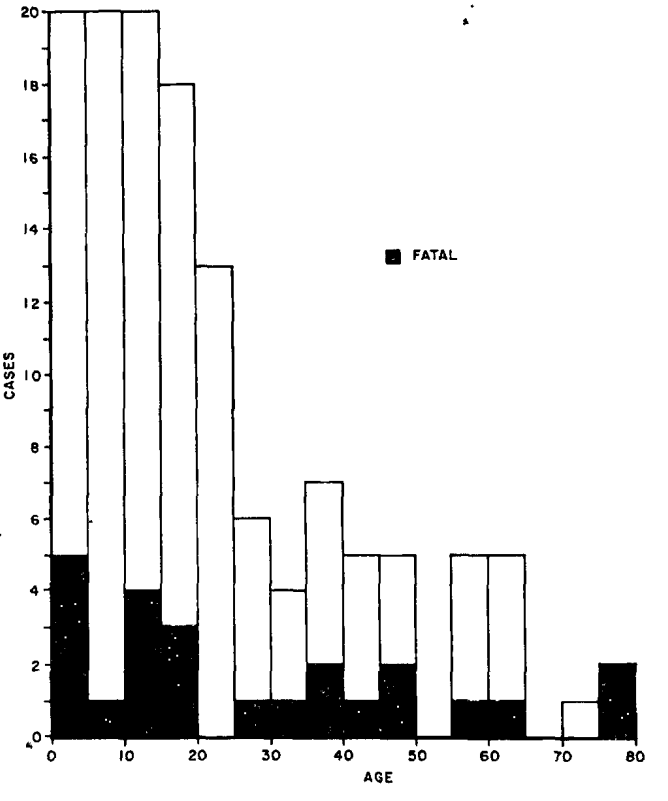
Of the 3 forms of plague, bubonic is the most common, accounting for over 85% of all cases reported in the United States in the past 25 years. Such cases are characterized by fever and painful lymphadenopathy. The inguinal, femoral, axillary, cervical, and epitrochlear nodes are most commonly involved, with 10%-15% of patients having enlarged nodes at several sites. Primary septicemic plague accounts for about 10% of cases and is characterized by fever and primary bacteremia without detectable lymphadenitis. Both of these forms of the disease may be complicated by pneumonia or meningitis. Patients who have pneumonia as a result of their primary infection are of particular concern because they may be a source of epidemic primary pneumonic plague.

Between 1925 and 1964, an average of 1 case of plague per year occurred in the United States (Figure 1). Since 1965, an increase in the annual average to 9 reported cases per year has been largely unexplained. In addition to this change, the geographic distribution of cases has shifted. Whereas 77% of the wild rodent-associated human plague cases reported in the United States from 1925-1950 occurred in California and Oregon, 81% of cases since 1950 have been acquired in New Mexico, Arizona, Colorado, and Utah. The seasonal distribution of plague has remained relatively constant, with 82% of patients having onset between May and September.

More than half of the persons who had plague in the period 1950-1979 were less than 20 years old. Males accounted for 61% of cases between 1960 and 1974, but since 1975, 57% (45/79) of the persons with confirmed cases have been females. Most patients have been white, although race-specific attack rates are significantly higher for Native Americans living in states with endemic plague. For the period 1925-1964, the case-fatality ratio was 52%, but it has since dropped to 14%.

When human plague cases are associated with an epizootic among wild mammals, control measures may in-

Figure 1. Plague—reported human cases and deaths by age group, United States, 1950-1978



clude 1) identifying the animal species involved, 2) determining the geographic extent of the epizootic, 3) using insecticides to control the flea population in the area, 4) reducing rodent harborage, and 5) selectively reducing, if appropriate, rodent populations. Although flea-borne bubonic plague usually affects only 1 person in a household, prophylactic antibiotics have occasionally been prescribed for other household members. Close contacts of patients with suspected or proven secondary plague pneumonia or primary pneumonic plague should receive prophylactic therapy (a tetracycline or sulfonamide).

The drugs of choice for treating patients with plague include streptomycin, chloramphenicol, and tetracycline. Although sulfonamides can be used for treating patients with uncomplicated bubonic plague, they should not be used for patients with pneumonic or septicemic plague. If a patient has suspected or confirmed plague meningitis, chloramphenicol may be the drug of choice.

An inactivated whole-cell plague vaccine is currently licensed for use in the United States. Mild reactions including pain, erythema, and swelling at the injection site are common. Localized or generalized urticarial reactions and sterile abscesses have rarely been observed. Although the efficacy of current plague vaccines has not been precisely determined, inactivated vaccine used by the American armed forces in Vietnam appears to have been effective in preventing clinical plague.

The low incidence of plague in the United States, even among residents of areas where plague is enzootic, makes vaccination against plague for this population impractical and unnecessary. However, selective vaccination is recommended for persons traveling to Vietnam, Kampuchea, or Laos. In addition, persons whose vocations bring them into frequent contact with wild rodents in areas where plague is enzootic and laboratory personnel who work with *Y. pestis* or plague-infected animals should be vaccinated.

Pneumococcal Disease

The pneumococcus (*Streptococcus pneumoniae*) is the most common cause of bacterial pneumonia and a frequent cause of otitis media and meningitis. Nearly all pneumococcal disease seen in the United States in recent decades has been endemic, although epidemics may occur among such institutionalized groups as soldiers and prisoners. The average incidence of pneumococcal meningitis in the United States is 1.5 to 2.5 cases per 100,000 population per year. The highest rates are for infants 6-8 months of age and for the elderly. There is no precise information available on the incidence of penumococcal pneumonia in the United States, but it has been estimated that several hundred thousand cases occur each year. Host factors strongly affect the risk of acquiring pneumococcal disease. Persons whose spleens are malfunctioning (e.g., those with sickle cell disease) or have been surgically removed are at high risk, as are those with cirrhosis, multiple myeloma, agammaglobulinemia, nephrotic syndrome, alcoholism, or congestive heart failure. Viral respiratory infections frequently precede pneumococcal pneumonia.

Before 1977, strains of pneumococci isolated from patients were consistently sensitive to penicillin, which is generally the drug of choice for patients who are not allergic. In 1977, pneumococcal strains resistant to a concentration of 4 μg of penicillin/ml of diluent were found in South Africa and in Minnesota. Many of the strains from South Africa were also resistant to most other antibiotics used in clinical practice. Surveillance of antibiotic sensitivity of pneumococci since 1977 has not shown widespread penicillin resistance of pneumococci outside South Africa, but continued surveillance will be of assistance in selecting alternative drugs if these organisms are found elsewhere.

Pneumococci have polysaccharide capsules, and more than 80 antigenically distinct capsular types have been identified. Fourteen of the types cause about 80% of the serious pneumonic disease in the United States. Before sulfonamides were introduced, type-specific antisera were used to treat persons with pneumococcal disease. Now strains are typed for epidemiologic studies and vaccine evaluation.

Vaccines against pneumococcal disease were first tested in about 1910. Purified capsular polysaccharide vaccines were shown during World War II to protect army troops; a vaccine similar to the one now in use was licensed briefly after the war but was not widely used because of the availability of penicillin. Additional testing in the last 10 years shows that polyvalent pneumococcal vaccines are immunogenic for persons over 2 years old. In 1977, a 14-valent pneumococcal vaccine was licensed. It is given as a single injection and contains 50 μg each of capsular polysaccharides of American types 1, 2, 3, 4, 6, 8, 9, 12, 14, 19, 23, 25, 51, and 56.

Poliomyelitis

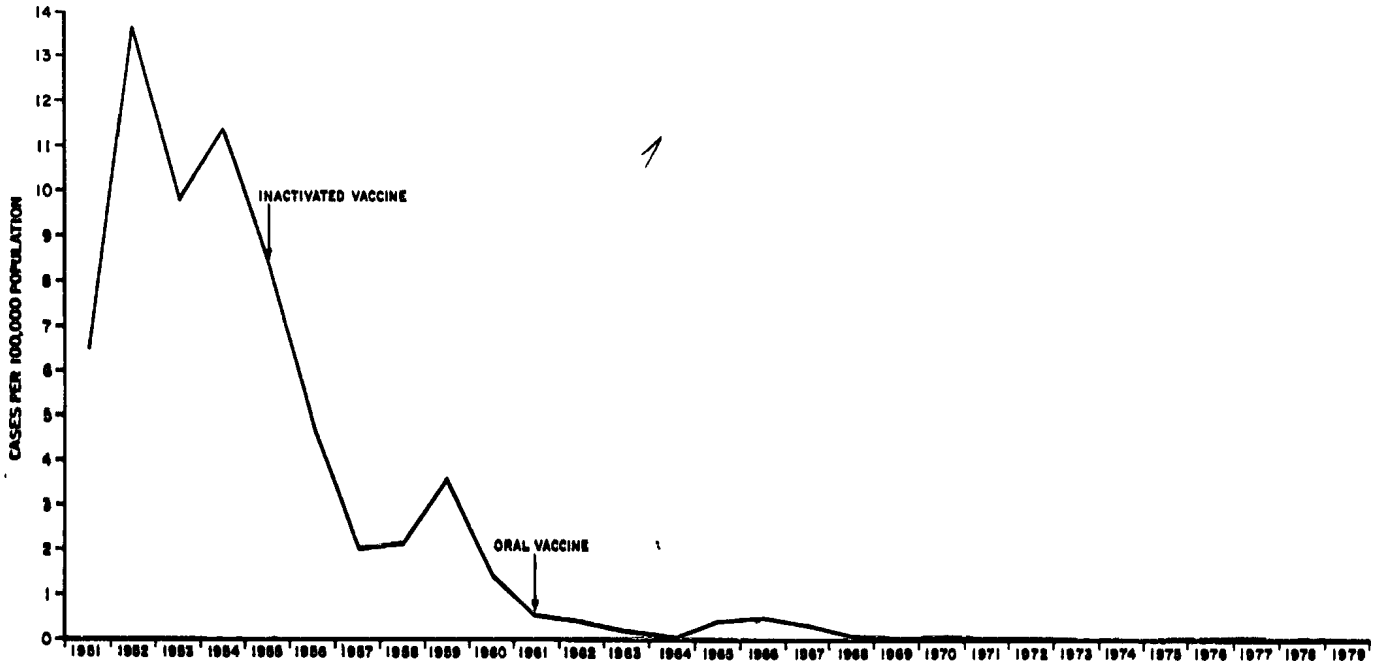
Poliomyelitis (formerly known as infantile paralysis) was recognized as a distinct entity with wide geographic distribution in the 19th century, although paralytic illness among infants had been known and described earlier. Small outbreaks were reported in both Europe and North America in the mid-19th 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. On the basis of studies of several epidemics, poliomyelitis was characterized as an infectious disease, spread via human contact, with both paralytic and nonparalytic expression. In 1909, Landsteiner discovered that poliomyelitis was caused by a virus. However, only after 40 years of increasingly intensive research were the 3 serotypes of poliovirus identified and propagated in tissue culture. The foundation was thus laid for the development of inactivated poliomyelitis vaccine (IPV), introduced for general use in 1955, and live-attenuated oral poliovirus vaccine (OPV), licensed in 1961.

Widespread use of the 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 a dramatic reduction in the number of reported paralytic cases from 13,850 in 1955 to 988 in 1961. When OPV became available, the incidence decreased further as a larger proportion of the population became immune. The number of paralytic cases decreased from 988 in 1961 to 9 cases in 1978 (Figure 1).

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 attack rates of paralytic illness for infants and young children, the incidence of paralytic poliomyelitis shifted upward for all age groups during the years of crippling epidemics. Now with the general availability of effective vaccines, poliomyelitis occurs only sporadically, usually affecting unvaccinated persons or those who have not had a complete vaccine series. However, 3 outbreaks caused by wild poliovirus strains occurred in this country in 1970, 1972, and 1979, the last 2 among populations that specifically refuse vaccination. Most sporadic cases in the past 10 years have been associated with exposure to OPV either by vaccine recipients or their close contacts.

In addition to improved epidemiologic and biologic understanding of poliomyelitis, reporting practices have also changed. Before 1951, paralytic poliomyelitis was not differentiated from nonparalytic poliomyelitis (aseptic meningitis caused by poliovirus) in national reporting. The cases were thought to be equally divided between the 2 classifications. We now know that many of the nonparalytic cases, formerly attributed to poliovirus infection on epidemiologic grounds, were probably caused by echoviruses and Coxsackie virus. These agents may also cause paralytic illness occasionally, although the paralysis tends to be

Figure 1. Poliomyelitis (paralytic)—reported case rates by year, United States, 1951-1979



transient and less severe. Thus, one of the epidemiologic criteria for paralytic poliomyelitis is the presence of residual paralysis or paresis at least 60 days after onset of illness. In fact, only paralytic poliomyelitis is included in current official poliomyelitis case counts. Nonparalytic poliomyelitis is also reported, but because of the incompleteness of recognition and reporting, it is discussed separately.

Causative Agent

The poliovirus is a ribonucleic acid (RNA) picornavirus and belongs to the enterovirus group along with Coxsackie virus and echoviruses. The 3 antigenically distinct poliovirus types (1, 2, and 3) may cross-react serologically to some extent; thus infection with a given type may provide some cross-protection against paralytic disease from infection with another type. Surveillance data from the past several years suggest that poliovirus type 1 isolates from patients with suspected paralytic poliomyelitis and from their contacts are more likely to be wild strains and that poliovirus type 2 or 3 isolates are more likely to be vaccine strains.

Clinical Description

The incubation period for poliomyelitis is commonly 6-20 days, with a range of from 3 to perhaps 35 days. The virus is introduced either through fecal-oral contamination or respiratory secretions. It multiplies first in the oropharynx and subsequently in the gut. Viremia probably accompanies most forms of the illness, including abortive and possibly inapparent forms (see below). In rare cases (1/50 to 1/1,000), the virus causes paralysis, entering the central nervous system (CNS) perhaps through the medulla oblongata or directly into the anterior horn cell area of the spinal cord.

Intestinal infection with the poliovirus or many other enteroviruses may lead to a wide spectrum of clinical manifestations. Infection with any of the 3 poliovirus types will assume 1 of 4 forms:

1. Inapparent infection (90%-95%): Virus may be recovered from the throat and/or stool, but the patient remains asymptomatic.

2. "Minor illness" (4%-8%): Also known as abortive illness. Three syndromes observed with this form of poliovirus infection include a) upper respiratory tract infection, b) gastroenteritis, and c) influenza-like illness.

3. Nonparalytic poliomyelitis (1%-2%): May occur as a prodromal illness like the "minor illness" described above, followed by invasion of the CNS and by clinical aseptic meningitis.

4. Paralytic poliomyelitis (0.1%-2%): Consists usually of prodromal illness ("minor illness" described above), meningeal irritation, with eventual asymmetric flaccid paralysis or paresis resulting from involvement of spinal or bulbar centers. Early in the course of spinal paralytic poliomyelitis, the older patient may complain of pain or cramping in the limbs. This discomfort is followed by onset of weakness within about 48 hours.

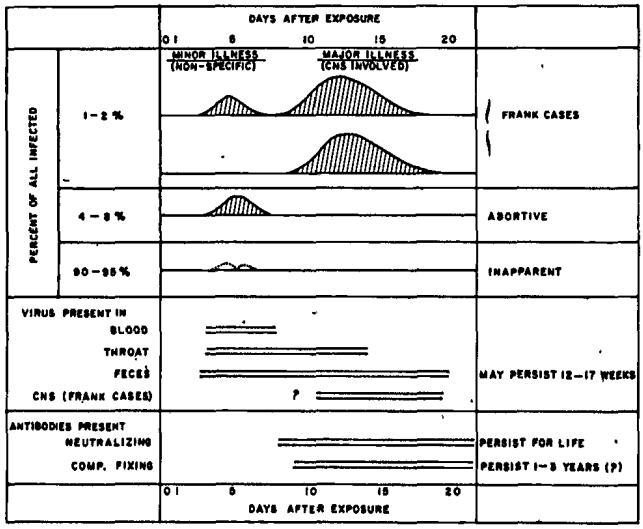
5. Bulbar paralysis may involve any combination of cranial nerves and brain-stem respiratory centers. Paralytic poliomyelitis is divided into 3 types: a) spinal, b)bulbar, and c) bulbospinal. Polio-encephalitis, another severe manifestation of poliovirus infection, may be accompanied by paralysis. Children may have bulbar paralysis without limb involvement, whereas adults with bulbar involvement generally also have limb paralysis. The probability that infection with poliovirus will lead to paralysis is increased by certain factors: a) more advanced age, b) triple seronegativity (absence of antibodies to all 3 poliovirus types), c) pregnancy, d) tonsillectomy, e) recent vaccinations, f) trauma, g) fatigue, and possibly h) the level of exposure.

Older patients and infants under 1 year of age generally have the most severe paralysis. Tonsillectomy may predispose persons to have paralysis of the affected limb(s). Physical exertion following the onset of CNS signs or symptoms may increase the severity of CNS involvement.

Poliovirus has been isolated from the stool as early as 19 days before onset of illness and as late as 3 months after onset. The mean duration of virus excretion cited in the literature is approximately 5 weeks after the onset of illness. The mean duration of excretion after OPV vaccination may also be about 5 weeks, beginning 2 days after vaccination. Figure 2 is a schematic diagram of the clinical and subclinical forms of poliovirus infection correlated with the times at which virus can be isolated from various anatomic sites and with the times of development of serum antibodies. Figures 3 and 4 illustrate the clinical course of both childhood and adult forms of acute poliomyelitis.

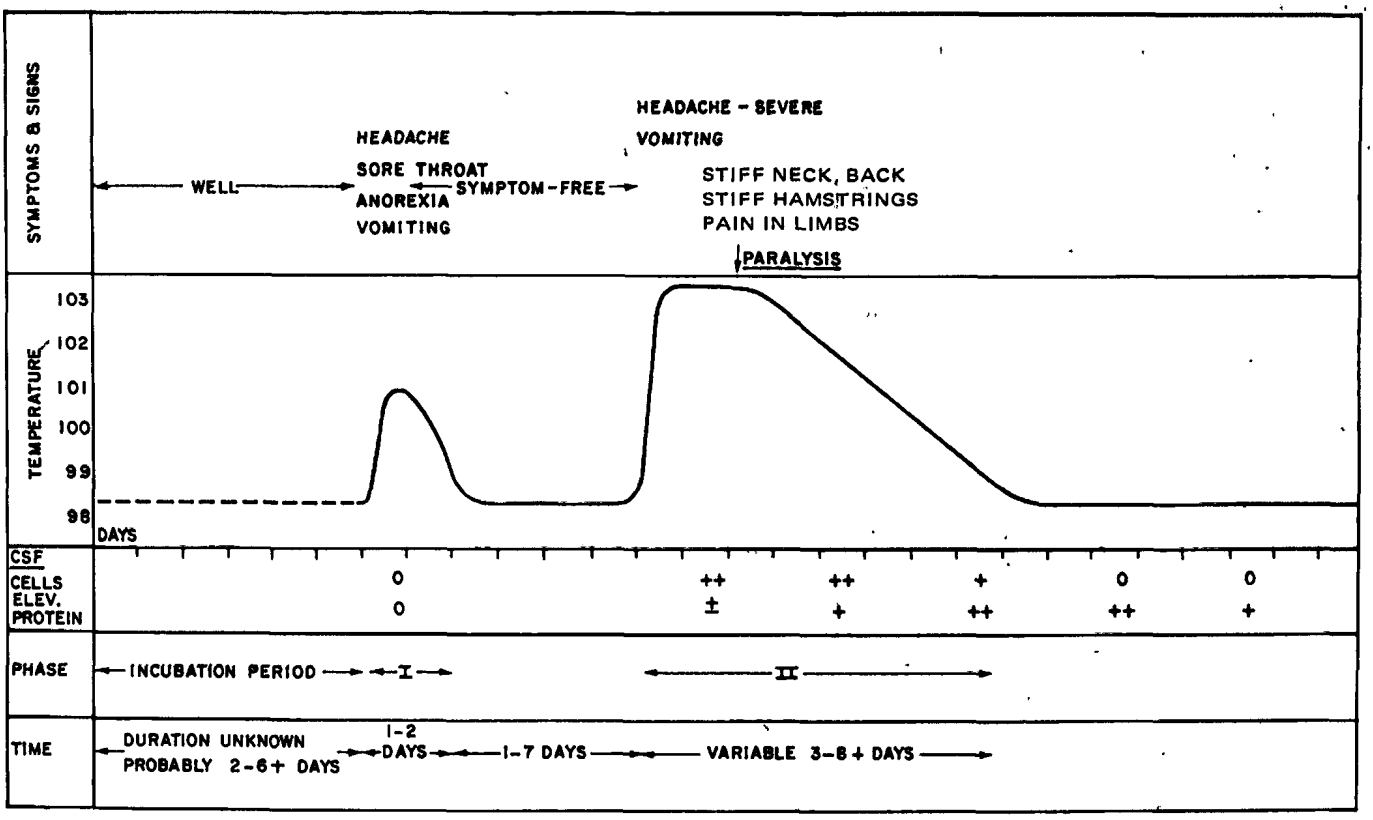
Treatment for poliomyelitis is essentially supportive. For nonparalytic disease, treatment is directed toward symptomatic relief of meningitis. Bed rest is encouraged.

Figure 2. Schema of clinical and subclinical poliomyelitis, correlated with virus isolation by site and with antibody production



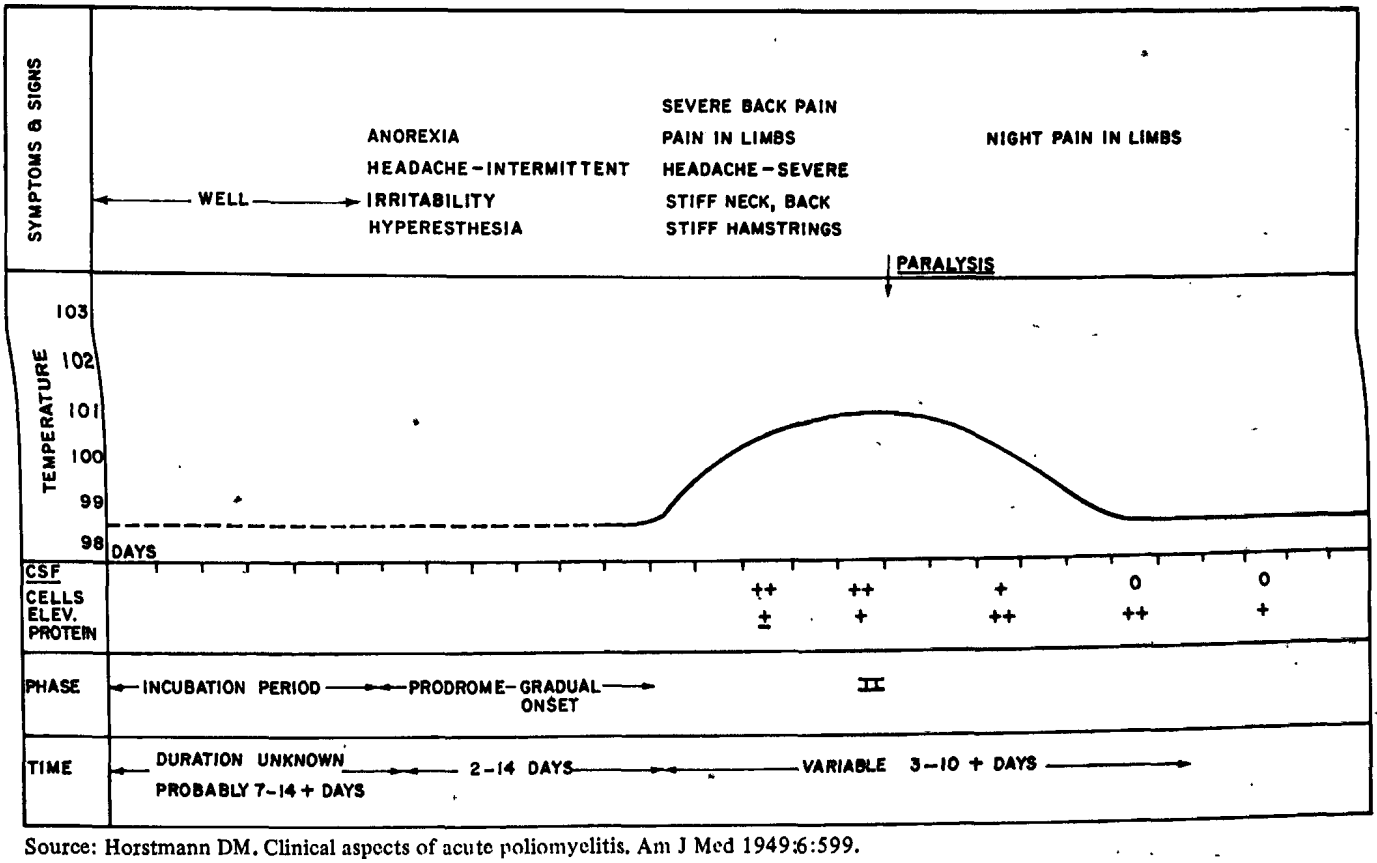
Source: Presented by Horstmann, DM, at the Symposium on Preventative Medicine, at the Thirty-Sixth Annual session of the American College of Physicians, Philadelphia, Pennsylvania, April 29, 1955.

Figure 3. Clinical course of "childhood-type" acute poliomyelitis



Source: Horstmann DM. Clinical aspects of acute poliomyelitis. Am J Med 1949;6:598.

Figure 4. Clinical course of "adult-type" acute poliomyelitis



Source: Horstmann DM. Clinical aspects of acute poliomyelitis. Am J Med 1949;6:599.

Treatment for paralytic poliomyelitis involves using all measures to save the life of the patient threatened by involvement of vital areas. Once the acute illness is over, weak muscles should be maintained in as good condition as possible, i.e., through physical therapy or bracing. Particular attention should be paid to emotional as well as social, economic, occupational, and physical rehabilitation considerations. Early in the course of the illness, a patient should avoid any physical exertion or chilling, as these may be predisposing factors to more severe CNS involvement.

Epidemiology

Since the beginning of the vaccine era, industrialized nations have for the most part effectively controlled poliomyelitis by using IPV or OPV. However, wherever pockets of susceptible persons remain, there is the potential for wild poliovirus transmission and hence for outbreaks of clinical poliomyelitis. This was demonstrated in 1978 in the Netherlands and in 1979 in the United States, when wild type 1 poliovirus circulated among members of religious groups that generally refuse vaccination.

In countries where poliomyelitis remains endemic, over 90% of cases affect children under 4-5 years of age. However, in industrialized areas, such as the United States, larger proportions of the few cases that continue to occur affect older children and young adults. This pattern probably reflects the slowing of the circulation of wild virus or its absence in the community as a result of the fact that a large proportion of the residents have been vaccinated or are otherwise immune as well as the fact that adults tend to have more severe illness than do children. The poliomyelitis attack rate for children is slightly higher for males, whereas for adults it is slightly higher for females.

The question of the correlation between poliovirus antibody titers and protection against infection or paralytic disease is often raised. Anyone with detectable neutralization antibodies should be considered immune to that specific poliovirus type. Many without detectable antibody are also immune, as can be demonstrated by a secondary-type IgG response upon rechallenge.

U.S. surveillance. Between 1969 and 1979 (through December 1), 186 cases of paralytic poliomyelitis were reported to the Center for Disease Control (CDC). Despite the small number of recent cases, a larger proportion —73 cases (39%)—were classified as vaccine-associated between 1969 and 1979 than in the previous comparable period. When data for the 43 cases occurring during the poliomyelitis epidemics of 1970, 1972, and 1979 are eliminated from calculations, 51% of these cases were associated with OPV. Vaccine-associated cases accounted for 21%-80% of the numbers reported each year of the 8 years in which no poliomyelitis outbreak occurred. Most vaccine-associated cases (68%) affected household contacts (53%) or nonhousehold contacts (15%) of vaccinees. The other 32% with vaccine-associated cases were OPV recipients.

An additional 11 cases affected immunodeficient persons vaccinated with OPV; data for these cases are included in the immune-deficient rather than the vaccine-associated category. There has been no recent documented cluster of vaccine-associated cases, either by vaccine lot or by transmission from a given patient.

The reported cases of paralytic poliomyelitis are classified epidemiologically into several categories:

I. Epidemic
   - A. No OPV 4-30 days before onset
   - B. OPV received 4-30 days before onset

II. Endemic
   - A. Endemic, not vaccine-associated
   - B. Recipient, vaccine-associated (OPV received 4-30 days before onset)
   - C. Contact, vaccine-associated (vaccinee received OPV 4-60 days before onset; contact within 30 days before onset)
     1. Household (vaccinee and patient regularly share same home for sleeping)
     2. Community or nonhousehold

III. Imported (poliovirus infection acquired outside the United States)
   - A. U.S. resident
   - B. Not U.S. resident

IV. Immune deficient

The total number of paralytic cases reported between 1969 and December 1, 1979, is shown by age group and epidemiologic classification in Table 1. Of the 186 persons affected, 125 (67%) had not been vaccinated against poliomyelitis (excludes implicated dose for persons with recipient, vaccine-associated cases), 55 (30%) had not had a complete vaccine series, 2 (1%) had had the complete series of 3 doses of trivalent OPV, and vaccination history was unknown for 4 (2%).

Laboratory Evaluation

Infection with poliovirus is confirmed by laboratory isolation of the virus or a 4-fold rise in antibody titer. However, a case of paralytic poliomyelitis is defined as a clinically compatible illness and 60-day residual paralysis *with or without* laboratory confirmation. This is particularly relevant to recipient, vaccine-associated cases, for which poliovirus isolation and antibody titer rise would be expected regardless of whether there is clinical illness.

Poliovirus is isolated most readily from the stool and can also be isolated early in the illness from the pharynx. Rarely, it can be isolated from the cerebrospinal fluid; the isolation of poliovirus from a CNS specimen is the strongest laboratory evidence that the clinical illness is indeed caused by poliovirus.

It is often important to characterize the poliovirus isolated as wild or vaccine-like. This is particularly important if the possibility of epidemic spread exists; to date, no documented epidemic has been attributed to vaccine-

Table 1. Age distribution of persons with poliomyelitis, by epidemiologic classification, 1969-1979[a]

	No. Cases (Class-Specific %)			
	Age in Years			
Epidemiologic Classification	<1-4	5-14	>15	Total
I. Epidemic	26(60)	6(14)	11(26)	43
II. Endemic				
A. Not Vaccine-Associated	18(46)	5(13)	16(41)	39
B. Recipient, Vaccine-Associated	21(91)	1(4)	1(4)	23
C. Contact, Vaccine-Associated	7(14)	1(2)	42(84)	50
III. Imported	10(50)	1(5)	9(45)	20
IV. Immunodeficient	10(91)	0	1(9)	11
Total	92	14	80	186
(Percentage of All Cases)	(49)	(8)	(43)	(4)

[a]Provisional data through December 1.

associated virus strains. The 4 tests currently used at CDC for strain characterization are a) temperature marker (rct), b) Wecker test (degree of virus breakthrough in the presence of specific anti-Sabin antiserum), c) van Wezel method (neutralization of test virus in the presence of cross-absorbed antisera to wild and Sabin strains), and d) oligonucleotide analysis (electrophoretic pattern of radiolabeled oligonucleotides of test virus).

Vaccines

Two poliomyelitis vaccines are available in the United States, IPV and OPV. When given as directed, both induce high titers for at least 95% of the vaccinees. The current vaccine of choice for routine use in this country is trivalent OPV, which has been available since 1963.

The OPV now being used is a trivalent oral vaccine. Three properly spaced doses should confer lifelong immunity, but a 1-time booster dose may be reccommended for adults who are at high risk of exposure to poliovirus. OPV vaccine provides not only sero-immunity to all 3 poliovirus types but intestinal immunity that protects the recipient from paralytic disease and in most cases prevents poliovirus carriage. OPV is a very safe and effective vaccine. Adverse reactions include the rare occurrence of paralytic poliomyelitis caused by OPV vaccination or contact with an OPV vaccinee. This reaction has been noted with about 1 of every 11 million doses of OPV distributed for recipient cases and with about 1 of every 5 million doses distributed for contact, vaccine-associated cases.

IPV is a killed-virus vaccine that was used extensively between 1955 and the early 1960's but has been largely replaced by OPV in the United States. IPV is recommended as the vaccine of choice in this country only for immunodeficient persons (or their household contacts) and for previously unvaccinated adults. A full series consists of 4 doses, 3 given 1 month apart and the 4th given 6 months after the 3rd. Booster doses are recommended every 5 years, but the need for them has not been well established. Adverse reactions to IPV include the small chance of hypersensitive reactions resulting from trace amounts of neomycin and streptomycin in the vaccine. A complete series of IPV provides excellent sero-immunity for at least 95% of persons vaccinated.

Vaccination Status

Two kinds of information indicative of the vaccination status of the U.S. population are available. One is the number of doses of poliovirus vaccine distributed each year in the United States. These data, as summarized for 1962-1978 in Table 2, represent the maximum possible utilization level rather than the actual number of doses given. More importantly, these data indicate trends in vaccination practice. The second source of information is the annual U.S. Immunization Survey.

After 1963, the rate at which IPV was distributed declined steadily to the low 1968 level of 2.7 million doses. Trivalent OPV was introduced in 1963, and the monovalent OPVs (types 1, 2, and 3) were no longer used by 1971. 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 vaccination series. Trivalent OPV is not the only *oral* vaccine in use. Essentially no IPV was used in the United States between 1969 and 1976. However, with the changes in recommendations of the Immunization Practices Advisory Committee (ACIP), in 1977 and again in 1979, which state that IPV should be used for vaccination of immunodeficient individuals and their families as well as for primary vaccination of adults, the demand and availability of IPV have increased. This trend is expected to continue. The overall decrease in the total number of doses of vaccine distributed each year since 1964 reflects a shift in emphasis from mass vaccination campaigns and community-wide programs to routine vaccination of infants. When OPV was introduced in the 1960s, adult recipients of the vaccine were found to be at increased risk of having paralytic poliomyelitis, and in 1965 routine vaccination of adults with OPV was discontinued.

The U.S. Immunization Survey is designed to estimate the immunization status of the population through a sample survey of the history of types and doses of vaccine received. Although this questionnaire method is not as accurate as surveillance involving serologic tests, it has

Table 2. Poliomyelitis vaccine distribution, net doses (millions) by year, United States, 1962-1978

Vaccine	1962[a]	1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978
IPV[b]	15.3	19.0	8.8	7.5	5.5	4.0	2.7	–	–	–	–	–	–	–	–	–	–
OPV[c]																	
MOPV[d]-1	33.1	38.7	24.9	4.7	1.4	1.3	0.5	0.4	0.3	0.2	–	–	–	–	–	–	–
MOPV-2	37.0	34.2	29.8	3.4	1.3	0.9	0.5	0.4	0.2	0.1	–	–	–	–	–	–	–
MOPV-3	13.7	54.2	28.4	3.7	1.4	1.0	0.6	0.4	0.3	0.2	–	–	–	–	–	–	–
TOPV[e]	–	4.2[f]	24.0	17.4	24.0	18.0	23.9	22.5	25.8	25.5	24.7	24.9	25.2	24.2	19.5	23.2	24.6
Total	99.1	150.3	115.9	36.7	33.6	25.2	28.2	23.7	26.6	25.9	24.7	24.9	25.2	24.2	19.5	23.2	24.6

[a] July-December (Biologics Surveillance Program began July 1962).
[b] Inactivated poliovirus vaccine.
[c] Live-attenuated oral poliovirus vaccine.
[d] Monovalent oral poliovirus vaccine (types 1, 2, and 3).
[e] Trivalent oral poliovirus vaccine.
[f] Production began in mid-1962.

proven useful in assessing the proportion of the population estimated to be immune to poliovirus infection.

Because 3 doses of trivalent OPV are considered a full primary series and because this is the vaccine used for most infants and children, percentages based on 3 or more doses of OPV serve as a satisfactory index of substantial protection, especially for schoolchildren. It is noteworthy that in 1978 only 61.4% in the 1- to 4-year-old group were thought to have substantial immunity. Of this age group, 7.9% had never been vaccinated, and the other 30.7% had not had a complete vaccine series. By the end of the National Childhood Immunization Initiative on September 30, 1979, over 90% of all school-age children had had a complete vaccine series.

Data for the 0- to 14-year olds who had received no poliovirus vaccine as of 1978 are presented in Table 3. Although percentages are small, they reflect the marked differences in the vaccination status of various segments of society, e.g., children in selected poverty and non-poverty areas. A similar gap is noted between vaccination status of whites and members of other races in the United States in general as well as in inner-city areas. There is a marked difference in the status of preschool versus school-age children that can be attributed mainly to vaccinations given when children are to enter school.

Immunization programs, especially the recent National Childhood Immunization Initiative, have gone far toward complete control of poliomyelitis in the United States. Nevertheless, even in a primarily immune population the potential for epidemic poliomyelitis exists wherever pockets of susceptible persons remain. The 1972 and 1979 outbreaks, both among religious sects that generally refuse vaccinations, illustrate this point. Continued importation of wild poliovirus strains from countries other than the United States that have ongoing epidemic and endemic poliomyelitis is reflected both by the occurrence of known imported cases and by the isolation of wild poliovirus from persons with cases classified as endemic, not vaccine-associated. The situation emphasizes the continued need to assure that a high proportion of persons in the United States are immune.

The U.S. surveillance data illustrate the changing picture

Table 3. Percentage of children 0-14 years of age with a history of ≥3 or of no doses of oral poliovirus vaccine, by race, SMSA,[a] United States Immunization Survey, 1978

Components and Geographic Divisions	≥3 Doses OPV	No OPV
United States Total	65.2	7.5
Race White	68.6	6.3
All Other Races	48.7	13.0
Poverty Status: Poverty	58.4	9.9
Nonpoverty	67.0	6.8
Non SMSA	66.5	7.3
Poverty Status: Poverty	62.3	8.7
Nonpoverty	68.8	6.5
Total SMSA Components	64.5	7.6
Total SMSAS Central Cities	60.1	9.1
Race: White	65.6	6.9
All Other Races	49.1	13.6
Poverty Status: Poverty	50.9	12.4
Nonpoverty	62.9	8.1
Remaining Areas in SMSA	67.4	6.6
Poverty	57.3	10.0
Nonpoverty	68.1	6.3
Geographic Divisions		
New England	69.0	4.7
Middle Atlantic	66.6	6.9
East North Central	64.3	7.7
West North Central	67.4	7.8
South Atlantic	60.5	8.7
East South Central	65.3	6.3
West South Central	65.2	7.9
Mountain	71.3	6.6
Pacific	64.9	8.1

[a] Standard Metropolitan Statistical Area.

of poliomyelitis in this country. In the prevaccine days, the overwhelming majority of people who had poliomyelitis were preschool-age children. With the present widespread use of the live-attenuated poliovirus vaccine (OPV), most cases are vaccine-associated and affect susceptible adult contacts of recently vaccinated children.

SELECTED BIBLIOGRAPHY

Abramson H, Greenberg M. Acute poliomyelitis in infants under one year of age: epidemiological and clinical features. Studies in epidemiology: selected papers of Morris Greenberg, M.D. New York: GP Putnam's Sons, 1965:182-95.

American Public Health Association. Poliomyelitis. In: Benenson AS. Control of communicable diseases in man. 12th ed. 1975:240-5.

Center for Disease Control. Follow-up on poliomyelitis—United States, Canada, MMWR 1979;28:309.

Center for Disease Control. Poliomyelitis surveillance report: 1974-1976. Atlanta, 1977.

Center for Disease Control. Poliomyelitis—United States, 1978-1979. MMWR 1979; 28:483.

Fenner FJ, White DO. Medical virology. 2nd ed. New York: Academic Press, 1976.

Horstmann DM. Clinical aspects of acute poliomyelitis. Am J Med 1949; 6:592-605.

Horstmann DM. Viral vaccines and their ways. In: Reviews of infectious diseases. 1979;1:502-8.

Schonberger LB, McGowan JE Jr, Gregg MB. Vaccine-associated poliomyelitis in the United States, 1961-1972. Am J Epidemiol 1976; 104:202-11.

Weinstein L. Poliomyelitis. In: Harrison's principles of internal medicine. 8th ed. New York: McGraw Hill, 1977:999-1005.

Rabies

Rabies, one of the oldest diseases known to society, is caused by a rhabdovirus. It is a bullet-shaped ribonucleic-acid (RNA) virus, 50 nm by 165 nm, and is readily inactivated by heat, light, and ultraviolet light. All warm-blooded animals are susceptible, but only certain species, primarily carnivores and bats, are usually important in the epidemiology of rabies. Rabies is usually transmitted by a bite of a rabid animal. After the virus enters an animal, it spreads through the peripheral nerves to the central nervous system. There it replicates, causes encephalitis that is usually fatal, and spreads to the periphery again through the nerves. A common site of peripheral infection is the salivary gland, and virus shed from an infected salivary gland can be transmitted to a person or another animal by a bite.

Democritus in the 5th century B.C. described the clinical picture of nonhuman rabies, and Celsus in A.D. 100 made the association between the bite of a rabid animal and human rabies. The first rabies in the United States was reported from the east coast in the 1750s, and by 1899 the disease had spread to California.

Animal Rabies

Until relatively recently, domestic animals accounted for most of the reported cases of rabies in the United States. In 1953, for example, domestic animals (primarily dogs and cats) accounted for 83% of reported cases of rabies, whereas wild animals accounted for only 17% (Figure 1). However, domestic animal vaccination and animal control programs implemented in 1946 gradually changed this situation. In 1960, reported cases of rabies among wild animals exceeded reported cases among domestic animals for the first time, and by 1978, only 14% of cases affected domestic animals and 86% affected wild animals. This shift resulted from a marked decrease in the incidence of canine and feline rabies—from 6,226 cases in 1953 to only 192 in 1978. Numbers of reports of rabies affecting wild animals rose from 1,479 in 1953 to 2,749 in 1978—possibly because of more effective surveillance.

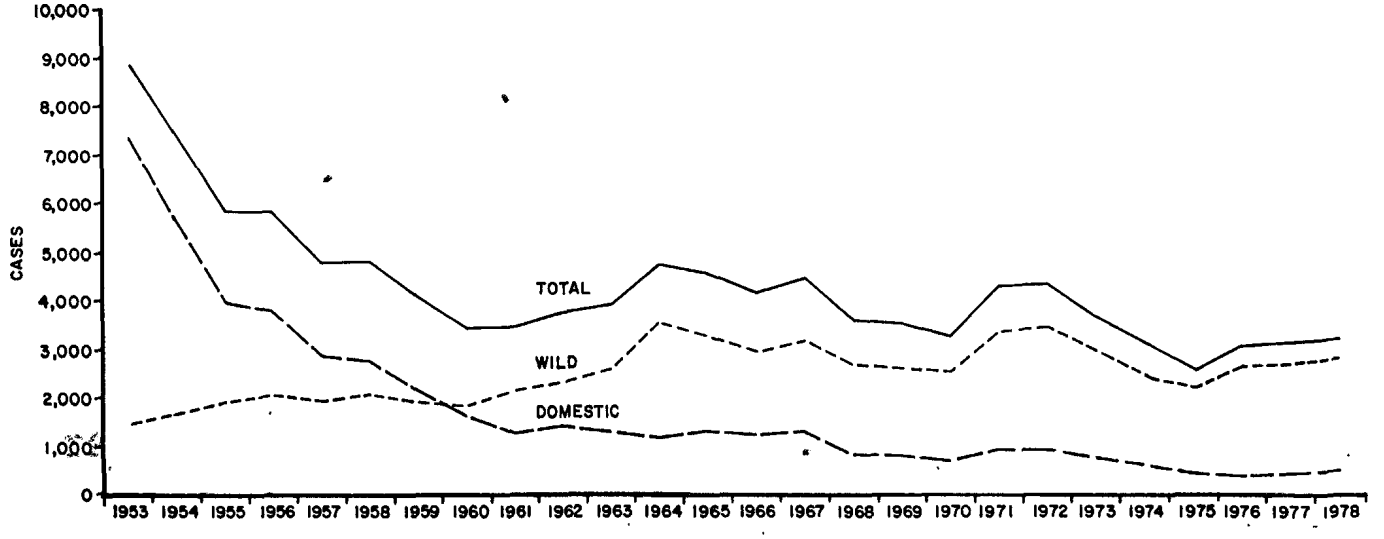
In 1978, the most common reports of rabies among domestic animals were for dogs (25.2%), cats (19.4%), and cattle (45.0%). In 1978, 98.8% of the 2,749 cases of rabies among wild animals affected skunks (59.4%), bats (19.4%), raccoons (14.8%), and foxes (5.2%).

Although rabies has been reported from all states except Hawaii, the primary animal species involved varies from state to state. For example, skunks are the principal species in the central and midwestern states, Texas, and California; raccoons predominate in Georgia, Florida, and parts of South Carolina and Alabama; rabid bats are reported throughout the country. Rodents and lagomorphs rarely have naturally acquired rabies. The extent of the rabies problem also varies from state to state, with Georgia, Minnesota, Oklahoma, Texas, and California each reporting over 200 rabid animals, and Delaware, Hawaii, Rhode Island, and Vermont each reporting fewer than 5 cases in 1977. Some regions within states have been free of terrestrial rabies for many years (Figure 2).

Human Rabies

Infection and diagnosis. The incidence of human rabies in the United States has declined markedly, from 33 cases in 1946 to between 1 and 5 cases per year since 1960 (Figure 3). This marked decrease in the number of human cases reflects the much lower incidence of rabies for cats and

Figure 1. Cases of rabies reported for wild and domestic animals by year, United States, 1953-1978



dogs. However, despite this fact, dog and cat bites still lead to approximately one-third of the estimated 30,000 postexposure rabies treatments given in the United States each year. Of the 173 persons who had rabies in the period 1946-1979 and whose source of exposure was known, 133 (77.3%) were bitten by dogs, 27 (15.7%) were bitten by wild animals, 10 (5.8%) were bitten by cats, 2 (1.2%) were infected through laboratory accidents, and 1 (0.6%) was infected by a transplanted cornea (Table 1). As human rabies becomes rarer in the United States, unusual exposures such as laboratory accidents and the corneal transplant incident, unknown sources of infection, and cases unsuspected until postmortem examination have received relatively more attention. In 1978 and 1979, the sources of 4 of 9 cases of human rabies could not be determined even after careful questioning of family members, friends, and fellow workers; 3 of the 9 cases were not even suspected until postmortem examination. These cases point up the difficulty of diagnosing rabies when no history of an exposure is obtained and the classic symptoms of rabies are not present. Rabies should be suspected when any patient has severe progressive encephalitis or atypical Guillain-Barré syndrome. Rabies can sometimes be diagnosed if fluorescent antibody (FA) tests of corneal impressions of

Figure 2. Counties reporting animal rabies, 1977

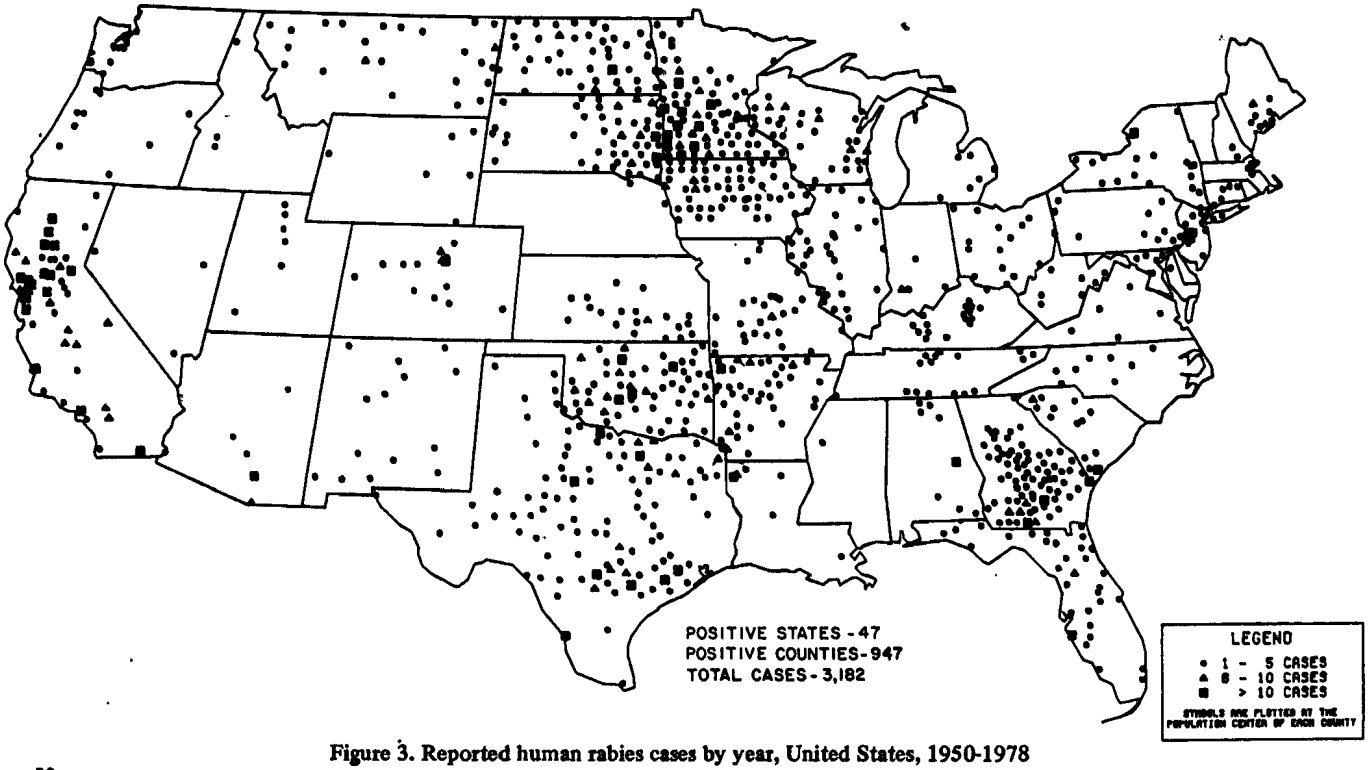
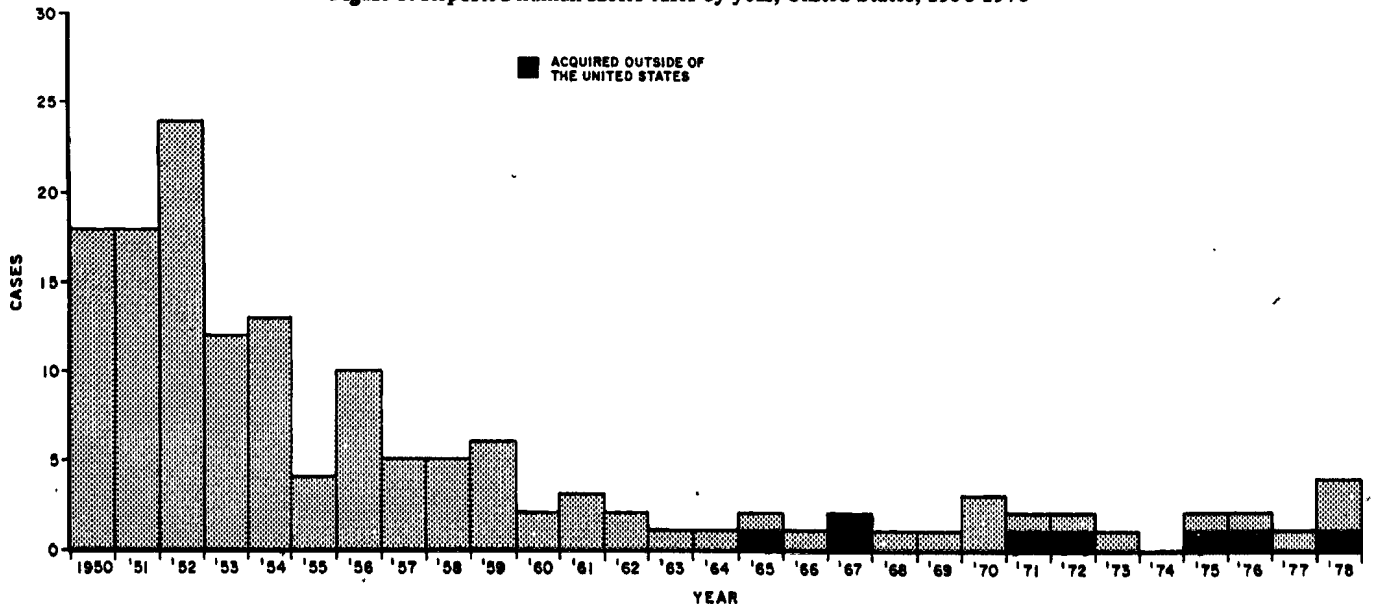


Figure 3. Reported human rabies cases by year, United States, 1950-1978



neck-skin biopsy specimens are done soon after the patient has clinical symptoms. The disease can also usually be diagnosed by the end of the second week of illness by testing serum or cerebrospinal fluid (CSF) for antibodies, and sometimes the virus can be isolated in saliva, respiratory secretions, CSF, and other specimens. If the patient dies, rabies is usually diagnosed on the basis of virus isolation or the results of FA testing of brain specimens, although the disease can also be diagnosed by identifying Negri bodies with light microscopy and rhabdovirus with electron microscopy.

Only 2 persons are known to have survived documented rabies infections in the United States. In 1970, a 6-year-old boy had clinical rabies 20 days after having been bitten by a proven rabid bat and then receiving 15 doses of duck embryo vaccine (DEV) without any antirabies serum or globulin. With intensive supportive care, the boy survived the acute illness in about 3 months and completely recovered his intellectual and motor functions. The second case affected a 32-year-old laboratory worker who presumably inhaled live rabies virus in the laboratory in April 1977. He had been vaccinated before being exposed and had had a rabies antibody titer of 32 as recently as November 1976. Although intensive supportive care enabled him to survive the acute illness, he apparently suffered substantial permanent neurologic damage.

Prophylaxis. Persons who have a rabies exposure that warrants postexposure prophylaxis should have the wound thoroughly cleansed with soap and water as soon as possible after the exposure and should be given human rabies immune globulin (HRIG) and rabies vaccine. HRIG (or antirabies serum if HRIG is not available) should be given at once at the beginning of therapy. Up to half the dose of HRIG should be injected at the site of the wound, and the rest should be given intramuscularly. The vaccine series should be started as soon as possible after the exposure. The vaccine of choice contains the human diploid cell strain (HDCV). The World Health Organization recommends that 6 doses of HDCV (1 each on days 0, 3, 7, 14, 30, and 90) be given intramuscularly. The Center for Disease Control is evaluating a 5-dose regimen that omits the 90-day dose.

If HDCV is not available, DEV can be given in a series of 21 doses (once a day for 21 days or twice a day for 7 days and then once a day for another 7 days plus 2 booster doses 10 and 20 days after the last dose of the primary series). Serum obtained when the last dose of HDCV or DEV is given should be tested for rabies antibody.

HDCV and DEV are safe enough to allow persons at substantial risk of rabies exposure to have preexposure vaccination. High-risk groups include veterinarians, animal handlers, certain laboratory workers, and persons—especially children—who live in or visit countries where rabies is a constant threat. If HDCV is available, 3 doses should be given intramuscularly (1 each on days 0, 7, and 21 or 28). If DEV is used, 2 doses should be given subcutaneously (1 each on days 0 and 30), followed by a third dose 6 to 7 months later, or 3 doses should be given subcutaneously (1 each on days 0, 7, and 14), followed by a fourth dose 3 months after the third. In every instance, serum should be tested for rabies antibody 2-3 weeks after the last dose of vaccine is given.

Table 1. Human rabies cases, by 4-year period and source of exposure, United States, 1946-1979

Year	Total Cases	No. Cases with Reported Exposure Source	Source of Exposure[a]							
			Domestic Animals			Wild Animals				
			Dog	Cat	% of Total	Fox	Skunk	Bat	Bob-Cat	% of Total
1946-1949	94	48	43	5	100	0	0	0	0	0
1950-1953	81	54	47	2	91	3	1	1	0	9
1954-1957	37	29	23	1	83	1	3	1	0	17
1958-1961	18	15	7	1	53	3	1	3	0	47
1962-1965	5	5	3[b]	0	60	0	1	1	0	40
1966-1969	5	4	2[b]	0	50	0	1	0	1	50
1970-1973	8	8[c]	2[b]	0	29	0	2	3[d]	0	71
1974-1979 (6 yrs)	15	10[e]	6[f]	1	70	0	0	1	0	10
Total	263	173	133	10	83	7	9	10	1	16

[a] Confirmed or most probable source.
[b] Exposure not in Continental United States.
[c] Includes 1 laboratory exposure.
[d] One person recovered.
[e] Includes 1 laboratory and 1 corneal transplant exposure.
[f] Includes 5 exposures not in the Continental United States.

Rh Hemolytic Disease

Prevention of Rh hemolytic disease of the newborn is among the recent major advances of preventive medicine. In 1932, 4 perinatal diseases (late fetal death with erythroblastosis, hydrops fetalis, icterus gravis neonatorum, and congenital anemia of the newborn) were recognized as manifestations of the same pathologic process—erythroblastosis fetalis or hemolytic disease of the newborn. The pathogenesis of the disease was determined 9 years later; over the next 25 years, improvements in diagnosis, the use of amniocentesis, and treatment with intrauterine transfusions and exchange transfusions significantly reduced mortality caused by hemolytic disease. Prevention of the disease became possible in 1968 when Rh immune globulin (official name, Rh [D] Immune Globulin [Human]) was licensed for use in the United States. This Rh immune globulin (RhIG), used appropriately, can reduce the incidence of Rh hemolytic disease among neonates to a very low level.

The Disease Process

The pathogenesis of the disease involves 2 sequential events and usually 2 separate pregnancies. The first event is sensitization of the Rh-negative woman to Rh antigen, and the second is maternal production of anti-Rh antibody. Maternal sensitization occurs when an adequate volume of fetal Rh-positive red blood cells passes into the maternal circulation. Low-volume transplacental fetal-maternal bleeding occurs throughout pregnancy but is not usually sufficient to cause maternal sensitization. However, about 1% of Rh-negative primigravidas with Rh-positive infants have dectectable anti-Rh antibodies at delivery, probably because of the earlier transplacental bleeding (*1*). A more common cause of maternal sensitization is the relatively extensive fetal-maternal bleeding associated with spontaneous and induced abortions, ectopic pregnancies, amniocentesis, and delivery. (Sensitization can also be caused by transfusing Rh-positive blood into an Rh-negative recipient, but this rarely happens in the United States.) Not all Rh-negative women exposed to Rh-positive blood will become sensitized, although we cannot yet predict which women will be sensitized. Maternal sensitization is permanent.

The second event, which occurs sometime during a later Rh-incompatible pregnancy, is accelerated production of anti-Rh antibody by the mother. During the incompatible pregnancy, newly formed maternal antibodies cross the placenta, enter the fetal circulation, and destroy the Rh-positive red blood cells of the fetus. The clinical severity of Rh hemolytic disease is related to the amount of fetal red blood cell destruction. A small amount of destruction may only cause jaundice or mild anemia, whereas a large amount will lead to the stillbirth of a severely hydropic infant. Clinical manifestations of hemolytic disease are most severe in Rh-incompatible, ABO-compatible pregnancies. Hemolytic disease becomes increasingly severe with each succeeding Rh-incompatible pregnancy.

Treatment

With the understanding of this sequence of events, investigators developed the concept of preventing maternal Rh sensitization by suppressing women's initial immune response. Giving women at risk of sensitization an injection of RhIG within 72 hours after abortion, amniocentesis, ectopic pregnancy, or delivery usually prevents maternal sensitization. Those at risk of Rh sensitization are unsensitized, Rh-negative or D^u-negative women with Rh-positive fetuses. Since the Rh status of in utero and aborted fetuses is unknown, they are assumed to be Rh positive, and therefore RhIG should be given to the Rh-negative, unsensitized mother after abortion or amniocentesis—except when the father is known to be Rh negative. (Since all offsprings will be Rh negative, RhIG is not required.) With random mating of individuals of the same race, 9.2% of the pregnancies of whites, 4.5% of those of blacks, and 0.9% of those of Native Americans and Asian Americans would be Rh incompatible (*2*).

The exact mechanism by which RhIG prevents maternal sensitization is not known, although a number of clinical trials have repeatedly documented its efficacy (*1*). In only about 1% of cases is RhIG reported not to prevent maternal sensitization.

Morbidity and mortality attributable to Rh hemolytic disease declined significantly in the 1970s. In the United States, after a rapid drop between 1970 and 1974, incidence continued to decline more slowly. In 1977, the national rate was estimated as 16.3 cases per 10,000 births, compared with the estimated rate of 40.7 cases per 10,000 births in 1970 (*3*). Although much of the decline can be attributed to the use of RhIG, trends toward smaller family size and the fact that the women who were sensitized before RhIG was available are leaving the childbearing age range have also helped reduce incidence.

Recommendations

Rh immune globulin should be given to all unsensitized Rh-negative women at risk of sensitization from contact with Rh-positive blood as a result of abortion, amniocentesis, ectopic pregnancy, or delivery. Potential recipients of RhIG are 1) women who are Rh negative and D^u-negative, 2) those who have no circulating anti-Rh antibodies (i.e., are unsensitized), 3) those whose infants are confirmed as being Rh positive or D^u positive by typing, and 4) those whose mates are of unknown Rh status or are Rh positive

and who have an abortion, ectopic pregnancy, or amniocentesis.

Delivery: The most common cause of Rh sensitization is the birth of an Rh-positive infant to an Rh-negative woman. Not all experts agree on the amount of the recommended postpartum dose. However, a dose of 300μg usually provides adequate protection. If a large fetal-maternal exchange is suspected, the volume should be measured, ant the dose of RhIG adjusted to reflect that volume. For each ml of fetal red blood cells in maternal circulation, 20 μg of RhIG should be given within 72 hours postpartum. An adequate dose of RhIG must be given after each Rh-positive child is born.

Prenatal Care. Routinely, when prenatal care begins, women should be blood and Rh typed and screened for antibody. For all Rh-negative women, screening should be repeated when they are 26-28 weeks pregnant and again at delivery. Repeated screening is necessary to detect antibody that may appear later in pregnancy. Presence of antibody indicates the need for special obstetric management.

Abortion: RhIG should be given to unsensitized, Rh-negative women within 72 hours after a spontaneous or induced abortion. Generally, a dose of 50 μg is sufficient to prevent sensitization after an abortion in the first trimester. However, if extensive fetal-maternal bleeding is suspected, or if the abortion occurs in the second trimester, the Kleihauer test should be performed to detect fetal red blood cells in the maternal circulation. For each ml of fetal red blood cells, 20 μg of RhIG should be given (*1*).

Ectopic pregnancy. All unsensitized, Rh-negative women should receive a protective dose of RhIG, as determined by the Kleihauer test, within 72 hours after the termination of an ectopic pregnancy. For each ml of fetal red blood cells in the maternal circulation, 20 μg of RhIG should be given.

Amniocentesis. Fetal-maternal bleeding can occur after amniocentesis done in the second or third trimester. However, data on the risk of sensitization after amniocentesis are not available. Unsensitized, Rh-negative women should be given a prophylactic dose of 300 μg of RhIG within 72 hours after amniocentesis. If RhIG is given in the second trimester, another 300-μg dose should be given at 28 weeks of pregnancy to maintain protective levels of RhIG through the third trimester. If the infant is Rh positive, RhIG must also be given postpartum.

Antepartum hemorrhage. The risk of sensitization after a spontaneous or traumatic antepartum hemorrhage has not been established. To avoid potential sensitization, RhIG is recommended if fetal red blood cells are found in the maternal circulation. The dose of RhIG should be calculated on the basis of the volume of fetal red blood cells in maternal circulation, allowing 20 μg of RhIG for every ml of fetal blood cells. The doses should be given as soon as possible, within 72 hours after the hemorrhage.

Transfusion error. Rarely, Rh-negative individuals may receive a transfusion of Rh-positive blood. To prevent sensitization, especially for the premenopausal woman, RhIG should be given within 72 hours after the transfusion. For each ml of Rh-positive whole blood transfused, 20 μg of RhIG is recommended. The dose of RhIG can be divided into multiple injections to be given at 12-hour intervals if the entire dose is given within 72 hours after the transfusion.

REFERENCES

1. Davey MG. McMaster Rh Conference Proceedings. Vox Sang, 1979; 36:50-64.

2. Lin-Fu JS. Prevention of hemolytic disease of the fetus and newborn due to Rh isoimmunization. Washington, D.C.: Government Printing Office, 1975.

3. Center for Disease Control. Rh hemolytic disease, United States, 1968-1977. MMWR 1978; 27:487-9.

Rocky Mountain Spotted Fever

Only 5 rickettsial diseases are known to occur in the United States at present: Rocky Mountain spotted fever, Brill's disease, murine typhus, Q fever, and rickettsialpox. Of these, only Rocky Mountain spotted fever is associated with substantial morbidity and mortality; it accounts for over 90% of the reported cases of human rickettsial disease in the United States. It was first recognized as a clinical entity in 1895, and the causative organism, *Rickettsia rickettsii*, was isolated in 1911 by Howard Taylor Ricketts.

Epidemiology

National surveillance data on Rocky Mountain spotted fever have been collected since 1920. The number of reported cases climbed steadily until the late 1940s and then declined sharply. This decline was attributed to the introduction of broad-spectrum antibiotics and the attendant decrease in the number of complications and mortality associated with this disease. However, in 1960 the number of cases reported each year began rising, and peaked at 1,153 in 1977. In 1978, the number of reported cases fell slightly to 1,063, and in 1979, reports of 1,035 cases were received. The distribution of reported cases for 1978 is shown in Figure 1. The overall increase largely reflects cases reported from the Southeast. In 1979, 595 cases (58%) were reported from the South Atlantic states of Delaware, Maryland, Virginia, West Virginia, North Carolina, South Carolina, Georgia, and Florida and from the District of Columbia. The Rocky Mountain states of Montana, Idaho, Wyoming, Colorado, New Mexico, Arizona, Utah, and Nevada, which gave the disease its name, reported only 17 cases, or 2% of all reports.

The incidence of cases of Rocky Mountain spotted fever reported in the United States per 100,000 population for the 3 decades 1950-1978 is shown in Figure 2. The pattern of rising incidence demonstrates that Rocky Mountain spotted fever is an unsolved public health problem, particularly in the East. The trend has been attributed to a continuing move to the suburbs, which leads to larger numbers of people living, working, and vacationing in areas where ticks are found.

Since 1970, the Center for Disease Control has collected epidemiologic data on individual cases of Rocky Mountain spotted fever. Most victims are children 2 to 14 years old, and 85% of cases occur between April and October. The most common symptoms are fever, malaise, macular rash, headache, and myalgia. In 1976, the overall case-fatality ratio was 4.9% but for patients over 40 years old, it was 14.9%. Over half the patients were reported to

Figure 1. Rocky Mountain spotted fever—reported cases by county, United States, 1978

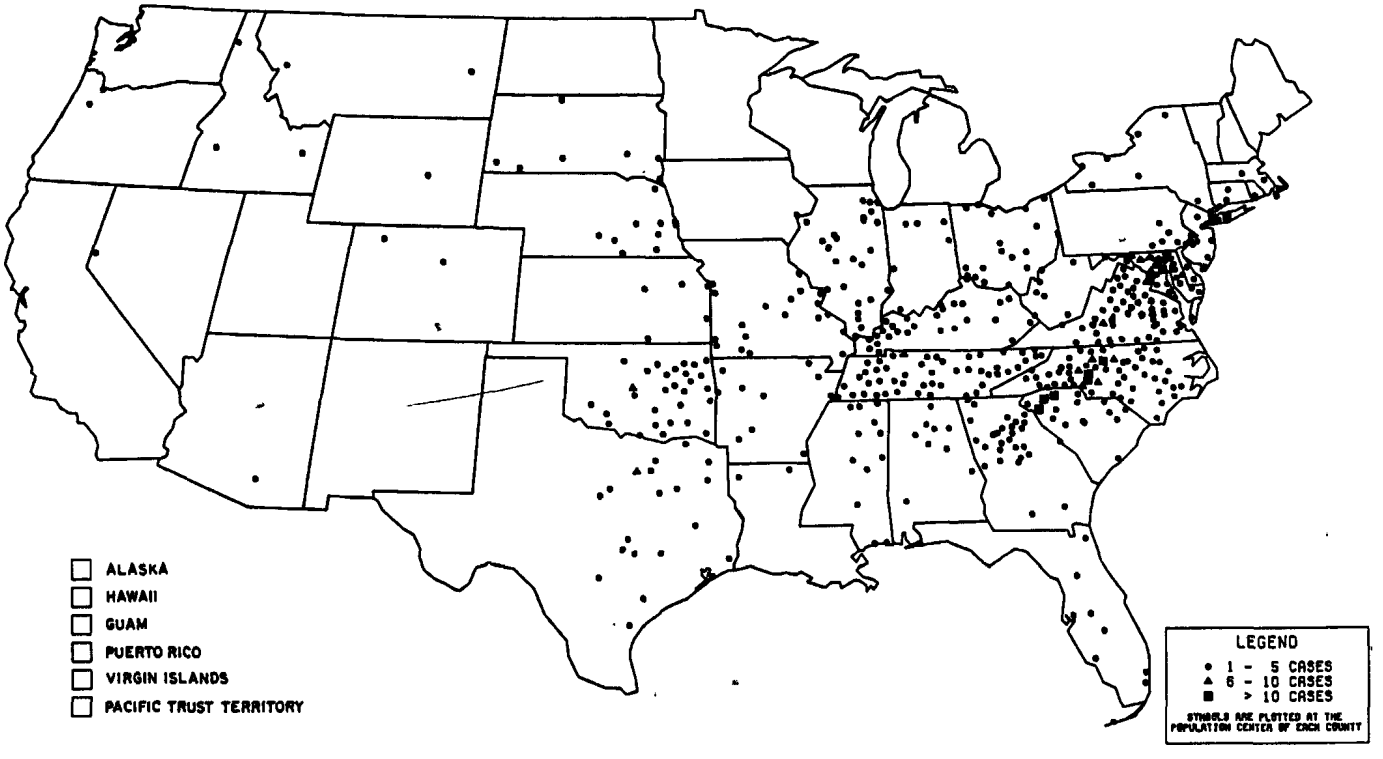
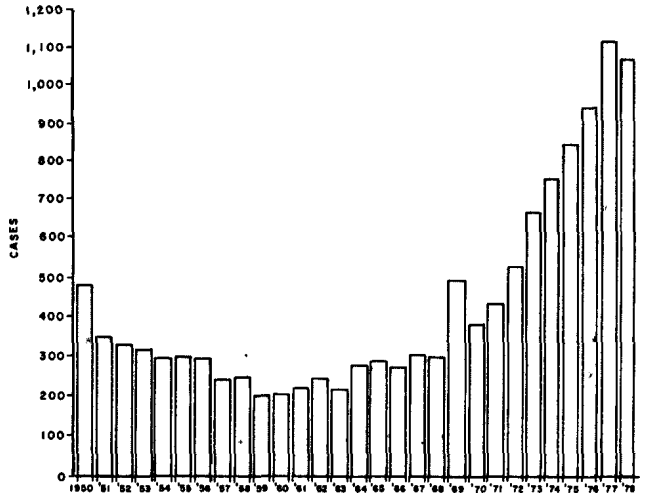


Figure 2. Reported cases of Rocky Mountain spotted fever, United States, 1950-1978



have tick bites or attached ticks and were reported to have been exposed to tick-infested woods or to dogs with ticks.

Vaccines

The first Rocky Mountain spotted fever vaccine, prepared from phenol-inactivated, homogenized, infected ticks, was extensively used in the Rocky Mountain region from 1927 to 1945. The vaccine appeared to reduce the severity of the disease but did not clearly reduce its incidence. In 1941, a vaccine containing *Rickettsia* grown in chick eggs was developed. This vaccine protected guinea pigs to some degree from Rocky Mountain spotted fever. Its efficacy for humans remained controversial, and because it failed to meet standards established by the Bureau of Biologics of the Food and Drug Administration, it is no longer available. A vaccine currently being developed to replace the older vaccines contains *Rickettsia* grown in cell cultures and has greater immunogenicity for humans.

The low incidence of Rocky Mountain spotted fever makes prophylactic use of a vaccine against it impractical for the population at large; however, the new vaccine can be given to laboratory personnel working with Rocky Mountain spotted fever organisms and to individuals continuously exposed to areas heavily infested with ticks. Regardless of whether vaccine is used, protective clothing and conscientious removal of ticks are important in preventing this disease. Because serologic test results do not confirm the presence of Rocky Mountain spotted fever in the first week of illness, treatment with appropriate antibiotics (tetracycline or chloramphenicol) should be started promptly when a case history or clinical findings suggest Rocky Mountain spotted fever.

Rubella (German Measles)

Rubella was first recognized as a distinct clinical entity in the early 1800s in Germany. It was regarded merely as a disease of children and young adults until 1941 when Gregg noted the association between rubella infection in early pregnancy and certain congenital defects, particularly cataracts and heart disease. His observations clearly established the public health significance of rubella and heightened interest in the disease. In 1962, 2 groups—Parkman, Beuscher, and Artenstein, and Weller and Neva—isolated the causative virus, thereby paving the way for developing a vaccine.

In 1964, a rubella pandemic swept the United States with dramatic results—an estimated 20,000-50,000 babies had congenital rubella syndrome (CRS), and excess fetal and neonatal deaths were in the thousands. Congenital heart disease, cataracts, and deafness were the predominant defects of affected infants. Several other abnormalities frequently observed included a thrombocytopenic purpura, long bone radiolucencies, hemolytic anemia, hepatitis, and jaundice. In addition, the ability of infants with CRS to shed virus for several months after birth was confirmed.

In 1966, rubella virus was attenuated by Parkman and Meyer. After extensive field trials, 3 live-attenuated virus vaccines were licensed in June 1969. Since then, approximately 100 million doses have been distributed in the United States. In February 1969, the strain of vaccine virus produced in human diploid cells was made available in the United States. Rubella vaccines have been shown to stimulate antibody production in at least 90% of vaccinees and to be 90%-95% protective. Although vaccine-induced neutralizing antibody titers are lower than those induced by naturally acquired rubella, they have been shown to persist for at least 9 years after vaccination. Most importantly, vaccine-induced immunity protects against viremia and transplacental passage.

Postnatal rubella is generally a mild disease, characterized by a 1- to 3-day rash, low-grade fever, and lymphadenopathy, especially postauricular and suboccipital. Transient arthralgia and arthritis frequently affect adult females and sometimes affect adult males and children. Up to 50% of all infections may be inapparent. Rare complications of rubella include postinfectious encephalitis and thrombocytopenic purpura. The incubation period for rubella is 14-21 days, usually 18 days. Infected persons can transmit the infection usually from 3-4 days before onset of rash to about 1 week after rash appears.

Current Trends

Rubella did not become a nationally reportable disease until 1966; however, many areas have maintained rubella surveillance for decades and have reported cases voluntarily to the Center for Disease Control (CDC). Since these data vary markedly in accuracy and completeness, they must be interpreted cautiously. Nevertheless, they depict trends of rubella in the United States.

The reported incidence of rubella from 1928 through 1978 in 10 selected areas is shown in Figure 1. The annual incidence of rubella has varied considerably. Major epidemics occurred in 1935, 1943, and 1964, and incidence was high in 1952 and 1958. On the basis of these data, a major epidemic was expected to occur in the early 1970s. It never materialized, however, probably because of the widespread vaccination of children, the primary transmitters of infection.

The number of reported rubella cases in the United States dropped dramatically with widespread use of the rubella vaccine to an all-time low of 11, 917 cases in 1974 (Figure 2). Although the incidence of reported rubella has fluctuated in recent years, the 18,269 cases reported in 1978 represent a 10.4% decrease from the 20,395 cases

Figure 1. Rubella incidence in 10 selected areas,* United States, 1928-1978

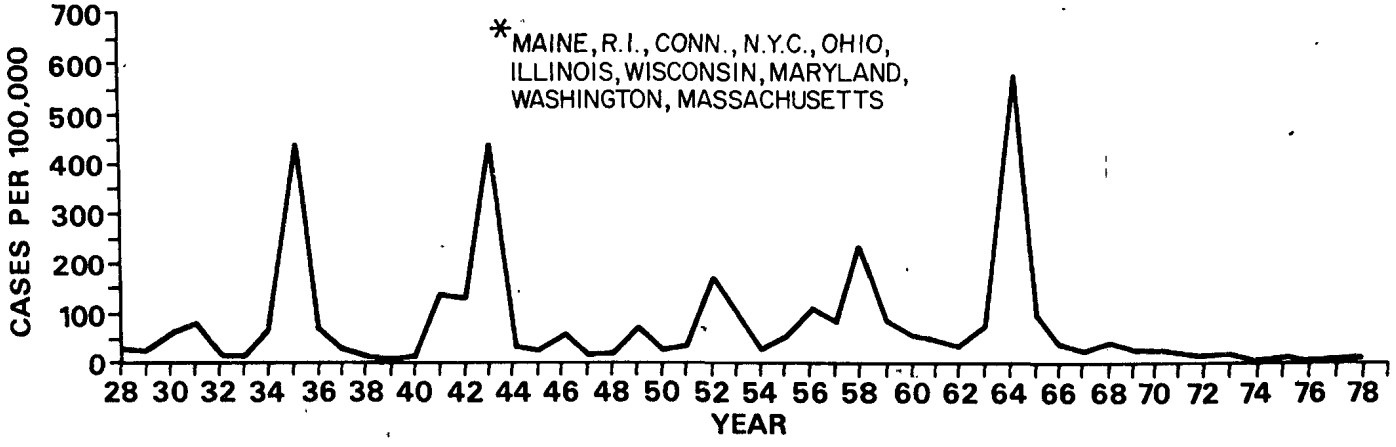


Figure 2. Rubella cases by year of report, United States, 1966-1979*

*1980 annual incidence rate for rubella was extrapolated from the number of cases for the first 30 weeks of 1980.

reported in 1975 but a 63.3% increase over the 12,491 cases reported in 1976.

Reported rubella has a seasonal pattern, with the number of cases rising in early winter, peaking in spring, and falling to a low point in late summer and autumn (Figure 3).

When the vaccine was licensed, serologic and epidemiologic data indicated that elementary school children were the primary reservoir for the rubella virus and were largely responsible for disseminating the virus in the community. Thus, rubella vaccination programs in the United States were directed at children ages 1 year to puberty, with the highest priority group being those in early grades of elementary school Secondary emphasis was placed on vaccinating susceptible postpubertal females. Since rubella vaccine began being used widely for young children, reported rubella incidence for this age group has declined markedly, and a greater proportion of cases have affected adolescents and young adults (Figure 4, Table 1). Outbreaks among high school and college students, military recruits, and certain employees (especially those in hospitals) have assumed increasing importance. Because of this trend, together with the fact that about 15% of all adults are still susceptible to rubella, vaccination for susceptible post-

Figure 3. Rubella cases by week of report, United States, 1972-1978

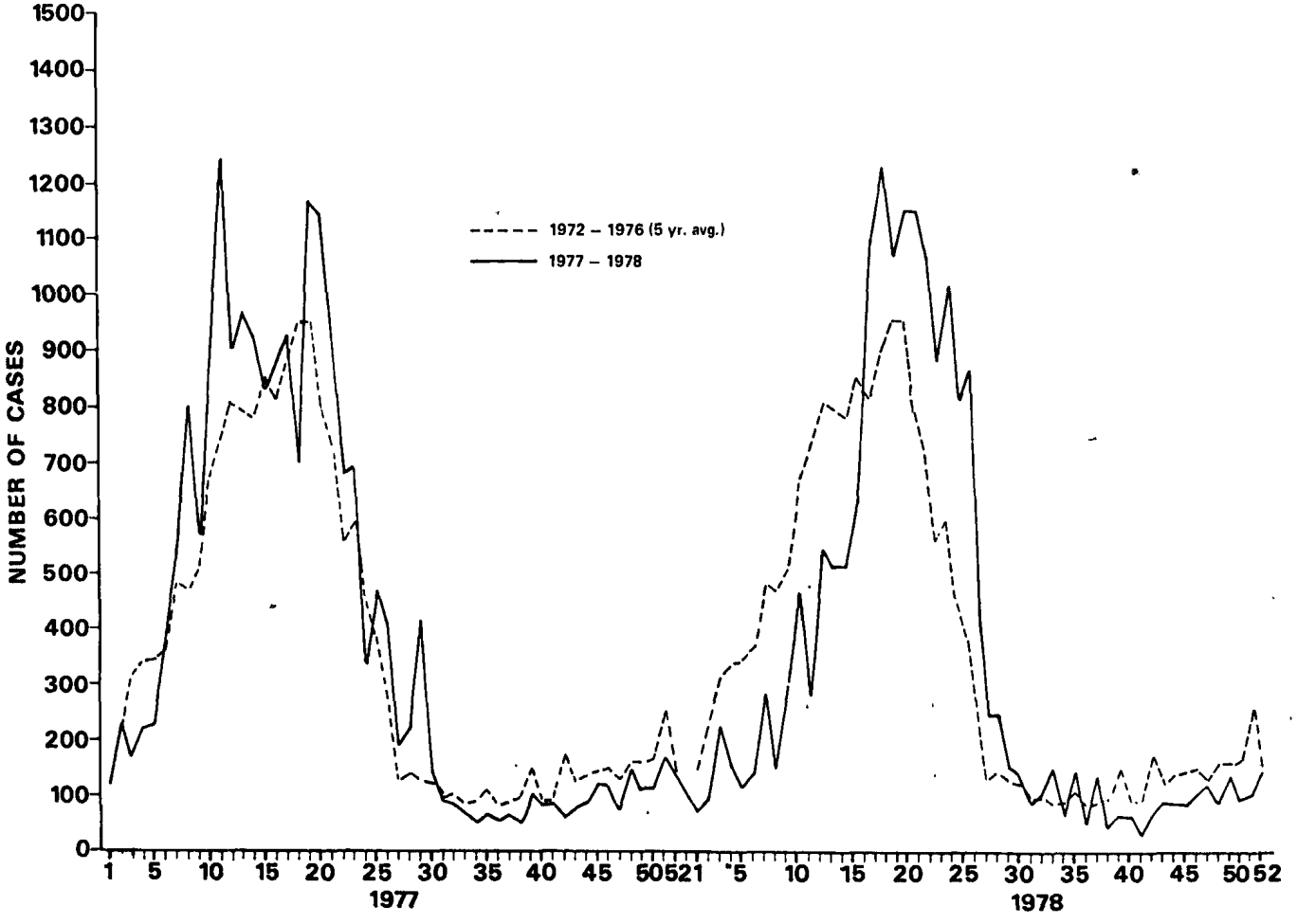
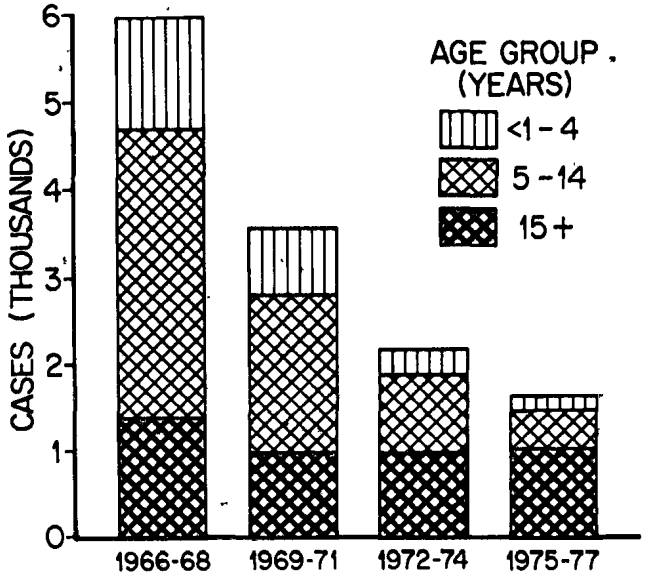


Figure 4. Average number of reported rubella cases in Massachusetts, New York City, and Illinois by age group, selected periods, 1966-1977



pubertal females should be more strongly emphasized. Although women known to be pregnant should not be vaccinated, the theoretical risk of damage to the fetus from the vaccine virus should not interfere with an effective vaccination program for women of childbearing age. In reports to CDC on more than 80 children born to susceptible women who either had been inadvertently vaccinated during pregnancy or had conceived within 3 months after being vaccinated, there was no evidence of a congenital defect caused by the vaccine virus. In view of the importance of protecting women of childbearing age against rubella, asking females if they are pregnant, excluding those who are, and explaining the theoretical risks to the others are reasonable precautions in a rubella vaccination program. Serologic testing of potential vaccines in the childbearing age group can be done when practical to determine whether they are susceptible to rubella.

The incidence of CRS is the most valid measure of the success or failure of our national rubella immunization strategy. Accordingly, in 1969 CDC established the National Registry for CRS, to which detailed reports of cases are submitted. Reports are processed through state health departments, whose methods of disease surveillance vary widely. The registry data are not necessarily complete but may reflect national trends. The reported numbers of CRS cases have paralleled reported rubella activity fairly closely since 1970 (Figure 2). The other source of data on CRS is the Birth Defects Monitoring Program (BDMP), which obtains information on about one-third of all the births in the United States. Although the BDMP has shown a decrease in the incidence of CRS, there has not been a consistent trend.

Table 1. Percentage distribution of reported rubella cases and incidence,[a] United States, 1975-1978

	1975			1976			1977			1978			Percentage Change 1975-1978	
Age (Years)	#	%	Incidence	#	%	Incidence	#	%	Incidence	#	%	Incidence	%	Rate
> 1-4	1,016	12.2	12.2	684	10.2	8.3	941	7.8	10.4	786	7.6	9.0	37.7	−29.7
5-9	938	11.3	10.9	629	9.4	6.8	1,012	8.4	10.0	619	6.0	6.5	46.9	−40.4
10-14	1,209	14.6	11.9	651	9.8	6.2	1,610	13.3	14.2	1,051	10.2	10.0	30.1	−16.0
15-19	3,836	46.2	36.8	2,927	43.8	25.9	5,867	48.6	47.0	4,543	44.1	38.3	4.5	+4.1
20-24	900	10.8	9.5	1,128	16.9	10.9	1,950	16.1	16.6	2,540	24.7	22.3	+128.7	+134.7
25-29	182	2.2	2.2	344	5.2	3.6	346	2.9	4.0	363	3.5	3.6	+ 59.1	+ 63.6
30+	223	2.7	0.4	315	4.7	0.6	352	2.9	0.6	394	3.8	0.6	+ 40.7	+ 50.0
Total with Known Age	8,304	49.9	–	6,678	53.4	–	12,078	59.2	–	10,296	56.4	–	–	–
Unknown Age	8,348	50.1	–	5,813	46.6	–	8,317	40.8	–	7,973	43.6	–	–	–
TOTAL	16,652	100.0	7.8	12,491	100.0	5.8	20,395	100.0	9.4	18,269	100.0	8.4	–	−10.6

[a]Incidence = cases per 100,000 population extrapolated from the age distribution of persons with documented cases from 40 (1975) to 47 (1978) reporting areas.

Smallpox

Vaccinia virus was the first agent to be used widely for human vaccination. 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 and fought to establish it as a routine public health procedure. He was supported in his efforts by Dr. Oliver Wendell Holmes and President Thomas Jefferson.

U.S. Smallpox Patterns

Smallpox was rampant in the early history of this country and decimated both the Indian tribes and the early settlers. Throughout the 1880s, variola major, with its high mortality rate, apparently coexisted with variola minor in many parts of the United States. At the turn of the 20th century, however, the death-to-case ratio reported for smallpox was low, which suggests that most of the cases were then caused by variola minor.

The incidence of smallpox declined markedly in the United States in the 1930s. The reasons for this are not completely clear. Routine vaccination may not have been solely responsible, for surveys showed that 60% of the residents of rural areas and more than 25% of the residents of selected urban areas with over 100,000 population had not been vaccinated. Anecdotal evidence suggests that intensive isolation procedures followed by local health authorities may have contributed substantially to the decline.

Small numbers of smallpox cases were officially reported in the late 1940s and early 1950s, but none of the cases reported after 1949 fulfilled the usual clinical criteria for smallpox, and no laboratory confirmation was obtained. 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. Both the Seattle and New York outbreaks, as well as the last European outbreaks, point up the special risks associated with the hospital as a focal point for smallpox transmission.

Worldwide Smallpox Eradication

The global smallpox eradication program began in 1967, when the disease was endemic in 6 countries in Asia, 3 in South America, and many in sub-Saharan Africa. Results have been dramatic (Figures 1-4). West and Central Africa became smallpox free in 1970, the Western Hemisphere in 1971, and Asia in 1975. The last known case of naturally acquired smallpox was reported from Somalia on October 26, 1977. A quickly contained outbreak of 2 cases occurred in England in 1978 as the result of a laboratory accident.

Smallpox was eradicated through intensive national and international efforts at outbreak detection, isolation of cases, and containment measures—chiefly the vaccination of contacts. These tactics reflect a departure from the traditional concept of establishing herd immunity through mass vaccination.

The World Health Organization certified that each region that had had endemic smallpox was free of the disease after carefully examining available records and doing intensive field searches to document the lack of current cases.

Current Vaccination Policy

In September 1971, the U.S. Public Health Service recommended that the policy of routine nonselective smallpox vaccination be changed to one of selective vaccination of individuals at special risk of acquiring smallpox.

Vaccination of children or other persons including hospital and health personnel is *not* recommended. Vaccination is indicated only for persons who are likely to come in contact with variola virus in a high-security laboratory and for travelers to countries that continue to require vaccination as a condition for entry.

Travelers to other countries should be aware of the vaccination requirements of each country to be visited. Most countries that require vaccination will exempt children under 1 year of age and persons with medical conditions that contraindicate smallpox vaccination. Such travelers should possess a written waiver from a physician indicating that smallpox vaccination is contraindicated for health reasons. Since the World Health Organization initially recommended that smallpox vaccination not be required for international travel, only a few nations in Asia and Africa have continued to enforce this regulation.

Figure 1. Reported cases of smallpox, worldwide, 1967-1978

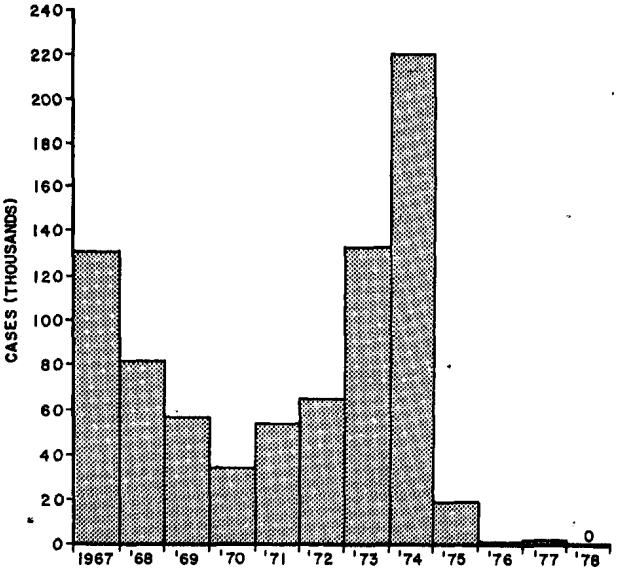


Figure 2. Areas with endemic smallpox, worldwide, 1966

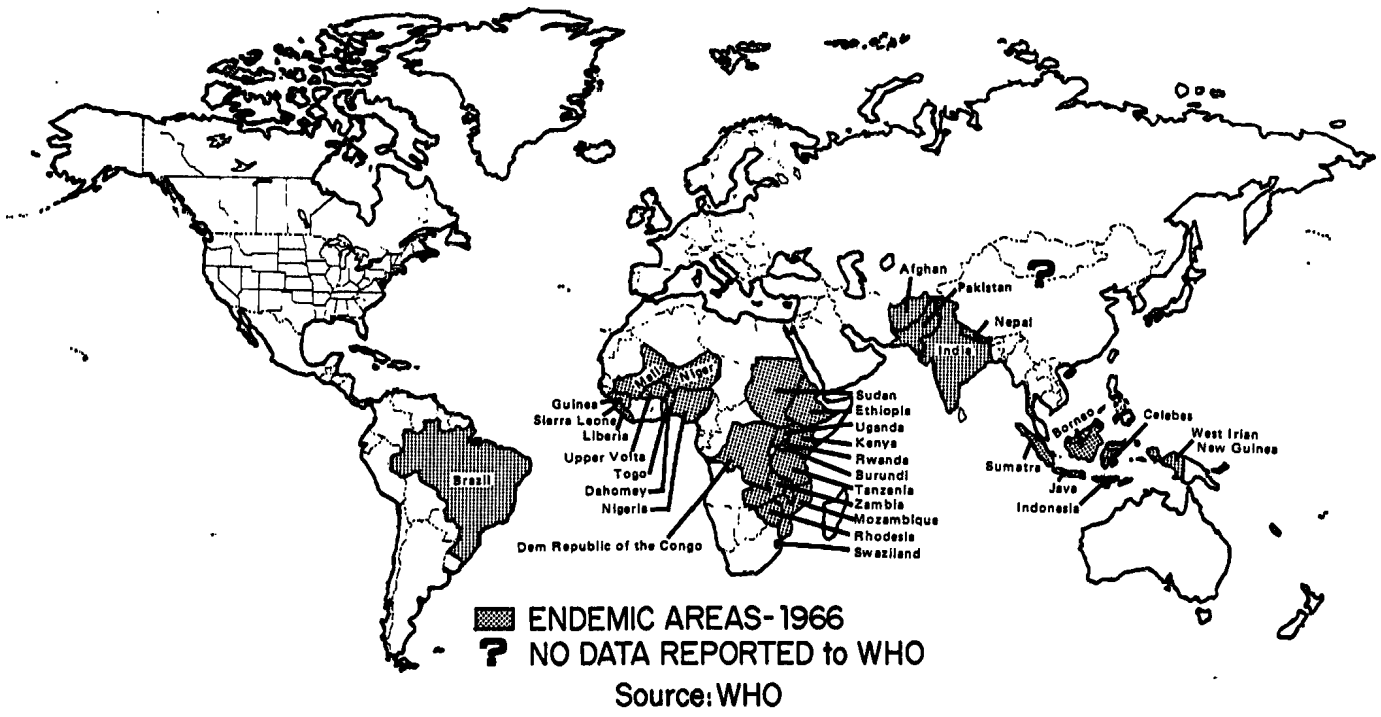


Figure 3. Areas with endemic smallpox, worldwide, 1971

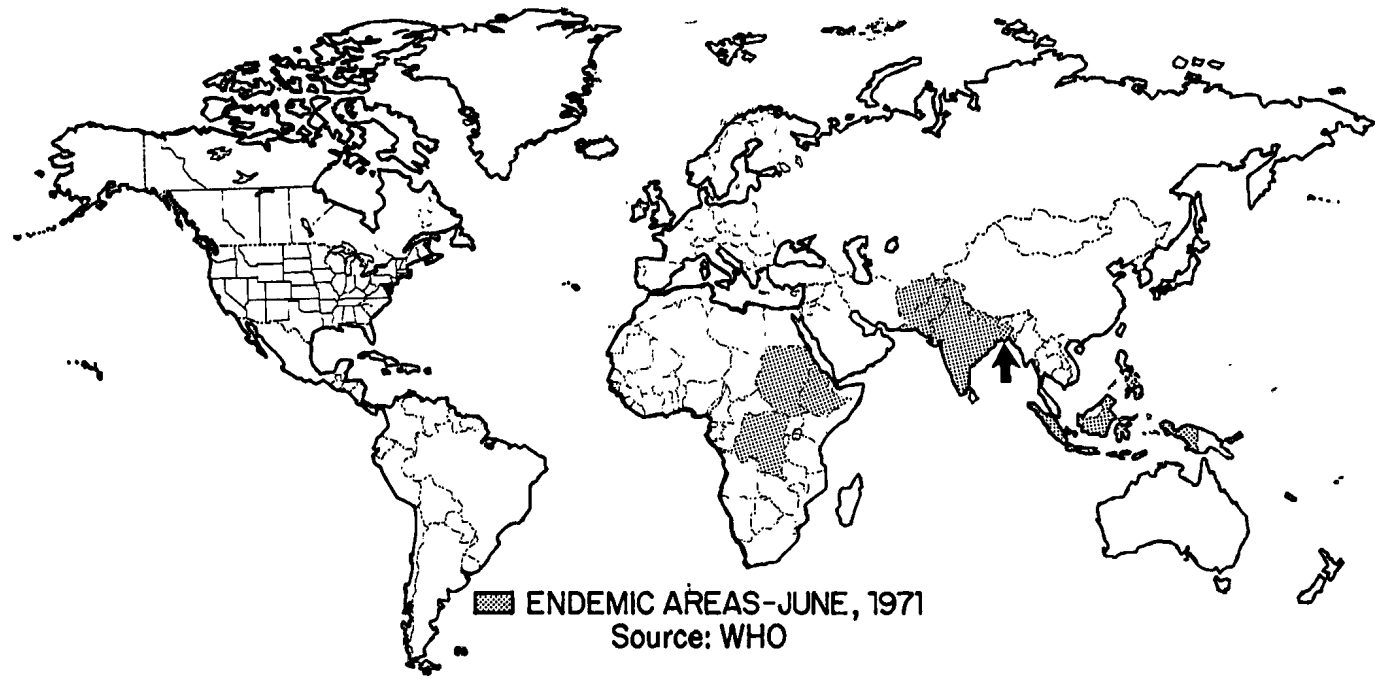
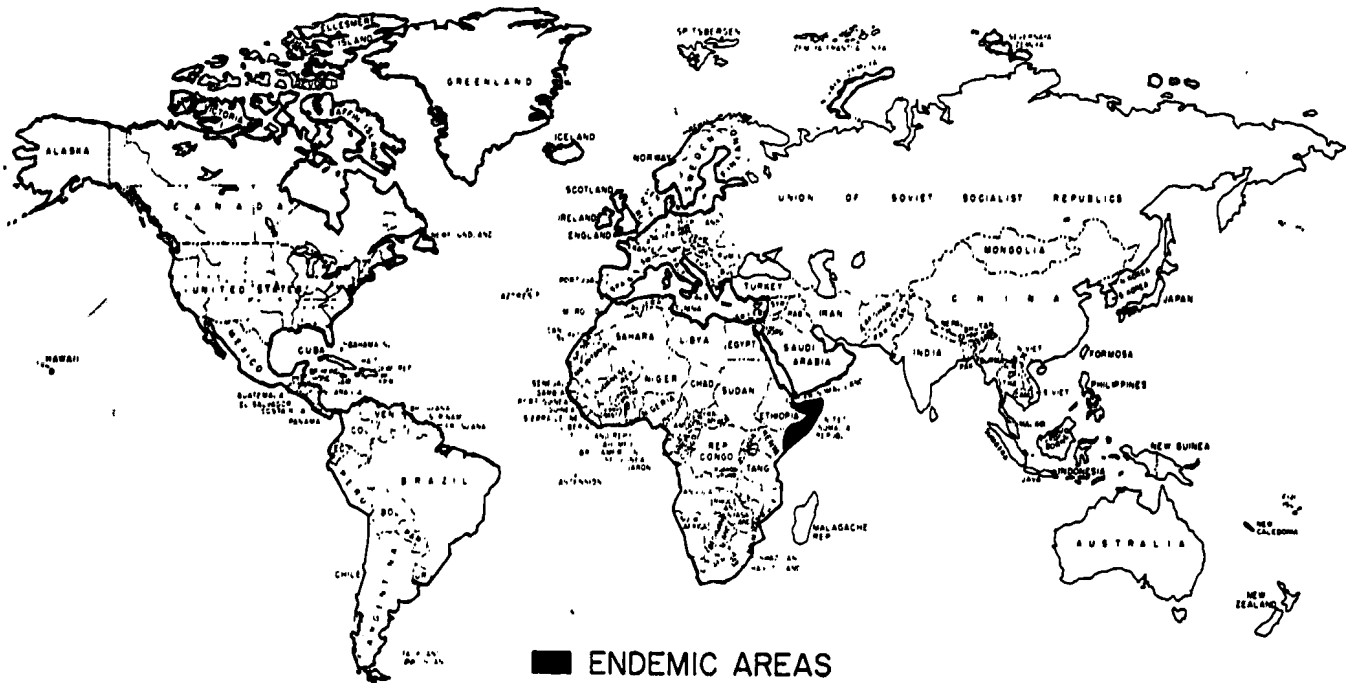


Figure 4. Areas with endemic smallpox, worldwide, 1977



Source: WHO, Geneva, Switzerland

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 *Clostridium tetani* in pure culture, and von Behring and Kitasato isolated tetanus toxin and produced tetanus antitoxin.

Experiences in World War I confirmed the value of prophylactic passive immunization with animal antitoxin. In 1925, Ramon introduced formalin-treated tetanus toxin as a toxoid for active immunization. During World War II, with routine toxoid use, the incidence of tetanus for American troops was only about 3% of that seen during World War I. In World War II, only 8 American military personnel with unequivocal histories of a complete vaccination series had documented tetanus. Japanese forces, who were not given tetanus toxoid, had a tetanus incidence in World War II comparable with that for American soldiers in World War I.

Since 1945, tetanus toxoid has been prescribed routinely for people of all ages. It is commonly available separately or in 2 combinations. Combined with diphtheria toxoid and pertussis vaccine (DTP), it is given to children ≤6 years old. It and diphtheria toxoid diluted to 15%-20% of normal (Td) are given in combination to older children and adults as both primary and booster vaccinations. Tetanus toxoid alone (T) is recommended for persons who are hypersensitive to diphtheria toxoid.

In each of the years 1975-1978, the number of tetanus cases reported to the Center for Disease Control averaged 88 (Figures 1 and 2). The incidence of tetanus has slowly decreased over the last 20 years, but the case-fatality ratio remains 40%-60% (Figure 3).

The incidence of tetanus in the United States in 1978 was highest for older persons, with the median age of tetanus patients being over 50 years.

Several Southern states have continued to have a higher incidence of tetanus than most other states (Figure 4).

Puncture wounds and lacerations preceded nearly 80% of tetanus cases in 1970-1971, the most recent years for which complete analysis is available. Seventy-seven percent of cases were associated with injuries in and around the home and garden. Eleven percent of people contracting the disease had no recollection of an associated injury. Most cases occurred between May and September, consistent with the hypothesis that the risk of acquiring tetanus is most strongly associated with outdoor activity and exposure to soil. Whites contracted the disease at 20% the rate at which members of other races did. Males with tetanus outnumbered females 3 to 2 overall, but of victims 20-40 years old, females outnumbered males.

Far fewer neonates have had tetanus recently than in earlier years. Tetanus affecting infants less than a month

Figure 1. Reported tetanus cases by year, United States, 1950-1978

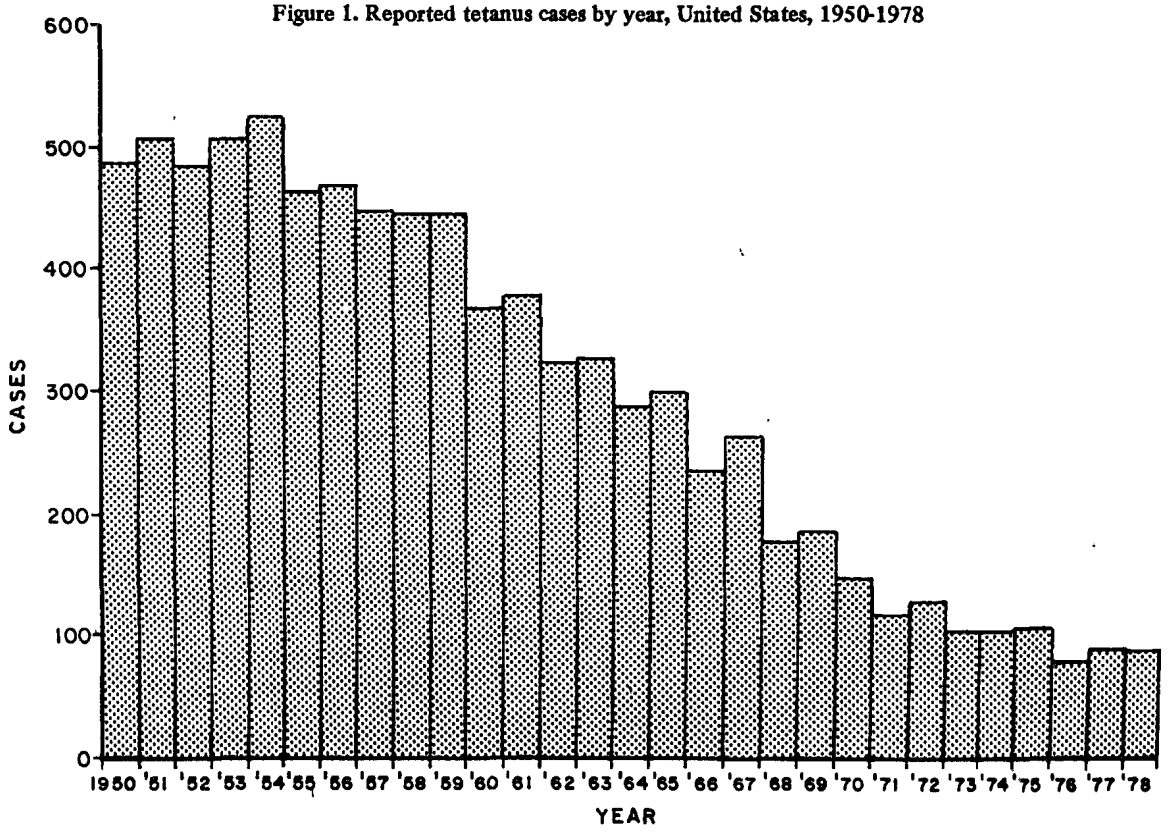


Figure 2. Reported tetanus cases by age group, United States, 1978

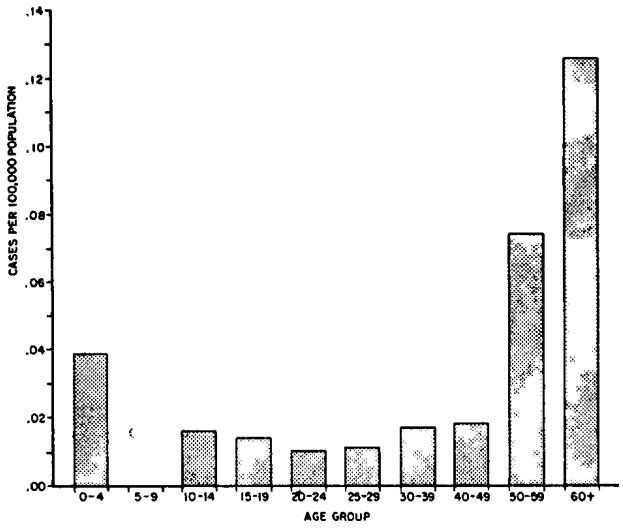
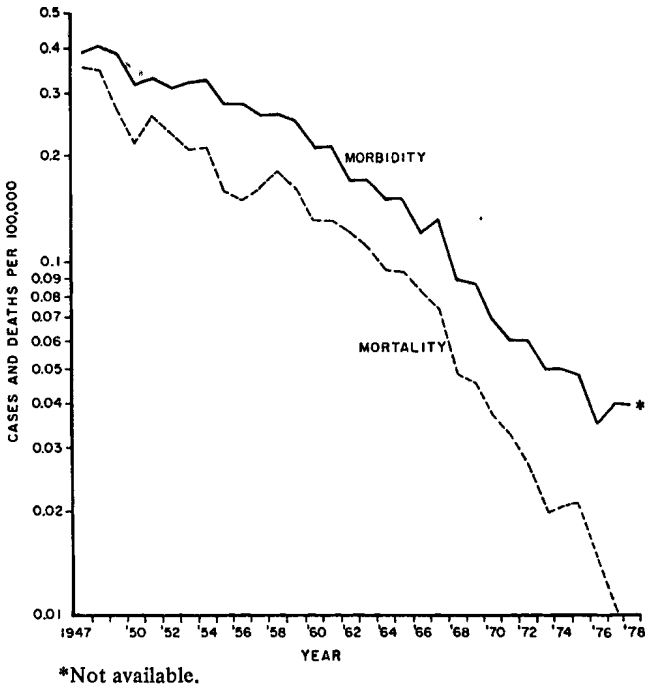


Figure 3. Tetanus morbidity and mortality per 100,000 population, United States, 1947-1978

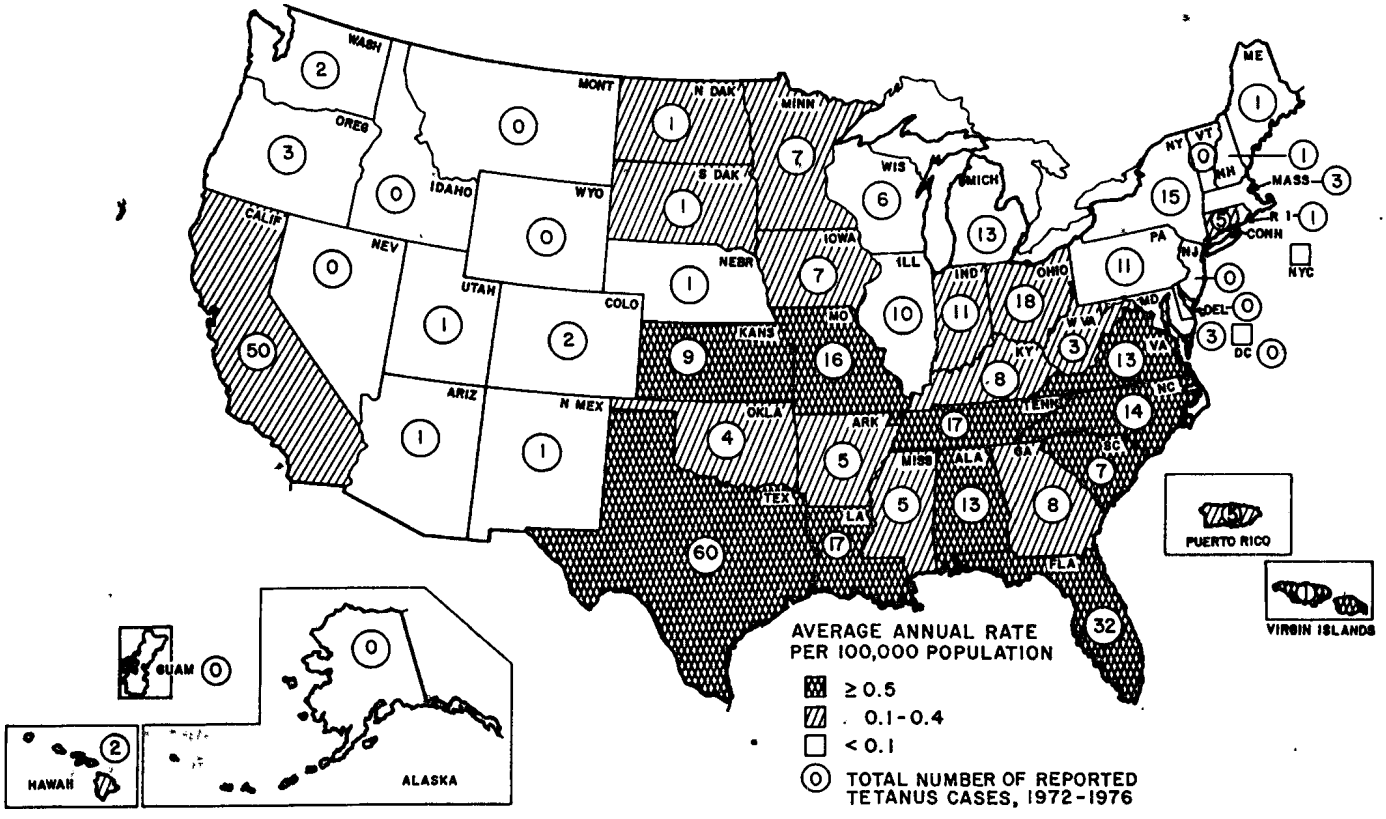


*Not available.

old is almost always associated with an unvaccinated mother and delivery unattended by a physician. Seven of the 10 neonates with tetanus in 1970-1971 were white. Four of the cases were reported from Texas and 4 from the Southeast. No person with a verified history of complete vaccination was reported to have tetanus in 1970 or 1971.

Although tetanus toxoid is among the most effective vaccines available, tetanus continues to occur even when a high percentage of the population has been vaccinated, because there is no herd immunity. Tetanus is still a significant problem primarily because of the ubiquity of the causative organism, the lack of naturally acquired immunity, and the fact that a significant proportion of the population, particularly persons over 40, are not adequately immunized.

Figure 4. Geographic distribution of tetanus cases and average incidence by state, 1972-1976



Tuberculosis

As far as can be determined, tuberculosis is as old as civilization. Infection with *Mycobacterium tuberculosis* has been called by many names, among them scrofula, phthisis, and consumption—the last, to describe the chronic wasting of the body believed to accompany late stages of infection. Clearer understanding of tuberculosis brought the realization that many patients reach far-advanced stages without appearing to be consumptive or emaciated. Indeed, even in its advanced stages, tuberculosis may be subclinical and unsuspected.

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

With Koch's discovery of the tubercle bacillus in 1882, interest in the communicability of tuberculosis reawakened, but not until the 1940s, almost 70 years later, was the route of transmission by droplet nuclei reasonably well understood. At that time, the tuberculosis incidence in the United States was around 90 cases per 100,000 population per year, and the death rate was 35 per 100,000.

The steady reduction in tuberculosis morbidity and mortality since the beginning of the 20th century has been attributed to several factors. Probably the most important in the past was public awareness of the disease and removal of patients with infectious disease from the community in order to isolate and treat them. Improved social conditions for most 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 were also major factors.

More recent scientific advances have provided the means to reduce the incidence of tuberculosis in the United States more rapidly. Antituberculosis drugs have proven effective for preventing tuberculosis and for treating patients who have the disease. Tuberculin skin test interpretation has been refined. In addition, the transmission and pathogenesis of tuberculosis are better understood, making possible a more rational approach to case finding, diagnosis, treatment, and prevention.

Recent Trends

In 1978, state health departments reported 28,521 tuberculosis cases, a 5.4% decline from the 30,145 cases recorded for the United States in 1977. The national incidence was 13.1 per 100,000 population in 1978 vs. 13.9 in 1977. Fewer than half as many tuberculosis cases were reported in 1978 as were reported 20 years ago (Table 1). Most of the decrease in tuberculosis incidence represents pulmonary cases. The number of reported extrapulmonary cases has remained virtually unchanged over the past decade. In 1978, extrapulmonary disease accounted for 14.6% of all tuberculosis cases, and pulmonary disease accounted for 85.4% (Figure 1).

There were 28,521 tuberculosis cases reported in 1978; bacteriologic results were available for 26,256 or 92.1%. Of these, 85.4% were confirmed to be positive, and 14.5% were negative. Although the overall case rates for whites are substantially lower than those for other races, the absolute number of cases reported for whites is larger than that for other races (Figure 2). Figure 2 also shows that both the numbers reported and the specific case rates rise with age. Case rates have generally been higher in the Southeast and in states along the Mexican border than in other parts of the country (Figure 3).

Statistics indicate that 2,830 persons died from tuberculosis in the United States in 1978, a death rate of 1.3 per 100,000 population. This represents a 7.1% decline in the death rate from 1977, continuing the steady downward trend of recent decades (Table 1).

Morbidity and mortality rates are 2 indices of the severity of the tuberculosis problem. A third index is the infection rate, which measures the level of transmission of tubercle bacilli from person to person. Although the rate has been high in the past, new infections among children are now rare in many parts of the country.

Prevention of Disease

The probability of having clinical tuberculosis is reduced by preventive treatment with the drug isoniazid or vaccination with "Bacille Calmette-Guérin" (BCG) vaccine. Preventive treatment is preferred in countries such as the United States, where there is a relatively low incidence of disease and an effective control program. BCG vaccine is recommended and widely used in some developing countries.

BCG Vaccine

The search for a 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 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 Guérin at the Pasteur Institute.

Table 1. Tuberculosis cases and deaths, United States, 1955-1978

	Cases				Deaths			
				% Change				% Change
Year	Number	Rate	Number	Rate	Number	Rate	Number	Rate
1955	77,368	46.9	−3.0	− 4.9	15,016	9.1	− 9.1	−10.8
1956	69,895	41.6	−9.7	−11.3	14,137	8.4	− 5.9	− 7.7
1957	67,149	39.2	−3.9	− 5.8	13,390	7.8	− 5.3	− 7.1
1958	63,534	36.5	−5.4	− 6.9	12,417	7.1	− 7.3	− 9.0
1959	57,535	32.5	−9.4	−11.0	11,474	6.5	− 7.6	− 8.5
1960	55,494	30.8	−3.5	− 5.2	10,866	6.0	− 5.3	− 7.7
1961	53,726	29.4	−3.2	− 4.5	9,938	5.4	− 8.5	−10.0
1962	53,315	28.7	−0.8	− 2.4	9,506	5.1	− 4.3	− 5.6
1963	54,042	28.7	+1.4	0.0	9,311	4.9	− 2.1	− 3.9
1964	50,874	26.6	−5.9	− 7.3	8,303	4.3	−10.8	−12.2
1965	49,016	25.3	−3.7	− 4.9	7,934	4.1	− 4.4	− 4.7
1966	47,767	24.4	−2.5	− 3.6	7,625	3.9	− 3.9	− 4.9
1967	45,647	23.1	−4.4	− 5.3	6,901	3.5	− 9.5	−10.3
1968	42,623	21.3	−6.6	− 7.8	6,292	3.1	− 8.8	−11.4
1969	39,120	19.4	−8.2	− 8.9	5,567	2.8	−11.5	− 9.7
1970	37,137	18.3	−5.1	− 5.7	5,217	2.6	− 6.3	− 7.1
1971	35,217	17.1	−5.2	− 6.6	4,501	2.2	−13.7	−15.4
1972	32,882	15.8	−6.6	− 7.6	4,376	2.1	− 2.8	− 4.5
1973	30,998	14.8	−5.7	− 6.3	3,875	1.8	−11.4	−14.3
1974	30,122	14.2	−2.8	− 4.1	3,513	1.7	− 9.3	− 5.6
1975	33,989	15.9	–	–	3,333	1.6	− 5.1	− 5.9
1976	32,105	15.0	−5.5	− 5.7	3,280	1.5	− 1.6	− 6.3
1977	30,145	13.9	−6.1	− 7.3	2,968	1.4	− 5.2	− 6.7
1978	28,521	13.1	−5.4	− 5.8	2,830[a]	1.3	− 4.6	− 7.1

[a]Provisional. Deaths are based on the National Center for Health Statistics' 10% sample of death certificates.
Note: Case data for years after 1974 are not comparable with those for earlier years because of changes in diagnostic and classification standards implemented in 1975.

Figure 1. Pulmonary and extrapulmonary tuberculosis cases, United States, 1964-1978

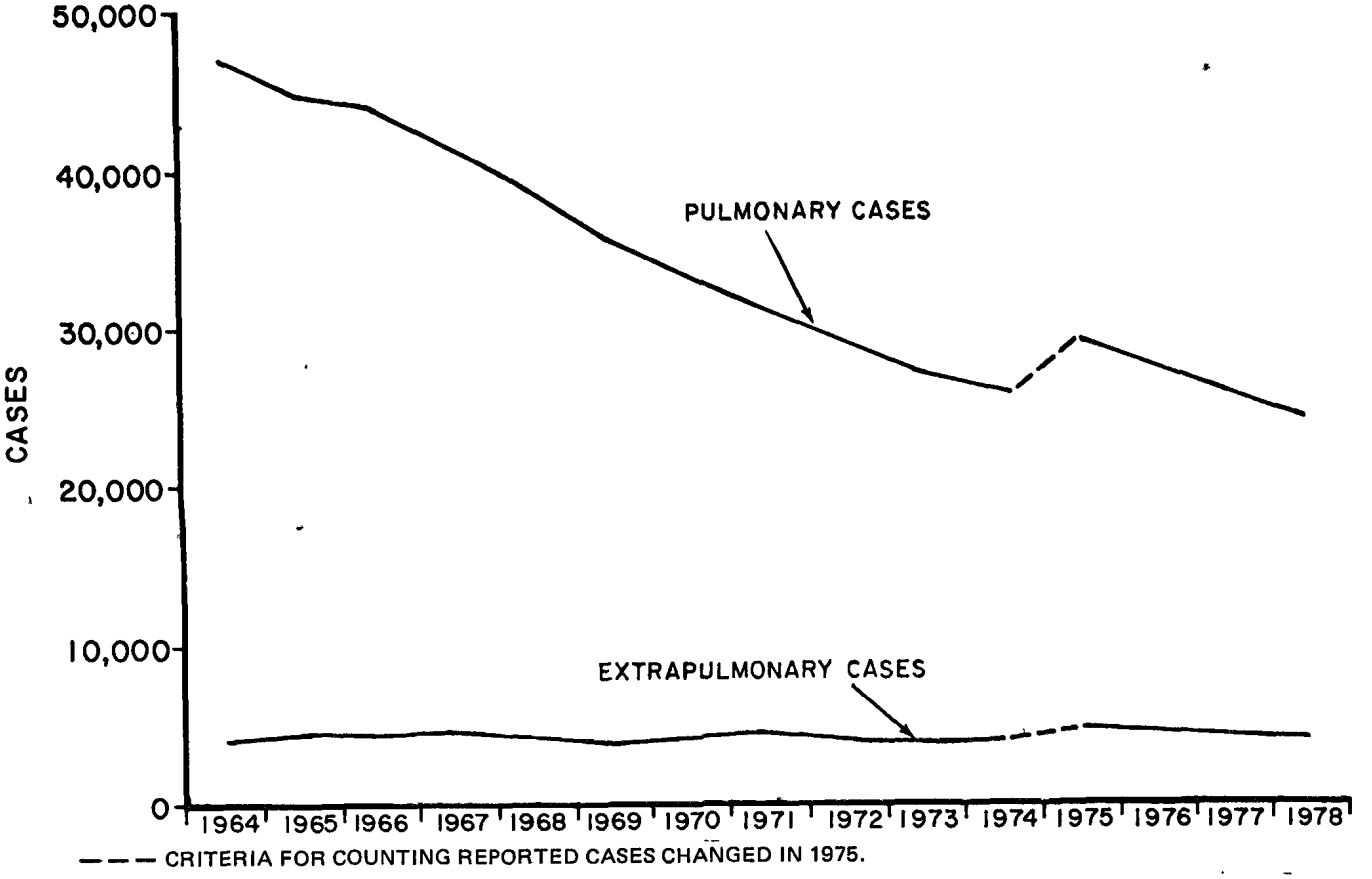
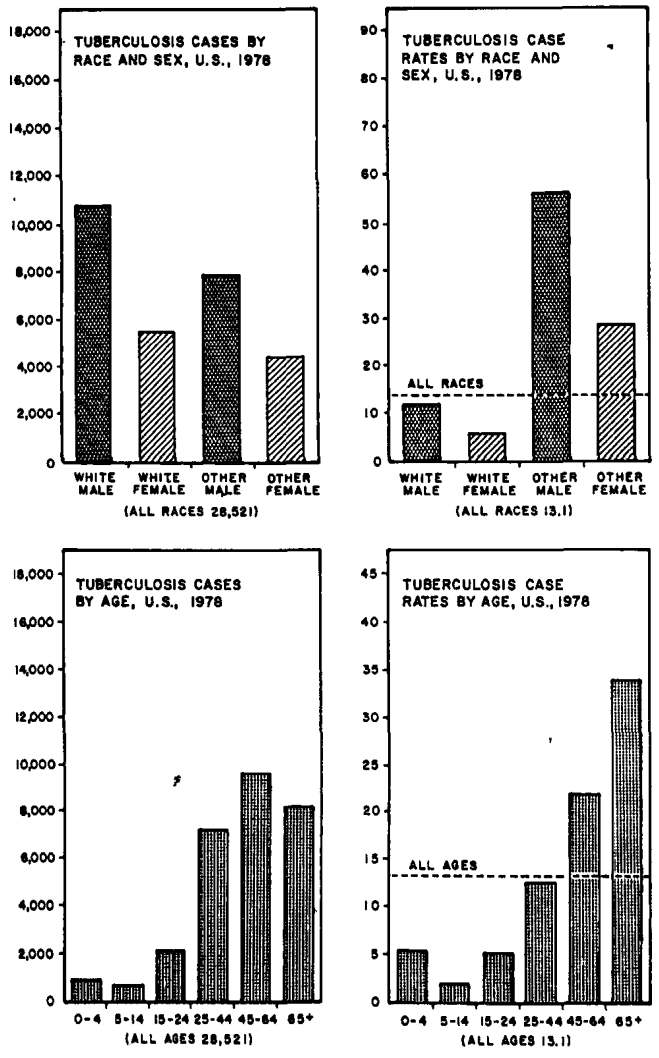


Figure 2. Tuberculosis—reported cases and cases per 100,000 population by race and sex and by age group, United States, 1978



No apparent harm resulted from using oral BCG vaccine for youngsters, and it was soon used throughout France despite appeals from some leading clinicians to have controlled studies of its effectiveness. Two major setbacks soon occurred. 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; then in the Hanseatic city of Lübeck in 1930, 73 children were mistakenly fed a culture of virulent bacilli instead of BCG and died from tuberculosis.

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 that became widely accepted as the campaigns spread throughout Europe and into the Middle East, Asia, and Latin America. The United Nations Children's Emergency Fund (UNICEF) provided early support, and by the mid-1950s the World Health Organization (WHO) took over the mass BCG vaccination campaigns as part of the tuberculosis control program for developing countries.

Questions again arose about the effectiveness of BCG vaccination. They led, this time, to the creation by WHO of a Tuberculosis Research Office (TRO), 1949-1955, and to the large-scale controlled trials that began in 1950, including those conducted by the U.S. Public Health Service and the British Medical Research Council. The work of the WHO/TRO was directed primarily toward answering questions about the nature of BCG vaccine, devising techniques of administration, and developing methods for selecting 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 that cause tuberculin sensitivity, all of which interfere with selection of candidates and efficacy of the vaccine. Results of the controlled trials have shown different degrees of effectiveness of the vaccine, related possibly to differences in the tuberculosis infection rates (higher in Britain), sources of other mycobacterial infections (more common in the United States), and various other factors, known as well as unknown.

Recently WHO, the Indian Council of Medical Research, and the U.S. Public Health Service sponsored a controlled community trial of BCG in South India. About 115,000 tuberculin-negative individuals were randomly allocated into study groups. After 7½ years of follow-up, no protective effect of BCG vaccine is evident.

The purpose of BCG vaccination is to modify the course of later infection with virulent tubercle bacilli and thereby reduce the risk of overt pulmonary disease and extrapulmonary complications, notably miliary tuberculosis and tuberculous meningitis. Thus, only the uninfected stand to benefit from vaccination, since infected persons have already responded to a natural challenge with tubercle bacilli. There is no indication that vaccination prevents tuberculous infection.

In the United States, BCG vaccination is recommended only for individuals who have a high probability of becoming infected, i.e., those who have unavoidable and continuous exposure to *M. tuberculosis* and cannot be kept under surveillance or given preventive treatment.

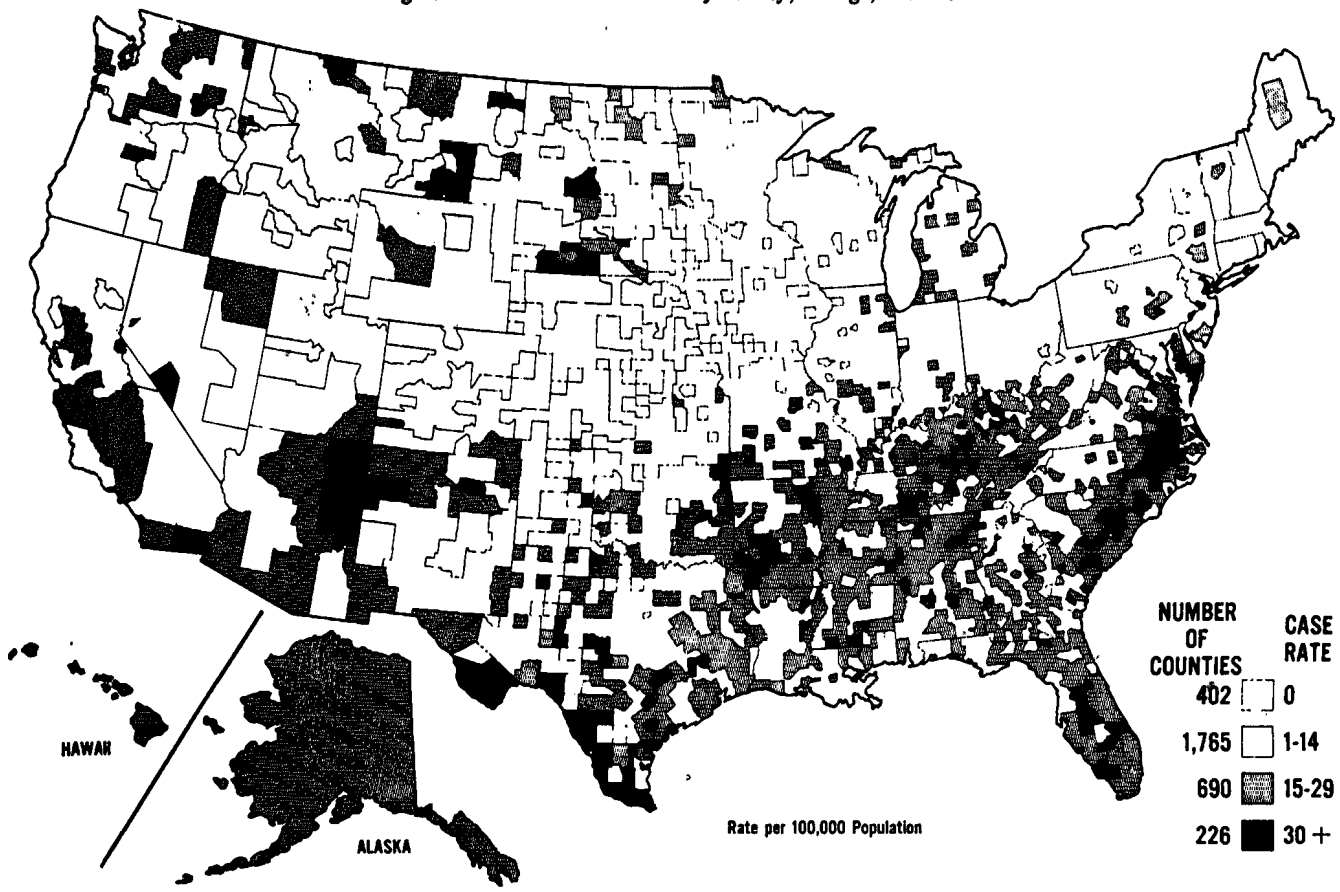
BCG vaccine is administered by the intracutaneous technique or the transcutaneous multiple-puncture technique. Specific instructions of the manufacturer should be carefully followed.

Preventive Treatment

Because of the low and still-falling infection rates in this country, relatively more of the tuberculosis cases diagnosed each year (an estimated 80% to 90% of all new cases) are from the already infected pool, estimated to comprise about 15 million persons. Preventive treatment can reduce the incidence of overt disease among infected individuals by 70%-90%. Top priority for preventive treatment is recom-

mended for persons as greatest risk: close contacts of infective persons, persons with abnormal chest X-ray findings, recent tuberculin converters, and persons with medical conditions that lower the natural resistance to disease. Isoniazid, 300 mg by mouth each day for a year, is the currently recommended preventive treatment for infected adults; for infected children, the recommended preventive treatment is 10 mg/kg body weight, not to exceed 300 mg daily, by mouth each day for a year. Although a course of preventive treatment for as little as 6 months reduces the probability that infected persons will have clinical disease, it appears to confer less protection than a 12-month course.

Figure 3. Tuberculosis case rates by county, average, 1975-1977



Typhoid Fever

Without any specific control programs, the incidence of typhoid fever in the United States and in other Western countries has progressively and substantially decreased over the past several decades (Figure 1). Although sporadic outbreaks still occur occasionally, improvements in sanitation and attrition among carriers have reduced the risk of acquiring typhoid fever in this country. In recent years, half the typhoid fever cases diagnosed in the United States have been acquired during travel to areas with endemic typhoid fever, chiefly Mexico and India. Therefore, a detailed history of travel should be obtained from each patient in the United States.

The organism that causes typhoid fever is transmitted almost exclusively in contaminated food and water. Because a moderately large inoculum (10^5 or more *Salmonella typhi* organisms) appears necessary to cause disease for most persons, typhoid fever is rarely transmitted by person-to-person spread or by fomites. Most of the recent outbreaks in the United States have been foodborne.

Indigenously acquired typhoid fever chiefly affects young adults and children over the age of 1 year. Most outbreaks involve only 2 or 3 cases, but several larger foodborne and waterborne outbreaks have occurred in the United States in the last decade. Persons with Hispanic surnames have been shown to be at a higher than average risk of acquiring typhoid. Substandard hygiene associated with poverty, a disproportionate segment of the population in the age group at greatest risk, and frequent interaction of Hispanic residents in the Southwestern United States with relatives, friends, associates, and other contacts from Latin America, where typhoid is endemic, probably contribute to the excess morbidity rates for the Hispanic population. Indigenous sporadic cases occur most frequently in the rural South.

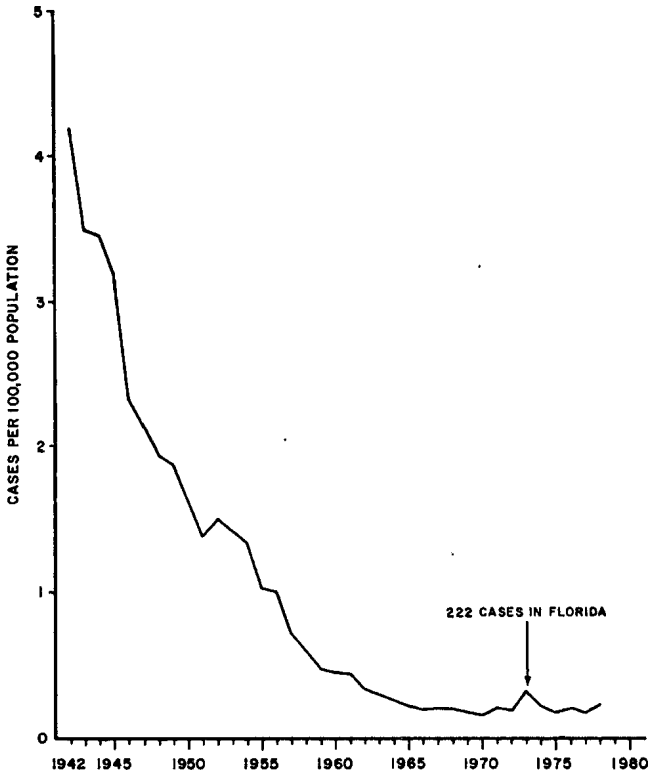
The typical patient with travel-associated typhoid fever is older and more likely than a patient with indigenous disease to be male, reflecting the demographic characteristics of foreign travelers. States with high attack rates of travel-associated typhoid are primarily those that border on Mexico or have major international ports.

Chloramphenicol-resistant strains of *S. typhi* have been reported from a number of countries, and a large outbreak of typhoid fever occurred in central Mexico in 1972 and 1973. For this reason, all strains of *S. typhi* isolated from patients with clinical illness should be tested for drug susceptibility, and if chloramphenicol resistance is demonstrated, any of 3 other drugs (i.e., ampicillin, amoxicillin, or the drug combination trimethoprim-sulfamethoxazole) should be used.

In the past, approximately 3% of patients with typhoid continued to excrete the organism for longer than a year regardless of antibiotic therapy, but this figure is highly age and sex dependent. Women over 40 years old with gallbladder disease are most likely to become carriers. Treatment for typhoid carriage is recommended, e.g., for persons whose livelihood depends on food handling.

In addition to the other indications for typhoid vaccination discussed in the recommendations by the Immunization Practices Advisory Committee (Section IV), laboratory workers who have frequent contact with *S. typhi* should be considered candidates for the vaccine.

Figure 1. Reported typhoid fever cases per 100,000 population by year, United States, 1942-1978



Typhus Fever (Epidemic)

Epidemic (louse-borne) typhus fever is caused by *Rickettsia prowazekii* 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 applies to febrile illness and clouded intellect. Gerhard, a Philadelphia physician, differentiated typhus from typhoid fever in 1837. In 1910, Brill described sporadic cases of a mild illness he saw affecting people in New York City who did not have lice. Zinsser suggested in 1934 that Brill's disease was recrudescent epidemic typhus, and in 1951 Murray and Snyder proved that it was by isolating *R. prowazekii* from lice that had been allowed to feed on patients with Brill's disease. Patients can now be effectively treated for typhus with a tetracycline or chloramphenicol, especially if treatment is started soon after the rash appears.

Another kind of typhus is murine (endemic) typhus, caused by *R. typhi (R. mooseri)* and transmitted by the rat flea. Clinically a somewhat milder form of epidemic typhus, it occurs endemically, especially in subtropical and tropical regions with large rat populations. The term "typhus" is also applied to scrub typhus or tsutsugamushi disease, a mite-borne rickettsial infection that 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 occur in various parts of the world.

Epidemic typhus fever has typically been seen in large epidemics associated with the disruption caused by wars and revolutions. The last large epidemic was in Eastern Europe and Russia in 1918-1922 and involved an estimated 30 million cases and 3 million deaths. In the World War II period, the disease was again seen there and also around the Mediterranean, but it has since disappeared from those areas. Recrudescent typhus, or Brill-Zinsser disease, continues to affect previously infected persons, even decades after the initial infection, and could initiate epidemics if lousiness were to return.

Today, epidemic typhus fever is seen primarily in mountainous areas of the tropics, where the climate is cool enough for the people to wear clothes. It may occur in epidemics of several hundred cases, as it recently did in Burundi, or in small outbreaks involving a few families. In the altiplano of South American, nearly all the people have been infected by the time they are adults, although clinical illness is rarely seen.

No outbreaks of epidemic typhus fever have occurred in the United States for several decades, and the recent cases seen here were imported from other countries. Because body lousiness is rare in the United States, cases of recrudescent typhus do not lead to epidemics, and epidemic typhus vaccine is therefore not indicated for the general civilian population. It has been recommended for military personnel and for civilians whose foreign travel will bring them in close contact with the populations of certain mountainous areas of the tropics. The risk for ordinary tourists is not significant. The vaccine provides little if any protection against murine typhus.

For the purpose of vaccine production, *R. prowazekii* is cultivated in the yolk sacs of embryonated chicken 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 vaccinating guinea pigs and testing their serum for antibodies capable of neutralizing the lethal effect that suspensions of viable *R. prowazekii* from infected yolk sacs have for mice. The protection provided to humans by the primary series is much improved by a booster dose 9-12 months later. This "booster effect" lasts for many years, and the primary series need not be repeated.

Varicella-Zoster Infections

Until 1767, when Heberden clinically differentiated varicella (chickenpox) and variola (smallpox), one was frequently misdiagnosed as the other. A century later, about the same time varicella was shown to cause an infectious disease, herpes zoster infection (shingles) was described. The relationship between varicella and herpes zoster infection was first postulated in 1888, but it was not until 1953 that virus isolation techniques allowed scientists to show that the 2 diseases are caused by the same virus. The concept is now generally accepted that chickenpox is the primary clinical response, and shingles is a delayed manifestation of infection with the varicella-zoster (V-Z) virus.

Varicella

Varicella is a disease of mildly fluctuating endemicity. Data from 8 states for the period 1955-1971 reveal no discernible epidemic cyclicity (Figure 1). This is in agreement with nationwide data available since 1972 (Figure 2, Table 1). The reported average annual incidence for the period 1972-1978 was 167,037 (78.4 cases per 100,000 population per year). Since varicella is a very contagious disease with a 60%-90% secondary attack rate for household members and with approximately 95% of all young adults having serologic evidence of infection at some time, the reported number of cases probably represents only about 6% of the actual number of infections (based on approximately 3 million births per year). The disease is most prevalent in late winter and in spring, i.e., between January and May (Figure 2). The illness is most common among children 5 to 9 years old, with 80% of reported cases affecting children less than 10 years old (Table 2). There has been no significant change in age distribution in recent years (Figure 3).

Varicella is a relatively benign illness for normal children. Inapparent infection is rare. The most common complication is secondary bacterial infection of the skin lesions. Children rarely have pneumonia as a complication of chickenpox; however, 16% of the group of apparently healthy military personnel tested had X-ray evidence of pneumonitis. Of this group, 25% had clinical signs of pneumonia. In clinical studies, postinfectious encephalitis has been reported at a rate of 1 case per 2,00-3,000 reported chickenpox cases. The rate reported to the Center for Disease Control (CDC) for the period 1972-1978 was 0.3 per 1,000 chickenpox cases (Table 1). Encephalitis secondary to chickenpox appears to be a severe illness, with a usual reported fatality rate of 10%-35%. Reye syndrome and hemorrhagic varicella are complications of chickenpox that occur less frequently. Deaths from chickenpox have been reported at a rate of 0.5 to 1 per 1,000 cases. Most persons who have serious complications or die are very young children (especially neonates), adults, and immunosuppressed individuals of all ages.

Figure 1. Reported varicella cases in eight states* by year, United States, 1955-1978

*Alabama, Arkansas, Arizona, Florida, Iowa, Massachusetts, Michigan, Washington.
**No Reporting for Arizona.

Figure 2. Reported varicella cases per 100,000 population by month, United States, 1972-1978

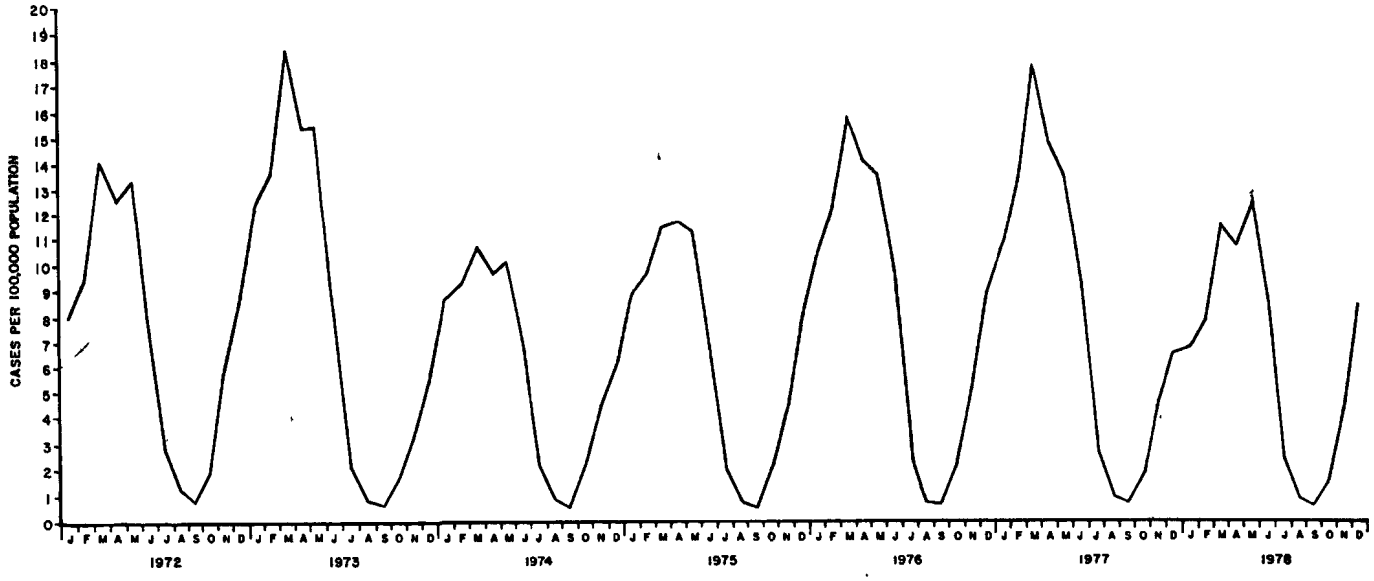


Table 1. Cases, deaths, and case-fatality ratios for chickenpox and chickenpox-associated encephalitis in the United States, 1972–1978

	Chickenpox			Chickenpox-Associated Encephalitis[a]		
Year	Cases	Deaths[b]	Deaths per 10,000 Cases	Cases	Deaths	Deaths per 100 Cases
1972	164,111	122	7.4	52	18	34.6
1973	182,927	138	7.5	102	14	13.7
1974	141,495	106	7.5	54	10	18.5
1975	154,248	83	5.4	54	12	22.2
1976	183,990	106	5.8	59	6	10.2
1977	188,396	89	4.7	43	1	2.3
1978	154,089	NA[c]	NA	NA	NA	NA

[a] Data from Viral Diseases Division, Bureau of Epidemiology, Center for Disease Control, Atlanta, Ga.
[b] Data from National Center for Health Statistics.
[c] NA = not available.

Table 2. Reported cases of chickenpox, by age group, for Massachusetts, New York City, and Illinois, 1972-1978

Age Group (Years)	Mean Annual Number of Cases (%)	Mean Annual Incidence per Population of 100,000
<5	3,399 (14.6)	208.5
5-9	14,887 (64.2)	739.0
10-14	3,720 (16.0)	181.4
15-19	761 (3.3)	32.9
>20	413 (1.8)	2.4
Total	23,180 (100.0)	94.8

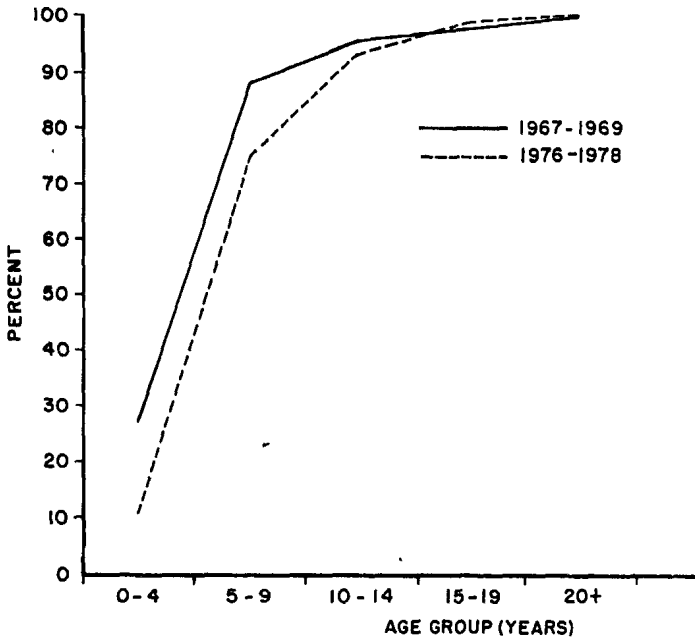
Herpes Zoster

Although herpes zoster infection is not a reportable condition, results of studies have shown no seasonal prevalence, supporting the contention that herpes zoster infections are not caused by exogenous reinfection after exposure to the V-Z virus. Cases have been reported to occur simultaneously with chickenpox and to affect persons for whom chickenpox had not been diagnosed. Although children do not usually have the disease, some infants born to mothers who had chickenpox while pregnant have been infected. In general, incidence rises with age. Patients with herpes zoster infection shed V-Z virus and thus can transmit varicella to susceptible contacts.

Prevention and Treatment

Experimental vaccines are being tested in Japan, Switzerland, and the United States, but none are currently available for routine use in the United States. High doses of pooled gamma globulin (0.6-0.9 cc/kg body weight) have modified the disease for normal children but are not effective in preventing chickenpox.

Figure 3. Cumulative percentage of varicella cases by age group, from selected areas,* 1967-1969 and 1976-1978



*Illinois, Massachusetts, New York City

Since January 1972, CDC has provided an investigational preparation, zoster immune globulin (ZIG), to more than 1,000 immunodeficient children within 96 hours after they were exposed to chickenpox. ZIG is prepared from the plasma of healthy donors convalescing from shingles or chickenpox. Data indicate that ZIG is effective in preventing or modifying varicella infection for immunodeficient patients if it is given soon after they are exposed to the virus.

Unfortunately, the supply of ZIG has not been constant because not enough plasma has been donated to meet the increasing number of requests. To meet the increasing demand, since 1977 CDC has contracted with the Sidney Farber Cancer Institute and the State Laboratory Institute of the Massachusetts State Department of Public Health to provide and distribute a supply of varicella-zoster immune globulin (VZIG) prepared from pooled plasma containing high levels of antibody against varicella virus. VZIG is also investigational and is available only in limited quantities. Unnecessary use can be minimized, when feasible, by determining whether children with immunodeficiency, leukemia, or lymphoma have V-Z virus antibody.

VZIG has been available at no cost since November 1, 1977, for patients meeting the criteria outlined in Table 3. A physician who desires treatment for such a patient should contact:

Division of Clinical Microbiology
Sidney Farber Cancer Institute
44 Binney Street
Boston, Massachusetts 02115
Telephone: 617-732-3121

Although former ZIG consultants and the Immunization Division, CDC (telephone: 404-329-3747), no longer have direct responsibility for distributing VZIG, they can be consulted about alternate modes of therapy such as zoster immune plasma (ZIP), adenosine arabinoside (Ara A), and interferon.

Table 3. Five criteria for obtaining varicella-zoster immune globulin (VZIG) to use as protection against varicella

I.	One of the following underlying illnesses or conditions:
	A. Leukemia or lymphoma
	B. Congenital or acquired immunodeficiency
	C. Person taking immunosuppressive medication
	D. Baby born to mother with varicella
II.	One of the following types of exposure to patient with varicella or zoster:
	A. Household contact
	B. Playmate contact (>1 hour play indoors)
	C. Hospital contact (in same 2- to 4-bed room or adjacent beds in a large ward)
	D. Newborn contact (newborn whose mother contracted varicella less than 5 days before delivery or within 48 hours after delivery)
III.	Negative or unknown disease history
IV.	Age less than 15 years
V.	Request for treatment must be initiated within 72 hours of exposure

Yellow Fever

Ecology

Yellow fever is an acute infectious disease caused by a group B arbovirus (flavivirus) transmitted to humans by the bite of an infected mosquito. Clinical illness may range from life-threatening disease with jaundice, coma, acute renal failure, and vomiting of blood, to a mild influenza-like syndrome, to an inapparent infection for infants. Case-fatality ratios have ranged from 5% in outbreaks involving natives of regions with endemic yellow fever to almost 50% in epidemics. The major variables include the attenuation of yellow fever virus strains in endemics and the protective effects of earlier infection with related arbovirus diseases. Those who recover are immune for life.

Comparable human infections occur after either urban or sylvatic cycles of yellow-fever-virus transmission. The urban cycle is human-mosquito-human, with humans remaining infectious for only 4-5 days, but after a 2-week incubation period, individual mosquitoes are infectious for life. In the Americas, *Aedes aegypti* is the only mosquito known to maintain the urban transmission cycle. The cycle may accompany explosive outbreaks in which large numbers of *Aedes aegypti* mosquitoes are in close contact with many susceptible persons or in less intense outbreaks in villages and rural areas where lower densities of humans and vectors as well as existing immunity may moderate the intensity of outbreaks. Sylvatic yellow fever is transmitted to monkeys in the rain forests of South and Central America principally by mosquitoes of the *Haemagogus* genus, and humans are infected more or less sporadically as they work or travel in forested areas and are bitten by *Haemogogus* spp. mosquitoes.

In Africa, the sylvatic cycle is maintained by mosquitoes such as *A. africanus* or *opok* that seldom bite humans but may cause sporadic human infection. In some parts of rural, tropical Africa, a cycle has been described in which humans contract the disease from the peridomestic mosquito *A. simpsoni*, which feeds on infected monkeys that periodically raid village gardens. Epidemiologic observation of widespread epidemics of human yellow fever, in the absence appreciable numbers of *A. aegypti* mosquitoes, indicates that in rural Africa humans may contract yellow fever through nonclassic, human-mosquito-human transmission cycles involving other aedine mosquitoes such as *A. luteocephalus* or *A. furcifertaylori*.

Recent observations have confirmed transovarial transmission of yellow fever virus in *A. aegypti*. This mode of transmission may be important in ensuring the persistence of the virus through dry seasons or in other situations unfavorable for its survival.

The virus has been repeatedly isolated from wild monkeys; they may have overt disease or die, depending on the species involved. There is also some evidence that other primates, especially "bush babies" (*Galago senegalensis*) the lemur species may be involved in transmitting the disease. Although isolates have been obtained in experiments with marsupials, edentates, rodents, and birds, serologic studies indicate that these animals are only casually involved in the enzootic cycles that preserve the virus.

History

Although the first generally acknowledged epidemic of yellow fever occurred in the Yucatan in 1648, the disease is thought to have originated in Africa and to have been introduced into the Americas early in the 17th century with the slave trade. Until early in the 20th century, it was one of the most feared of all epidemic diseases. There were thousands of deaths from yellow fever, but the cause and means of spread of the disease were unknown, and no control measures were available. This situation changed when the concept of transmission by mosquitoes was proposed in Havana in 1881 by Finlay, and confirmed by Reed in Cuba in 1900. In 1901, mosquito control measures were applied successfully by Gorgas in Havana.

The first successful transmission of yellow fever to nonhuman subjects, i.e., rhesus monkeys (*Macaca mulatta*), was reported by Stokes and co-workers in 1928. This study and the later use of white mice as laboratory hosts provided proof that African and American yellow fever are the same disease and led to the development of an effective yellow fever vaccine in the 1930s.

Current Status

Today, despite the availability of effective vaccines and initial results of *A. aegypti* eradication campaigns in the Americas, yellow fever is still a significant world health problem. Table 1 shows the numbers of cases and deaths by country officially reported to the World Health Organization for the period 1959-1978. In many instances, the similarity of numbers of cases and deaths reflects the common practice of reporting autopsy- or liver biopsy-proven cases. When interpreting these data, one should be aware that there is considerable underreporting, and official figures are only rough indicators of the prevalence. For example, retrospective investigation identified 63 deaths associated with the outbreak in Gambia during 1977 and 1978, and surveys indicated that there had been from 1,000 to 1,700 deaths. Only 30 cases had been officially reported.

The geographic distribution of reported yellow fever cases since 1959 is shown in Figures 1 and 2 and corresponds well with the endemic yellow fever zones classified as infected areas by many countries. As shown in Table 1 and Figure 1, there have been major African outbreaks

Table 1. Yellow fever cases reported by country, 1959-1978

Country	No. of Cases & Deaths	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978
AFRICA																					
Angola	C	–	–	–	–	–	–	–	–	–	–	–	–	65	–	–	–	–	–	–	–
	D	–	–	–	–	–	–	–	–	–	–	–	–	42	–	–	–	–	–	–	–
U Rep of Cameroon	C	–	–	–	–	–	–	–	–	–	–	–	1	–	2	1	–	2	1	–	–
	D	–	–	–	–	–	–	–	–	–	–	–	1	–	2	–	–	2	–	–	–
Ethiopia	C	–	–	3,000	10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
	D	–	–	3,000	6	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Gambia	C	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	30
	D	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	30
Guinea-Bissau	C	–	–	–	–	–	6	–	–	–	–	–	–	–	–	–	–	–	–	–	–
	D	–	–	–	–	–	6	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Equatorial Guinea	C	–	–	–	–	–	–	–	–	–	–	–	4	–	–	–	–	–	–	–	–
	D	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Ghana	C	2	–	–	–	–	–	–	–	–	–	307	12	–	4	5	1	1	1	110	213
	D	2	–	–	–	–	–	–	–	–	–	2	7	–	4	4	1	–	–	33	40
Liberia	C	–	–	–	–	–	–	–	–	5	–	–	–	–	–	–	–	–	–	–	–
	D	–	–	–	–	–	–	–	–	3	–	–	–	–	–	–	–	–	–	–	–
Mali	C	–	–	–	–	–	–	–	–	–	–	21	–	–	–	–	–	–	–	–	–
	D	–	–	–	–	–	–	–	–	–	–	12	–	–	–	–	–	–	–	–	–
Nigeria	C	–	–	–	–	–	–	–	–	–	–	208	4	–	–	3	23	–	–	–	–
	D	–	–	–	–	–	–	–	–	–	–	60	1	–	–	1	10	–	–	–	–
Senegal	C	–	–	–	–	–	–	243	–	–	–	–	–	–	–	–	–	–	–	–	–
	D	–	–	–	–	–	–	216	–	–	–	–	–	–	–	–	–	–	–	–	–
Sierra Leone	C	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	130	–	–	–
	D	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	36	–	–	–
Sudan	C	120	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
	D	88	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Togo	C	–	–	–	–	–	–	–	–	–	–	1	2	–	–	–	–	–	–	–	–
	D	–	–	–	–	–	–	–	–	–	–	1	2	–	–	–	–	–	–	–	–
Uganda	C	–	–	–	–	–	1	–	–	–	–	–	–	–	–	–	–	–	–	–	–
	D	–	–	–	–	–	1	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Upper Volta	C	–	–	–	–	–	–	–	–	–	–	87	–	–	–	–	–	–	–	–	–
	D	–	–	–	–	–	–	–	–	–	–	44	–	–	–	–	–	–	–	–	–
Zaire	C	11	7	4	–	–	–	–	–	–	–	–	–	2	–	–	–	–	–	–	–
	D	8	7	1	–	–	–	–	–	–	–	–	–	2	–	–	–	–	–	–	–
AMERICAS																					
Argentina	C	–	–	–	–	–	–	2	51	1	–	–	–	–	–	–	–	–	–	–	–
	D	–	–	–	–	–	–	2	16	1	–	–	–	–	–	–	–	–	–	–	–
Bolivia	C	2	30	2	–	81	14	19	68	–	27	8	2	8	9	86	12	147	18	2	11
	D	–	–	–	–	–	–	–	–	–	–	–	–	5	–	39	1	80	11	1	4
Brazil	C	4	1	2	1	–	13	14	22	2	2	4	2	11	12	67	13	1	1	10	27
	D	..	..	..	..	..	12	14	22	–	–	4		9	7	67	11	1	1	10	7
Colombia	C	23	12	12	38	21	10	2	3	5	11	7	7	9	3	16	29	11	45	9	109
	D	21	11	9	30	10	9h	2	3	5	11	7	-	7	3	16	29	10	21	9	20
Ecuador	C	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	3	1	–	1
	D	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	3	1	–	1
Guyana	C	–	–	2	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
	D	–	–	2	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Panama	C	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	4	–	–	–	–
	D	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1	–	–	–	–
Paraguay	C	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	9	–	–	–	–
	D	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	3	–	–	–	–
Peru	C	1	6	53	20	49	59	45	10	3	5	28	75	–	7	33	2	1	1	82	89
	D	–	–	–	–	–	–	–	–	–	–	–	–	–	7	19	–	1	1	63	56
Surinam	C	–	–	–	–	–	–	–	–	–	1	1	–		1	–	–	–	–	–	–
	D	–	–	–	–	–	–	–	–	–	1	1	–	–	1	–	–	–	–	–	–
Trinidad & Tobago	C	1	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
	D	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Venezuela	C	1	2	14	1	1	2	5	5	–	–	–	–	–	22	7	–	–	–	–	3
	D	1	2	14	1	1	2	5	4	–	–	–	–	–	22	7	–	–	–	–	3

.. Data not available.
– Number zero or negligible.
C Cases notified to health authorities.
D Deaths notified to health authorities.

These are data from the World Health Organization.
Many are preliminary incomplete, or estimated.
Anyone who wishes to cite this information specifically should check with WHO or the reporting country.

since 1960 in Ethiopia (1961), Senegal (1965), Ghana (1969), Nigeria and Upper Volta (1969), Angola (1971), Sierra Leone (1975), and Gambia and Ghana (1978).

In the Americas, significant numbers of jungle yellow fever cases continue to be reported each year, with occasional outbreaks also involving settlements on the edge of the jungle. No large urban epidemics have occurred in the Americas since the 1928-1929 epidemic in Rio de Janeiro, Brazil (738 cases, 436 deaths), but significant outbreaks of jungle yellow fever occurred near urban areas of northern Colombia and Trinidad in 1979.

Credit for preventing yellow fever in urban areas of the Americas is generally attributed to the success of programs of *A. aegypti* control and eradication coordinated through the Pan American Health Organization. The status of these programs has declined in recent years. Major problems include inadequate financial support and the finding that areas earlier freed from *A. aegypti* are being reinfested by importation from the northern part of South America, from the United States, and from the Caribbean. No equivalent programs have been conducted in Africa, and *A. aegypti* is widely distributed throughout the "endemic yellow fever zone" there. Yellow fever has never been reported from many areas where *A. aegypti* is found, notably the Indian subcontinent, Southeast Asia, and the South Pacific. We do not know why these areas have escaped the disease, but the risk probably rises with urbanization and spreads as more people travel with greater speed throughout the world.

Indications for Vaccination

In the words of F. L. Soper, Past Director of the Pan American Health Organization: "Yellow fever is not a disease which has been conquered. It is not a disease which has been eliminated from consideration as a permanent threat . . . . For the jungle populations and for rural workers who have to go into the forest, yellow fever carries the same threat that it previously had for the people in the cities." Yellow fever is far less a threat for the typical traveler, and effective, safe vaccines are available. The 2 reasons that travelers should receive yellow fever vaccination are 1) vaccination may be required by some African countries for all entering travelers and by a number of countries for entering travelers who live in or have visited infected areas and 2) vaccination will protect travelers who may be at risk of acquiring infection in areas where yellow fever virus is present. Details of vaccine requirements for international travel can be obtained from local health departments or in *Health Information for International Travel* (see Section IV). Travelers who limit their stay to uninfected urban areas in the Americas or Africa are not likely to be at risk of contracting yellow fever. On the other hand, those who plan to reside or travel outside the urban centers of countries in endemic yellow fever zones of the Americas or Africa may well be exposed to yellow fever.

Figure 1. Yellow fever in Africa, number of cases by country, 1959-1978*

Figure 2. Yellow fever in the Americas, number of cases by country, 1959-1978*

*A number of countries classify these areas as infected and require an *International Certificate of Vaccination against Yellow Fever* from travelers arriving from them.

SECTION II:
BIOLOGICS SURVEILLANCE

Biologics Surveillance

In July 1962, the Public Health Service and the major U.S. producers of biologics agreed to collaborate on compiling data about the distribution of the most common biologic agents used as vaccines 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 summarized in quarterly reports from the Immunization Division, Bureau of State Services, Center for Disease Control, and an annual summary is included in the last quarterly report for that year. The data shown represent the total initial distribution of vaccine minus doses reported to be returned to 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 3 producers market and report figures for essentially the same product. This is a basic agreement of the Biologics Surveillance Program. In some instances, when adequate time has elapsed since production and distribution, the manufacturers have allowed data to be released when not all the criteria of confidentiality could be met. The addition of these data to the summaries completes the "natural history" of patterns of vaccine utilization.

Biologics Surveillance Program Participants

Armour Pharmaceutical Company
Connaught Laboratories
Hyland Laboratories
Lederle Laboratories
Eli Lilly & Company
Massachusetts Department of Public Health
Merck Sharp & Dohme
Michigan Department of Health
Parke, Davis & Company
Sclavo, Inc.
Wyeth Laboratories

Table 1. Biologic surveillance by product, selected years, 1965-1978.

Product Description	Biologic Surveillance					
	Number Net Doses Distributed					
	1965	1970	1975	1976	1977	1978
Influenza Virus Vaccine (All Types)	10,548,058	18,588,050	24,198,025	85,418,860	26,949,072	20,410,980
Diphtheria Toxoid with Tetanus Toxoid (Pediatric)	–	2,071,673	1,060,365	1,111,653	904,966	823,326
Diphtheria and Tetanus Toxoids with Pertussis Vaccine	20,035,808	19,490,108	17,333,487	19,021,934	16,862,740	17,992,360
Tetanus Toxoid with Diphtheria Toxoid (Adult)	–	8,780,988	8,763,624	9,843,770	9,650,244	9,191,122
Diphtheria Toxoid	28,986,870	10,374	[a]	3,716	3,590	960
Tetanus Toxoid	47,352,918	17,526,774	13,343,429	17,721,235	12,942,190	10,971,238
Pertussis Vaccine	20,885,893	116,785	47,766	91,133	21,110	100,610
Poliomyelitis Vaccine (Inactivated)	7,462,277	[a]	[a]	[a]	[a]	[a]
Poliovirus Vaccine, Live, Trivalent [b]	17,379,175	25,836,701	24,804,475[c]	19,474,835	23,211,560	24,579,120
Measles Virus Vaccine, Live, Attenuated	6,172,918	4,546,922[d]	7,378,229[d]	7,478,646[d]	10,675,623[d]	8,931,344[d]
Mumps Virus Vaccine, Live	–	2,836,000	4,811,000	4,417,000[d]	4,092,773[d]	4,648,810[d]
Rubella Virus Vaccine, Live	–	29,324,972[e]	7,809,057[d]	6,398,353[d]	7,698,639[d]	7,552,861[d]

[a] Not shown since fewer than 3 distributors reported.
[b] Also includes poliovirus vaccine, live, oral, types 1, 2, 3.
[c] Poliovirus vaccine, live, oral, types 1, 2, 3, not included since fewer than 3 distributors reported.
[d] All products containing this vaccine.
[e] From licensure through 12/70.

Table 2. Biologic products by distributor, United States, 1979-80

Products	Distributors of Specified Biologics in the United States									
	Armour Pharmaceutical Company	Connaught Laboratories	Hyland Laboratories	Lederle Laboratories	Massachusetts Department of Public Health	Merck Sharp & Dohme	Michigan Department of Health	Parke, Davis & Company	Sclavo, Inc.	Wyeth Laboratories
Influenza Virus Vaccine (All Types)		X		X		X		X		X
Diphtheria Toxoid with Tetanus Toxoid (Pediatric)				X	X		X		X	X
Diphtheria and Tetanus Toxoids with Pertussis Vaccine		X		X	X		X		X	
Tetanus Toxoid with Diphtheria Toxoid (Adult)		X		X	X		X			X
Diphtheria Toxoid							X			
Tetanus Toxoid		X		X	X	X	X	X	X	X
Pertussis Vaccine				X			X			
Poliomyelitis Vaccine (Inactivated)		X								
Poliovirus Vaccine, Live, Trivalent				X						
Measles Virus Vaccine, Live, Attenuated				X		X				
Mumps Virus Vaccine, Live						X				
Rubella Virus Vaccine, Live						X				
Immune Serum Globulin	X		X		X	X	X	X		X
Tetanus Immune Globulin			X		X	X	X	X		X

SECTION III

Immunization and Health Program for Hospital Employees

An immunization and health program for hospital personnel (defined as employees, physicians, and other professional staff, volunteers, and other persons having regular contact with patients, laboratories, and other areas of the hospital) is an essential component of a hospital's infection control program. Patient-care and laboratory employees of an acute-care hospital are at greater risk than the average person in the community of being exposed to selected communicable diseases. A personnel health program is important, therefore, in assessing risks in the hospital, providing indicated vaccination or other prophylaxis against preventable diseases to which personnel might be exposed, and diagnosing promptly and arranging for management of diseases they might contract. The program also reduces the risk of nosocomial infection for hospitalized patients by protecting the health of personnel, thereby reducing the risk that a staff member with a communicable disease will infect a susceptible patient.

A comprehensive personnel health program may include prevention of, screening for, diagnosis of, or treatment for any disease, but the following discussion is limited to communicable disease aspects of the program. Although the discussion is complete for the more commonly occurring problems, it does not attempt to cover all infectious diseases or to provide full recommendations for the management of personnel exposed to or infected by any of the numerous possible pathogens; a more complete discussion of personnel health services and the control of infections among hospital personnel has been published (*1*). Recommendations for vaccination are based on exposures that personnel are likely to have in the hospital. Those who are exposed to certain diseases in the community or who have altered host susceptibility to infection may also need to have vaccinations not routinely recommended for hospital personnel.

Vaccination and health programs for hospital personnel will vary from hospital to hospital, but most should include the elements discussed below.

Initial Health Evaluation

A complete history of communicable disease must be obtained from all personnel before or at the time they are employed or when they first provide service in the hospital. This should include a history of vaccination; tuberculosis exposure, infection, disease, and treatment; and exposure to tuberculosis, hepatitis, or other communicable conditions as appropriate. History or presence of chronic exfoliative, pustular, or other types of skin lesions should be obtained or documented because certain patient-care activities can worsen these conditions, and heavy colonization of the lesions with microbial pathogens may increase risk of nosocomial infection for patients. The history and current status of diabetes, malignant or other immunodeficient conditions, and acute and chronic gastrointestinal, cardiovascular, and respiratory diseases should also be determined.

Certain medical conditions may increase the risk of disease for hospital personnel, endangering not only them but perhaps also patients with whom they have contact. For example, although it has not been documented, personnel who are immunosuppressed might be more susceptible than the average person to infection. Also, any female employee exposed during pregnancy to diseases such as rubella or cytomegalovirus through work in the nursery or dialysis or transplantation units might be at greater risk of bearing an infant with a congenital infection. Work assignments for persons with special needs or risks should therefore be carefully considered.

The health service may elect to complete the physical examination and obtain laboratory studies on personnel for whom reliable results are not available from another source.

The following tests should be done as part of the initial health evaluation.

Tuberculin skin test. If the reaction to the first test with 5 units of Tween-stabilized purified protein derivative (PPD) is less than a 10-mm induration, a second intradermal test should be done at least 1 week and no more than 3 weeks after the first test. The results of the second test should be recorded in millimeters of induration and used as the baseline for determining subsequent conversion, treatment, and follow-up. The rationale for the current recommendation for 2 tests is a better understanding of the booster phenomenon. Persons with remote sensitivity to tuberculin who have not had recent exposure to the skin test antigen may not react to the initial skin test (false-negative result); later, however, because of the stimulation by the recent skin test, they may have a positive reaction. The 2-test technique identifies persons with initial false-negative results and avoids an erroneous assumption later that the individual has a positive skin test reaction because of current tuberculous infection (*2-5*).

Chest X-ray films. Persons with positive tuberculin skin test results should have X-ray films made. Although it may be useful to have a baseline X ray for persons who do not have earlier films available, there is no need to obtain a chest film of asymptomatic, tuberculin-negative persons.

Rubella serum antibody titer. This test is essential for women of childbearing age who work in pediatric and nursery areas. Because of the risk that personnel will acquire rubella and transmit it to susceptible pregnant patients (*6,7*), this test should also be performed on other personnel, both male and female, who might have close contact with pregnant women anywhere in the hospital.

Screening for HbsAg and anti-HBs. Hepatitis B surface antigen (HbsAg) screening for patient-care personnel assigned to hemodialysis units is extremely important (*8-10*). To provide complete information about those likely to be exposed to or to transmit hepatitis B virus (HBV), screening for both HBsAg and antihepatitis B antigen (anti-HBs) is recommended. In dialysis units, personnel positive for anti-HBs should be assigned to care for HBsAg-positive patients. Personnel working in other areas of the hospital such as some clinical laboratories or hematology-oncology, pathology, or surgery units may be exposed more frequently or intensely than most other personnel to blood from HBsAg-positive patients. Knowledge about antigen and antibody carriage can be important for evaluating the clinical status of individuals and for controlling the spread of hepatitis B; therefore, some hospitals may require initial and periodic serologic testing for personnel who are at high risk of acquiring hepatitis B (*1*).

Other tests may be required by state or local codes or may be suggested by special circumstances (e.g., serologic test for measles) (*1*). Some, such as a serologic test for syphilis, may be of value to the individual but are not central elements of the infection control program.

Serum banks in which a baseline serum specimen from each staff member is stored are not maintained in most hospitals. Although the potential value of this service has not been fully established, it is often valuable to have a serum specimen available to provide baseline values or to assist in epidemiologic investigation of problems that occur later.

Vaccinations for Hospital Personnel

Background epidemiologic information about each disease for which preventive therapy is available is provided in this and other publications (*1*). Specific information on the indications, dosage, preparation, and contraindication for each of the vaccines, toxoids, and immune globulins is discussed in other sections of this manual. These recommendations must be consulted before the products are used.

Specific recommendations for hospital personnel are shown below.

Diphtheria and tetanus toxoids. Hospital personnel are at no greater risk than the average person of acquiring tetanus, but they may be exposed to and acquire diphtheria from infected patients. Susceptible personnel should have primary vaccination against diphtheria and tetanus with adult-type (Td) toxoids. Each employee should have a booster vaccination of the adult toxoids every 10 years, or more often if exposed to a patient with diphtheria or if injured while in contact with a tetanus-prone wound.

Pertussis vaccine. Hospital personnel, especially those on the pediatric service, may acquire pertussis from infected patients. However, pertussis vaccination is not recommended for persons more than 6 years old because of potential reactions to the vaccine and because adults usually do not have the severe and perhaps fatal complications that infants with the disease sometimes do. It must be stressed that hospital personnel who contract pertussis can transmit the disease to susceptible patients. Nosocomial pertussis infection of infants is of special concern (*11*). Standard recommendations for the management of problems associated with pertussis, including the use of pertussis vaccine, have not been formulated and tested.

Measles and mumps vaccines. Susceptibility to measles and mumps should be ascertained by a history of either disease or vaccination. Serologic screening for antibody against measles is also available. Susceptible employees should have the vaccines for these diseases.

Rubella vaccine. The most serious consequences of rubella are the fetal anomalies frequently associated with rubella infection acquired by a mother in early pregnancy. In order to prevent congenital rubella syndrome for children of hospital personnel, women of childbearing age who work with pediatric patients or newborn infants must be immune to the disease. It is also possible for susceptible male personnel to acquire rubella and transmit it to pregnant patients. Therefore, all personnel, including physicians, who might have contact with pregnant women through the hospital or its clinics should be immune to rubella (*6,7*). Since histories of rubella infection are unreliable, susceptibility should be ascertained by serologic testing at the time of the initial health evaluation or documented by a record of rubella vaccination. Susceptible personnel working in high-risk areas should be vaccinated according to current recommendations for the vaccine. Pregnant women should not be vaccinated, and women of childbearing age should be cautioned not to become pregnant for at least 3 months after being vaccinated. Women of childbearing age who refuse susceptibility testing or vaccination should be advised of the risk of damage to the fetus should they become infected while pregnant.

Poliomyelitis vaccine. Most adults in the United States are immune to poliomyelitis, the risk of exposure to infection is generally low, and the risk of vaccine-associated paralysis is slightly higher for adults than for children given trivalent oral poliovaccine (OPV). Even in the prevaccine era when poliomyelitis was epidemic and hospitals treated many infected patients, the disease was rarely acquired through hospital contact. However, susceptible

hospital personnel who are in close contact with patients who might be shedding poliovirus should have a primary vaccination series with inactivated poliomyelitis vaccine as recommended by the Immunization Practices Advisory Committee (ACIP).

Influenza vaccine. Because influenza vaccine is reformulated frequently to contain antigen against the current strains of influenza viruses, the latest recommendations of the Immunization Practices Advisory Committee (ACIP) should be consulted. In general, vaccination may be considered for hospital personnel to reduce the potential for nosocomial infection and to reduce the incidence of illness and levels of absenteeism. The decision to vaccinate for these reasons, however, must be made in each hospital, with consideration given to the inherent benefits, risks, and costs of the program (*12*). Elderly personnel, those with chronic diseases (particularly those with disease of the cardiopulmonary system or kidneys or those with metabolic disease), and those who work with high-risk patients should be considered for annual vaccination against influenza, according to the current ACIP recommendations.

Typhoid vaccine. Routine typhoid vaccination is not recommended for hospital personnel.

Smallpox vaccine. The world is now considered free of smallpox; the last naturally acquired case was reported in October 1977. Therefore, smallpox vaccination is not only *not* indicated for hospital personnel, its use is discouraged because a few vaccinees have had serious side effects. The only exception to this general recommendation against smallpox vaccination is for persons working in the few laboratories in the world that continue to maintain stocks of variola virus.

Meningococcal polysaccharide vaccines. Routinely giving hospital personnel meningococcal polysaccharide vaccines is not recommended. Appropriate antibiotic prophylaxis has been the principal means of reducing the risk of secondary cases among personnel who have intimate respiratory contact (e.g., mouth-to-mouth resuscitation) with persons with meningococcal disease (*13*). Vaccination as an adjunct to antibiotic chemoprophylaxis for hospital personnel in close contact with patients with meningococcal disease has not been evaluated. Vaccination of hospital personnel during an epidemic of meningococcal disease caused by serogroups A or C should be considered as an aspect of the total community vaccination effort.

Pneumococcal polysaccharide vaccine. Routinely giving pneumococcal polysaccharide vaccination is not recommended for hospital personnel.

BCG vaccine for tuberculosis. Routine use of BCG vaccine for hospital personnel is not recommended; surveillance of personnel for evidence of newly acquired tuberculosis infection, as discussed below under Surveillance, is preferable. Some groups suggest that a BCG vaccination program should be considered for hospital personnel when there is a documented high rate of newly acquired tuberculosis infection (*14,15*). However, surveillance of patients and other infection control measures that prevent exposure are more important because they protect both patients and employees (*2,5*). It should be unusual for a hospital in the United States to have such poor infection control and disease surveillance that using BCG, a vaccine of questionable efficacy, would be necessary.

Immune globulins for hepatitis A. The risk of hepatitis A transmission in the hospital is quite small. Therefore, giving immune serum globulin (ISG) to hospital personnel as either preexposure or postexposure prophylaxis for hepatitis A is not indicated if they have only routine contact with infected patients. Personnel who have had direct oral or parenteral contact with infected patients soon after they become ill should be given ISG (*16,18-20*). Emphasis should be placed on prevention by using sound hygienic practices and good patient-care techniques (*16*). Continuing education programs about the risk of exposure to hepatitis A and recommended precautions should be provided for hospital personnel who have close contact with infective materials or with patients with hepatitis A.

Immune globulins for hepatitis B. Hepatitis B immune globulin (HBIG) is recommended as prophylaxis against hepatitis B for susceptible personnel who have a single, acute parenteral, oral, or mucosal exposure to HBsAg-infected blood, secretions, or excretions (*16,18-20*). If HBIG is not available, ISG can be used because recent batches of ISG have usually had moderately high titers of anti-HBs that appear to provide similar protection. Persons with antibody to HBV can be assumed to be immune and to need no immunoprophylaxis. No prophylaxis is recommended for HBsAg-positive individuals.

Surveillance

Hospital personnel at high risk of being exposed to certain diseases should be periodically monitored with appropriate laboratory tests and clinical evaluations. The hospital program to prevent transmission of hepatitis B should emphasize routine serologic screening for personnel working in hemodialysis units and provide intensive continuing education about the risk of exposure and recommended precautions and control practices (*8-10,16-20*). In addition, some hospitals may periodically screen selected personnel working in other high-risk areas of the hospital; the frequency of screening should be based on epidemiologic factors including the estimated risk of exposure.

If exposed to a patient with infectious tuberculosis, hospital personnel who were tuberculin negative when last tested should have skin tests performed immediately, and if results are negative they should be retested 10 weeks later. If there is a risk of frequent exposure to undiagnosed and untreated infectious tuberculosis in the hospital or in the community, regular skin testing should be performed at 6-month to 1-year intervals. Those for whom the risk of exposure is small or infrequent should be retested every 1 to 2 years (*2,5,14*).

Specific evaluation and treatment programs should be established for the management of personnel who begin to have positive tuberculin tests or show evidence of tuber-

culosis on chest X ray (*2,5,21,22*). These employees should have another chest X ray and be provided chemoprophylaxis if they do not have clinical disease. Employees who are initially tuberculin positive should have a chest X ray and be considered for chemoprophylaxis if they do not have clinical disease. Employees already vaccinated with BCG should be skin tested and managed as if BCG had not been given (*15,23*). Employees who have completed a course of chemoprophylaxis or a course of therapy for tuberculosis do not need additional X-ray examinations unless they begin to have clinical symptoms (*24*). Those who are unable to tolerate chemoprophylaxis should be kept under surveillance. A chest X ray should be made periodically, with the frequency depending on the exposure, history, and the level of risk to the employee and to patients.

Routinely taking specimens for cultures from personnel to determine asymptomatic carriage of *Staphylococcus, Streptococcus, Salmonella,* or *Shigella* is not recommended, although cultures of appropriate specimens can provide useful information in investigating outbreaks (*1*). Local and state regulations for screening food handlers should be followed.

The vaccination status of personnel should be monitored and kept current.

Laboratory Accidents

Routine personnel health policies and procedures as well as special contingency programs should be developed to identify and protect employees exposed to patients with previously unsuspected communicable disease. Among diseases in this category are tuberculosis, hepatitis A and B, meningococcal disease, rubella, varicella, and exotic diseases such as rabies, smallpox, Lassa fever, and Marburg virus disease. Occasionally a laboratory accident involving highly infectious agents may occur. To be prepared for such accidents, the personnel health service and the infection control committee and laboratory director should formulate a series of contingency plans describing the management of persons exposed to communicable diseases (*25-27*). The protocols should include 1) criteria to determine the risk of having infection or disease, considering host susceptibility and the type and duration of exposure to the pathogen, 2) individual personnel and administrative responsibilities, and 3) patient management, including isolation and treatment.

Continuing Education

Continuing education programs should be developed and used for personnel in order to emphasize specific hazards of communicable diseases to which they might be exposed and appropriate methods for managing patients and reducing the risk of transmission. The responsibility of each individual to report being ill and to seek therapy for even minor infectious problems must be emphasized. All personnel should be made aware of common symptoms of communicable diseases and the risk to patients from a person with a contagious illness. Personnel with any of the following signs of, symptoms of, or exposure to infectious diseases should report promptly to personnel health for evaluation: fever or chills, acute skin eruption, purulent drainage, jaundice, sore throat, productive cough, influenza-like illness, diarrhea, or exposure of susceptible personnel to specific illnesses such as rubella, chickenpox, hepatitis, and tuberculosis.

Personnel with communicable diseases that do not otherwise affect their ability to work but do constitute a risk for patients should be assigned to activities not involving patient care. Alternatively, they may be required or allowed to be absent from duty without penalty or loss of pay, even if their allotted sick leave has been exhausted. Taking punitive action against personnel because of minor illnesses that are potentially dangerous to patients or failing to provide them with an alternative to patient-care activities may cause them to conceal or ignore problems that they think are trivial but that are actually extremely dangerous for others.

REFERENCES

1. Kaslow RA, Garner JS. Hospital personnel. In: Bennett JV, Brachman PS, eds. Hospital infections. Boston: Little, Brown, and Co., 1979:17-52.

2. Center for Disease Control. Guidelines for prevention of TB transmission in hospitals. Atlanta: Center for Disease Control, 1979. (HEW Publication No. [CDC] 79-8371).

3. Atkinson ML, Farer LS. TB testing for hospital employees: new recommendations. Hosp Med Staff 1979; 1:16-20.

4. Comstock GW, Woolpert SF. Tuberculin conversions: true or false? Am Rev Respir Dis 1978;118: 215-7.

5. American Thoracic Society, Ad Hoc Committee of the Scientific Assembly on Tuberculosis. Screening for pulmonary tuberculosis in institutions. Am Rev Respir Dis 1977;115:901-6.

6. McLaughlin MC, Gold LH. The New York rubella incident: a case for changing hospital policy regarding rubella testing and immunization Am J Public Health 1979;69:287-9.

7. Center for Disease Control. Exposure of patients to rubella by medical personnel—California. Morbidity Mortality Weekly Report 1978;27:123.

8. Public Health Service Advisory Committee on Immunization Practices. Perspectives on the control of viral hepatitis, type B. Morbidity Mortality Weekly Report 1979;25(Suppl):1-12.

9. Snydman DR, Bryan JA, Dixon RE. Prevention of nosocomial viral hepatitis type B (hepatitis B). Ann Intern Med 1975;83:838-45.

10. Center for Disease Control. Hepatitis—control measures for hepatitis B in dialysis centers. Atlanta: Center for Disease Control, 1977. (Viral Hepatitis: Investigations and Control Series) (HEW Publication No. [CDC] 78-8358).

11. Linnemann CC, Raimundo N, Perlstein PH, et al. Use of pertussis vaccine in an epidemic involving hospital staff. Lancet 1975;2:540-3.

12. Hoffman PC, Dixon RE. Control of influenza in the hospital. Ann Intern Med 1977;87:725-8.

13. Jacobson JA, Fraser DW. A simplified approach to meningococcal disease prophylaxis. JAMA 1976;236: 1053-4.

14. American Hospital Association. Guidelines on tuberculosis control programs for hospital employees. Hospitals, JAHA 1975;49:57-60.

15. Public Health Service Advisory Committee on Immunization Practices. BCG vaccines. Morbidity Mortality Weekly Report 1970;28:241-4.

16. Public Health Service Advisory Committee on Immunization Practices. Immune globulins for protection against viral hepatitis. Morbidity Mortality Weekly Report 1977;26:425-8, 441-2.

17. Favero MS, Maynard JE, Leger RT, Graham DR, Dixon RE. Guidelines for the care of patients hospitalized with viral hepatitis. Ann Intern Med 1979;91:872-6.

18. Grady GF, Lee VA, Prince AM, et al. Hepatitis B immune globulin for accidental exposures among medical personnel: final report of a multicenter controlled trial. J Infect Dis 1978;138:625-38.

19. Hoofnagle JH, Seeff LB, Bales ZB, Wright, EC, Zimmerman HJ, the Veterans Administration Cooperative Study Group. Passive-active immunity from hepatitis B immune globulin. Ann Intern Med 1979;91:813-8.

20. Mosley JW. Hepatitis B immune globulin: some progress and some problems. Ann Intern Med 1979;91: 914-6.

21. Joint Statement of the American Thoracic Society, American Lung Association, and the Center for Disease Control. Preventive therapy of tuberculous infection. Am Rev Respir Dis 1974;110:371-4.

22. American Thoracic Society, Ad Hoc Committee of the Scientific Assembly on Tuberculosis. Treatment of mycobacterial disease. Am Rev Respir Dis 1977;115:185-6.

23. American Thoracic Society, Ad Hoc Committee on the Scientific Assembly on Tuberculosis. Tuberculosis in the foreign born. Am Rev Respir Dis 1977;116:561-4.

24. American Thoracic Society, Ad Hoc Committee on the Scientific Assembly on Tuberculosis. Discharge of tuberculosis patients from medical surveillance. Am Rev Respir Dis 1976;113:709-10.

25. Center for Disease Control. The role of the microbiology laboratory in surveillance and control of nosocomial infections. Atlanta: Center for Disease Control, 1977. (National Nosocomial Infections Study Report, Annual Summary 1974) (DHEW Publication No. [CDC] 77-8257).

26. Center for Disease Control. Prevention of laboratory-acquired infection. Atlanta: Center for Disease Control, 1978. (National Nosocomial Infections Study Report, Annual Summary 1976) (HEW Publication No. [CDC] 78-8257).

27. Center for Disease Control. Isolation techniques for use in hospitals. 2nd ed. Washington: Government Printing Office, 1975. (HEW Publication No. [CDC] 78-8314).

Immunization During Pregnancy

The increase in the number of available vaccines in the past 2 decades has left many physicians uncertain about the indications for their use. The Public Health Service and the American Academy of Pediatrics publish general recommendations for vaccination but have given limited advice for special groups such as pregnant women. Because many effects of diseases and of vaccines on the pregnant woman or her fetus are unknown, this compilation of current information will be subject to change.

A fundamental assumption behind these guidelines is that the use of vaccines during pregnancy should be limited to a few defined situations. Live-virus vaccines, in particular, should not be given except when susceptibility and exposure are highly probable and the disease to be prevented is more hazardous than vaccination for the woman or fetus.

The vaccines discussed are of 4 types: toxoids, killed bacterial and viral vaccines, live-virus vaccines, and immune serum globulin preparations. Toxoids are preparations of chemically altered bacterial exotoxin, killed vaccines contain heat-inactivated or chemically inactivated microorganisms, and live-virus vaccines are strains of virus selected for their reduced virulence. This lowered virulence may be a selected property of the virus or may be produced by serial passages of the wild virus in tissue culture (attenuation). In all cases, the vaccine shares sufficient antigenic properties with the infectious agent to stimulate protective immunity without producing significant illness. The fourth type of vaccine, immune serum globulin, is a protein fraction of human plasma that can produce transient, passive antibody protection in the recipient. Pooled gamma globulin is useful for protection against hepatitis, measles, tetanus, or rabies when possibly significant exposure has occurred or will soon occur and when available active vaccines are used as recommended.

A systematic approach toward vaccinating women of childbearing age is needed in order to protect both the woman and her fetus from preventable, serious diseases while avoiding the risk that accompanies unnecessary or hazardous vaccination. The series of factors listed below should be weighed by the health-care provider who considers vaccinating any adult female patient.

Confirmation of Pregnancy

It should first be determined whether the woman is pregnant. Because of the theoretical risk to the fetus, females of childbearing age should receive measles, rubella, and mumps vaccines only if they are not pregnant and understand that they should not become pregnant for 3 months after vaccination. In view of the importance of protecting this age group against measles and rubella, asking women if they are pregnant, excluding those who are, and explaining the theoretical risks to the others are reasonable precautions.

Determination of Susceptibility

If the woman is pregnant, it should be determined whether she is susceptible to the particular vaccine-preventable disease. A thorough history of illness and of previous vaccinations may reveal that the patient is immune and therefore does not need to be vaccinated. A history of physician-diagnosed measles or documentation of measles vaccination is usually a reliable indicator of immunity. However, if the history is in question, serologic testing, when practical, can be used to determine susceptibility. Unfortunately, at this time, serologic tests are not readily available for most vaccine-preventable diseases other than rubella.

Risk of Exposure

The third factor to be weighted is the patient's risk of exposure to a disease. During pregnancy, it is preferable to reduce exposure when possible rather than to vaccinate with live-virus vaccines. A pregnant woman can avoid certain diseases by not entering areas in which these diseases are endemic. In particular, she can be advised against travel in areas with endemic plague or yellow fever unless she was vaccinated against these diseases before becoming pregnant. In addition, sanitary precautions will decrease the chance of exposure to typhoid, cholera, and hepatitis. Obviously it is not feasible to prevent exposure to diseases endemic in the United States, such as rubella or measles, or to periodically epidemic diseases, such as influenza. However, an epidemic in this country of a currently rare disease, for example poliomyelitis, might significantly alter a woman's chance of exposure and therefore alter the decision about vaccination.

Once it has been determined that exposure is likely or unavoidable, the hazards of the disease must be balanced against the potential deleterious effects of vaccination.

Risk from Disease

If the woman is pregnant, susceptible, and at risk of exposure, it is important to assess the potential morbidity and mortality caused by the disease for the pregnant woman and the fetus. Pregnancy may significantly alter the rate at which some complications occur and the health-care provider must be aware of special problems that pregnancy may impose. In the case of tetanus, for example, the high morbidity and mortality do not change during pregnancy. Because poliomyelitis has been reported to produce paralysis more frequently during pregnancy, vaccination is

recommended when the risk of exposure is high. Tetanus toxoid should be given to all susceptible pregnant women.

Risk from Vaccines

Once the above factors have been considered, the vaccine must be assessed in terms of its effectiveness in conferring immunity and its potential for complicating pregnancy. Data on effectiveness exist for most of the agents listed in Table 1. Cholera vaccine is notable for the poor or transient immunity it confers, and influenza vaccine provides protection for only about a year. The other vaccines discussed have been shown to produce stable immunity for over 90% of vaccinees.

Little information is available on the deleterious effects that vaccines may have on the fetus. Rubella vaccine has probably been the most thoroughly studied in this regard. A total of 84 women known to be susceptible who received rubella vaccine shortly before becoming pregnant or early in pregnancy were followed to term. All the infants were clinically normal, though 2 had serologic evidence of rubella virus infection. The risk that rubella vaccine virus will cause congenital deformity therefore appears to be less than 5%, considerably less than the risk from the disease itself.

Nevertheless, pregnancy is a contraindication to rubella vaccination, as well as to measles and mumps vaccination, because of the theoretical risk of damage to the fetus. In general, killed vaccines may be the least threatening, although their actual effects are unknown, and exaggerated febrile responses by the mother may also pose some risk.

Although live measles vaccine should not be given to a pregnant woman, immune serum (gamma) globulin will usually protect a susceptible person from measles if given within 48 hours after exposure. It is important to administer the globulin when indicated, because measles has been reported to cause up to 50% of infected pregnant women to abort. On the other hand, pooled gamma globulin has not been shown to prevent infection after exposure to rubella or mumps.

Immune Serum Globulins

Immune serum (gamma) globulin preparations are available for persons exposed to or anticipating exposure to measles, hepatitis A, hepatitis B, tetanus, or rabies. Some of these preparations are prepared from high-titer immune globulin pools and are marketed as hepatitis B immune globulin, tetanus immune globulin (humna), and rabies immune globulin (human). Globulin preparations provide passive (and thus temporary) protection only.

Indications for using these preparations are the same for pregnant and nonpregnant women. These and other human immune serum globulin preparations, although not to be used indiscriminately, pose no known threat to the pregnant woman or her fetus.

Vaccinia immune globulin, previously available for use with smallpox vaccination, is no longer available.

For 2 reasons, immune serum globulin is *not* the best therapy for pregnant women exposed to rubella infection: 1) subclinical infection may still occur, with attendant risk to the fetus, and 2) the passively acquired antibody will hinder accurate serologic diagnosis of rubella infection.

Table 1 summarizes information on vaccine-preventable diseases in terms of the 5 categories outlined above. Using the approach described, the health-care provider should be better able to decide whether a specific vaccine is indicated for a pregnant patient. If the information available is inadequate or further questions arise, the health-care provider should seek advice from local or state health authorities or from infectious disease specialists.

In order to improve knowledge about adverse effects of live-virus vaccines given to pregnant women, situations in which pregnant women are inadvertently vaccinated should be reported to the Immunization Division, Bureau of State Services, Center for Disease Control (404-329-3741). Women who become pregnant within 3 months after such vaccination may also be at risk, and such occurrences should also be reported.

Inquiries for additional information or requests for consultation for specific problems can also be directed to the Immunization Division.

Table 1. Information on vaccination during pregnancy, by vaccine type

	RISK FROM DISEASE TO PREGNANT FEMALE	RISK FROM DISEASE TO FETUS OR NEONATE	VACCINE	RISK FROM VACCINE TO FETUS	INDICATIONS FOR VACCINATION DURING PREGNANCY	DOSE/ SCHEDULE	COMMENTS
LIVE VIRUS VACCINES:							
MEASLES	Significant morbidity, low mortality, not altered by pregnancy.	Significant increase in abortion rate. May cause malformations.	Live-attenuated virus vaccine.	Non confirmed.	Contraindicated. See immune serum globulins.	Single dose.	— — —
RUBELLA	Low morbidity and mortality, not altered by pregnancy.	High rate of abortion and congenital rubella syndrome in first trimester.	Live-attenuated virus vaccine.	None confirmed.	Contraindicated.	Single dose.	Teratogenicity of vaccine suspected but not confirmed.

Table 1. Information on vaccination during pregnancy, by vaccine type (Continued)

	RISK FROM DISEASE TO PREGNANT FEMALE	RISK FROM DISEASE TO FETUS OR NEONATE	VACCINE	RISK FROM VACCINE TO FETUS	INDICATIONS FOR VACCINATION DURING PREGNANCY	DOSE/ SCHEDULE	COMMENTS
MUMPS	Low morbidity and mortality, not altered by pregnancy.	Questionable association with fibroelastosis in neonates.	Live-attenuated virus vaccine.	None confirmed.	Contraindicated.	Single dose.	– – –
SMALLPOX	Mortality increased to 90% during pregnancy (variola major).	Possible increased abortion rate. Congenital smallpox reported.	Live-vaccinia virus.	Rare cases of congenital vaccinia	Contraindicated, Avoid in pregnancy except for unavoidable exposure.	Single dose.	Disease has been eradicated. Only use is for those exposed to variola virus in the laboratory.
YELLOW FEVER	Significant morbidity and mortality, not altered by pregnancy.	Unknown.	Live-attentuated virus vaccine.	None confirmed.	Contraindicated except for unavoidable exposure.	Single dose.	Postponing travel perferable to vaccination.
RABIES	Near 100% fatality not altered by pregnancy.	Determined by maternal disease.	Killed virus vaccine. Rabies immune globulin.	None confirmed.	Pregnancy does not alter indications for prophylaxis. Each case must be considered individually.	Consult public health authorities for indications and dosage.	– – –
INACTIVATED VIRUS VACCINES:							
POLIOMYELITIS	No increased incidence in pregnancy, but may increase risk of more severe disease.	Anoxic fetal damage reported. 50% mortality in neonatal disease.	Trivalent live-attenuated virus (Sabin) and inactivated (Salk) vaccine[a].	None confirmed.	Not routinely recommended for adults in USA. Immunize all persons at increased risk of exposure.	Trivalent. Primary series of 3 doses at 1-2 month intervals, or booster dose.	Vaccine indicated for susceptible women travelling in endemic areas.
INFLUENZA	Possible increase in morbidity and mortality during epidemic of new antigenic strain.	Possible increased abortion rate. No malformations confirmed.	Inactivated type A and type B virus vaccines.	None confirmed.	Usually recommended only for patients with serious underlying diseases. Consult public health authorities for current recommendation.	*Primary:* 2 doses 4-weeks apart in early fall for those under 27 years; single dose for those ≥27. *Booster:* Single dose.	Criteria for vaccination of pregnant women same as for nonpregnant population.
INACTIVATED BACTERIAL VACCINES:							
CHOLERA	Significant morbidity and mortality, not altered by pregnancy.	Unknown.	Killed bacterial vaccine.	None confirmed.	Only to meet international travel requirements.	2 injections 4-8 weeks apart.	Vaccine of low efficacy.
TYPHOID	Significant morbidity and mortality, not altered by pregnancy.	Unknown.	Killed bacterial vaccine.	None confirmed.	Not recommended routinely except for close continued exposure or travel to endemic areas.	*Primary immunization:* 2 injections 4 weeks apart. *Booster:* Single dose.	– – –
PLAGUE	Significant morbidity and mortality, not altered by pregnancy.	Unknown	Killed bacterial vaccine.	None Confirmed.	Very selective vaccination of exposed persons.	Consult public health authorities for indications and dosage.	– – –

Table 1. Information on vaccination during pregnancy, by vaccine type (Continued)

	RISK FROM DISEASE TO PREGNANT FEMALE	RISK FROM DISEASE TO FETUS OR NEONATE	VACCINE	RISK FROM VACCINE TO FETUS	INDICATIONS FOR VACCINATION DURING PREGNANCY	DOSE/ SCHEDULE	COMMENTS
MENINGOCOCCUS	No increased risk during pregnancy. No increase in severity of disease.	Unknown	Killed bacterial vaccine.	No data available on use during pregnancy.	Pregnancy does nor alter indications. Vaccinated only in unusual outbreak situations.	Consult public health authorities.	---
PNEUMOCOCCUS	No increased risk during pregnancy. No increase in severity of disease.	Unknown.	Killed bacterial vaccine.	No data available on use during pregnancy.	Pregnancy does not alter indications. Vaccine used only for particular high-risk individuals.	Consult public health authorities.	---
TOXOIDS: TETANUS-DIPHTHERIA	Severe morbidity Tetanus mortality 60%, diphtheria mortality 10% unaltered by pregnancy.	Neonatal tetanus mortality 60%	Combined tetanus diphtheria toxoids preferred: request adult Td from pharmacist.	None confirmed.	Lack of primary series, or no booster within past 10 years.	*Primary:* 3 doses at 1-2 month intervals. *Booster:* Single dose.	Updating of immune status should be be part of antepartum care.
IMMUNE SERUM GLOBULIN:	Morbidity and mortality not altered by pregnancy.	Congenital and/or neonatal disease known to be associated with hepatitis and measles; risk uncertain for others.	Immune serum globulin or specific globulin preparations.	None reported. See text: "Immune Serum Globulins."	Exposure or anticipated exposure to measles, hepatitis A, hepatitis B, rabies, or tetanus.	See package insert of specific preparation.	Does not provide active or lasting immunity.

[a]Inactivated polio vaccine (Salk) recommended for susceptible adults at increased risk.

In order to provide better knowledge about effects of live-virus vaccines given during pregnancy, we ask that situations in which pregnant women are inadvertently vaccinated or in which women become pregnant within 3 months after vaccination be reported to the Immunization Division, Bureau of State Services, Center for Disease Control, Atlanta, GA 30333 (Tel. 404-329-3741).

Immunization for Infants and Children

Table 1*
Recommended schedule for active immunization of normal infants and children

2 mo	DTP[1]	TOPV[2a]
4 mo	DTP	TOPV
6 mo	DTP	2b
1 yr		Tuberculin Test[3]
15 mo	Measles,[4] Rubella[4]	Mumps[4]
1½ yr	DTP	TOPV
4-6 yr	DTP	TOPV
14-16 yr	Td[5]—repeat every 10 years	

1 DTP—diphtheria and tetanus toxoids combined with pertussis vaccine.

2a TOPV—trivalent oral poliovirus vaccine. This recommendation is suitable for breast-fed as well as bottle-fed infants.

2b A third dose of TOPV is optional but may be given in areas of high endemicity of poliomyelitis.

3 Frequency of repeated tuberculin tests depends on risk of exposure of the child and on the prevalence of tuberculosis in the population group. For the pediatrician's office or outpatient clinic, an annual or biennial tuberculin test, unless local circumstances clearly indicate otherwise, is appropriate. The initial test should be done at the time of, or preceding, the measles immunization.

4 May be given at 15 months as measles-rubella or measles-mumps-rubella combined vaccines.

5 Td—combined tetanus and diphtheria toxoids (adult type) for those more than 6 years of age, in contrast to diphtheria and tetanus (DT) toxoids, which contain a larger amount of diphtheria antigen. *Tetanus toxoid at time of injury:* For clean, minor wounds, no booster dose is needed by a fully immunized child unless more than 10 years have elapsed since the last dose. For contaminated wounds, a booster dose should be given if more than 5 years have elapsed since the last dose.

Concentration and Storage of Vaccines

Because the concentration of antigen varies in different products, the manufacturer's package insert should be consulted regarding the volume of individual doses of immunizing agents.

Because biologics are of varying stability, the manufacturer's recommendations for optimal storage conditions (e.g., temperature, light) should be carefully followed. Failure to observe these precautions may significantly reduce the potency and effectiveness of the vaccines.

* From the *Report of the Committee on Infectious Diseases,* 1977, 18th edition. Copyright American Academy of Pediatrics 1977.

Table 2*
Primary immunization for children not immunized in early infancy[1]

Under 7 Years of Age	
First visit	DTP, TOPV, Tuberculin Test
Interval after first visit	
1 mo	Measles,[2] Mumps, Rubella
2 mo	DTP, TOPV
4 mo	DTP, TOPV[3]
10 to 16 mo or preschool	DTP, TOPV
Age 14-16 yr	Td—repeat every 10 yr
7 Years of Age and Over	
First visit	Td, TOPV, Tuberculin Test
Interval after first visit	
1 mo	Measles, Mumps, Rubella
2 mo	Td, TOPV
8 to 14 mo	Td, TOPV
Age 14-16 yr	Td—repeat every 10 years

1 Physicians may choose to alter the sequence of these schedules if specific infections are prevalent at the time. For example, measles vaccine might be given on the first visit if an epidemic is under way in the community.

2 Measles vaccine is not routinely given before 15 months of age (see Table 1).

3 Optional.

* From the *Report of the Committee on Infectious Diseases,* 1977, 18th edition. Copyright American Academy of Pediatrics 1977.

SECTION IV:
ACIP RECOMMENDATIONS

RECOMMENDATIONS OF THE IMMUNIZATION PRACTICES ADVISORY COMMITTEE

Here are the most current recommendations of the Immunization Practices Advisory Committee (ACIP) on the vaccines or diseases indicated below. These recommendations are frequently reviewed, and revisions or updates are published in the *Morbidity and Mortality Weekly Report* (MMWR). If you wish to be included on the MMWR mailing list to be sure you are kept abreast of future revisions, send your request to: Distribution Services, GSO, Center for Disease Control 1/SB-36, Atlanta, Georgia 30333.

- ☐ General Recommendations on Immunization
- ☐ BCG Vaccines
- ☐ Cholera Vaccine*
- ☐ Diphtheria/Tetanus Toxoids/Pertussis Vaccine
- ☐ Immune Globulins for Viral Hepatitis
- ☐ Influenza Vaccine
- ☐ Measles Prevention
- ☐ Meningococcal Polysaccharide Vaccines
- ☐ Mumps Vaccine
- ☐ Plague Vaccine*
- ☐ Pneumococcal Polysaccharide Vaccine
- ☐ Poliomyelitis Prevention
- ☐ Rabies Prevention
- ☐ Rubella Vaccine
- ☐ Smallpox Vaccine*
- ☐ Typhoid Vaccine*
- ☐ Typhus Vaccine*
- ☐ Yellow Fever Vaccine*
- *☐ Vaccines for Selective Use in International Travel (collection of individual reprints)

The attached statements are current as of_____. Additional copies may be ordered from: Public Inquiries, Center for Disease Control 1/B63, Atlanta, Georgia 30333.

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Recommendation of the Immunization Practices Advisory Committee (ACIP)

General Recommendations on Immunization

This revision of the "General Recommendations on Immunization" represents an updating of the 1976 statement, based on current knowledge and experience. Major changes from the 1976 statement clarify the recommendations on simultaneous administration of vaccines and emphasize the need to report adverse reactions to vaccines.

INTRODUCTION

Certain basic principles underlie the immunization practices recommended for infants, children, and adults. Most of these principles depend on scientific knowledge about active and passive immunization. Others represent judgments of public health officials and specialists in clinical and preventive medicine. Thus, recommendations on immunization practices represent a balancing of scientific evidence of benefits and risks in order to achieve optimal levels of protection against infectious or communicable diseases.

MULTIPLE-DOSE VACCINES

Some vaccines must be given in more than 1 dose for full protection. In recommending the times and intervals for multiple doses, the Committee takes into account current risks from disease and the objective of inducing satisfactory clinical immunity. Intervals between doses that are longer than those recommended do not usually lead to a reduction in final antibody levels. Therefore, it is not necessary to restart an interrupted series of vaccinations or to add extra doses.

SIMULTANEOUS ADMINISTRATION OF CERTAIN VACCINES

Experimental evidence and extensive clinical experience are strengthening the scientific basis for giving certain vaccines at the same time. Most of the widely used antigens can safely and effectively be given simultaneously. This knowledge is particularly helpful when circumstances call for giving several vaccines at the same time—such as imminent exposure to several infectious diseases, preparation for foreign travel, or uncertainty that the patient will return for future vaccinations.

In general, inactivated vaccines can be administered simultaneously at separate sites. It should be noted, however, that when vaccines commonly associated with local or systemic side effects—such as cholera, typhoid, and plague vaccines—are given simultaneously, the side effects theoretically could be accentuated. Generally, persons known to experience such side effects should be given these vaccines on separate occasions.

An inactivated vaccine and a live, attenuated-virus vaccine can be administered simultaneously at separate sites, with the precautions that apply to the individual vaccines.

Previously it has been recommended that individual live-virus vaccines be given at least 1 month apart whenever possible. The reason for this was the theoretical concern that more frequent or severe side effects as well as diminished antibody responses might otherwise result. Field observations indicate, however, that simultaneous administration of the most widely used live-virus vaccines has not resulted in impaired antibody response or increased rates of adverse reactions.

Observation of children indicates that antibody responses to trivalent oral polio vaccine (OPV) given simultaneously with licensed combination measles-mumps-rubella vaccine are comparable to those obtained when the same vaccines are given at different times. It is reasonable to expect equivalently good immunologic responses when other licensed, combination, live attenuated-virus vaccines or their component antigens are given simultaneously with OPV.

Direct evidence on the response to simultaneous administration of diphtheria and tetanus toxoid and pertussis vaccine (DTP), OPV, and measles-mumps-rubella vaccines is lacking. However, field experience and antibody data regarding simultaneous administration of either DTP and measles vaccine or DTP and OPV indicate that the protective response is satisfactory and that the incidence of side effects is not increased. Therefore, simultaneous administration of all of these antigens is feasible, particularly if there is doubt that the recipient will return to receive further doses of vaccine.

There is no evidence to indicate that simultaneous administration of individual measles, mumps, or rubella antigens at different sites will yield different results from administration of the combined vaccines in a single site.

Simultaneous administration of pneumococcal polysaccharide vaccine and whole-virus influenza vaccine has been found to give satisfactory antibody response without increasing the incidence of side effects. Although not yet studied, simultaneous administration of the pneumococcal vaccine and split-virus influenza vaccine may also be expected to yield satisfactory results.

HYPERSENSITIVITY TO VACCINE COMPONENTS

Vaccine antigens produced in systems or with substrates that contain allergenic substances—for example, those antigens derived from growing microorganisms in the embryonated eggs of chickens or ducks—may cause hypersensitivity reactions. These may possibly include anaphylaxis, when the final vaccine contains a significant amount of the allergen. Such antigens include those grown in eggs and used against typhus, rabies (duck embryo vaccine), and yellow fever. Vaccines with such characteristics should not be given to persons known to be hypersensitive to components of the substrates. Contrary to this generalization, influenza vaccine antigens, although prepared from viruses grown in embryonated eggs, are highly purified during preparation and have only very rarely been reported to be associated with hypersensitivity reactions. Screening persons by history of ability to eat eggs without adverse effects is a reasonable way to identify those possibly at risk from influenza vaccination. Individuals with anaphylactic hypersensitivity to eggs should not be given influenza vaccine. This would include persons who, upon ingestion of eggs, develop swelling of the lips or tongue or who experience acute respiratory distress or collapse.

Live-virus vaccines prepared by growing viruses in cell cultures are essentially devoid of potentially allergenic substances related to host tissue. No severe hypersensitivity reactions have been reported with the live, attenuated measles, mumps, or rubella vaccines prepared from viruses grown in cell cultures. These vaccines can be given safely regardless of a history of allergy to eggs or egg protein.

Vaccines, such as cholera, DTP, plague, and typhoid, that are derived from organisms grown in simple bacteriologic media, are frequently associated with local, and occasionally systemic, side effects, but they do not appear to be allergenic *per se*. They should not be given, however, to individuals who have experienced any serious side effects from them.

Some vaccines contain preservatives or trace amounts of antibiotics to which patients may be hypersensitive. Those giving vaccines should review carefully the information provided with the package insert before deciding whether the rare patients with known hypersensitivity to such preservatives or antibiotics can be vaccinated safely.

ALTERED IMMUNITY

Virus replication after administration of live, attenuated-virus vaccines may be enhanced in persons with immune deficiency diseases, and in those with suppressed capability for immune response, as occurs with leukemia, lymphoma, generalized malignancy, or therapy with corticosteroids, alkylating agents, antimetabolites, or radiation. Patients with such conditions should not be given live, attenuated-virus vaccines. Similarly, individuals residing in the household of a susceptible immunocompromised individual should not receive OPV because vaccine viruses are excreted by the recipient of the vaccine and are communicable to other persons.

SEVERE FEBRILE ILLNESSES

Vaccination of persons with severe febrile illnesses should generally be deferred until these persons have recovered. This precaution is to avoid superimposing adverse side effects from the vaccine on the underlying illness or mistakenly identifying a manifestation of the underlying illness as having been caused by the vaccine. The presence of minor illnesses such as mild upper-respiratory infections should not preclude vaccination.

LIVE VACCINES AND PREGNANCY

On grounds of a theoretical risk to the developing fetus, live, attenuated-virus vaccines are not generally given to pregnant women or to those likely to become pregnant within 3 months after vaccination. With some of these antigens, particularly rubella, measles, and mumps vaccines, pregnancy is a contraindication to the vaccination. With OPV and yellow fever vaccine, however, vaccine should be given if there is a substantial risk of exposure to natural infection. There is no convincing evidence of risk to the fetus from vaccination of pregnant women with inactivated viral vaccines, bacterial vaccines, or toxoids.

RECENT ADMINISTRATION OF IMMUNE SERUM GLOBULIN OR HYPERIMMUNE GLOBULIN

Passively acquired antibody can interfere with the response to live, attenuated-virus vaccines. Therefore, administration of such vaccines should be deferred until approximately 3 months after passive immunization. By the same token, immunoglobulins should not be administered for at least 2 weeks after a vaccine has been given, if possible. Inactivated vaccines are sometimes administered concurrently with passive antibody to induce active immunity, as is done for postexposure rabies prophylaxis.

REPORTING ADVERSE REACTIONS

All vaccines have been reported to cause some adverse effects. These range from minor local reactions to severe systemic illness such as paralysis associated with OPV. To improve knowledge about adverse effects, all severe reactions should be evaluated and reported in detail to local or state health officials and to the manufacturer.

Replaces previous recommendation on this subject, published in MMWR 1976;25:349-50,355.

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Recommendation of the Immunization Practices Advisory Committee (ACIP)

BCG Vaccines

INTRODUCTION

Tuberculosis cases and deaths in the United States have declined steadily since reporting began in the 19th century. In 1977 there were approximately 30,000 reported cases and 3,000 deaths, for rates of 13.9 (cases) and 1.4 (deaths) per 100,000 population. These rates are 40% and 60% lower than the corresponding rates for 1967. The rate of infection, judged by the prevalence of positive tuberculin skin tests, has also declined, particularly for susceptible groups, such as young children. The prevalence of positive reactors among children entering school is now estimated to be 0.2%, and among adolescents, 0.7%. The current annual infection rate is estimated to be 0.03%, based on the prevalence among 6-year-olds.

The incidence of tuberculosis cases varies broadly among different segments of the population and in different localities. Cases occur twice as frequently in males as in females. Rates increase sharply with age in both sexes and all races. More than 80% of reported cases are in persons over 25 years of age, most of whom were infected several years previously. Reported cases are generally typical post-primary pulmonary disease. The risk of infection is greatest for those who have repeated exposure to persons with unrecognized or untreated sputum-positive pulmonary tuberculosis. Chemotherapy rapidly reduces the infectivity of cases.

Efforts to control tuberculosis in the United States are directed toward the early identification and treatment of cases and preventive therapy with isoniazid for infected persons at high risk of developing disease. In this country, vaccine prepared from the Bacillus of Calmette and Guérin (BCG) has been used mainly for selected groups of uninfected persons who live or work where they have an unavoidable risk of exposure to tuberculosis.

BCG VACCINES

BCG was derived from a strain of *Mycobacterium bovis* attenuated through years of serial passage in culture by Calmette and Guérin at the Pasteur Institute, Lille, France. It was first administered to humans in 1921.

There are many BCG vaccines* available in the world today; all are derived from the original strain, but they vary in immunogenicity, efficacy, and reactogenicity. Variation probably has been the result of genetic changes in the bacterial strains; differences in techniques of production; methods and routes of vaccine administration; and characteristics of the populations and environments in which vaccine has been studied. Controlled trials—all conducted prior to 1955—of liquid vaccines prepared from different BCG strains showed protection ranging from 0 to 80%.

The vaccines now available in the United States differ from products used in the field trials in that additional culture passages have since taken place, and there have been various modifications in methods of preparation and preservation. The efficacy of these current vaccines has not been demonstrated directly and can only be inferred.

Production standards for BCG vaccines (Bureau of Biologics, Food and Drug Administration) specify that they be freeze-dried products containing live bacteria from a documented strain of the Bacillus of Calmette and Guérin. The strain must demonstrate various specified characteristics of safety and potency and be capable of inducing tuberculin sensitivity in guinea pigs and humans. (The assumed relationship between sensitivity and immunity has not been proven.)

Freeze-dried vaccine should be reconstituted, protected from exposure to light, and used within 8 hours.

VACCINE USAGE

General Recommendations

Modern methods of case detection, chemotherapy, and preventive treatment can be highly successful in controlling tuberculosis. Nevertheless, an effective BCG vaccine may be useful under certain circumstances. In particular, BCG may benefit uninfected persons with repeated exposure to infective cases who cannot or will not obtain or accept treatment.

Recommended Vaccine Recipients

1. BCG vaccination should be seriously considered for individuals, such as infants in a household, who are tuberculin skin-test negative (*1*) but who have repeated exposure to persistently untreated or ineffectively treated patients with sputum-positive pulmonary tuberculosis.

2. BCG vaccination should be considered for groups in which an excessive rate of new infections can be demonstrated and the usual surveillance and treatment programs have failed or are not feasible. Such groups might exist among those without a regular source of health care.

Adequate surveillance and control measures should be possible to protect groups such as health workers (*2*). However, some health workers may be at increased risk of repeated exposure, especially those working in institutions serving major urban population centers in which the endemic prevalence of tuberculosis is relatively high. BCG vaccine should be considered when the frequency of skin-test conversion representing new infections (*3*) exceeds 1% annually.

Schedule

BCG should be reserved for persons who are skin-test negative to 5 TU* of tuberculin, PPD.† Those who receive BCG should have a tuberculin skin test 2-3 months later. If that skin test is negative and the indications for BCG remain, a second dose of vaccine should be given. Dosage is indicated by the manufacturer in the package labeling; one-half of the usual dose should be given to persons under 28 days old. If the indications for immunization persist, these children should receive a full dose after attaining 1 year of age.

Administration Technique

The World Health Organization recommends that BCG be given by the intradermal route in order to provide a uniform and reliable dose. In the United States, however, vaccines for intradermal and for percutaneous administration are licensed, and vaccination should be only by the route indicated in the package labeling.

*Official name: BCG Vaccine.

*Tuberculin unit.
†*Purified protein derivative* of tuberculin.

RISKS AND SIDE EFFECTS

BCG vaccine has been associated with adverse reactions including severe or prolonged ulceration at the vaccination site, lymphadenitis, and—very rarely—osteomyelitis, lupoid reactions, disseminated BCG infection, and death. Available data on adverse reactions do not necessarily pertain to the vaccines currently licensed in the United States, and the reported frequency of complications has varied greatly, depending in part on the extent of the surveillance effort. For example, the frequency of ulceration and lymphadenitis has been reported to range from 1% to 10%, depending on the vaccine, the dosage, and the age of vaccinees. Osteomyelitis has been reported to occur in 1 per 1,000,000 vaccinees, although limited information indicates that with newborns it may be higher. Disseminated BCG infection and death are very rare (1-10 per 10,000,000 vaccinees) and occur almost exclusively in children with impaired immune responses.

PRECAUTIONS AND CONTRAINDICATIONS

Altered Immune States

BCG for prevention of tuberculosis should not be given to persons with impaired immune responses such as occur with congenital immunodeficiency, leukemia, lymphoma, or generalized malignancy, and when immunologic responses have been suppressed with steroids, alkylating agents, antimetabolites, or radiation.

Pregnancy

Although no harmful effects of BCG on the fetus have been observed, it is prudent to avoid vaccination during pregnancy unless there is an immediate excessive risk of unavoidable exposure to infective tuberculosis.

Interpretation of Tuberculin Test

After BCG vaccination, it is usually not possible to distinguish between a tuberculin reaction caused by virulent supra-infection and one resulting from persistent postvaccination sensitivity. Therefore, caution is advised in attributing a positive skin test to BCG (except in the immediate postvaccination period), especially if the vaccinee has recently been exposed to infective tuberculosis.

Tuberculosis in Vaccinated Persons

Since full, lasting protection from BCG vaccination cannot be assured, tuberculosis should be included in the differential diagnosis of any tuberculosis-like illness in a BCG vaccinee.

SURVEILLANCE

All suspected adverse reactions to BCG should be carefully investigated and reported to health authorities. These reactions occasionally occur as long as a year or more after vaccination.

References

1. American Lung Association: Diagnostic standards and classification of tuberculosis and other mycobacterial diseases. New York, American Lung Association, 1974
2. CDC: Guidelines for Prevention of TB Transmission in Hospitals (HEW Pub. No. [CDC] 79-8371). Atlanta, CDC, Jan 1979
3. Thompson N, Glassroth JL, Snider D, Farer LS: The booster phenomenon in serial tuberculin testing. Am Rev Respir Dis 119:587-597, 1979

SELECTED BIBLIOGRAPHY

CDC: Tuberculosis in the United States 1977 (HEW Pub. No. [CDC] 79-8322). Atlanta, CDC, Mar 1979

Eickhoff TC: The current status of BCG immunization against tuberculosis. Annu Rev Med 28:411-423, 1977

National Institutes of Health: Status of Immunization in Tuberculosis in 1971: Report of a Conference on Progress to Date, Future Trends, and Research Needs (HEW Pub. No. [NIH] 72-68). Washington, Government Printing Office, 1972

Rouillon A, Waaler H: BCG vaccination and epidemiological situation: A decision making approach to the use of BCG. Adv Tuberc Res 19:64-126, 1976

World Health Organization: Ninth Report of the Expert Committee on Tuberculosis (WHO Tech Rep No. 552). Geneva, WHO, 1974

Replaces previous recommendations on BCG Vaccines published in Morbidity and Mortality Weekly Reports (MMWR) 15:350-351, 1966 and 24:69-70, 1975.

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Recommendation of the Immunization Practices Advisory Committee (ACIP)

Diphtheria and Tetanus Toxoids and Pertussis Vaccine

INTRODUCTION

Routine immunization against diphtheria, tetanus, and pertussis in infancy or childhood has been widely advocated and generally practiced in the United States for the past 30 years. Its effectiveness is reflected in the marked decrease in cases and deaths from these 3 diseases.

DIPHTHERIA

Reported cases of diphtheria in the United States remain at 200-300 annually with some variation due to a few focal epidemics. (In 1970, for instance, there were 435 cases.) While diphtheria is generally uncommon, localized outbreaks continue to occur in many parts of the United States. Many of the reported cases are severe, and 10% of respiratory diphtheria cases are fatal.

Although outbreaks of diphtheria in adults (including cutaneous diphtheria) are becoming increasingly common in urban areas, most diphtheria cases occur in children. The majority of cases are in unimmunized or inadequately immunized persons. Diphtheria immunity does not prevent pharyngeal carriage of the organism, but it does significantly reduce the occurrence and severity of clinical disease. Antitoxin persists at protective levels for 10 years or more in adequately immunized persons.

TETANUS

Although its incidence in the United States has declined in recent years, tetanus remains an important health problem. In 1975, 102 cases of tetanus were reported. All occurred in unimmunized persons, partially immunized persons, or persons whose immunization history was uncertain. More than half of the patients were 50 years of age or older.

Since the tetanus organism is ubiquitous and there is no natural immunity to the tetanus toxin, immunization is a universal necessity regardless of age. Immune pregnant women provide maternal antibodies to their infants, thus protecting them against neonatal tetanus.

Tetanus toxoid has proved to be an excellent immunizing agent. It is highly effective and provides long-lasting protection. Hypersensitivity reactions are uncommon with primary immunization. They do occasionally occur in persons who have received an excessive number of booster injections.

PERTUSSIS

The severe complications and high mortality from pertussis in infancy are the major reasons for immunization early in life. Pertussis is highly communicable, and attack rates of up to 90% are reported for unimmunized household contacts. Most cases occur in infants and young children. In 1972, a typical year, two-thirds of the reported pertussis deaths occurred in infants less than 1 year of age.

Cases and consequently deaths from pertussis have declined dramatically with increasingly widespread use of standardized pertussis vaccines beginning in the late 1940s. Because the incidence, severity, and fatality of pertussis decrease with age, routine pertussis vaccination is not generally needed or recommended for persons 7 years of age or older. (See "VACCINE USAGE.")

PREPARATIONS USED FOR IMMUNIZATION

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

The toxoids are available in both fluid and adsorbed forms. Comparative tests show that adsorbed toxoids induce higher antitoxin titers and more durable protection than fluid toxoid, although the rate of appearance of antibody is essentially equivalent. Thus, adsorbed toxoids are preferable.

The toxoids and pertussis vaccine 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 toxoids (Td) is only about 10-25% of that in standard DTP.

VACCINE USAGE

Primary Immunization

Age: *For children 6 weeks through 6 years (up to the seventh birthday)*, the manufacturers' recommended dose of DTP should be given intramuscularly on 4 occasions, 3 doses at 4- to 8-week intervals and a fourth dose approximately 1 year after the third. Ideally, immunization should begin at 2-3 months of age or at the 6-week check-up, if this is an established routine.

For schoolchildren and adults, a series of 3 doses of Td should be given intramuscularly with the second dose 4-8 weeks after the first, and the third dose 6 months to 1 year after the second. Td is considered the agent of choice for immunization of school-age children (above school-entering age) on the basis of data regarding its adequacy in primary immunization of older children and adults and because of increasing frequency of reactions to full doses of diphtheria toxoid with age.

With regard to adult immunity, prior military service should not be considered as a guarantee of diphtheria immunity since diphtheria toxoid was not regularly administered until the mid-1950s.

Dose: The concentration of antigens varies in different manufacturers' products. The package literature gives specific information on the proper volume of a single dose.

Booster Immunization

Age: *For children 3 through 6 years (up to the seventh birthday — preferably at the time of entrance to kindergarten or elementary school)*, a single injection of the recommended dose of DTP should be given intramuscularly.

Thereafter and for all other persons, the recommended dose of Td should be given intramuscularly every 10 years. If a dose is given sooner as part of wound management, the next booster is not needed for 10 years thereafter. (See "Tetanus Prophylaxis in Wound Management.") More frequent booster doses are not indicated and may be associated with increased incidence and severity of side effects.

DIPHTHERIA ANTITOXIN FOR CASE CONTACTS

All *asymptomatic, unimmunized* household contacts of patients with diphtheria should be managed with: 1) prompt prophylaxis using either an intramuscular injection of benzathine penicillin (600,000 units for persons less than 6 years of age and 1,200,000

units for those 6 years of age and older) or a 7-day course of oral erythromycin with bacteriologic cultures before and after treatment, 2) vaccination with diphtheria toxoid, and 3) daily surveillance for 7 days for evidence of diphtheria.

Where close surveillance of unimmunized household contacts is impossible, they should receive intramuscular benzathine penicillin, diphtheria toxoid, and, in addition, diphtheria antitoxin. Intramuscular benzathine penicillin is preferred to oral erythromycin to avoid the problem of non-compliance with an oral drug regimen. Diphtheria antitoxin is recommended because: 1) intramuscular penicillin is not totally effective in eradicating the organism; 2) antibiotics may not prevent development or progression of disease due to toxin, 3) the factors that make surveillance difficult may contribute to delay in administering antitoxin therapy should diphtheria develop, and 4) the first dose of diphtheria toxoid in an unimmunized person does not result in protective levels of antitoxin.

Although some experts recommend diphtheria antitoxin routinely for asymptomatic, unimmunized, exposed persons, the risk of allergic reactions to horse serum has led others to recommend its more limited use. The proportion of immediate hypersensitivity reactions in adults receiving large doses of an equine antitoxin is reported to be 7% and of serum sickness reactions, 5%. This risk must be weighed against the risk of diphtheria in unimmunized household contacts — about 20% before the antibiotic era — and the risk of death from diphtheria which increases significantly each day treatment with antitoxin is delayed.

The possible adverse effects of equine antitoxin and the severity of diphtheria underscore the need for prompt investigation, antibiotic prophylaxis of contacts, and daily surveillance of diphtheria cases.

This recommendation for household contacts should also apply to other unimmunized diphtheria contacts whose exposures were unusually intimate (for example, mouth-to-mouth resuscitation).

TETANUS PROPHYLAXIS IN WOUND MANAGEMENT

The physician often needs to consider active and passive immunization in managing a patient with a wound. The decision should be based on the history of previous tetanus vaccinations and the condition of the wound.

Available evidence indicates that complete primary immunization with tetanus toxoid provides long-lasting, protective antitoxin levels. Few documented cases of tetanus have occurred in persons with adequate primary immunization. After a person is completely immunized, antitoxin persists at sufficiently high levels that in managing his or her wounds it is unnecessary to give booster injections more than every 5 years.

For some persons without a full series of tetanus toxoid injections in the past, tetanus toxoid plus simultaneous passive immunization may be needed at the time of wound cleansing and debridement. A guide to wound management is given in the table. It is based on observations that antitoxic antibodies develop rapidly following a dose of tetanus toxoid in persons who have previously received at least 2 doses. The condition of the wound further influences the recommended practice. For persons whose tetanus immunization is still incomplete following wound management, the remainder of the recommended series of toxoid injections should be given.

If passive immunization is to be used, tetanus immune globulin (TIG) is the product of choice. It provides longer protection than does antitoxin of animal origin and causes no undesirable reactions. The currently recommended prophylactic dose of TIG is 250 units for wounds of average severity. When tetanus toxoid and TIG are given concurrently, separate syringes and separate sites should be used. (Adsorbed Td or tetanus toxoid is preferred over fluid toxoid for concurrent administration with TIG.)

Guide to tetanus prophylaxis in wound management

History of tetanus immunization (doses)	Clean, minor wounds		All other wounds	
	Td	TIG	Td	TIG
Uncertain	Yes	No	Yes	Yes
0-1	Yes	No	Yes	Yes
2	Yes	No	Yes	No[1]
3 or more	No[2]	No	No[3]	No

[1] Unless wound more than 24 hours old
[2] Unless more than 10 years since last dose
[3] Unless more than 5 years since last dose

SELECTED BIBLIOGRAPHY

Diphtheria

Center for Disease Control: Diphtheria Surveillance Report No. 11, December 31, 1971

Doull JA: Factors influencing selective distribution in diphtheria. J Prev Med 4:371-404, 1930

Ipsen J: Circulating antitoxin at the onset of diphtheria in 425 patients. J Immunol 54:325-347, 1946

Merson MH, Hughs JM, Dowell VR, et al: Current trends in botulism in the United States. JAMA 229:1305-1308, 1974

Neiditch MJ, Bower AG: Diphtheria — A study of 1,433 cases observed during a ten-year period at the Los Angeles County Hospital. Am J Med 17:229-245, 1954

Russell WT: The Epidemiology of Diphtheria during the Last Forty Years (Medical Research Council Special Report No. 247). London, 1943

Scheibel I, Bentzon MW, Christensen PE, et al: Duration of immunity to diphtheria and tetanus after active immunization. Acta Pathol Microbiol Scand 67:380-392, 1966

Tasman A, Lansberg HP: Problems concerning the prophylaxis, pathogenesis, and therapy of diphtheria. Bull WHO 16:939-973, 1957

World Health Organization: Diphtheria and Pertussis Vaccination, Report of Conference of Heads of Laboratories producing Diphtheria and Pertussis Vaccines, Part I — Diphtheria (WHO Tech Rep Series No. 61). Geneva, 1953

Tetanus

Center for Disease Control: Tetanus Surveillance Report No. 4, March 31, 1974

Eckmann L (ed): Principles on Tetanus: Proceedings of the International Conference on Tetanus, Bern, July 15-19, 1966. Beru, Huber, 1967

Gottlieb S, Martin M, McLaughlin FX, et al: Long-term immunity to diphtheria and tetanus: A mathematical model. Am J Epidemiol 85:207-219, 1967

LaForce FM, Young LS, Bennett JV: Tetanus in the United States (1965-1966): Epidemiologic and clinical features. N Engl J Med 280:569-574, 1969

Peebles TC, Levine L, Eldred MC, et al: Tetanus-toxoid emergency boosters: A reappraisal. N Engl J Med 280:575-581, 1969

Rubbo SD: New approaches to tetanus prophylaxis. Lancet 2: 449-453, 1966

Scheibel I, Bentzon MW, Christensen PE, et al: Duration of immunity to diphtheria and tetanus after active immunization. Acta Pathol Microbiol Scand 67:380-392, 1966

Volk VK, Gottshall RY, Anderson HD, et al: Antigenic response to booster dose of diphtheria and tetanus toxoids: Seven to thirteen years after primary inoculation of noninstitutionalized children. Public Health Rep 77:185-194, 1962

White WG, Barnes GM, Griffith AH, et al: Duration of immunity after active immunization against tetanus. Lancet 2:95-96, 1969

Pertussis

Berg JM: Neurologic complications of pertussis immunization. Br Med J 2:24-27, 1958

Bradford WL: The Bordetella group. In Dubos RJ, Hirsch JG: Bacterial and Mycotic Infections of Man. 4th ed. Philadelphia, JB Lippincott, 1965, pp 742-751

Eldering G: Some laboratory aspects of a pertussis surveillance program, in proceedings of the Fifth Annual Immunization Conference, San Diego, California. U.S. Department of Health, Education, and Welfare, PHS, HSMHA. National Communicable Disease Center, 1968, pp 91-95

Gordon J, Hood RL: Whooping cough and its epidemiological anomalies, Am J Med Sci 222: 333-361, 1951

Lambert HJ. Epidemiology of a small pertussis outbreak in Kent County, Michigan. Public Health Rep 80:365-369, 1965

Replaces previous recommendation on DTP, published in MMWR 20:396-7, 1971.

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Recommendation of the Immunization Practices Advisory Committee (ACIP)

Immune Globulins for Protection Against Viral Hepatitis*

INTRODUCTION

The term "viral hepatitis," as commonly used, applies to at least 3 clinically similar disease entities that are distinct in their virology, immunology, and epidemiology. Two of these diseases, hepatitis A (formerly "infectious hepatitis") and hepatitis B (formerly "serum hepatitis"), have been recognized as separate entities since the early 1940s and account for most cases of viral hepatitis. The third one, "other hepatitis viruses" (non-A, non-B viral hepatitis), has only recently been identified as a separate entity and is a diagnosis of exclusion once hepatitis A and B have been ruled out by appropriate diagnostic tests. This diagnosis appears to encompass the majority of post-transfusion hepatitis cases in the United States today.

Immune serum globulin (ISG)† offers effective protection against the clinical manifestations of hepatitis A. Recent evidence also suggests that immune globulin preparations containing varying quantities of specific antibody against hepatitis B (anti-HBs) may be partially effective against this disease as well. At the present time there is no evidence to suggest immune globulins are effective against non-A, non-B hepatitis. Clinically, it is extremely difficult to distinguish between individual cases of viral hepatitis. Classification is therefore dependent upon careful evaluation of epidemiologic evidence and the use of appropriate serologic tests.

Hepatitis A

Hepatitis A is caused by infection with hepatitis A virus (HAV), a small 27-nm virus that has not yet been fully characterized. Illness produced by HAV infection is characteristically of abrupt onset, with fever, malaise, anorexia, nausea, abdominal discomfort, and jaundice. Morbidity is age-related, with asymptomatic infection and anicteric illness predominating in childhood. Mortality in clinical cases is quite low (less than 1%). Transmission occurs primarily by the fecal-oral route under conditions of poor sanitation and close contact between infected persons, although common-source exposures via contaminated food and water do occur. The incubation period of hepatitis A is 15-45 days (average 25-30 days). HAV has consistently been demonstrated in the stools of infected persons, with peak viral excretion occurring during the late incubation and early prodromal phase of illness. Viral excretion falls off rapidly with the onset of jaundice. The period of maximal infectivity occurs during the 2-week period before the onset of jaundice. Viremia is of short duration, and a chronic blood carrier state for HAV has not been demonstrated. HAV is not a significant cause of post-transfusion hepatitis.

*This recommendation is in process of revision at the time of this reprinting (March 1980). Once approved, the revised version will be published in MMWR, and reprints will be available from Public Inquiries, CDC-T/B63, Atlanta, Ga. 30333.

†See section, "Immune Globulins." The class of serum proteins of which ISG is an example are called immunoglobulins or immune globulins.

Serum antibody against HAV (anti-HAV) has recently been demonstrated by radioimmune assay, immune adherence hemagglutination, and complement-fixation techniques. Antibody remains detectable in serum for years and apparently confers life-long immunity to reinfection. Preliminary sero-epidemiologic studies have documented that hepatitis A is a common infection in the United States with over half the population having serologic evidence of past infection by mid-adult life.

Hepatitis B

Hepatitis B is caused by the hepatitis B virus (HBV), a 42-nm, double-shelled virus originally known as the "Dane particle." Two well defined antigen-antibody systems have been associated with the HBV virion. Hepatitis B surface antigen (HBsAg), formerly known as the "Australia antigen," is the antigen found on the surface of the virus and on the accompanying 22-nm spherical and tubular forms. Various subtypes of HBsAg have been described and have proven to be useful epidemiologic markers of infection.

Hepatitis B core antigen (HBcAg) is the antigen found within the core of the virus, and HBV specific DNA polymerase and circular double-stranded DNA have been associated with it. HBsAg can be identified in the serum 1-2 months after exposure and may persist for a variable period. The frequency of the chronic carrier state for HBsAg is variable but appears to be related both to the age at which infection is acquired and to the immunologic competence of the host. It has been estimated that as many as 10% of HBV infections result in chronic carriage of HBsAg. The carrier state can be completely asymptomatic, or, less commonly, it may be associated with active liver disease. While the carrier state appears to be important in perpetuating transmission of hepatitis B in a given population, recent evidence suggests that HBsAg carriers possess varying degrees of infectivity.

A newly described antigen-antibody system, the "e" system, appears to be of value in identifying those HBV carriers who are most likely to develop active liver disease and to be efficient disseminators of infection. The presence of HBeAg in the serum appears to be a marker for degree of infectivitiy and has been associated with active forms of chronic liver disease and with a poor prognosis for the chronic HBsAg carrier.

Several routes of exposure to HBV have been documented. Based on available data, the principal modes of transmission include:

1. direct percutaneous inoculation by needle of contaminated serum or plasma or transfusion of infected blood or blood products;
2. non-needle, percutaneous transfer of infected serum or plasma such as may occur through minute skin cuts or abrasions;
3. introduction of infective serum or plasma on mucosal surfaces such as may occur through inadvertent introduction of this material into buccal or ocular surfaces;
4. introduction of other known infective secretions such as saliva or semen into mucosal surfaces as through sexual contact; and
5. indirect transfer of serum or plasma via vectors or inanimate environmental surfaces.

Experimental data suggest that airborne transmission of infection is not important in virus transfer and that transmission of infection via an intestinal route does not occur.

The onset of hepatitis B is generally insidious and consists of a variable combination of the following: anorexia, malaise, nausea, vomiting, abdominal pains, jaundice, as well as arthralgias and arthritis. Morbidity and mortality are variable and may be a function of HBV dose and the age of the patient. Older individuals typically have higher mortality. The incubation period of hepatitis B is characteristically long, ranging from 60-180 days (average 90 days).

HEPATITIS SURVEILLANCE

Viral hepatitis has been a nationally reportable disease since 1952. In 1966 the reporting system was changed to permit classification of cases into 2 categories: 1) hepatitis A and hepatitis unspecified and 2) hepatitis B. Since 1974 hepatitis A and hepatitis unspecified have been reported separately. From 1952 to 1966, the annual number of reported viral hepatitis cases has varied. The lowest number of reported cases occurred in 1957 (14,922), flanked by major peaks in 1954 and 1961. After the 1961 peak (72,651), a decrease in reported cases occurred until the most recent low was reached in 1966 (34,356).

For the period of separate reporting (1966-present), the incidence of hepatitis A peaked in 1971 (59,606) and has been declining since. For the 3 years for which figures are available for hepatitis unspecified, the rate has remained nearly constant. The incidence of hepatitis B has continued to rise during the period of separate reporting. In 1966 there were 1,497 reported cases of hepatitis B (1.8 cases per 100,000 population), and in 1976 there were 14,850 cases (6.9 cases per 100,000 population). This represents a 10-fold increase in the number of reported cases and an almost 4-fold increase in case rate.

Currently, the age group most vulnerable to viral hepatitis is young adults (20-24 years), followed by the 15- to 19 and the 25- to 29-year-olds. For hepatitis A, there is a preceding but smaller peak in incidence in the 5- to 9-year olds. For hepatitis B immediately evident are the lack of cases in persons less than 15 years old. All reported hepatitis cases show an overall case-fatility rate of approximately 1.0%, a rate which increases with increasing age. The case-fatility rate appears to be similar for hepatitis A and B. Since 1966, surveillance has revealed that the seasonal variation for viral hepatitis has diminished remarkably.

IMMUNE GLOBULINS

Immune globulins are sterile solutions for intramuscular use containing antibody derived from human blood. They are 16.5% protein obtained by cold ethanol fractionation of large pools of blood plasma. ISG, one of the immune globulins, contains specified amounts of antibody against diphtheria, measles, and one type of poliovirus and varying amounts of antibody against hepatitis A and hepatitis B, depending on the preparation. Neither hepatitis A nor hepatitis B has been transmitted by immune globulins.

ISG AND HEPATITIS A

Numerous field studies during the past 2 decades have documented the protection against hepatitis A conferred by ISG administered before exposure and during the incubation period. Its relative effectiveness depends on timing and dose. When administered before or within 1-2 weeks after exposure to hepatitis A in the appropriate dose, it prevents illness in 80-90% of those exposed. Also, because ISG may not suppress inapparent infection, long-lasting, natural immunity may result.

The decision to give ISG is based on assessing the possible hepatitis exposure. If the exposure could have resulted in infection, ISG should be given.

ISG should be given as soon as possible after a known exposure. Its prophylactic value is greatest when given early in the incubation period and decreases with time after exposure. The use of ISG more than 2 weeks after exposure or after onset of clinical illness is not indicated.

Dosage

The dosage patterns of ISG in common use have been derived primarily from field and clinical observations. The dose of ISG may vary with the setting in which it is used. In postexposure prophylaxis a dose of 0.02 ml per kilogram of body weight is recom-

mended. In pre-exposure settings, the dosage varies not only with body weight but also with the length of time protection is needed. Specific dosages in specific settings are given below.

Postexposure Prophylaxis

Close personal contact: Close personal contact, as among permanent and even temporary household residents, is important in the spread of hepatitis A. Secondary attack rates are particularly high for children and teenagers. Rates are somewhat lower for adults, but illness tends to be more severe. ISG is recommended for all household contacts who have not already had hepatitis A.

School contacts: Although there is a high incidence of hepatitis A among school-age children, contact at school is usually not an important means of transmitting this disease. Routine administration of ISG is not indicated for pupil or teacher contacts of a patient. However, when epidemiologic study has clearly shown that a school- or classroom-centered outbreak exists, it is reasonable to administer ISG to persons at risk.

Institutional contacts: The conditions in institutions, such as prisons and facilities for the mentally retarded, favor transmission of hepatitis A. While sporadic cases do occur, periodic epidemics of disease are generally most common. The administration of ISG to residents and staff contacts of hepatitis A cases may effectively limit the spread of disease.

Hospital contacts: Routine prophylactic administration of ISG to hospital personnel is not indicated. Emphasis should be placed on sound hygienic practices. Intensive, continuing education programs that point out the risk of exposure to hepatitis A as well as recommended precautions should be directed toward hospital personnel who have close contact with patients or infective materials.

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

Common-source exposure: When food, water, or other such vehicle is clearly identified as a common source of infection for multiple hepatitis cases, administration of ISG to others exposed to the same source theoretically could be expected to offer some degree of protection. In actual practice, however, the administration of ISG in this setting has not been shown to confer benefit. The apparent lack of efficacy of ISG appears to result from inherent delays in outbreak recognition with administration of ISG too late in the incubation period to significantly alter clinical manifestations of illness. Therefore, the use of ISG in this setting cannot be routinely recommended.

Pre-exposure Prophylaxis

Exposure to non-human primates: Sporadic cases and outbreaks of hepatitis have occurred among persons in close contact with recently imported non-human primates, primarily chimpanzees. Because of the similarity between chimpanzee-associated hepatitis and hepatitis A, prophylactic ISG has been used with apparent success in doses of 0.05 ml/k of body weight administered every 4 months to those in close contact with newly imported animals. Emphasis should also be placed on other measures, such as scrupulous hygienic practices, use of protective clothing, and limited human contact with the animals.

Travelers to foreign countries: The risk of hepatitis A for U.S. residents traveling abroad appears to be small. It varies with living conditions, the prevalence of hepatitis in the areas visited, and particularly the length of stay.

Travelers may be at no greater risk than in the United States when their travel involves ordinary tourist routes and lasts less than 3 months. ISG is not routinely recommended in such instances. However, travelers to tropical areas and developing countries who bypass ordinary tourist routes may be at greater risk of acquiring hepatitis A. If ISG is admin-

istered, the dosage should be 0.02 ml/k of body weight.

Travelers planning to stay 3 or more months in tropical areas or developing countries where hepatitis A is common and where they may be exposed to infected persons and contaminated food and water are at greater risk of acquiring hepatitis. A single injection of ISG in a dose of 0.05 ml/k of body weight is recommended for them.

For persons residing abroad in tropical areas or developing countries, the risk of hepatitis appears to persist. Experience has shown that regular administration of ISG offers at least partial protection against hepatitis. It is recommended that prophylactic ISG be repeated every 4-6 months at doses of 0.05 ml/k of body weight.

IMMUNE GLOBULINS AND HEPATITIS B

Early attempts to use ISG in the passive prophylaxis of viral hepatitis revealed this material to be of little or no benefit in the prevention of post-transfusion hepatitis. Based on early findings, passive immunization against hepatitis B was not generally recommended. The majority of initial studies were, however, conducted before the discovery of HBsAg and the development of serologic procedures for detection of the variety of immunologic markers currently associated with HBV infection. Thus, in early post-transfusion study settings, the dose of presumed HBV inoculum was high, hepatitis B and non-B cases could not be accurately distinguished, and specific anti-HBs content of utilized immune globulin preparations could not be assessed.

In the United States over half of the lots of ISG manufactured before 1972 contained no detectable anti-HBs, and, therefore, could not be presumed to be of any value in the prevention of hepatitis B. In contrast, most ISG manufactured subsequent to 1972 has contained detectable anti-HBs for which some specific effectiveness in passive prophylaxis might be inferred. The development of serologic tests enabling accurate diagnosis of hepatitis B and measurement of the specific anti-HBs content of immune globulins has resulted in re-evaluation of passive prophylaxis for this disease.

Unified interpretation of results of recent immune globulin prophylaxis studies has been rendered difficult by: 1) the use of immune globulin preparations of differing anti-HBs titers from a variety of manufacturers; 2) differences in dosage and timing of immune globulin administration; and 3) defects in design of some studies, the most important of which has been failure to include placebo controls.

In regard to anti-HBs titers of immune globulins, those of high anti-HBs titer (generally greater than 1:100,000 by passive hemagglutination [PHA]) prepared from donor pools preselected for anti-HBs content are now generally designated as hepatitis B immune globulin (HBIG). Such material was compared, in several studies, with globulins of lower or no detectable anti-HBs content. In general, such latter globulins have been prepared from donor pools not initially preselected for anti-HBs content. It is important to note that the term HBIG refers to quantity of anti-HBs and not to its presence or absence in the manufactured product. Thus, ISG may be expected to contain some anti-HBs — in the United States, this would generally have a titer >1:64 by PHA.

Studies of passive immunization may be temporally divided into 2 categories, pre-exposure prophylaxis and post-exposure prophylaxis. An early randomized comparison of ISG containing a moderate titer of anti-HBs with true placebo among military personnel in a hepatitis B endemic area provided evidence that this globulin provided significant protection against disease in a pre-exposure prophylactic setting where hepatitis B was presumably transmitted by close personal contact.

In a study in a custodial institution of children who were experimentally inoculated with HBV, HBIG was found to have significantly greater protective effect in preventing ensuing hepatitis B than ISG with a low titer of anti-HBs when administered 4 hours after inoculation of virus. In this postexposure prophylactic setting, maximum effectiveness achieved for HBIG was 70%. The incubation period was significantly prolonged when

hepatitis B did occur in the group given HBIG (mean of 118 days in comparison to 48 days in the group given ISG). Also, the low titer globulin appeared to be partially effective when compared to untreated controls.

It was against the background of evidence suggesting some effectiveness of ISG, but perhaps greater efficacy of HBIG, that subsequent trials of passive immunization against hepatitis B were undertaken. While none of these trials incorporated a true placebo control, they may be divided into 2 categories based on type of comparison groups used: those that incorporated ISG containing no detectable anti-HBs (placebo globulin) and those that compared the efficacy of HBIG to globulins with low to intermediate anti-HBs titers.

When compared to placebo globulin, HBIG has been found to be of significant value in pre-exposure prophylaxis of patients in hemodialysis units where hepatitis B is endemic and in postexposure prophylaxis of medical personnel following HBsAg-positive needle sticks, of spouse contacts of acute hepatitis B cases, and of infants born to HBsAg-positive mothers.

Results are less clear in studies which have compared the relative efficacy of HBIG with ISG that has low tiers of anti-HBs. In a pre-exposure prophylactic study of new admissions to 3 institutions for the mentally retarded, HBIG and low anti-HBs titered immune globulins appeared to be equally effective in preventing hepatitis B when compared to an untreated control group. Furthermore, there was some evidence that individuals receiving low titered immune globulin may have developed active anti-HBs response in the absence of disease (passive-active immunity). In 2 large multicenter studies, the first involving pre-exposure prophylaxis of dialysis patients and staff, and the second, post-exposure prophylaxis of medical personnel exposed to HBsAg-positive needle sticks, the effectiveness of HBIG was compared to immune globulins of low and intermediate anti-HBs titer.

When the results of these studies were compared after 6 and 8 months of follow-up, a significant relative reduction in the incidence of hepatitis B was observed in the HBIG treated individuals. However, at 9 and 12 months of follow-up, no statistically significant differences in the incidence of hepatitis B between the globulin groups could be observed due to the occurrence of late-onset cases in HBIG recipients. The pre-exposure study among dialysis patients and staff also provided additional evidence that administration of low titered globulin may have been associated with the development of passive-active immunity in recipients.

One recent study of ISG in postexposure prophylaxis has indicated that hepatitis B was prevented in infants who received this material within a week of birth to mothers who had experienced acute hepatitis B in the third trimester of pregnancy.

The above studies provide independent evidence for the efficacies of both ISG containing low titers of anti-HBs and of HBIG in both pre-exposure and postexposure prophylaxis of hepatitis B. With the exception of the previously cited experimental study of postexposure prophylaxis among children in a custodial institution, there is no statistically or epidemiologically convincing evidence of the superiority of HBIG over such ISG preparations under circumstances permitting these comparisons.

It has been proposed that the late-onset cases in HBIG recipients in the 2 multicenter studies were due to re-exposure at a time when the protective effect of HBIG had diminished, thus masking an inferred relative superiority of HBIG over low anti-HBs titered globulins. It has also been proposed, however, that administration of HBIG itself prolongs the incubation period of hepatitis B for those cases which do break through after passive immunization.

Whereas there are no extant data to support the re-exposure hypothesis, there is convincing evidence cited above that HBIG does prolong the incubation period of hepa-

titis B. Additional support for this interpretation is provided from a recent study in which hepatitis B incubation periods of 7 and 8 months were documented following HBIG administration. Further, it is difficult to explain, under circumstances of adequate randomization, as reported in the multicenter studies, an excess late re-exposure to HBV occurring in HBIG recipients only. On balance it seems likely that the late-onset cases in HBIG recipients in the multicenter studies were due, in part, to prolongation of the incubation period of hepatitis B. Therefore, the relative superiority of HBIG over ISG in these 2 studies cannot be convincingly affirmed.

In all studies reviewed to date there has been no evidence of infectivity of HBIG or ISG or of increased incidence of HBsAg carriage among infected individuals given anti-HBs containing globulins. Therefore, passive immunization for hepatitis B is considered to be safe. Efficacy of immune globulins in the prevention of hepatitis B varies from 40 to 70%. For this reason, passive immunization should not replace other forms of infection control that can be expected to be more efficacious in the prevention of hepatitis B. This is of particular significance for reducing disease in hemodialysis unit patients and staff. Data have shown that hepatitis B transmission may be virtually eliminated through appropriate environmental containment procedures involving early identification and segregation of HBsAg-positive individuals.

In cases of massive single exposure to HBV, such as accidental transfusion of HBsAg-positive blood or high-risk plasma derivatives, there are no available data from controlled studies which indicate that immune globulins containing anti-HBs may be effective. Therefore, control of post-transfusion hepatitis B should be approached through elimination of HBsAg-positive transfused products by routine testing using the most sensitive available methods.

GUIDELINES FOR PROPHYLAXIS OF HEPATITIS B

The following guidelines are believed to reflect the best available synthesis of current data. It is understood that these guidelines may be subject to change as new information becomes available. Use of ISG refers to lots of material which contain some anti-HBs detectable by PHA techniques. Lots of such material currently manufactured in the United States may be reasonably expected to contain such antibody.

Postexposure Prophylaxis

Acute exposure: The major indication for use of HBIG is following a single acute exposure to a relatively large inoculum of HBV, such as occurs following accidental needlestick or mucosal exposure to blood known to contain HBsAg. HBIG in a dose of 0.05-0.07 ml/k of body weight may be administered as soon as possible within a 7-day period after exposure, with a second, identical dose administered 25-30 days after the first. If HBIG is not available, ISG can be given in the same dosage schedule.

Fetal exposure: Infants born to mothers with acute hepatitis B in the third trimester of pregnancy and HBsAg seropositivity at time of delivery may be given either HBIG or ISG within 7 days of birth. HBIG has been administered as a single dose of 0.13 ml/k of body weight. ISG has been similarly administered at a dose of 0.5 ml/k of body weight.

Pre-exposure Prophylaxis

In certain endemic settings where HBV transmission is known to occur and repeated chronic virus exposure is fully documented, passive immunization may be considered. In these situations, routine serologic monitoring of the HBsAg and anti-HBs status of candidate persons should be a routine component of hepatitis prevention and control.

Although HBIG has been shown in one study to prevent hepatitis B in spouses of individuals with acute HBV infection, recommendations for passive immunization to prevent hepatitis B, presumably acquired by sexual or other such intimate contact, should

await further estimates of the magnitude of risk of disease transmitted by these routes, as well as studies of the relative prophylactic efficacies of HBIG vs. ISG.

Hemodialysis units: Passive immunization is not routinely recommended for staff and patients of hemodialysis units. Rather, hepatitis B prevention and control should be based on routine serologic screening, as described above, as well as implementation of hygienic measures. Under conditions where such hygienic measures cannot be implemented, passive immunization may be considered for anti-HBs-negative staff and patients. HBsAg-positive individuals should not be included. All passive immunization should be discontinued when evidence for endemic HBV transmission ceases to exist. Since there is no convincing evidence for a superior efficacy of HBIG, and in order to take advantage of the possibility of acquisition of passive-active immunity, prophylaxis with ISG may be preferred. A dose of 0.05-0.07 ml/k of body weight has been administered at 4-month intervals. Individuals receiving prophylaxis should be tested for anti-HBs prior to reimmunization. Those found to be anti-HBs-positive may be removed from further prophylaxis under presumption of the acquisition of active anti-HBs response.

Custodial institutions for the mentally retarded: Under conditions of demonstrable HBV transmission with repeated chronic virus exposure and where routine serologic monitoring for HBsAg and anti-HBs status of patients and staff is undertaken, passive immunization of anti-HBs-negative individuals can be considered. ISG administered in the same dosage, at the same intervals, and under the same conditions for discontinuation as outlined for hemodialysis units may be preferred.

PRECAUTIONS

Immune globulin preparations should not be administered intravenously because of the possibility of severe hypersensitivity reactions.

Intramuscular administration of immune globulins rarely causes adverse reactions. Discomfort may occur at the site of injection, especially with larger volumes. A few instances of hypersensitivity have been reported, but in view of the very large numbers of persons who receive immune globulins, the risk is small. Antibody against gamma globulin may appear following administration of immune globulins, although its significance is unknown. When immune globulin is needed, this theroretical consideration should not preclude its administration.

The induction of immune complex disorders following the administration of HBIG to HBsAg-positive persons is a potential concern, but such reactions have not been observed. Although HBsAg testing of potential HBIG recipients is not mandatory, HBIG should not knowingly be given to HBsAg positives.

Pregnancy is not a contraindication to using ISG or HBIG as recommended.

A Selected Bibliography was published as part of this recommendation in MMWR 1977;26:442. Copies of this bibliography are available upon request.

Recommendation of the Public Health Service
Advisory Committee on Immunization Practices

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Influenza Vaccine

INTRODUCTION

Influenza virus infections occur every year in the United States, but they vary greatly in incidence and geographic distribution. Infections may be asymptomatic, or they may produce a spectrum of manifestations, ranging from mild upper respiratory infection to pneumonia and death. Influenza viruses A and B are responsible for only a portion of all respiratory disease. However, they are unique in their ability to cause periodic widespread outbreaks of febrile respiratory disease in both adults and children. Influenza epidemics are frequently associated with deaths in excess of the number normally expected. During the period from 1968 to 1979, more than 150,000 excess deaths are estimated to have occurred during epidemics of influenza A in the United States.

Efforts to prevent or control influenza in the United States have been aimed at protecting those at greatest risk of serious illness or death. Observations during influenza epidemics have indicated that influenza-related deaths occur primarily among chronically ill adults and children and in older persons, especially those over age 65. Therefore, annual vaccination is recommended for these "high-risk" individuals.

Influenza A viruses can be classified into subtypes on the basis of 2 antigens: hemagglutinin (H) and neuraminidase (N). Four subtypes of hemagglutinin (H0-H3) and 2 subtypes of neuraminidase (N1, N2) are recognized among viruses causing widespread disease among humans. Immunity to these antigens reduces the likelihood of infection and reduces the severity of disease in infected persons. However, there may be sufficient antigenic variation within the same subtype over time (antigenic drift) that infection or immunization with 1 strain may not induce immunity to distantly related strains. As a consequence, the antigenic composition of the most current strains is considered in selecting the virus strain(s) to be included in the vaccine.

The predominant influenza strain in the United States during 1978-79 was A/Brazil/78—a variant of the H1N1 prototype A/USSR/77. This strain caused outbreaks in schools, colleges, and military bases, as had been the case with the prototype strain. People over 25 years of age generally were not affected, presumably because of previous infection with antigenically related strains that had circulated throughout the world in the early 1950s. Strains of the subtype H3N2 were not isolated in the United States, but other countries reported the isolation of both H1N1 and H3N2 strains. Since it is uncertain which strain will predominate in the future, continued circulation of strains related to A/Texas/77 (H3N2) and A/Brazil/78 (H1N1) must be anticipated.

Outbreaks caused by influenza B viruses occur less frequently than influenza A epidemics, but influenza B infection can also cause serious illness or death. Influenza B viruses have shown much more antigenic stability than influenza A viruses. Strains of influenza B that were isolated in 1978 and 1979 in the United States and elsewhere resembled the B/Hong Kong/5/72 virus.

INFLUENZA VIRUS VACCINE FOR 1979-80

Influenza vaccine for 1979-80* will consist of inactivated trivalent preparations of antigens representative of influenza viruses expected to be prevalent: A/Brazil/78 (H1N1), A/Texas/77 (H3N2), and B/Hong Kong/72. The formulation will contain 7 micrograms of hemagglutinin of each antigen in each 0.5 ml dose. Persons 27 years and older will

*Official name: Influenza Virus Vaccine, Trivalent.

Influenza Vaccine — Continued

require only 1 dose. Because of lack of previous contact with H1N1 strains, persons less than 27 who did not receive at least 1 dose of the 1978-79 trivalent vaccine will require 2 doses of the 1979-80 vaccine. Those who received the 1978-79 vaccine will require only 1 dose. The vaccine will be available as whole virion (whole-virus) and subviron (split-virus) preparations. Based on past data, split-virus vaccines have been associated with somewhat fewer side effects than whole-virus vaccines in children. Thus, only split-virus vaccines are recommended for persons less than 13 years of age. The vaccines prepared for the 1978-79 respiratory disease season contained A/USSR/77 as the H1N1 component. Because of the antigenic similarities between the A/USSR/77 and the A/Brazil/78 strains, the stocks of vaccine remaining from last year may be used, until the expiration date, according to the instructions on the package insert.

VACCINE USAGE

General Recommendations

Annual vaccination is strongly recommended for all individuals at increased risk of adverse consequences from infections of the lower respiratory tract. Conditions predisposing to such risk include (1) acquired or congential heart disease associated with altered circulatory dynamics, actual or potential (for example, mitral stenosis, congestive heart failure, or pulmonary vascular overload); (2) any chronic disorder with compromised pulmonary function, such as chronic obstructive pulmonary disease, bronchiectasis, tuberculosis, severe asthma, cystic fibrosis, neuromuscular and orthopedic disorders with impaired ventilation, and residual pulmonary dysplasia following the neonatal respiratory distress syndrome; (3) chronic renal disease with azotemia or the nephrotic syndrome; (4) diabetes mellitus and other metabolic diseases with increased susceptibility to infection; (5) chronic, severe anemia, such as sickle cell disease; and (6) conditions which compromise the immune mechanism, including certain malignancies and immunosuppressive therapy.

Vaccination is also recommended for older persons, particularly those over age 65, because excess mortality in influenza outbreaks occurs in this age group.

In considering vaccination of persons who provide essential community services or who may be at increased risk of exposure, such as medical care personnel, the inherent benefits, risks, and cost of vaccination should be taken into account.

Table 1 summarizes vaccine and dosage recommendations by age group for 1979-80.

TABLE 1. Influenza vaccine* dosage, by age, 1979-80

Age group	Product	Dosage (ml)	Number of doses
27 years and older	whole virion (whole virus) or subvirion (split virus)	0.5	1
13-26 years	whole virion (whole virus) or subvirion (split virus)	0.5	2**
3-12 years	subvirion (split virus)	0.5	2**
6-35 months***	subvirion (split virus)	0.25	2**

* Contains 7 μg each of A/Brazil/78, A/Texas/77, B/Hong Kong/72 hemagglutinin antigens in each 0.5 ml.

** 4 weeks or more between doses; both doses essential for good protection, unless the individual received at least 1 dose of 1978-79 vaccine.

*** Based on limited data. Since the likelihood of febrile convulsions is greater in this age group, special care should be taken in weighing relative risks and benefits.

Influenza Vaccine — Continued

Use in Pregnancy

Although the issue has been much discussed, only in the pandemics of 1918-19 and 1957-58 has strong evidence appeared relating influenza infections with increased maternal mortality. Although several studies have reported an increased risk of congenital malformations and childhood leukemia among children born to women who had influenza infection during pregnancy, other studies have not shown an increased risk; the issue is not settled.

Physicians prudently limit prescription of drugs and biologics for pregnant women. However, no evidence has been presented to suggest that influenza vaccination of pregnant women poses any special maternal or fetal risk. Furthermore, because influenza vaccine is an inactivated viral preparation, it does not share the theoretical risks that impel caution in the use of live virus vaccines. Taking the above uncertainites into account, physicians should evaluate pregnant women for influenza immunization according to the same criteria applied to other persons. (See VACCINE USAGE—General Recommendations.)

SIDE EFFECTS AND ADVERSE REACTIONS

Recent influenza virus vaccines have been associated with few side effects. Local reactions, consisting of redness and induration at the site of injection lasting 1 or 2 days, have been observed in less than one-third of vaccinees. Three types of systemic reactions to influenza vaccines have been described.

1. Fever, malaise, myalgia, and other systemic symptoms of toxicity, although infrequent, occur more often in children and others who have had no experience with influenza viruses containing the vaccine antigen(s). These reactions, which begin 6-12 hours after vaccination and persist 1-2 days, are usually attributed to the influenza virus itself (even though it is inactivated) and constitute most of the side effects of influenza vaccination.

2. Immediate—presumably allergic—responses, such as flare and wheal or various respiratory expressions of hypersensitivity occur extremely rarely after influenza vaccination. They probably derive from sensitivity to some vaccine component, most likely residual egg protein. Although current influenza vaccines contain only a small quantity of egg protein, on rare occasions they can provoke hypersensitivity reactions. Individuals with anaphylactic hypersensitivity to eggs should not be given influenza vaccine. This would include persons who, upon ingestion of eggs, develop swelling of the lips or tongue or who experience acute respiratory distress or collapse.

3. Guillain-Barré syndrome (GBS) is an uncommon illness characterized by ascending paralysis which is usually self-limited and reversible. Though most persons with GBS recover without residual weakness, approximately 5% of cases are fatal. Before 1976, no association of GBS with influenza vaccination was recognized. That year, however, GBS appeared in excess frequency among persons who had received the A/New Jersey/76 influenza vaccine. For the 10 weeks following vaccination the excess risk was found to be approximately 10 cases of GBS for every million persons vaccinated—an incidence 5-6 times higher than that in unvaccinated persons. Younger persons (under 25 years) had a lower relative risk than others and also had a lower case-fatality rate. Preliminary analysis of data from GBS surveillance during the 1978-79 influenza season suggests that, in contrast to the 1976 situation, the risk of GBS in recipients of the 1978-79 vaccine was not significantly higher than that in non-vaccinees. Nonetheless, persons who receive influenza vaccine should be made aware of this possible risk as compared with the risk of influenza and its complications.

Influenza Vaccine – Continued

SELECTED BIBLIOGRAPHY

Clinical studies on influenza vaccines—1976. (A conference held at the National Institutes of Health, Bethesda, Maryland, January 20-21, 1977.) J Infect Dis 136 (Suppl): S345-S742, 1977

Dowdle WR, Coleman MT, Gregg MB: Natural history of influenza type A in the United States, 1957-1972. Prog Med Virol 17:91-135, 1974

Eickhoff TC: Immunization against influenza: Rationale and recommendations. J Infect Dis 123: 446-454, 1971

Kilbourne ED (ed): The Influenza Viruses and Influenza. New York, Academic Press, 1975

Leneman F: The Guillain-Barre syndrome. Arch Intern Med 118:139-144, 1966

Parkman PD, Galasso GH, Top FH, Noble GR: Summary of clinical trials of influenza vaccines. J Infect Dis 134:100-107, 1976

Wright PF, Dolin R, LaMontagne JR: Summary of clinical trials of influenza vaccines II. J Infect Dis 134:633-638, 1976

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Recommendation of the Immunization Practices Advisory Committee (ACIP)

Measles Prevention

These revised ACIP Measles Prevention recommendations represent an effort to address more directly some of the key issues in measles prevention and control.

The issues discussed in previous statements on Measles Vaccine (MMWR 25:359-360, 365, 376, 1976) and Measles Outbreak Control (MMWR 26:294, 299, 1977) have been combined in this statement. The relative increase in reported measles cases in adolescents prompted an extension and clarification of recommendations for immunization of adolescents, both males and females. The usefulness of school immunization requirements has been emphasized. The definition of measles susceptibles and revaccination recommendations for them have been more clearly established.

INTRODUCTION

Measles (rubeola) is often a severe disease, frequently complicated by middle ear infection or bronchopneumonia. Encephalitis occurs in approximately 1 of every 1,000 cases; survivors often have permanent brain damage and mental retardation. Death, predominantly from respiratory and neurologic causes, occurs in 1 of every 1,000 reported measles cases. The risks of encephalitis and death are known to be greater in infants, and suspected to be greater in adults, than in children and adolescents.

Measles illness during pregnancy increases fetal risk. Most commonly, this involves premature labor and moderately increased rates of spontaneous abortion and of low birth weight (*1*). One retrospective study in an isolated population suggests that measles infection in the first trimester of pregnancy was associated with an increased rate of congenital malformations (*2*).

Before measles vaccine was available, more than 400,000 measles cases were reported annually in the United States. Since the introduction of vaccine in 1963, the collaborative efforts of professional and voluntary medical and public health organizations in vaccination programs have resulted in a 90% reduction in the reported incidence of measles. In 1977, 57,345 cases were reported. In the pre-vaccine era, the majority of measles cases occurred in preschool and young school-age children. In 1977, more than 60% of cases in which the age was known occurred in persons 10 or more years old. More than 20% were reported in the 15- to 19-year-old age group.

With the highly effective, safe measles vaccines now available, the degree of measles control in the United States depends largely on the effectiveness of the continuing effort to vaccinate all susceptible persons who can safely be vaccinated.

MEASLES VIRUS VACCINE

Live measles virus vaccine* available in the United States is prepared in chick embryo cell culture. The vaccine virus strain primarily used at present has been attenuated beyond the level of the original Edmonston B strain and is therefore known as a further attenuated strain. Vaccine prepared with the further attenuated measles virus is generally

*Official name: Measles Virus Vaccine, Live, Attenuated

preferred, in part because it causes fewer reactions than its predecessor. It is available in monovalent (measles only) form and in combinations: measles-rubella (MR) and measles-mumps-rubella (MMR) vaccines. All vaccines containing measles antigen are recommended for use at about 15 months of age. MMR is encouraged for use in routine infant-child vaccination programs. In all situations where measles vaccine is to be used, consideration should be given to using a combination vaccine when recipients are likely to be susceptible to rubella and/or mumps as well as to measles. Edmonston B measles vaccine is not available in combined form and is now rarely used.

Measles vaccine produces a mild or inapparent, non-communicable infection. Measles antibodies develop in at least 95% of susceptible children vaccinated at about 15 months of age or older with the current further attenuated vaccine. Evidence now extending to 15-year follow-up indicates that, although titers of vaccine-induced antibodies are lower than those following natural disease, the protection conferred appears to be durable.

Vaccine Shipment and Storage

Failure of protection against measles may result from the administration of improperly stored vaccine. During shipment and storage prior to reconstitution, measles vaccine must be kept at a temperature between 2-8 C (35.6-46.4 F). It must also be protected from light, which may inactivate the virus.

VACCINE USAGE

General Recommendations

Persons can be considered immune to measles only if they have documentation of:
(1) Physician-diagnosed measles or laboratory evidence of measles immunity, or
(2) Adequate immunization with live measles vaccine when 12 or more months of age.

Most persons born before 1957 are likely to have been infected naturally and generally need not be considered susceptible. All other children, adolescents, and adults are considered susceptible and should be vaccinated, if not otherwise contraindicated.

Dosage

A single dose of live measles vaccine (as a monovalent or combination product) should be given subcutaneously in the volume specified by the manufacturer. Immune serum globulin (ISG) should **NOT** be given with further attenuated measles virus vaccine. It is indicated only if Edmonston B vaccine is used.

Age at Vaccination

Measles vaccine is indicated for persons susceptible to measles, regardless of age, unless otherwise contraindicated. Current evidence indicates that for a maximum rate of seroconversion, measles vaccine should preferably be given when children are about 15 months of age. Whenever there is likely exposure to natural measles, infants as young as 6 months should be vaccinated. However, to ensure protection of infants vaccinated before 12 months of age, they should be revaccinated when they are about 15 months old. It is particularly important to vaccinate infants before they might encounter measles in day-care centers or other such environments.

Because of the upward shift in age distribution of reported cases, the immune status of all adolescents should be evaluated. Complete measles control will require protection of all susceptibles; therefore, increased emphasis must be placed on vaccinating susceptible adolescents and young adults. Susceptible persons include those who received inactivated vaccine or who were given live measles virus vaccine before they were 12 months of age, as well as those who were never vaccinated or never had measles.

Revaccination of Persons Vaccinated According to Earlier Recommendations

Persons vaccinated with live measles vaccine before 12 months of age and those vaccinated at any age with inactivated vaccine (available from 1963 to 1967) should be

identified and revaccinated. Persons who are unaware of their age at vaccination or who were vaccinated prior to 1968 with a vaccine of unknown type should also be revaccinated. In addition, persons who received live measles vaccine in a series within 3 months of inactivated measles vaccine should be revaccinated.

There has been some confusion concerning the immunity of children vaccinated against measles at 12 months of age. This is because some recent data have indicated a slightly lower rate of seroconversion among children vaccinated at 12 months of age than among those vaccinated at 13 months or later. This difference is not sufficient to warrant routinely revaccinating persons in the former group; the vast majority are fully protected. If, however, the parents of a child vaccinated when 12 to 15 months old request revaccination for the child, there is no immunologic or safety reason to deny the request.

Individuals Exposed to Disease

Use of vaccine: Exposure to measles is not a contraindication to vaccination. Available data suggest that live measles vaccine, if given within 72 hours of measles exposure, may provide protection. If the exposure does not result in infection, the vaccine should induce protection against subsequent measles infection.

Use of ISG: To prevent or modify measles in a susceptible person exposed less than 6 days before, ISG, 0.25 ml/kg (0.11 ml/lb) of body weight, should be given (maximum dose—15 ml). ISG may be especially indicated for susceptible household contacts of measles patients, particularly contacts under 1 year of age, for whom the risk of complications is highest. Live measles vaccine should be given about 3 months later, when the passive measles antibodies should have disappeared, if the child is then at least 15 months old. *ISG should not be used in an attempt to control measles outbreaks.*

SIDE EFFECTS AND ADVERSE REACTIONS

Experience with more than 100 million doses of measles vaccine distributed in the United States through early 1978 indicates an excellent record of safety. About 5%-15% of vaccinees may develop fever ≥103 F (≥39.4 C) beginning about the sixth day after vaccination and lasting up to 5 days. Most reports indicate that persons with fever are asymptomatic. Transient rashes have been reported rarely. Central nervous system conditions including encephalitis and encephalopathy have been reported approximately once for every million doses administered. Limited data indicate that reactions to vaccine are not age-related.

Subacute sclerosing panencephalitis (SSPE) is a "slow virus" infection of the central nervous system associated with a measles-like virus. Results from a recent study indicate that measles vaccine, by protecting against measles, significantly reduces the chance of developing SSPE (*3,4*). However, there have been reports of SSPE in children who did not have a history of natural measles but did receive measles vaccine. Some of these cases may have resulted from unrecognized measles illness in the first year of life or possibly from the measles vaccine. The recent decline in numbers of SSPE cases in the presence of careful surveillance is additional strong presumptive evidence of a protective effect of measles vaccination.

Revaccination Risks

There is no evidence of enhanced risk from receiving live measles vaccine for one who has previously received live measles vaccine or had measles. Specifically, there does not appear to be any enhanced risk of SSPE. The previously cited study showed no association between SSPE and either receiving live measles vaccine more than once or receiving it after having had measles.

On exposure to natural measles, some children previously inoculated with inactivated measles virus vaccine have developed atypical measles, sometimes with severe symptoms.

Reactions, such as local edema and induration, lymphadenopathy, and fever, have at times been observed when live measles virus vaccine was administered to recipients of inactivated vaccine. However, despite the risk of local reaction, children who have previously been given inactivated vaccine (whether administered alone or followed by a dose of live vaccine within 3 months) should be revaccinated with live vaccine to avoid the severe atypical form of natural measles and to provide full and lasting protection.

PRECAUTIONS AND CONTRAINDICATIONS

Pregnancy: Live measles vaccine should not be given to females known to be pregnant. This precaution is based on the theoretical risk of fetal infection, which applies to administration of any live virus vaccine to females who might be pregnant or who might become pregnant shortly after vaccination. Although no evidence exists to substantiate this theoretical risk from measles vaccine, concern about it has constrained measles vaccination programs for adolescent girls. Considering the importance of protecting adolescents and young adults against measles with its known serious risks, asking females if they are pregnant, excluding those who are, and explaining the theoretical risks to the others are reasonable precautions in a measles immunization program.

Febrile illness: Vaccination of persons with febrile illness should be postponed until recovery. Minor illnesses such as upper respiratory infections, however, do not preclude vaccination.

Allergies: Live measles vaccine is produced in chick embryo cell culture. It has not been reported to be associated with allergic reactions and can be given to all who need it, including persons with allergies to eggs, chickens, and feathers. Some vaccines contain trace amounts of antibiotics to which patients may be allergic. Those administering vaccines should review the label information carefully before deciding whether patients with known allergies to such antibiotics can be vaccinated safely. Live measles virus vaccine does not contain penicillin.

Recent Administration of ISG: Vaccination should be deferred for about 3 months after a person has received ISG because passively-acquired antibodies might interfere with the response to the vaccine.

Tuberculosis: Tuberculosis may be exacerbated by natural measles infection. There is no evidence, however, that the live measles virus vaccine has such an effect. Therefore, tuberculin skin testing need not be a prerequisite for measles vaccination. The value of protection against natural measles far outweighs the theoretical hazard of possibly exacerbating unsuspected tuberculosis. If there is a need for tuberculin skin testing, it can be done on the day of vaccination and read 48 to 72 hours later. If a recent vaccinee proves to have a positive skin test, appropriate investigations and, if indicated, tuberculosis therapy should be initiated.

Altered immunity: Replication of the measles vaccine virus may be potentiated in patients with immune deficiency diseases and by the suppressed immune responses that occur with leukemia, lymphoma, or generalized malignancy or with therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. Patients with such conditions should not be given live measles virus vaccine. Their risks of being exposed to measles may be reduced by vaccinating their close susceptible contacts. Management of such persons, should they be exposed to measles, can be facilitated by prior knowledge of their immune status.

Management of Patients with Contraindications to Measles Vaccine

If immediate protection against measles is required for persons for whom live measles virus vaccine is contraindicated, passive immunization with ISG, 0.25 ml/kg (0.11 ml/lb) of body weight, should be given as soon as possible after known exposure (maximum

dose—15 ml). It is important to note, however, that ISG, which will usually prevent measles in normal children, may not be effective in children with acute leukemia or other conditions associated with altered immunity.

Simultaneous Administration of Certain Live Virus Vaccines

See current ACIP statement, "General Recommendations on Immunization."

MEASLES CONTROL

Ongoing Programs

The best means of reducing the incidence of measles is by having an immune population. 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 vaccinating children against measles at about 15 months of age should be established by all communities. In addition, all other persons, regardless of age, thought to be susceptible should be vaccinated when they are identified, unless vaccine is otherwise contraindicated.

Official health agencies should take whatever steps are necessary, including development and enforcement of school immunization requirements, to assure that all persons in schools and day-care settings are protected against measles. Enforcement of such requirements has been correlated with reduced measles incidence.

Measles outbreaks have been and continue to be reported from places where young adults are concentrated, such as colleges and military bases. Measles control in these places may require careful evaluation of susceptibility and vaccination of those who are susceptible.

Concern is often expressed because of observations during outbreaks that cases occur in persons with a history of proper vaccination. Even under optimal conditions of storage and use, measles vaccine may have a 5% failure rate. A 90% or greater reduction in attack rates has been demonstrated consistently in appropriately vaccinated persons when compared to others. As greater numbers of susceptibles become vaccinated and as measles incidence is further reduced, there will be a relative increase in the proportion of cases seen among appropriately vaccinated persons.

Outbreak Control

The danger of a measles outbreak exists whenever a measles case is reported in a community. Once an outbreak occurs, preventing dissemination of measles depends on promptly vaccinating susceptible persons. Ideally, they will have been identified before the outbreak (by school record reviews, for example); if not, they must be quickly identified.

Speed in implementing control programs is essential in preventing the spread of measles. All persons who cannot readily provide a *documented* history of measles or of vaccination with live measles virus vaccine when more than 12 months of age should be vaccinated or excluded from school. If a person's measles immunity is in doubt, he/she should be vaccinated.

An effective means of terminating outbreaks and increasing rates of immunization quickly is to exclude from school all children or adolescents who cannot present valid evidence of immunity through vaccination or prior disease. Exclusion should include pupils who have been exempted from measles vaccination because of medical, religious, or other reasons. Exclusion should continue until at least 2 weeks after the onset of the last case of measles in the community. Less rigorous approaches such as voluntary appeals for vaccination have not been effective in terminating outbreaks.

ISG should not be used in an attempt to control measles outbreaks.

SURVEILLANCE

Known or suspected measles cases should be reported immediately to local health departments. Effective surveillance of measles and its complications can delineate inadequate levels of protection, further define groups needing special attention, and assess the effectiveness of control activities. Continuous and careful review of adverse reactions is also important. All serious reactions in vaccinated children should be evaluated and reported in detail to local and state health officials as well as to the manufacturer.

References

1. Siegel M, Fuerst HT: Low birth weight and maternal virus diseases: A prospective study of rubella, measles, mumps, chicken-pox, and hepatitis. JAMA 197:680-684, 1966
2. Jesperson CS, Lettauer J, Segild U: Measles as a cause of fetal defects. Acta Paediatr Scand 66:367-372, 1977
3. Modlin JF, Jabbour JT, Witte JJ, et al: Epidemiologic studies of measles, measles vaccine, and subacute sclerosing panencephalitis. Pediatrics 59:505-512, 1977
4. Center for Disease Control: Subacute sclerosing panencephalitis and measles. MMWR 26:309, 1977

SELECTED BIBLIOGRAPHY

Albrecht P, Ennis FA, Saltzman EJ, et al: Persistence of maternal antibody in infants beyond 12 months: Mechanism of measles vaccine failure. J Pediatr 91:715-718, 1977

Barkin RM: Measles mortality. Analysis of the primary causes of death. Am J Dis Child 229:307-309, 1975

Berkovich S, Starr S: Use of live-measles-virus vaccine to abort an expected outbreak of measles within a closed population. N Engl J Med 269:75-77, 1963

Center for Disease Control: Atypical measles—California. MMWR 25:245-246, 1976

Horowitz O, Grunfeld K, Lysgaard-Hansen B, et al: The epidemiology and natural history of measles in Denmark. Am J Epidemiol 100:136-149, 1974

Kamin PB, Fain BT, Britton HA: Use of live, attenuated measles virus vaccine in children allergic to egg protein. JAMA 193:1125, 1965

Krugman RD, Rosenberg R, McIntosh K, et al: Further attenuated measles vaccines: The need for revised recommendations. J Pediatr 91:766-767, 1977

Landrigan PJ, Witte JJ: Neurologic disorders following live measles vaccination. JAMA 223:1459-1462, 1973

Langmuir AD: Medical importance of measles. Am J Dis Child 103:34-56, 1962

Linnemann CC: Measles vaccine. Immunity reinfection and revaccination. Am J Epidemiol 97:365-371, 1973

Marks JS, Halprin TJ, Orenstein WA: Measles vaccine efficacy in children previously vaccinated at 12 months of age. Pediatrics (in press)

Orenstein WA, Halsey NA, Hayden GF, et al: Current status of measles in the United States 1973-1977. J Infect Dis 137:847-853, 1978

Shasby DM, Shope TC, Downs H, et al: Epidemic measles in a highly vaccinated population. N Engl J Med 296:585-589, 1977

Shelton JD, Jacobson JE, Orenstein WA, et al: Measles vaccine efficacy: The influence of age at vaccination versus duration of time since vaccination. Pediatrics (in press)

Wilkins J, Wehrle PF: Evidence for reinstatement of infants 12 to 14 months of age into routine measles immunization programs. Am J Dis Child 132:164-166, 1978

Yeager AS, Davis JH, Ross LA, et al: Measles immunization successes and failures. JAMA 273:347-351, 1977

Replaces previous recommendation on this subject, "Measles Vaccine" (MMWR 25:359-360, 365, 376, 1976) and Measles Outbreak Control (MMWR 26:294, 299, 1977).

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Recommendation of the Immunization Practices Advisory Committee (ACIP)

Meningococcal Polysaccharide Vaccines

INTRODUCTION

Polysaccharide vaccines against diseases caused by *Neisseria meningitidis* serogroups A and C are now licensed in the United States. They are prepared as monovalent and as bivalent antigens. The purpose of this statement is to summarize available information on these antigens and to offer general guidance regarding their role in the control of epidemics of meningococcal disease in the civilian population of the United States.

MENINGOCOCCAL DISEASE

Meningococcal disease is endemic in the United States and throughout the world. It caused serious epidemics approximately every 10 years from 1900 to 1945 in this country. The fact that it also regularly caused outbreaks among military recruits was a catalyst for the development of serogroup-specific vaccines.

During the last decade an estimated 3,000-6,000 cases a year of meningococcal disease occurred in the United States. From 1964 to 1968 and since 1972, the serogroup most often isolated from patients has been serogroup B. From 1969 through 1971 serogroup C was most common in the civilian and military populations. Serogroup A was only rarely identified until the occurrence recently of small outbreaks in several cities of the Pacific Northwest. In 1971 the Armed Forces began administering serogroup C meningococcal polysaccharide vaccine routinely to all recruits. Since then, the incidence of meningococcal disease in the military has declined sharply, and serogroup C disease has been virtually eliminated in that population.

Sulfa-sensitive serogroup B strains currently cause the majority of U.S. cases. Highest attack rates are in infants. Serogroup C strains account for about one-third of cases. Although the highest age-specific attack rate for serogroup C is also in infants, about 70% of serogroup C cases occur in persons over 2 years old. More than two-thirds of all meningococcal disease occurs in patients less than 20 years old.

In recent years meningococcal disease in civilians has occurred primarily as single isolated cases or, infrequently, as small, localized clusters. Secondary cases occur more frequently in household contacts than in the general population, and appropriate antibiotic prophylaxis has been the principal means of reducing the risk for immediate contacts of cases.

MENINGOCOCCAL VACCINES

Three meningococcal polysaccharide vaccines, monovalent A, monovalent C, and bivalent A-C vaccine*, are licensed for selective use in the United States. These vaccines are chemically defined antigens consisting of purified bacterial capsular polysaccharide, each inducing specific serogroup immunity. The duration of immunity conferred by each vaccine is unknown.

Serogroup A vaccine was evaluated in 62,000 Egyptian schoolchildren 6-15 years old and appeared to be highly effective and not to induce any serious side effects. When used to control an outbreak in Brazil, it appeared to be effective in all age groups beyond the

*Official names: Meningococcal Polysaccharide Vaccine, Group A; or , Group C; or , Groups A & C

first year of life. Further confirmation of effectiveness was found in children of ages 3 months-5 years in a vaccine trial carried out in Finland. Serogroup A vaccine has also been used to control outbreaks in the United States in Portland, Seattle, Anchorage, and Fairbanks.

Serogroup C vaccine has been given routinely to American military recruits since October 1971. More than 500,000 young adults have been vaccinated without significant adverse reactions. Serogroup C vaccine has been studied in infants, preschool and school-age children, and adults. It elicited antibody in all age groups, although older children and young adults had the highest levels. Serogroup C vaccine does not appear to be effective in children less than 2 years of age.

VACCINE USAGE

General Recommendations

Routinely vaccinating civilians with meningococcal polysaccharide vaccines is **not** recommended because of insufficient evidence of its value when the risk of infection is low. The serogroup-specific monovalent vaccines should be used, however, to control outbreaks of meningococcal disease caused by *N. meningitidis* serogroup A or C.

Vaccine may be of benefit for some travelers planning to visit countries recognized as having epidemic meningococcal disease. Although cases among Americans traveling in such areas are rare, prolonged contact with the local populace could enhance the risk of infection and make vaccination a reasonable precaution.

Vaccination should be considered an adjunct to antibiotic chemoprophylaxis for household contacts of meningococcal disease cases caused by serogroups A or C. This is because half the secondary family cases occur more than 5 days after the primary case—long enough to yield potential benefit from vaccination if the antibiotic chemoprophylaxis has not been successful.

Primary Immunization

For both adults and children, vaccine is administered parenterally as a single dose in the volume specified by the manufacturer.

PRECAUTIONS AND CONTRAINDICATIONS

Reactions

Adverse reactions to meningococcal vaccine are infrequent and mild, consisting principally of localized erythema lasting for 1-2 days.

Pregnancy

The safety of meningococcal vaccines in pregnant women has not been established. On theoretical grounds, it is prudent not to use them unless there is a substantial risk of infection.

EPIDEMIC CONTROL

In an epidemic of meningococcal disease due to serogroups A or C, the population at risk should be identified. It should be delineated by neighborhood, census tract, or other reasonable boundary. If there is ample vaccine, all residents in that area should be vaccinated. If not, persons expected or known to be at highest risk of disease by virtue of age, socioeconomic status, or area of residence should receive priority vaccination.

SELECTED BIBLIOGRAPHY

Artenstein MS, Winter PE, Gold R, et al: Immunoprophylaxis of meningococcal infection. Milit Med 139:91-95, 1974

Peltola H, Mäkelä PH, Käyhty H, et al: Clinical efficacy of meningococcus group A capsular polysaccharide vaccine in children three months to five years of age. N Engl J Med 297:686-691, 1977

Wahdan MH, Rizk F, el-Akkad AM, et al: A controlled field trial of a serogroup A meningococcal polysaccharide vaccine. Bull WHO 48:667-673, 1973

Replaces previous recommendation on this subject, MMWR 24:381-382, 1975.

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Recommendation of the Immunization Practices Advisory Committee (ACIP)

Mumps Vaccine

This revised ACIP recommendation on mumps vaccine represents an updating of the 1977 recommendation, based on current knowledge and practice. Major changes include a clearer definition of individuals to be vaccinated, a definition of susceptibles, and a statement regarding the possible association of mumps and diabetes.

INTRODUCTION

Mumps is primarily a disease of young, school-age children; only about 15% of reported cases occur in adolescents and adults. It is generally self-limited, but it may be moderately debilitating. Benign meningeal signs appear in up to 15% of cases, but permanent sequelae are rare. Nerve deafness is one of the most serious of the rare complications involving the central nervous system (CNS).

Orchitis (usually unilateral) has been reported as a complication in up to 20% of clinical mumps cases in postpubertal males, although sterility is very rare. Symptomatic involvement of other glands and organs has been observed less frequently.

There are limited experimental, clinical, and epidemiologic data that pancreatic damage may result from injury caused by direct viral invasion. However, further research is indicated to determine whether mumps infection contributes to the pathogenesis of diabetes mellitus.

Naturally acquired mumps infection, including the estimated 30% of cases that are subclinical, confers durable immunity.

MUMPS VIRUS VACCINE

Live mumps virus vaccine* is prepared in chick-embryo cell culture. Since it was introduced in December 1967, more than 40 million doses have been distributed in the United States. The vaccine produces a subclinical, non-communicable infection with very few side effects.

Parotitis after vaccination has been reported rarely. Allergic reactions, including rash, pruritus, and purpura, have been associated temporally with mumps vaccination but are uncommon and usually mild and of brief duration. Very rarely, effects of CNS involvement, such as febrile seizures, unilateral nerve deafness, and encephalitis within 30 days of mumps vaccination, are reported. No deaths have been reported among patients with such complications, and almost all have recovered completely. It should be emphasized that reports of nervous system illness following mumps vaccination do not necessarily connote an etiologic relationship between the illness and the vaccine. The frequency of CNS dysfunction following mumps vaccination is lower than the observed background incidence of CNS dysfunction in the normal population.

More than 90% of persons susceptible to mumps develop measurable antibody which, although of considerably lower titer than that following natural infection, is protective and long-lasting. The duration of vaccine-induced immunity is unknown, but observations

*Official name: Mumps Virus Vaccine, Live.

over 12 years of vaccine use indicate both continuing protection against infection and the presence of antibody.

VACCINE USAGE

(See also the current ACIP statement, "*General Recommendations on Immunization.*")

General Recommendations

Susceptible children, adolescents, and adults should be vaccinated against mumps, unless vaccination is contraindicated. Persons can be considered susceptible to mumps unless they have documentation of 1) physician-diagnosed mumps or laboratory evidence of immunity, or 2) adequate immunization with live mumps virus vaccine when 12 or more months of age. Persons born before 1957 are likely to have been infected naturally and generally may be considered immune.

Since there is no evidence that persons who have previously either received the vaccine or had mumps are at enhanced risk from receiving live mumps vaccine, testing for susceptibility before vaccination is unnecessary. Furthermore, such testing is usually either unreliable (mumps skin test) or non-specific (complement-fixation antibody test). Those tests which are reliable (neutralization, ELISA, and radial hemolysis antibody tests) are not readily available.

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

Age: Live mumps virus vaccine is recommended for all children at any age after 12 months. It should not be administered to younger infants because persisting maternal antibody may interfere with seroconversion. The vaccine may be administered either by itself or in combination with measles and/or rubella vaccines. The combined vaccine is preferred for routine use in young children because of convenience and economy. When given in a combined vaccine that includes measles antigen, it should be administered when a child is about 15 months of age to achieve the maximum rate of measles seroconversion. Mumps vaccine can be of particular value for children approaching puberty and for adolescents and adults, especially males, who have not had mumps.

Use of Vaccine Following Exposure

When given after exposure to mumps, live mumps vaccine may not provide protection. However, if the exposure did not result in infection, the vaccine should induce protection against subsequent infection.

Neither mumps immune globulin nor immune serum globulin (ISG) has been of established value in postexposure prophylaxis, and neither is recommended.

PRECAUTIONS AND CONTRAINDICATIONS

Pregnancy

Although mumps virus is capable of infecting the placenta and fetus, there is no good evidence that it causes congenital malformations in humans. Mumps vaccine virus also has been shown to infect the placenta, but the virus has not been isolated from the fetal tissues from susceptible women who were vaccinated and underwent elective abortions. However, because of the theoretical risk of fetal damage, it is prudent to avoid vaccinating pregnant women.

Allergies

Live mumps vaccine is produced in chick-embryo cell culture. It has not been reported to be associated with allergic reactions, and there is no evidence to indicate it should not be given to persons with allergies to eggs, chickens, and feathers. Some vaccines contain

trace amounts of antibiotics to which patients may be allergic. Those administering vaccines should review the label information carefully before deciding whether patients with known allergies to such antibiotics can be vaccinated safely. Live mumps virus vaccine does not contain penicillin.

Recent Administration of Immune Serum Globulin

Passively acquired antibody can interfere with the response to live, attenuated-virus vaccines. Therefore, administration of mumps vaccine should be deferred until approximately 3 months after passive immunization.

Immune Deficiency Conditions

Live mumps virus vaccine should not be given to persons with severe febrile illness; those with congenital immunodeficiency; those with leukemia, lymphoma, or generalized malignancy; or those receiving immunosuppressive therapy.

Other

There is no proven association between mumps vaccination and pancreatic damage or subsequent development of diabetes mellitus.

SURVEILLANCE

There is a continuing need to improve the reporting of mumps cases and mumps complications and to document the duration of vaccine effectiveness. Continuous and careful review of adverse reactions is also important. All severe reactions in vaccinated individuals should be evaluated and reported in detail to local or state health officials and to the manufacturer.

SELECTED BIBLIOGRAPHY

Drash AL. The etiology of diabetes mellitus. N Engl J Med 1979;300:1211-2.

Harris RW, Turnbull CD, Isacson P, Karzon DT, Winkelstein W Jr. Mumps in a northeast metropolitan community. Am J Epidemiol 1968;88:224-33.

Hayden GF, Preblud SR, Orenstein WA, Conrad JL. The current status of mumps and mumps vaccine in the United States. Pediatrics 1978;62:965-9.

Hilleman MR, Buynak EB, Weibel RE, Stokes J Jr. Live, attenuated mumps virus vaccine. N Engl J Med 1968;278:227-32.

Ennis FA, Hopps HE, Douglas RD, Meyer HM Jr. Hydrocephalus in hamsters: induction by natural and attenuated mumps viruses. J Infect Dis 1969;119:75-9.

Sinaniotis CA, Daskalopolou E, Lapatsanis P, Doxiadis S. Diabetes mellitus after mumps vaccination. Arch Dis Child 1975;50:749.

Weibel RE, Buynak EB, McLean AA, Hilleman MR. Persistence of antibody after administration of monovalent and combined live attenuated measles, mumps, and rubella vaccines. Pediatrics 1978;61:5-11.

Witte JJ, Karchmer AW: Surveillance of mumps in the United States as background for use of vaccine. Public Health Rep 1968;83:95-100.

Yamauchi T, Wilson C, St. Geme JW. Transmission of live, attenuated mumps virus to the human placenta. N Engl J Med 1974;290:710-2.

Replaces previous recommendation on this subject, published in MMWR 1977;26:393-4.