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(ACIP)

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DEFINITIONS OF ABBREVIATIONS AND TERMS USED IN THIS PUBLICATION

ACIP	Immunization Practices Advisory Committee
AIDS	Acquired immunodeficiency syndrome
CDC	Centers for Disease Control
CNS	Central nervous system
CRS	Congenital rubella syndrome
GBS	Guillain-Barré syndrome
H	Hemagglutinin
HB	Hepatitis B
HBIG	Hepatitis B immune globulin
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HDCV	Human diploid cell rabies vaccine
HRIG	Human rabies immune globulin
ID	Intradermal, intradermally
IG	Immune globulin
IM	Intramuscular, intramuscularly
IPV	Inactivated poliovirus vaccine
MMR	Measles, mumps, rubella vaccine
N	Neuraminidase
OPV	Oral poliovirus vaccine
SC	Subcutaneous, subcutaneously
Td	Tetanus and diphtheria combined toxoids (for adult use)
TIG	Tetanus immune globulin
VZIG	Varicella-zoster immune globulin
WHO	World Health Organization

This statement on adult immunization is a supplement to the "General Recommendations on Immunizations" of the Immunization Practices Advisory Committee (ACIP) (1). *It presents an overview of immunizations for adults and makes specific immunization recommendations. The statement provides information on vaccine-preventable diseases; indications for use of vaccines, toxoids, and immune globulins recommended for adults; and specific side effects, adverse reactions, precautions, and contraindications associated with use of these immunobiologics. It also gives immunization recommendations for adults in specific age groups and for those who have special immunization requirements because of occupation, lifestyle, travel, environmental situations, and health status.*

This statement, a compendium of ACIP recommendations, will not be updated regularly. The ACIP periodically reviews individual immunization statements, and revised statements are published in the MMWR. The reader must use the detailed, up-to-date individual statements in conjunction with this compendium in order to keep abreast of current information.

INTRODUCTION

In general, immunization policies have been directed towards vaccinating infants, children, and adolescents. While immunization is a routine measure in pediatric practice, it is not usually routine in the practice of physicians who treat adults.

The widespread and successful implementation of childhood immunization programs has greatly reduced the occurrence of many vaccine-preventable diseases. However, successful childhood immunization alone will not necessarily eliminate specific disease problems. A substantial proportion of the remaining morbidity and mortality from vaccine-preventable diseases now occurs in older adolescents and adults. Persons who escaped natural infection or were not immunized with vaccines and toxoids against diphtheria, tetanus, measles, mumps, rubella, and poliomyelitis may be at risk of these diseases and their complications.

To reduce further the unnecessary occurrence of these vaccine-preventable diseases, all those who provide health care to older adolescents and adults should provide immunizations as a routine part of their practice. In addition, the epidemiology of other vaccine-preventable diseases (e.g., hepatitis B, rabies, influenza, and pneumococcal disease) indicates that individuals in certain age, occupational, environmental, and lifestyle groups and individuals who have special health problems are at increased risk of these illnesses and should be immunized. Travelers to some countries may be at increased risk of exposure to vaccine-preventable illnesses. Finally, foreign students, immigrants, and refugees may be susceptible to these diseases.

A systematic approach to immunization is necessary to ensure that every adult is appropriately protected against vaccine-preventable diseases. Every visit by an adult to a health-care provider should be an opportunity to provide this protection. Several factors need to be considered before any patient is vaccinated. These include the susceptibility of the patient, the risk of exposure to the disease, the risk from the disease, and the benefits and risks from the immunizing agent. Physicians should maintain detailed information about previous vaccinations received by each individual, including type of vaccination, date of receipt, and adverse events, if any, following vaccination. Information should also include the person's history of vaccine-preventable illnesses, occupation, and lifestyle. Vaccine histories ideally should be based on written documentation to ascertain whether vaccines and toxoids were administered at appropriate ages and at proper intervals. Close attention to factors such as military service and age may be helpful in determining whether any vaccines or toxoids are advisable for an individual. After the administration of any immunobiologic, the patient should be given written documentation of its receipt and information on which vaccines or toxoids will be needed in

the future. For this purpose an immunization record form such as the suggested form found in Appendix 1 should be used routinely.

The patient or responsible person should be given information on the risks of immunobiologics as well as their major benefits in preventing disease both in individuals and in the community. No formal, legally acceptable statement has been universally adopted for the private medical sector. Thus, the ACIP recommends that there be ample opportunity for questions before each immunization. CDC has developed "Important Information Statements" for use with federally purchased vaccines given in public health clinics. Practitioners may wish to consider these or similar materials for patients. Examples of "Important Information Statements" can be obtained from state and many local health departments.

Modern immunobiologics are extremely safe and effective, but not completely so. All immunobiologics have had adverse events reported after administration. These range from frequent, minor, local reactions to extremely rare, severe systemic illness, such as paralysis associated with oral poliovirus vaccine (OPV). It is frequently impossible to establish cause-and-effect relationships when untoward events occur after vaccination since temporal association alone does not necessarily indicate causation. To improve knowledge about adverse reactions, all temporally associated events severe enough to require the recipient to seek medical attention should be evaluated and reported in detail to local or state health officials and to the manufacturer of the immunobiologic.

General immunization considerations and recommendations are found in the ACIP statement "General Recommendations on Immunization" (*1*).

The following recommendations apply generally to individuals in the indicated groups. For more detailed information on immunobiologics, including indications, side effects, adverse reactions, precautions, contraindications, dosage, and route of administration, providers are urged to refer to the following section on individual immunobiologics, the ACIP statements on specific immunobiologics (Appendix 2), and the tables and appendices at the back of this supplement. Appendix 3 provides a list of vaccines, toxoids, and immune globulins available in the United States as of June 1984.

Age Groups

The following text and Table 1 summarize the vaccines and toxoids recommended for most adults in the specific age groups. The reader is referred to the section on specific immunobiologics for essential information.

Adults 18-24 Years Old

All young adults should complete a primary series of diphtheria and tetanus toxoids. A primary series for adults is three doses of preparations containing tetanus and diphtheria toxoids, with the first two doses given at least 4 weeks apart and the third dose given 6-12 months after the second. Those who have completed a primary series should receive a booster dose every 10 years. There is no need to repeat doses when the series schedule is delayed. The combined tetanus-diphtheria toxoids for adult use, Td, should be used to enhance protection against both diseases. Persons with unknown or uncertain histories of receiving tetanus or diphtheria toxoids should be considered unimmunized and should receive a full three-dose primary series of Td.

Young adults should also be immune to measles, rubella, and mumps. Persons are considered immune to measles and mumps if they have a dated record of vaccination with live vaccines on or after their first birthday, documentation of physician-diagnosed disease, or laboratory evidence of immunity. Persons vaccinated in the period 1963-1967 with inactivated-

measles-virus vaccine or with a measles vaccine of unknown type should be revaccinated with live-measles-virus vaccine to prevent measles disease or atypical measles syndrome if exposed to wild measles virus. Persons are considered immune to rubella only if they have a record of vaccination with rubella vaccine on or after their first birthday or laboratory evidence of immunity. The combined measles, mumps, rubella (MMR) vaccine is the vaccine of choice if recipients are likely to be susceptible to more than one of the three diseases. Persons lacking adequate documentation as noted above should be vaccinated.

Adults 25-64 Years Old

All adults 25-64 years of age should complete a primary series of tetanus and diphtheria toxoids. A primary series for adults is three doses of preparations containing tetanus and diphtheria toxoids, with the first two doses given at least 4 weeks apart and the third dose given 6-12 months after the second. Those who have completed a primary series should receive a booster dose every 10 years. The combined toxoids for adult use, Td, should be used to enhance protection against both diseases. Persons with unknown or uncertain histories of receiving tetanus or diphtheria toxoids should be considered unimmunized and should receive a full three-dose primary series of Td.

Adults born in 1957 or later should receive measles vaccine unless they have a dated record of vaccination with live-measles vaccine on or after their first birthday, documentation of physician-diagnosed disease, or laboratory evidence of immunity. Adults born before 1957 can be considered immune to measles, since measles was a universal infection before measles vaccine became available. While most adults are likely to have been infected naturally with mumps, mumps vaccine may be given to adults, especially males, who are considered susceptible. Unless proof of vaccination with rubella vaccine or laboratory evidence of immunity is available, rubella vaccine is recommended for women of childbearing age and for other adults who may find themselves in places where rubella transmission is likely to occur, such as hospitals, all types of schools, and other places where young people are likely to congregate. The combined MMR vaccine is the vaccine of choice if recipients are likely to be susceptible to more than one of these three diseases.

Adults 65 Years Old or Older

All older adults should complete a primary series of tetanus and diphtheria toxoids. A primary series for adults is three doses of preparations containing tetanus and diphtheria toxoids, with the first two doses given at least 4 weeks apart and the third dose given 6-12 months after the second. Those who have completed a primary series should receive a booster dose every 10 years. The combined toxoids for adult use, Td, should be used to enhance protection against both diseases. Persons with unknown or uncertain histories of receiving tetanus or diphtheria toxoids should be considered unimmunized and should receive a full three-dose primary series of Td.

All older adults should receive influenza vaccine annually. They should also receive a single dose of pneumococcal polysaccharide vaccine.

Special Occupations

Persons in specific occupations may be at increased risk of exposure to certain vaccine-preventable illnesses. Such persons may need selected vaccines and toxoids in addition to those routinely recommended for their age group. Table 2 provides a summary of immunobiologics recommended for various special occupational groups. The reader is referred to the section on specific immunobiologics for essential information.

Health-Related Occupations

Medical, dental, laboratory, and other support personnel who may have contact with blood or blood products should be immune to hepatitis B virus (HBV) infection. The groups at highest risk for acquiring HBV infection and for whom HB vaccine is recommended include medical technicians, operating room staff, phlebotomists, physicians (particularly surgeons and pathologists), nurses (particularly intravenous-therapy nurses and nurses on oncology and dialysis units), dentists and oral surgeons, laboratory and blood-bank technicians, and emergency-room staff. Morticians and their assistants who have routine contact with blood and secretions are also at high risk of HBV infection. Selected staff of institutions for the mentally retarded may be at increased risk of HBV infection because of exposure to bites and contact with skin lesions, saliva, and other potentially infected secretions in addition to blood.

Among health-care personnel with frequent exposure to blood, the prevalence of serologic evidence of HBV infection is estimated to range between 10% and 30%. Since the cost effectiveness of serologic screening to detect susceptible individuals among health-care personnel depends on the prevalence of infection, each institution must decide whether serologic screening is cost effective. Vaccination of individuals who already have antibodies to HBV has not been shown to cause adverse effects.

The duration of protection from a three-dose series of HB vaccine or the need for booster doses has not yet been determined.

Transmission of rubella in health facilities (hospitals, physician or dentist offices, clinics, etc.) can disrupt hospital or office routines and cause considerable expense. Although no cases of congenital rubella syndrome (CRS) have been reported in association with rubella transmission in health facilities, therapeutic abortions have been sought by pregnant staff members following rubella infection (*2*). To prevent such situations, all medical, dental, laboratory, and other support health personnel, both male and female, who might be at risk of exposure to patients infected with rubella, or who might have contact with pregnant patients, should be immune. Rubella vaccine is recommended for all such personnel unless they have either proof of vaccination with rubella vaccine on or after their first birthday or laboratory evidence of immunity. Combined MMR vaccine is the vaccine of choice if recipients are likely to be susceptible to measles and/or mumps as well as to rubella.

Measles transmission in health facilities can also be disruptive and costly. To prevent such situations, all health personnel born in 1957 or later who may have contact with patients infected with measles should be immune. Such persons can be considered immune only if they have documentation of having received live-measles vaccine on or after their first birthday, a record of physician-diagnosed measles, or laboratory evidence of immunity. Measles vaccine is recommended for all persons lacking such documentation. Combined MMR vaccine is the vaccine of choice if recipients are likely to be susceptible to rubella and/or mumps as well as to measles. Adults born before 1957 can be considered immune to measles since measles was a universal infection before the availability of measles vaccine.

Poliovirus vaccine is not routinely recommended for persons older than high school age (18-19 years old). However, hospital personnel having close contact with patients who may be excreting wild polioviruses, and laboratory personnel handling specimens that may contain wild polioviruses, should have completed a primary series of poliovirus vaccine. For personnel who do not have proof of having completed a primary series, completion is recommended with inactivated poliovirus vaccine (IPV). IPV is preferred because there is a slightly increased risk in adults of vaccine-associated paralysis following receipt of OPV. In addition, since vaccine poliovirus may be excreted by OPV recipients for 30 or more days, the use of OPV increases the risk of acquiring vaccine-associated paralytic poliomyelitis among susceptible immunocompromised contacts and susceptible close contacts of OPV recipients.

Smallpox vaccination is indicated only for laboratory workers involved with orthopox viruses or in producing and testing smallpox vaccine. When indicated, smallpox vaccination should be given at least every 3 years.

Plague vaccine is indicated for laboratory personnel working with *Yersinia pestis* possibly resistant to antimicrobial agents and for persons performing *Y. pestis* aerosol experiments.

Preexposure rabies vaccination is indicated for laboratory workers directly involved with testing or isolating rabies virus.

Veterinarians and Animal Handlers

Veterinarians and animal handlers are at risk of rabies exposure because of occupational contact with both domestic and wild animals. They should receive preexposure rabies-vaccine prophylaxis with human diploid cell rabies vaccine (HDCV). Preexposure vaccination against rabies does *not* eliminate the need for additional therapy after exposure to rabies; it does, however, simplify postexposure therapy by eliminating the need for human rabies immune globulin (HRIG) and by decreasing the number of postexposure doses of vaccine needed. Persons at continued risk of frequent exposure should receive a booster dose of HDCV every 2 years or have their serum tested for rabies antibody every 2 years and, if the titer is inadequate (< 5 by the rapid fluorescent-focus inhibition test), receive a booster dose.

Selected Field Personnel

Plague vaccine is indicated for field personnel who cannot avoid regular exposure to potentially plague-infected wild rodents and rabbits and their fleas.

Preexposure rabies vaccine prophylaxis should be considered for field personnel who are likely to have contact with potentially rabid dogs, cats, skunks, raccoons, bats, or other wildlife species.

Sewage Workers

Sewage workers, as all other adults, should be adequately vaccinated against diphtheria and tetanus.

Poliovirus and typhoid vaccines and immune globulin are not routinely recommended for sewage workers.

Lifestyles

Various lifestyles may increase the risk of exposure to certain vaccine-preventable illnesses. Persons with these lifestyles may require vaccines in addition to those routinely recommended for their age group. Table 2 provides a summary of the vaccines recommended.

Homosexually Active Males

Homosexually active males are at high risk of HBV infection. Between 35% and 80% have serologic evidence of HBV infection. Susceptible homosexual males should be vaccinated with HB vaccine as early as possible after they begin homosexual activity because they can be expected to acquire HBV infection at a rate of 10%-20% per year. The duration of protection from a three-dose series of HB vaccine and the need for booster doses have not yet been determined. Because of the high prevalence of infection, prevaccination serologic screening of homosexual males may be cost effective regardless of their age or of how long they have been homosexually active.

Users of Illicit Injectable Drugs

Users of illicit injectable drugs are at high risk of HBV infection. Serologic evidence of HBV infection has been found in 60%-80% of these individuals. Efforts should be made to vaccinate susceptible users with HB vaccine as early as possible after their drug use begins because they can be expected to acquire HBV infection at a rate of 10%-20% per year. The duration of protection from a three-dose series of HB vaccine and the need for booster doses have not yet been determined. Because of the high prevalence of infection, prevaccination serologic screening of users of illicit injectable drugs to avoid unnecessary immunization is cost effective.

These drug users are also at increased risk of tetanus, and their tetanus immunization status should be kept up to date with Td.

Environmental Situations

Certain environments may place an individual at increased risk of certain vaccine-preventable diseases. Table 2 summarizes additional vaccines recommended for persons in selected environments. The reader is referred to the section on specific immunobiologics for essential information.

Inmates of Long-Term Correctional Facilities

Serologic evidence of HBV infection has been found in 10%-80% of male prisoners. Although the frequency of transmission during imprisonment has not been documented, the environment of long-term correctional facilities may be associated with a high risk of transmission of HBV infection because of the frequency of use of illicit injectable drugs and of homosexual behavior. In selected long-term institutional settings, prison officials may elect to undertake serologic HBV screening and vaccination programs. The duration of protection from a three-dose series of HB vaccine and the need for booster doses have not yet been determined.

Residents of Institutions for the Mentally Retarded

Institutions for the mentally retarded provide a setting conducive to the transmission of HBV infection through bites and contact with blood, skin lesions, saliva, and other potentially infectious secretions. Serologic evidence of HBV infection has been found in 35%-80% of residents of such institutions. New admissions to these institutions should be vaccinated as soon as possible. For current residents, screening and vaccination of susceptible residents is recommended. Because of the high prevalence of infection, preimmunization serologic screening of those already institutionalized may be cost effective; however, screening of new admissions very likely will not be. Residents of group homes, foster homes, and similar settings who have household contact with a carrier of HBV should also be vaccinated. The duration of protection from a three-dose series of HB vaccine and the need for booster doses have not yet been determined.

Travel

The risk of acquiring illness during international travel depends on the areas of the world to be visited and the extent to which the traveler is likely to be exposed to vaccine-preventable diseases. When considering travel, people often seek advice from health-care personnel on immunization. This provides a good opportunity to review the person's immunization status and administer primary series or booster doses, if needed.

In most countries, measles, mumps, and rubella remain uncontrolled. Therefore, the risk of acquiring these diseases while traveling outside the United States is greater than the risk incurred within the United States. Approximately 50% of imported measles cases reported for 1980-1983 occurred in citizens returning to the United States (*3*). To minimize importations by U.S. citizens, all travelers born in 1957 or later should be immune to measles. Women travelers of childbearing ages should be immune to rubella before leaving the United States.

In developed countries such as Japan, Canada, Australia, New Zealand, and the European countries, the risk of acquiring other vaccine-preventable diseases such as poliomyelitis, diphtheria, and tetanus is usually no greater than the risk incurred while traveling in the United States. In contrast, travelers to developing countries are, in general, at increased risk of exposure to many infections, including wild polioviruses and diphtheria. Accordingly, such travelers should be immune to poliomyelitis and diphtheria, in particular.

For protection against poliomyelitis, unimmunized adults should receive at least two doses of IPV 1 month apart, and preferably a complete primary series, before traveling to a developing country. If an individual's travel plans do not permit this interval, then a single dose of OPV is recommended. For adults previously incompletely immunized with OPV or IPV, the remaining doses of either vaccine required for completion of the primary series should be given, regardless of the interval since the last dose or the type of vaccine previously received. A single additional dose of either OPV or IPV should be given to travelers who have previously completed a primary series of OPV or IPV.

Selective immunization of travelers with vaccines against yellow fever, cholera, typhoid, plague, meningococcal disease, rabies, or HBV infection or administration of immune globulin (IG) to prevent hepatitis A is recommended on the basis of known, or perceived, disease-specific risks in the country(ies) to be visited and the type and duration of travel within a country. In the instances of cholera and yellow fever, vaccination requirements may have been established by the country to be visited. Countries currently reporting yellow fever, cholera, and plague are identified biweekly in the *Summary of Health Information for International Travel*, and information on known or probably infected areas is published annually in *Health Information for International Travel*, which also lists specific requirements for cholera and yellow fever vaccinations for each country. All state health departments and many county and city health departments receive both publications. For entry into countries requiring yellow fever or cholera vaccination, travelers must have an International Certificate of Vaccination validated by an appropriate authority. State or local health departments can provide the addresses of persons or centers able to validate certificates.

More information on specific vaccine-preventable illnesses that a traveler might encounter is provided in the sections describing specific vaccines.

Foreign Students, Immigrants, and Refugees

In many countries children and adolescents are not routinely immunized against diphtheria, tetanus, measles, mumps, rubella, and poliomyelitis. As a result, persons entering the United States to pursue college and postgraduate studies or as immigrants or refugees may be susceptible to one or more of these diseases.

Unless foreign students, immigrants, and refugees can provide a vaccination record documenting the receipt of recommended vaccines or toxoids at appropriate ages and intervals or laboratory evidence of immunity, they should receive the appropriate vaccines for their age as noted in age-specific recommendations (see page 2S) and in Table 1. Poliovirus vaccines are not recommended, in general, for persons 18 years of age or older.

Special Health Status

Some vaccines may be contraindicated for persons with certain health problems; other vaccines may be indicated because of an underlying health condition. Table 3 provides a summary of immunobiologics indicated or contraindicated for persons with selected health problems.

Pregnancy

When any vaccine or toxoid is to be given during pregnancy, waiting until the second or third trimester, when possible, is a reasonable precaution to minimize concern about possible teratogenicity.

Pregnant women not vaccinated previously against tetanus and diphtheria should receive two doses of Td properly spaced. Those who have previously received one or two doses of tetanus or diphtheria toxoid should complete their primary series during pregnancy. A primary series is three doses of preparations containing tetanus and diphtheria toxoids, with the first two doses given at least 4 weeks apart and the third dose given 6-12 months after the second. Pregnant women who have completed a primary series should receive a booster dose of Td if 10 or more years have elapsed since their last dose.

Because of a theoretical risk to the developing fetus, live-virus vaccines should not usually be given to pregnant women or to those likely to become pregnant within 3 months. If, however, immediate protection against poliomyelitis or yellow fever is needed because of imminent exposure, OPV or yellow fever vaccine may be given. If the only reason to vaccinate a pregnant woman with yellow fever vaccine is an international travel requirement, efforts should be made to obtain a waiver letter (see page 19S).

It is strongly recommended that rubella vaccine be administered in the postpartum period to women not known to be immune, preferably before discharge from the hospital.

Information about immunobiologics and vaccine-preventable diseases during pregnancy is summarized in Appendix 4.

Conditions That Compromise the Immune System

Persons with conditions that compromise their immune responses (e.g., leukemia, lymphoma, and generalized malignancy or immunosuppressive therapies) should receive annual influenza vaccination with the currently formulated vaccine. Persons with conditions associated with increased risk of pneumococcal disease or its complications should receive a single dose of pneumococcal polysaccharide vaccine. The effectiveness of these vaccines in such persons may be limited, but the risk of disease is substantial and adverse reactions are minimal.

In general, live-virus vaccines should not be given to persons who are immunocompromised as a result of immune deficiency diseases, leukemia, lymphoma, or generalized malignancy or are immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. However, susceptible patients with leukemia in remission who have not had chemotherapy for at least 3 months may receive live-virus vaccines. The exact interval between discontinuing immunosuppressives and regaining the ability to respond to individual vaccines is not known. Estimates of experts vary from 3 months to 1 year.

Short-term (less than 2 weeks) corticosteroid therapy, topical steroid therapy (e.g., nasal or skin), and intraarticular, bursal, or tendon injections with corticosteroids should not be immunosuppressive and do not necessarily contraindicate vaccination with live-virus vaccines. Vaccination should be avoided if systemic immunosuppressive levels are achieved by topical application.

Hemodialysis

Persons receiving hemodialysis have been at high risk of infection with HBV, although environmental control measures have reduced this risk during the past few years. Nationwide, an estimated 15% of hemodialysis patients have serologic evidence of HBV infection, and routine serologic screening of hemodialysis patients is currently recommended. Susceptible patients who will soon require or are currently receiving long-term hemodialysis should receive three double doses of HB vaccine as soon as possible. Double the normal dose is recommended for these patients because of lower vaccine immunogenicity in this group. Postvaccination screening to demonstrate antibody to hepatitis B surface antigen (HBsAg) is recommended in this group. Approximately 60% of hemodialysis patients who receive double doses of HB vaccine demonstrate antibodies against HBV. The duration of protection from a three-dose series of HB vaccine and the need for booster doses have not yet been determined.

Because persons with chronic renal disease are at increased risk of adverse consequences from infections of the lower respiratory tract, hemodialysis patients should receive annual influenza vaccination with the current formulated vaccine. These patients are also at increased risk of developing pneumococcal infection, as well as of experiencing more severe pneumococcal disease, and should receive pneumococcal polysaccharide vaccine.

Splenic Dysfunction or Anatomic Asplenia

Persons with splenic dysfunction or anatomic asplenia are known to be at increased risk of contracting fatal pneumococcal bacteremia and should receive pneumococcal polysaccharide vaccine. Persons scheduled for elective splenectomy should receive pneumococcal polysaccharide vaccine at least 2 weeks before the operation.

Factor VIII and IX Deficiencies

Patients with clotting disorders who receive factor VIII or IX concentrates have an increased risk of HBV infection. Vaccination with HB vaccine is recommended for susceptible patients. The degree and duration of protection from a three-dose series of HB vaccine and the need for booster doses have not yet been determined.

Prevaccination serologic screening for HBV markers is recommended for patients who have already received multiple infusions of these products.

Chronic Alcoholism

Persons with chronic alcoholism may be at increased risk of contracting a pneumococcal infection or having a more severe pneumococcal illness. Such persons, especially those with cirrhosis, should receive pneumococcal polysaccharide vaccine.

High-Risk Diseases

Persons with disease conditions that increase the risk of adverse consequences from lower-respiratory-tract infections should receive annual influenza vaccination with the current formulated vaccine. These conditions include:

(a) Acquired or congenital heart disease with actual or potentially altered circulatory dynamics.
(b) Any chronic disorder or condition that compromises pulmonary function.
(c) Diabetes mellitus or other metabolic diseases that increase the likelihood that infections will be more severe than for persons without such conditions.

(d) Chronic renal disease with azotemia or nephrotic syndrome.

(e) Chronic, severe anemia, such as sickle cell disease.

Some chronic illnesses (e.g., chronic pulmonary disease, congestive heart failure, diabetes mellitis) predispose individuals to an increased risk of pneumococcal illness or its complications. While data on the effectiveness of pneumococcal polysaccharide vaccine for chronically ill persons are not conclusive, such persons should receive the vaccine.

VACCINE-PREVENTABLE DISEASES AND THEIR IMMUNOBIOLOGICS

Vaccines, toxoids, and immune globulins are available for use in the prevention of a number of diseases. These diseases and their specific immunobiologics are presented in this section. For each immunobiologic, dosage, route of delivery, indications for use, side effects, adverse reactions, precautions, and contraindications to be considered before administration are described here and are summarized in Table 4.

Toxoids

Diphtheria

The occurrence of diphtheria has decreased dramatically in the United States, largely because of the widespread use of diphtheria toxoid. Only 11 cases of diphtheria were reported in the period 1980-1982. From 1977 through 1982, 56% of the 34 reported cases of respiratory diphtheria occurred in adults 20 years of age or older, and 24% of the cases occurred in adults 50 years of age or older. The age distribution for persons who died from diphtheria was similar. Diphtheria occurs primarily among unimmunized or inadequately immunized individuals. Limited serosurveys done since 1977 indicated that 62% of adults 18-39 years of age and 41%-84% of those 60 years of age or older lacked protective levels of circulating antitoxin against diphtheria (*4-6*).

- **Diphtheria toxoid**

Complete and appropriately timed immunization is at least 95% effective in preventing diphtheria. The combined preparation Td is recommended for use in adults since a large proportion of adults lack protective levels of circulating antibody against tetanus (*4-6*). Furthermore, Td contains much less diphtheria toxoid than other diphtheria toxoid-containing products, and as a result, reactions to the diphtheria component are less likely. Immunization with toxoid does not, however, prevent or eliminate carriage of *Corynebacterium diphtheriae*.

- **Toxoid indications**

All adults lacking a completed primary series of tetanus and diphtheria toxoids should complete the series with Td. A primary series for adults is three doses of preparations containing tetanus and diphtheria toxoids, with the first two doses given at least 4 weeks apart and the third dose given 6-12 months after the second. All adults for whom 10 years or more have elapsed since completion of their primary series or since their last booster dose should receive a dose of Td. Thereafter, a booster dose of Td should be administered every 10 years. There is no need to repeat doses if the schedule for the primary series or booster doses is delayed. (For toxoid side effects and adverse reactions, and precautions and contraindications, see page 12S).

Tetanus

The occurrence of tetanus has decreased dramatically, largely because of the widespread use of tetanus toxoid. Nevertheless, the number of cases remained relatively constant from

1973 through 1982, averaging 88 reported cases per year. Tetanus occurs almost exclusively in unimmunized or inadequately immunized individuals. Immune pregnant women confer temporary protection against tetanus to their infants through transplacental maternal antibody. In the period 1977-1982, persons 20 years of age or older accounted for 89% of the 504 reported tetanus cases for which patient ages were known; persons 60 years of age or older accounted for 55%. The age distribution of persons who died from tetanus was similar. Serosurveys done since 1977 indicated that 11% of adults 18-39 years of age and 49%-66% of those 60 years of age or older lacked protective levels of circulating antitoxin against tetanus (*4-6*).

- **Tetanus toxoid**

Complete and appropriately timed immunization is nearly 100% effective in preventing tetanus. The combined preparation, Td, is the preferred preparation for active tetanus immunization of adults since a large proportion of adults lack protective levels of circulating antitoxin against diphtheria (*4-6*).

- **Toxoid indications**

All adults lacking a complete primary series of tetanus and diphtheria toxoids should complete the series with Td. A primary series for adults is three doses of preparations containing tetanus and diphtheria toxoids, with the first two doses given at least 4 weeks apart and the third dose given 6-12 months after the second. All adults for whom 10 years or more have elapsed since completion of their primary series or since their last booster dose should receive a booster dose of Td. Thereafter, a booster dose of Td should be administered every 10 years. There is no need to repeat doses if the primary schedule for the series or booster doses is delayed.

The recommended pediatric schedule for DTP vaccine includes a booster dose at age 4-6 years. The first Td booster is recommended at age 14-16 years (10 years after the dose at age 4-6 years). One means of ensuring that persons continue to receive boosters every 10 years is to vaccinate persons routinely at mid-decade ages, e.g., 25 years, 35 years, etc.

For wound management the need for active immunization, with or without passive immunization, depends on the condition of the wound and the patient's immunization history. A summary of the indications for active and passive immunization is provided in Table 5. Only rarely have cases of tetanus occurred in persons with a documented primary series of toxoid injections.

Evidence indicates that complete primary immunization with tetanus toxoid provides long-lasting protection—10 years or more in most recipients. Consequently, after complete primary tetanus immunization, boosters are recommended at 10-year intervals. For clean and minor wounds occurring during the 10-year interval no additional booster is recommended. For other wounds, a booster is appropriate if the patient has not received tetanus toxoid within the preceding 5 years. Antitoxin antibodies develop rapidly in persons who have previously received at least two doses of tetanus toxoid.

Persons who have not completed a full primary series of injections or whose immunization status is unknown or uncertain may require tetanus toxoid and passive immunization at the time of wound cleaning and debridement. It is not sufficient to ascertain the interval since the most recent toxoid dose. A careful attempt should be made to determine whether a patient has previously completed primary immunization and, if not, how many doses have been given. Persons with unknown or uncertain previous immunization histories should be considered to have had no previous tetanus toxoid doses.

Td is the preferred preparation for active tetanus immunization in managing the wounds of adults. Td is used to enhance protection against diphtheria concurrently, since a large propor-

tion of adults are susceptible. Thus, if advantage is taken of visits for care of acute health problems, such as for wound management, some patients who otherwise would remain susceptible can be protected against both diseases. Primary immunization should ultimately be completed for persons documented to have received fewer than the recommended number of doses, including doses given as part of wound management.

If passive immunization is needed, human tetanus immune globulin (TIG) is the product of choice. The currently recommended prophylactic dose of TIG for wounds of average severity is 250 units, intramuscularly (IM). When tetanus toxoid and TIG are given concurrently, separate syringes and separate sites should be used. Most experts consider the use of adsorbed toxoid mandatory in this situation.

Toxoid (Td) Side Effects and Adverse Reactions

Local reactions, generally erythema and induration with or without tenderness, can occur after the administration of Td. Fever and other systemic symptoms are less common.

Arthus-type hypersensitivity reactions characterized by severe local reactions generally starting 2-8 hours after an injection and often associated with fever and malaise may occur, particularly in persons who have received multiple boosters of tetanus toxoid.

Rarely, severe systemic reactions such as generalized urticaria, anaphylaxis, or neurologic complications have been reported after administration of tetanus and diphtheria toxoids. Peripheral neuropathy has been reported rarely after administration of tetanus toxoid, although a causal relationship has not been established.

Toxoid (Td) Precautions and Contraindications

Although there is no evidence that tetanus and diphtheria toxoids are teratogenic, waiting until the second trimester of pregnancy to administer Td is a reasonable precaution to minimize any concern over teratogenicity.

A history of a neurologic reaction or a severe hypersensitivity reaction (e.g., generalized urticaria or anaphylaxis) following a previous dose is a contraindication to tetanus and diphtheria toxoids. Local side effects alone do not preclude continued use. If a prior systemic reaction is suspected of representing allergic hypersensitivity, appropriate skin testing to document immediate hypersensitivity may be useful before tetanus toxoid immunization is discontinued (7). Mild, nonspecific skin-test reactivity to tetanus toxoid is common. Most vaccinees develop cutaneous delayed hypersensitivity to the toxoid.

Persons experiencing severe Arthus-type hypersensitivity reactions to a prior dose of tetanus toxoid usually have very high serum tetanus antitoxin levels and should not be given even emergency booster doses of Td more frequently than every 10 years.

Although a minor illness, such as a mild upper-respiratory infection, should not be cause for postponing vaccination, a severe febrile illness is reason to defer routine vaccination.

Live-Virus Vaccines

Measles

In 1983, only 5.6% of the 3,139 counties in the United States reported cases of measles. Indigenous transmission of measles has been eliminated from most of the United States because of widespread vaccination. However, importations of disease are frequent (more than 100 each year), and there is a continued risk of exposure, particularly for young adults attending college or universities or traveling abroad.

In 1982, 11.7% of measles patients whose ages were reported were 20 years of age or older. Outbreaks continue to occur in universities and colleges and other places where young

adults congregate. In the first half of 1983, 51% of reported cases were among college students or were epidemiologically linked to campus outbreaks. It is estimated that as many as 20% of young adults lack detectable antibody and may be susceptible to measles.

Encephalitis or death follows measles disease in approximately one case per 1,000. The risk of encephalitis is greatest in adult patients. Aside from infants, the highest measles case-fatality ratio occurs in adults.

Measles illness during pregnancy increases rates of spontaneous abortion, premature labor, and low birth weight for infants. Although cases of congenital malformation following measles infection during pregnancy have been reported, no consistent patterns have been demonstrated.

- **Measles vaccine**

Measles vaccine produces a mild or inapparent noncommunicable infection. A single subcutaneously (SC) administered dose of live-measles vaccine provides durable protection against measles illness in approximately 95% of vaccinees, extending probably for their lifetime. Combined MMR vaccine is the vaccine of choice if recipients are likely to be susceptible to rubella and/or mumps as well as to measles. Although reactions following measles, mumps, and rubella vaccines in persons previously immune have been reported, evidence and experience overwhelmingly suggest that vaccination with MMR of persons who were previously immune to one or more of its components is not associated with significant adverse effects.

- **Vaccine indications**

Measles vaccine is indicated for all persons born in 1957 or later who lack documentation of receipt of live-measles vaccine on or after their first birthday, physician-diagnosed measles, or laboratory evidence of immunity. Persons born before 1957 can generally be considered immune since measles was a universal infection before measles vaccine became available. Individuals who received vaccine before their first birthday, killed-measles vaccine, killed-measles vaccine followed within 3 months by live-measles vaccine, or a measles vaccine of unknown type in the period 1963-1967 should be revaccinated. An estimated 600,000-900,000 persons in the United States received killed-measles vaccine in the years 1963-1967.

Because the risk of acquiring measles outside the United States is greater than the risk incurred in the United States, travelers should be immune to measles before leaving the United States.

Generally, young adults who are exposed to measles and who have no or uncertain documentation of live-measles vaccination on or after their first birthday, no record of physician-diagnosed measles, and no laboratory evidence of immunity should be vaccinated within 72 hours after exposure, when vaccination is most likely to be protective. If the exposure did not result in infection, the vaccine should induce protection against subsequent measles infection. An acceptable alternative is to use IG, which can prevent or modify infection if administered within 6 days after exposure. IG is principally indicated when measles vaccine is contraindicated. IG should not be used in an attempt to control measles outbreaks. The recommended dose of IG is 0.25 ml/kg IM, not to exceed 15 ml. Live-measles vaccine should be given 3 months after IG is administered, by which time the passive measles antibodies should have disappeared.

- **Vaccine side effects and adverse reactions**

Reactions to measles vaccine do not appear to be age related. About 5%-15% of vaccinees may develop a temperature of 103°F (39.4°C) or higher, generally beginning between days 5 and 12 after vaccination; fever usually lasts 1-2 days and, rarely, up to 5 days. Transient

rashes have been reported in approximately 5% of vaccinees. The incidence rate of encephalitis or encephalopathy following measles vaccination is lower than the observed background incidence rate of encephalitis of unknown etiology and much lower than that following natural measles.

Reactions after live-measles vaccination occur in 4%-55% of prior recipients of killed-measles vaccine. The reactions are generally mild, consisting of a local reaction with or without a low-grade fever of 1-2 days' duration. Such reactions are considerably milder than atypical measles syndrome, an illness which may affect prior recipients of killed-measles vaccine who are exposed to natural measles.

- **Vaccine precautions and contraindications**

Vaccination should not be postponed because of a minor illness, such as a mild upper-respiratory infection. However, vaccination of persons with severe febrile illnesses should be postponed until recovery. Vaccine should be given 14 days before or deferred for at least 6 weeks, and preferably 3 months, after a person has received IG, whole blood, or other blood products containing antibody.

Because of a theoretical risk to the developing fetus, measles vaccine should not be given to pregnant women.

Measles vaccine should not be given to persons who are immunocompromised as a result of immune deficiency diseases, leukemia, lymphoma, or generalized malignancy or are immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. (See "Conditions That Compromise the Immune System," page 8S.)

There is no evidence that live-measles vaccine exacerbates tuberculosis. If tuberculin skin testing is needed, it should be done on the day of vaccination and read 48-72 hours later. For a recent vaccinee, it is prudent to wait 4-6 weeks after receipt of measles vaccine before administering a tuberculin skin test since measles vaccination may temporarily suppress tuberculin reactivity.

Persons with a history of any sign or symptom of an anaphylactic reaction (i.e., hives, swelling of the mouth and throat, difficulty in breathing, hypotension, or shock) following ingestion of eggs or receipt of neomycin should be given measles vaccine only with extreme caution. Protocols have been developed for vaccinating such persons (*8*). Persons with reactions that are not anaphylactic are not at increased risk and can be vaccinated.

Mumps

The occurrence of reported mumps cases in the United States has decreased steadily since the introduction of live-mumps-virus vaccine. In 1983, a record low of 3,297 cases were reported provisionally; this number represented a 98% decline from the 185,691 cases reported in 1967, the year live-mumps vaccine was licensed. In 1982, 5,270 cases were reported, of which 9% occurred in persons 20 years of age or older.

Although mumps disease is generally self-limiting, meningeal signs may appear in up to 15% of cases, and orchitis in up to 20% of clinical cases among postpubertal males. Sterility is a rare sequela of mumps orchitis among males. Deafness occurs at a rate of one case per 15,000 cases of mumps.

Serologic surveys indicate that most individuals have been infected with mumps by 20 years of age.

- **Mumps vaccine**

Live-mumps vaccine has been available since 1967. A single dose of live-mumps vaccine administered SC provides protective and long-lasting levels of antibody in over 90% of recipients. Reported clinical vaccine efficacy ranges between 75% and 90%. MMR is the vaccine

of choice if recipients are likely to be susceptible to measles and/or rubella as well as to mumps. Although reactions following measles, mumps, and rubella vaccines in persons previously immune have been reported, evidence and experience overwhelmingly suggest that the vaccination with MMR of persons who were previously immune to one or more of its components is not associated with significant adverse effects.

- **Vaccine indications**

Mumps vaccine is indicated for all adults, particularly males, believed to be susceptible. Most adults are likely to have been infected naturally and generally can be considered immune, even if they did not have clinically recognizable mumps disease. Killed-mumps vaccine was available from 1950 until 1978. Persons who received killed-mumps vaccine might benefit from vaccination with live-mumps vaccine.

- **Vaccine side effects and adverse reactions**

Parotitis after vaccination has been reported rarely. Allergic reactions including rash, pruritus, and purpura have been associated temporally with mumps vaccination but are uncommon, usually mild, and of brief duration. The frequency of reported central nervous system (CNS) dysfunction following mumps vaccination is lower than the observed background incidence rate in the general population.

- **Vaccine precautions and contraindications**

Vaccine should be given at least 14 days before or deferred for at least 6 weeks, and preferably 3 months, after a person has received IG, whole blood, or other blood products containing antibody.

Because of the theoretical risk of fetal damage following administration of a live-virus vaccine to a pregnant woman, it is prudent to avoid giving mumps vaccine to pregnant women.

Mumps vaccine should not be given to persons who are immunocompromised as a result of immune deficiency diseases, leukemia, lymphoma, or generalized malignancy or are immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. (See "Conditions That Compromise the Immune System," page 8S.)

Persons with a history of any sign or symptom of an anaphylactic reaction (i.e., hives, swelling of the mouth and throat, difficulty in breathing, hypotension, or shock) following ingestion of eggs or receipt of neomycin should be vaccinated only with extreme caution. Protocols have been developed for vaccinating persons with severe egg allergy (*8*). Persons with reactions that are not anaphylactic are not at increased risk and can be vaccinated.

Rubella

Preventing fetal infection and consequent CRS are the objectives of rubella immunization. Fetal infection occurring during the first trimester of pregnancy can lead to CRS in up to 80% of fetuses. In addition, fetal wastage due to miscarriage or therapeutic abortion following maternal rubella disease or exposure during the first trimester remains a frequent occurrence.

The number of reported rubella cases has decreased steadily from over 56,000 cases in 1969, the year rubella vaccine was licensed, to 2,325 cases in 1982. In 1982, only 11.7% of the 3,137 counties in the United States reported cases of rubella. The 1983 provisional total of 954 cases is an all-time low. Because, until recently, many adolescents and young adults had not been vaccinated, decreases in incidence rates of reported rubella were observed primarily for children. Recent efforts to increase delivery of vaccine to college-age and older persons have led to the current decline in the incidence rates for these age groups. However, an estimated 10%-15% of young adults remain susceptible to rubella, and limited outbreaks continue to be reported in universities, colleges, and places of employment—notably hospitals.

Vaccination of young children has prevented widespread epidemics of rubella and of CRS and eventually will lead to the elimination of CRS as vaccinated cohorts enter the childbearing age. However, increased efforts to ensure that all women of childbearing age, in particular, are vaccinated will hasten the elimination of rubella and CRS in the United States. Additional aids to elimination of rubella and CRS include 1) achieving and maintaining high immunization levels, 2) maintaining vigorous surveillance, and 3) practicing aggressive outbreak control.

- **Rubella vaccine**

A single SC administered dose of live, attenuated rubella vaccine provides long-term, probably lifetime, immunity in approximately 95% of vaccinees. Moreover, there is no risk to susceptible contacts of vaccinees. MMR is the vaccine of choice if recipients are likely to be susceptible to measles and/or mumps as well as to rubella. Although reactions following administration of measles, mumps, and rubella vaccines to persons previously immune have been reported, evidence and experience overwhelmingly suggest that the vaccination with MMR of persons who are already immune to one or more of its components is not associated with significant adverse effects.

- **Vaccine indications**

Rubella vaccine is recommended for adults, particularly females, unless proof of immunity is available (i.e., documented rubella vaccination on or after the first birthday or a positive serologic test) or unless the vaccine is specifically contraindicated. In particular, nonpregnant susceptible women of childbearing age should be provided rubella vaccination 1) during routine internal medicine and gynecologic outpatient care, 2) during routine care in a family planning clinic, 3) following premarital screening, 4) before discharge from a hospital for any reason, and 5) after childbirth or abortion. Ideally, any contact with the health-care system should be used as an opportunity to vaccinate susceptible women. In addition, evidence of rubella immunity should be required for all individuals in colleges and universities. Health-care programs in work places and in other places where women of childbearing age congregate should ensure that the rubella immune status of every employee is ascertained and that rubella immunization is made available. All hospital personnel (male and female) who might be at risk of exposure to patients infected with rubella or who might have contact with pregnant patients or personnel should be immune to rubella. Consideration should be given to making rubella immunity a condition for employment. Finally, since the risk of acquiring rubella while traveling outside the United States is greater than the risk incurred within the United States, all women travelers, particularly those of childbearing age, should be immune before leaving the United States.

- **Vaccine side effects and adverse reactions**

Up to 40% of susceptible adult vaccinees in large-scale field trials have had joint pain, usually of the small peripheral joints, after vaccination; frank arthritis is reported infrequently. Arthralgia and transient arthritis occur more frequently and tend to be more severe in susceptible women than in children. When joint symptoms or other types of pain and paresthesias do occur, they generally begin 3-25 days after vaccination, persist for 1-11 days, and rarely recur. Adults with joint problems usually have not had to disrupt work activities. Complaints of transient peripheral neuritis such as paresthesias and pain in the arms and legs have occurred very rarely and only in susceptible vaccinees.

- **Vaccine precautions and contraindications**

Rubella vaccine should be given at least 14 days before administration of IG or deferred for at least 6 weeks, and preferably 3 months, after administration. On the other hand, previous administration of whole blood or other blood products containing antibody (e.g., human anti-Rho [D] immune globulin) does not generally interfere with an immune response and is not a contraindication to postpartum vaccination. However, in this situation, serologic testing should be done 6-8 weeks after vaccination to assure that seroconversion has occurred.

Rubella vaccine should not be given to pregnant women or to those likely to become pregnant within 3 months after receiving the vaccine. Through 1983, CDC monitored prospectively 214 susceptible pregnant women who had received rubella vaccine within 3 months before or after conception and carried their pregnancies to term (94 received Cendehill or HPV-77, 119 received RA 27/3, and one received an unknown strain of vaccine). None of the infants had malformations compatible with CRS. The ACIP believes that the risk of vaccine-associated malformation is so small as to be negligible. Although a final decision must rest with the individual patient and her physician, the ACIP believes that rubella vaccination during pregnancy should not ordinarily be a reason to recommend interruption of pregnancy.

Because of the theoretical risk to the fetus, reasonable precautions should be taken before women of childbearing age are vaccinated. These precautions include 1) asking women if they are pregnant, 2) excluding those who say they are, and 3) explaining the theoretical risks of the vaccine to the others and counseling them not to become pregnant for 3 months after vaccination. If a pregnant woman is vaccinated or if a woman becomes pregnant within 3 months after vaccination, she should be counseled on the theoretical risks to the fetus. Instances of vaccination of *known* susceptible women who are pregnant or become pregnant within 3 months should be reported through state health departments to the Division of Immunization, CDC.

In general, rubella vaccine should not be given to persons who are immunocompromised as a result of immune deficiency diseases, leukemia, lymphoma, or generalized malignancy or are immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. (See "Conditions That Compromise the Immune System," page 8S.)

Rubella vaccine is prepared in human diploid cell cultures and has not been reported to be associated with allergic reactions. The vaccine does contain trace amounts of neomycin to which patients may be allergic. Persons with a history of any sign or symptom of an anaphylactic reaction (i.e., hives, swelling of the mouth and throat, difficulty in breathing, hypotension, or shock) following receipt of neomycin should not receive rubella vaccine. Persons with reactions to neomycin that are not anaphylactic are not at increased risk and can be vaccinated. Rubella vaccine does not contain penicillin.

Smallpox

In May 1980, the World Health Organization (WHO) declared the world free of smallpox. A smallpox vaccination certificate is not required by any country as a condition of entry for international travelers. In May 1983, the distribution of smallpox vaccine for civilian use in the United States was discontinued.

- **Vaccine indications**

There is no evidence that smallpox vaccination has therapeutic value in the treatment of recurrent herpes simplex infection, warts, or any other disease. Smallpox vaccine should never be used therapeutically for these or any other conditions.

Except for persons working with orthopox viruses or involved in producing and testing smallpox vaccine, there are *no* indications for the use of smallpox vaccine in civilian populations. When indicated, smallpox vaccination should be given at least every 3 years. For advice on vaccine administration and contraindications, contact the International Health Program Office, CDC, Atlanta, Georgia 30333.

Yellow Fever

Cases of yellow fever are reported only from Africa and South America. Two forms of yellow fever—urban and jungle—are distinguishable epidemiologically. Clinically and etiologically they are identical.

Urban yellow fever is an epidemic viral disease transmitted from infected to susceptible persons by the *Aedes aegypti* mosquito. In areas where the *A. aegypti* mosquito has been eliminated or suppressed, urban yellow fever has disappeared. In West Africa, *A. aegypti*-transmitted epidemics involving town and village populations continue to occur at frequent intervals.

Jungle yellow fever is an enzootic viral disease transmitted among nonhuman hosts by a variety of mosquito vectors. It is currently observed only in forested areas of South America and forest-savannah zones of tropical Africa, but occasionally extends into Central America and the Caribbean. In tropical America 200-400 cases are recognized annually, mainly among persons with occupational exposure to the vector in forested areas; the disease is, however, believed to be greatly underreported. In Africa, epidemics that are spread by forest mosquito vectors affect tens of thousands of persons every few years, but few cases are officially reported. The jungle yellow fever cycle may be active but unrecognized in forested areas of countries within the zone with endemic yellow fever (Figure 1).

- **Yellow fever vaccine**

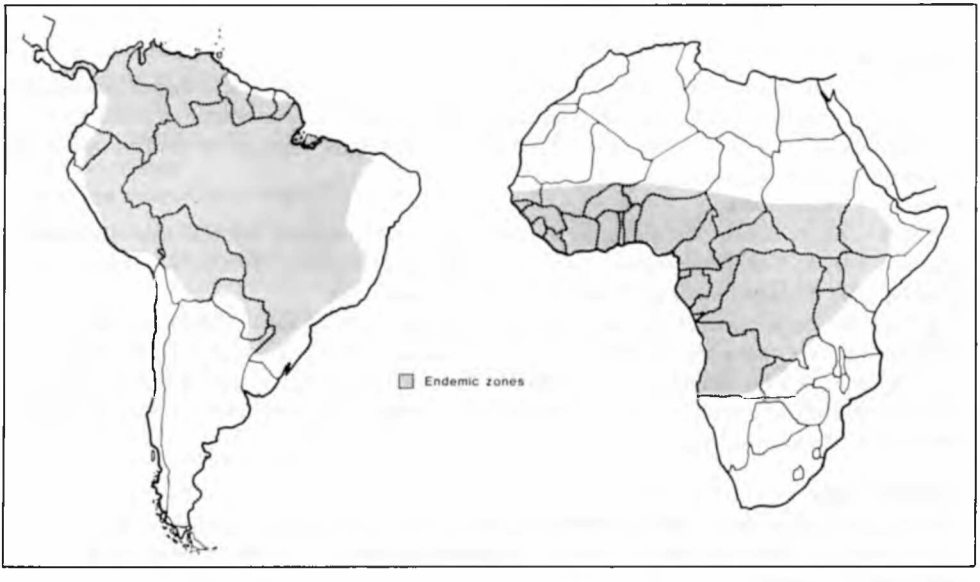
The yellow fever vaccine available in the United States is an attenuated, live-virus vaccine prepared from the 17D strain of virus grown in chick embryo. Immunity is induced by a single SC injection of 0.5 ml of reconstituted vaccine and persists for more than 10 years.

Yellow fever vaccines must be approved by WHO and administered at an approved Yellow Fever Vaccination Center. Centers can be identified by contacting state and local health departments. Vaccinees should have an International Certificate of Vaccination filled out, dated, signed, and validated with the stamp of the center where the vaccine is given. Vaccine must be received 6 days to 10 years before travel in order for the certificate to be valid.

- **Vaccine indications**

Vaccination is recommended for persons traveling or living in areas where yellow fever infection occurs—currently parts of Africa and South America. Information on known or probably infected areas are published annually in *Health Information for International Travel.* Coun-

FIGURE 1. Yellow fever endemic zones



tries currently reporting yellow fever are noted biweekly in *Summary of Health Information for International Travel.* All state health departments and many county and city health departments receive these publications. It should be emphasized that the actual areas of yellow fever activity far exceed the zones officially reported to be infected. Vaccination is also recommended for laboratory personnel who might be exposed to virulent yellow fever virus.

Booster doses are needed at 10-year intervals.

Some countries, especially in Africa, require evidence of vaccination from all entering travelers. Other countries may waive the requirements for travelers coming from noninfected areas and staying less than 2 weeks. Some countries require a traveler, even if only in transit, to have a valid certificate if the traveler has visited any country thought to harbor yellow fever virus. Requirements of individual countries may change, and the most current information is published biweekly in *Summary of Health Information for International Travel* and summarized annually in *Health Information for International Travel.*

- **Vaccine side effects and adverse reactions**

Reactions to 17D yellow fever vaccine are generally mild. From 2% to 5% of vaccinees have mild headache, myalgia, low-grade fever, or other minor symptoms 5-10 days after vaccination. Fewer than 0.2% curtail regular activities. Immediate hypersensitivity reactions, characterized by rash, urticaria, and/or asthma, are extremely uncommon and occur principally in persons with a history of egg allergy. Although more than 34 million doses of vaccines have been distributed, only two cases of encephalitis temporally associated with vaccinations have been reported in the United States; in one fatal case, 17D virus was isolated from the brain.

- **Vaccine precautions and contraindications**

Yellow fever vaccine should not be given to persons who are immunocompromised as a result of immune deficiency diseases, leukemia, lymphoma, or generalized malignancy or are immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. (See "Conditions That Compromise the Immune System," page 8S.)

Although specific information is not available on adverse effects of yellow fever vaccine on the developing fetus, it is prudent on theoretical grounds to avoid vaccinating pregnant women and to advise that they postpone travel to areas where yellow fever occurs until after delivery. Pregnant women who must travel to areas where the risk of yellow fever is high should be vaccinated. It is believed that under these circumstances, the risk of yellow fever infection far outweighs the small theoretical risk to mother and fetus from vaccination. However, if international travel regulations constitute the only reason to vaccinate a pregnant woman or a patient hypersensitive to eggs, efforts should be made to obtain a letter of waiver from a physician clearly stating the contraindication to vaccination. Ideally, this letter should be written on letterhead stationery and bear the stamp used by health departments and official immunization centers to validate the International Certificates of Vaccination. Such a letter of waiver has been acceptable to some governments. Under these conditions, it is also useful for the traveler to obtain specific, authoritative advice from the country or countries he or she plans to visit. Their embassies or consulates may be contacted, and a letter substantiating the waiver of requirements obtained.

Since live yellow fever vaccine is produced in chick embryos, persons with a history of any signs or symptoms of an anaphylactic reaction (i.e., hives, swelling of the mouth and throat, difficulty in breathing, hypotension, or shock) after eating eggs should not receive yellow fever vaccine. If vaccination of an individual with a questionable history of egg hypersensitivity is considered essential because of a high risk of exposure, an intradermal (ID) test dose may be administered under close medical supervision. Specific directions for skin testing are found in the package insert.

Some data have indicated that persons given yellow fever and cholera vaccines simultaneously or 1-3 weeks apart had lower-than-normal antibody responses to both vaccines. Unless there are time constraints, cholera and yellow fever vaccines should be administered at a minimal interval of 3 weeks. If the vaccines cannot be administered at least 3 weeks apart, then they should preferably be given simultaneously.

Yellow fever vaccine and commercially available IG may be given simultaneously.

Both Live-Virus and Inactivated-Virus Vaccines

Poliomyelitis

The risk of poliomyelitis is very small in the United States; however, epidemics could occur if the high immunity level of the general population is not maintained by immunizing children routinely or if wild poliovirus is introduced into susceptible populations in communities with low immunization levels. In the United States inapparent infection with wild poliovirus strains no longer contributes significantly to establishing or maintaining immunity. Most adults are already immune.

- **Poliovirus vaccines**

Two types of poliovirus vaccines are currently licensed in the United States: OPV and IPV. A primary vaccination series with either vaccine produces immunity to all three types of poliovirus in more than 95% of recipients. The primary series of OPV consists of three doses: two doses given 6-8 weeks apart and a third dose given at least 6 weeks and customarily 6-12 months after the second. The primary series for IPV consists of four doses: three doses each given 4-8 weeks apart and a fourth dose given 6-12 months after the third. In general, it is not necessary to give a primary vaccine series to adults living in the United States who have not had a primary series as children. However, for adults who have not had a primary series and who are at greater risk than the general population of exposure to wild polioviruses because of foreign travel or health occupation, IPV is preferred since the risk of OPV-associated paralysis is slightly higher in adults than in children.

Poliovirus vaccine is not routinely recommended for persons older than high school age (18-19 years old).

- **Vaccine indications**

Travelers to areas where wild poliovirus is epidemic or endemic should have completed a primary series of poliovirus vaccine. For previously unimmunized persons, IPV is indicated. However, if less than 4 weeks are available before protection is needed, a single dose of OPV is recommended. Travelers who have previously received less than a full primary course of OPV or IPV should be given the remaining required doses of either vaccine, regardless of the interval since the last dose and the type of vaccine previously received. Travelers to developing countries who have previously completed a primary series of OPV should receive a single dose of OPV. Additional booster doses of OPV are probably not necessary. Those who have previously received a primary series of IPV should receive a dose of either OPV or IPV. If IPV is used exclusively, an additional dose may be given every 5 years if exposure continues or recurs, although the need for these boosters has not been established.

Health-care personnel in close contact with patients who may be excreting wild polioviruses, and laboratory personnel handling specimens that may contain wild polioviruses, should have completed a primary series of poliovirus vaccine. IPV is indicated because of the slightly increased risk to adults of vaccine-associated paralysis after OPV administration; also, virus may be shed after receipt of OPV vaccine and inadvertently expose susceptible immunocompromised contacts to live vaccine virus.

- **Vaccine adverse reactions**

Inactivated poliovirus vaccine. No serious side effects of currently available IPV have been documented. Since IPV contains trace amounts of streptomycin and neomycin, hypersensitivity reactions are possible in individuals sensitive to these antibiotics. Persons with signs and symptoms of an anaphylactic reaction (i.e., hives, swelling of mouth and throat, difficulty in breathing, hypotension, or shock) following receipt of streptomycin or neomycin should not receive IPV. Persons with reactions that are not anaphylactic are not at increased risk and can be vaccinated.

Oral poliovirus vaccine. In rare instances, administration of OPV has been associated with paralysis in healthy recipients and their contacts. Although the risk of vaccine-associated paralytic poliomyelitis is extremely small for immunologically normal vaccinees (approximately one case per 9 million doses distributed) and their susceptible, immunologically normal household contacts (approximately one case per 7 million doses distributed), vaccinees should be informed of this risk.

- **Vaccine precautions and contraindications**

Inactivated poliovirus vaccine. There is no convincing evidence of adverse effects of IPV for the pregnant woman or developing fetus; regardless, it is prudent on theoretical grounds to avoid vaccinating pregnant women. However, if immediate protection against poliomyelitis is needed, OPV, not IPV, is recommended.

Oral poliovirus vaccine. Unlike other live-virus vaccines, which are administered parenterally, OPV is administered orally. IG and other antibody-containing blood products do *not* appear to interfere with the immune response to OPV.

OPV should not be given to persons who are or may be immunocompromised as a result of immune deficiency diseases, leukemia, lymphoma, or generalized malignancy or immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. (See "Conditions That Compromise the Immune System," page 8S.) If immunization against poliomyelitis is indicated in such persons, IPV should be used, and some protection may result.

OPV should not be used for immunizing household contacts of patients immunocompromised as a result of immune deficiency disease, leukemia, lymphoma, or generalized malignancy or immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. If protection is indicated, IPV should be used for immunizing household contacts of such patients. OPV should not be given to anyone in a family with a known family history of immunodeficiency until the immune status of all family members is documented.

When children in the household are given OPV, adults who are not adequately immunized against poliomyelitis are at a very small risk of contracting OPV-associated paralytic poliomyelitis. Because of the overriding importance of ensuring prompt and complete immunization of the child and the extreme rarity of OPV-associated disease in contacts of vaccinees, the ACIP recommends the administration of OPV to a child regardless of the poliovirus-vaccine status of adult household contacts. This is the usual practice in the United States. The responsible adult should be informed of the small risk involved and of precautions to be taken, such as hand washing after changing a diaper. An acceptable alternative, if there is strong assurance that ultimate, full immunization of the child will not be jeopardized or unduly delayed, is to immunize adults with IPV or OPV, as appropriate to their immunity status, before giving OPV to the child.

Inactivated-Virus Vaccines

Hepatitis B Virus Infection

The estimated lifetime risk of acquiring HBV infection in the United States is approximately 5% for the population as a whole but may approach 100% for the highest risk groups. Annually, an estimated 100,000 symptomatic cases of hepatitis B disease occur in the United States, leading to approximately 10,000 hospitalizations and 190 fulminant cases. Three-fourths of persons with fulminant disease die.

In 1982, 88% of hepatitis B cases for which patient age was known occurred in persons 20 years of age or older. Between 6% and 10% of adults with HBV infection become carriers. The United States currently has 400,000-800,000 carriers. Chronic active hepatitis occurs in 25% of carriers. Each year in the United States, approximately 4,000 persons die of HBV-related cirrhosis, and 800, of HBV-related liver cancer.

- **Hepatitis B vaccine**

A series of three 1-ml IM doses of HB vaccine, each containing 20 μg/ml of HBsAg protein, provides protective antibody in over 90% of healthy adult recipients and is 80%-95% effective in preventing infection for at least 2 years. The first two doses should be given 1 month apart, and the third dose, 5 months after the second. The duration of vaccine-induced protection and the need for booster doses are not yet known. For susceptible hemodialysis patients, three 2-ml doses given at the above intervals are recommended. Because the prevalence of HBV varies widely among various population groups, serologic screening to detect susceptible individuals before vaccination may or may not be cost effective. Cost effectiveness depends on the known or perceived risk of infection, the cost of screening, and the cost of HB vaccine.

- **Vaccine indications**

Immunization is recommended for adults at increased risk of occupational, social, family, environmental, or illness-related exposure to HBV. These include homosexual males, users of illicit injectable drugs, household and sexual contacts of HBV carriers, workers in health-related occupations requiring frequent exposure to blood, residents and staff of institutions for the mentally retarded, hemodialysis patients, recipients of factor VIII or IX concentrates, and morticians and their assistants. Inmates in some long-term correctional facilities may also be candidates for vaccination.

Vaccination should also be considered for persons who plan to reside for more than 6 months in areas with high levels of endemic HBV and who will have close contact with the local population and for travelers intending a short stay who are likely to have contact with blood from or sexual contact with residents of areas with high levels of endemic disease (particularly areas of eastern Asia and Sub-Saharan Africa). Such persons should allow 6 months before travel in order to complete the HB vaccine primary series.

HB vaccine is intended primarily for preexposure prophylaxis. However, it has recently been recommended for postexposure use in certain situations, particularly for persons who belong to a high-risk group for whom preexposure administration of vaccine is recommended (*9*). HB vaccine in combination with HBIG provides sustained protective levels of antibody and obviates the need for a second dose of HBIG in such exposures. Therefore, a normal series of HB vaccine, combined with a single dose (0.06 ml/kg or 5 ml for adults) of HBIG given at a different site, is recommended for postexposure prophylaxis of health workers following accidental percutaneous or mucous-membrane exposure to blood containing HBsAg, and of susceptible homosexual men following sexual exposure to an HBsAg-positive man. HBIG alone (in the same dose) is recommended for postexposure prophylaxis of persons with heterosexual exposures.

- **Vaccine side effects and adverse reactions**

In vaccine trials, soreness at the site of injection was the only side effect that occurred more frequently for vaccinees than for controls. Since its licensure in 1981 through August 1983, HB vaccine is estimated to have been administered to over 350,000 individuals in the United States. As of May 1984, adverse events following immunization had been reported for 890 vaccinees. The reported adverse events represent temporal associations with vaccination and are not necessarily caused by the vaccine. Forty-eight persons had serious events such as transverse myelitis, grand mal seizures, aseptic meningitis, erythema multiforme, or Guillain-Barré syndrome (GBS).

- **Vaccine precautions and contraindications**

Pregnancy should not be considered a contraindication to vaccinating women who are otherwise candidates for receiving HB vaccine. While data are not available on the safety of the vaccine for the developing fetus, HB vaccine contains only noninfectious HBsAg particles and should pose no risk to the fetus. In contrast, HBV infection in a pregnant woman may result in a severe disease for the mother and chronic infection for the newborn.

Since HB vaccine is made from human plasma, the possibility that it may contain an etiologic agent of acquired immunodeficiency syndrome (AIDS) has been raised. The purification and inactivation process used in preparing HB vaccine inactivates representatives of all known groups of viruses. There are no microbiologic, epidemiologic, or empiric data to suggest that the HB vaccine carries any etiologic risk for AIDS.

Influenza

Influenza viruses have continually demonstrated the ability to cause major epidemics of respiratory disease. High attack rates of acute illness and the frequent occurrence of lower-respiratory-tract complications usually result in dramatic rises in visits to physicians' offices and hospital emergency rooms. Furthermore, influenza frequently infects individuals who, because of their age or underlying health status, are poorly able to cope with the disease and often require medical attention, including hospitalization. Such persons are considered to be medically at "high risk" in epidemics. In one recent study, for example, rates of hospitalization for adults with "high-risk" medical conditions increased during major epidemics by about two- to fivefold in different age groups, reaching a maximum rate of about 800 per 100,000 population.

Influenza epidemics cause excess mortality, which is attributable not only to influenza pneumonia, but also to cardiopulmonary disease. Fifteen times in the years 1957-1982, epidemics have been associated with 10,000 or more excess deaths; in 1983, excess mortality again exceeded the epidemic threshold.

The greatest impact of influenza is normally seen when new strains appear against which most of the population lacks immunity. In these circumstances (e.g., 1957 and 1968), pandemics occur. During pandemics, a quarter or more of the United States population have been affected over a period of 2-3 months.

Because the proportion of elderly persons in the United States is increasing, and because age and its associated chronic diseases are risk factors for severe influenza illness, the toll of influenza may also increase unless control measures are used more vigorously than in the past.

- **Influenza vaccine**

Influenza A viruses are classified into subtypes on the basis of two antigens: hemagglutinin (H) and neuraminidase (N). Three subtypes of hemagglutinin (H1, H2, H3) and two subtypes of neuraminidases (N1, N2) are recognized among influenza A viruses that have caused widespread human disease. Immunity to these antigens, especially hemagglutinin, reduces the

likelihood of infection and the severity of disease if a person does become infected. However, there may be sufficient antigenic variation (antigenic drift) within the same subtype over time, so that infection or vaccination with one strain may not induce immunity to distantly related strains of the same subtype. Although influenza B viruses have shown much more antigenic stability than influenza A viruses, antigenic variation does occur. As a consequence, the antigenic characteristics of current strains provide the basis for selecting virus strains to be included in the vaccine for a given year.

Potency of present vaccines is such that nearly all vaccinated young adults develop hemagglutination-inhibition antibody titers that are likely to protect them against infection by strains like those in the vaccine, and often by related variants that emerge. The elderly, the very young, and patients with certain chronic diseases may develop lower postvaccination antibody titers than do young adults. Under these circumstances, influenza vaccine may be more effective in preventing lower-respiratory-tract involvement, or other complications of influenza, than in preventing upper-respiratory-tract involvement. Influenza vaccine will not prevent primary illnesses caused by other respiratory pathogens.

- **Vaccine indications**

Use of inactivated influenza vaccine is the single most important measure in the prevention and/or attenuation of influenza infection. Since 1963, annual vaccination against influenza has been recommended for individuals at high risk of lower-respiratory-tract complications and death following influenza infection (i.e., the elderly and persons with chronic disorders of the cardiovascular, pulmonary, and/or renal systems; metabolic diseases; severe anemia; and/or compromised immune function). These groups have been identified primarily by review of death certificate data, supported by hospital-based or population-based studies. Within each broadly defined "high-risk" category, however, some persons are more likely than others to suffer severe complications from influenza infection.

Among nursing-home residents, chronic diseases and other debilitating conditions are common, and spread of influenza can often be explosive, with attack rates as high as 60% and case-fatality ratios up to 30% or higher. In addition, recent retrospective studies of noninstitutionalized patients suggest that chronic underlying diseases, particularly those that affect the cardiovascular and pulmonary systems, may contribute more to the severity of illness than does age alone.

Medical personnel may transmit influenza infections to their high-risk patients while they are themselves incubating an infection, undergoing a subclinical infection, or working while they have mild symptoms. Nosocomial outbreaks of influenza are reported. The potential for introducing influenza to a high-risk group such as patients with severely compromised cardiopulmonary or immune systems or infants in neonatal intensive care units should be reduced by targeted vaccination programs of medical personnel.

Based on these observations, the previous, broadly defined "high-risk" adult groups have been further assigned priority for receiving vaccine in order that special efforts can be directed at providing vaccine to those who may derive the greatest benefit.

1. Adults at high risk of severe influenza illness who most warrant active, targeted vaccination efforts:
   (a) Adults with chronic disorders of the cardiovascular or pulmonary systems that are severe enough to require regular medical follow-up or to have caused hospitalization during the preceding year.
   (b) Residents of nursing homes and other chronic-care facilities (e.g., institutions housing patients of any age with chronic medical conditions). Achievement of high vaccination rates (e.g., 80%) may induce herd immunity in such populations and thereby

lower the frequency of outbreaks, as well as reducing the frequency of severe illness when outbreaks do occur.

2. Physicians, nurses, and other personnel who have extensive contact with high-risk patients (e.g., primary-care and certain specialty clinicians and staff of intensive-care units). These persons should receive influenza vaccination annually to reduce the possibility for nosocomial spread of influenza to high-risk patients.
3. Other adults who are at moderately increased risk of serious illness compared with the general population. Special programs to make vaccine readily available to these groups should also be given high priority:
   (a) Healthy individuals over 65 years of age.
   (b) Adults with a chronic metabolic disease (including diabetes mellitus), renal dysfunction (including those in chronic dialysis), anemia, immunosuppression, or asthma that is severe enough to require regular medical follow-up or to have caused hospitalization during the preceding year.

In addition, influenza vaccine may be offered to persons who provide essential community service or to any adult who wishes to reduce the likelihood of an influenza infection.

Effective programs for giving influenza vaccine are needed in nursing homes and other chronic-care facilities, in physicians' offices, and in hospital settings. Residents of nursing homes and chronic-care facilities should receive routine annual vaccination. Other adult high-priority groups should receive influenza vaccine at the time of regular medical follow-ups in the fall, or should be notified to come in specifically to receive the vaccine. Patients with high-risk conditions who are hospitalized during the fall should be considered for influenza vaccine before discharge from the hospital.

There is considerable overlap in the target groups for influenza vaccination and those for pneumococcal polysaccharide vaccine. Pneumococcal polysacchraride vaccine and influenza vaccine can be given at the same time at different sites without an increase in side effects; however, it should be emphasized that whereas influenza vaccine is given annually, pneumococcal polysaccharide vaccine should be given only once to adults. Detailed immunization records should be provided to each patient to help ensure that additional doses of pneumococcal polysaccharide vaccine are not given.

Amantadine hydrochloride, an antiviral drug, can prevent influenza A or be used therapeutically to reduce symptoms of influenza A infections. It is *not* a substitute for vaccine. Specific circumstances in which amantadine prophylaxis is recommended are described in the ACIP recommendations on prevention and control of influenza.

- **Vaccine side effects and adverse reactions**

Vaccines used in recent years have generally been associated with only a few reactions. Fewer than one-third of vaccinees have been reported to develop local redness or induration for 1 or 2 days at the site of injection.

Systemic reactions have been of two types. First, malaise, myalgia, and other systemic symptoms of toxicity, although infrequent, most often affect those who have had no experience with the influenza virus antigens contained in the vaccine. These reactions, which begin 6-12 hours after vaccination and persist for 1-2 days, are usually attributed to the influenza antigens (even though the virus is inactivated) and constitute most of the systemic side effects of influenza vaccination.

Second, immediate, presumably allergic, responses such as flare and wheal or various respiratory-tract symptoms of hypersensitivity occur extremely rarely after influenza vaccination. These symptoms probably result 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 vaccine can induce hypersensitivity reactions. Unlike the

1976 swine influenza vaccine, vaccines used subsequently have not been associated with an increased frequency of GBS.

- **Vaccine precautions and contraindications**

Pregnancy has not been demonstrated to be a risk factor for severe influenza infection except in the largest pandemics of 1918-1919 and 1957-1958. Influenza vaccine is considered to be generally safe for pregnant women. Nonetheless, when vaccine is to be given during pregnancy, waiting until the second or third trimester is a reasonable precaution to minimize any concern over theoretical teratogenicity.

Persons with a history of any signs or symptoms of an anaphylactic reaction (i.e., hives, swelling of the mouth and throat, difficulty in breathing, hypotension, or shock) after eating eggs should not be given inactivated influenza vaccine.

Persons with acute febrile illnesses normally should not be vaccinated until their temporary symptoms have abated.

Rabies

Although rabies rarely affects humans in the United States, thousands of persons receive rabies vaccine every year, principally for postexposure prophylaxis. The likelihood of human exposure to rabies from domestic animals has decreased greatly in recent years. In every year since 1976, more than 85% of all reported cases of animal rabies have been among wild animals, the most important source of possible infection for humans in the United States. However, for persons traveling overseas to developing countries with endemic rabies, the dog remains the animal most likely to transmit rabies.

- **Rabies vaccine**

Both whole-virion and subvirion human diploid cell rabies vaccines (HDCV) are available. For preexposure rabies prophylaxis a three-dose series of HDCV of either type given as 1-ml doses IM on days 0, 7, and 28 provides adequate antibody levels in virtually all recipients (*10*). The CDC currently accepts a titer of 5 by the rapid fluorescent-focus inhibition test as adequate.

The whole-virion HDCV produced by the Merieux Institute has been used for preexposure immunization in a regimen of three 0.1-ml doses given intradermally (ID) in the lateral aspect of the upper arm in the deltoid area, one dose on each of days 0, 7, and 28. Experience gained with over 2,000 persons vaccinated in the United States by the ID route has shown that antibody is produced in all recipients, although the mean response is somewhat lower and may be of shorter duration than with comparable IM immunization. Except for persons suspected of being immunosuppressed, postvaccination serology is not necessary following IM or ID immunization in the United States. Antibody response in some groups vaccinated ID outside the United States has been found to be inadequate for reasons not yet determined (*11*). Preliminary data suggest that concurrent administration of malaria chemoprophylaxis may be a factor in the lowered immunologic response of persons vaccinated overseas. It should be noted that Merieux Institute, the manufacturer, has not yet met the packaging and labeling requirements necessary to obtain approval by the FDA for the ID route of administration. The 1-ml vial presently available is intended for IM use and contains no preservatives. To minimize the risk of contamination and loss of vaccine potency, the reconstituted vaccine must be used immediately. Data on ID immunization are not available for Wyeth Laboratories vaccine.

Proper postexposure rabies prophylaxis is determined by whether or not the person has had previous preexposure or postexposure prophylaxis. 1) Persons who (a) have previously received postexposure prophylaxis with HDCV, (b) have received a three-dose IM preexposure regimen of HDCV, (c) have received a three-dose ID preexposure regimen of HDCV in the

United States, or (d) have a previously documented adequate rabies titer should receive two 1-ml IM doses of HDCV—one dose on each of days 0 and 3. HRIG is not recommended in these circumstances. 2) Persons not meeting the above criteria should be treated with a single, 20-international units (IU)/kg dose of HRIG and five 1-ml doses IM of HDCV—one on each of days 0, 3, 7, 14, and 28. HRIG should be administered at the beginning of HDCV postexposure prophylaxis but can be given up to the eighth day after the first dose of HDCV was given. The HRIG dose should be divided; up to half should be infiltrated into the area of the wound, if possible, and the rest administered IM, but not in the same site as HDCV. *Only* IM administration of HDCV is indicated for postexposure prophylaxis.

- **Vaccine indications**

Preexposure immunization should be considered for high-risk groups: animal handlers, certain laboratory workers and field personnel, and persons planning to be in countries or areas of countries for more than 1 month where rabies is a constant threat. Persons whose vocations or avocations bring them into contact with potentially rabid animals should also be considered for preexposure immunization. Persons with continuing risk of exposure should receive a booster dose every 2 years or have their serum tested for rabies antibody every 2 years and, if the titer is inadequate, be given a booster dose. If there is substantial risk of exposure to rabies, preexposure rabies prophylaxis may be indicated during pregnancy.

The decision to provide specific postexposure antirabies treatment should include the following considerations:

1. Type of exposure—rabies is transmitted primarily by the bite of infected animals. It may also be transmitted by introducing the virus into open cuts or wounds in skin or via mucous membranes by saliva or other potentially infectious material from a rabid animal and, rarely, by aerosol exposure.
2. Species of biting animal—carnivorous wild animals (especially skunks, raccoons, and foxes) and bats are most commonly infected with rabies in the United States. Elsewhere in the world, dogs, cats, carnivorous wildlife, and bats are the major vectors. The likelihood that domestic cats or dogs in the United States will be infected varies from region to region. Rodents are rarely infected. Consultations with the state or local health department may be helpful.
3. Circumstances of biting incident—an unprovoked attack is more indicative of a rabid animal than a provoked attack.

- **Vaccine side effects and adverse reactions**

Following postexposure prophylaxis, local reactions, such as pain, erythema, and swelling or itching at the injection site, are very common, and mild systemic reactions, such as headache, nausea, abdominal pain, muscle aches, and dizziness, are reported by about 20% of recipients. Systemic allergic reactions ranging from hives to anaphylaxis occur in an estimated 11 per 10,000 vaccinees. Mild immune-complex-like hypersensitivity reactions consisting of hives, itching, and angio-edema have occurred 2-21 days after booster doses of HDCV and are the most frequently reported allergic reactions (*12*). Four cases of transient neuroparalytic illness have been temporally associated with HDCV administration: two following administration of whole-virion vaccine and two following administration of subvirion vaccine (*13*). No permanent sequelae or deaths have been associated with administration of HDCV.

- **Vaccine precautions and contraindications**

Corticosteroids and other immunosuppressive agents can interfere with the development of active immunity and should not be administered during preexposure therapy. When rabies postexposure prophylaxis is administered to persons known or suspected of being immunosuppressed, or to those who are receiving steroids or immunosuppressive therapy, it is especially important that serum be tested to ensure an adequate rabies antibody response.

If a person experiences an anaphylactic reaction (i.e., hives, swelling of the mouth and throat, difficulty in breathing, hypotension, or shock) after receiving HDCV, no further preexposure doses of HDCV should be given. By contrast, if a person needing postexposure therapy has had a previous anaphylactic reaction to HDCV or has such a reaction during the postexposure course, HDCV therapy should continue; however, the person should receive the required doses in an appropriate medical setting.

Inactivated-Bacteria Vaccines

Cholera

Cholera continues to be a health risk in Africa and Asia. Countries currently reporting cholera are listed in the biweekly publication *Summary of Health Information for International Travel.* All state health departments and many county and city health departments receive this publication. Persons who follow the usual tourist itinerary and who use tourist accommodations in countries affected by cholera are at virtually no risk of infection. The traveler's best protection against cholera is avoiding food and water that might be contaminated.

- **Cholera vaccine**

The vaccine may be administered as a 0.5-ml dose SC or IM or as a 0.2-ml dose ID. Although a single dose of vaccine is sufficient for entry into most countries, some countries may require evidence of a complete primary series of two doses given 1 week to 1 month or more apart, or a booster dose within 6 months before arrival.

The currently available cholera vaccine has been shown in field trials to be only about 50% effective in preventing clinical illness for a period of 3-6 months. The vaccine does not prevent transmission of infection. The risk of cholera to most U.S. travelers is so low that it is doubtful that vaccination is of benefit. WHO no longer recommends cholera vaccination for travel to or from cholera-infected areas. However, some countries affected or threatened by cholera require evidence of cholera vaccination as a condition of entry. Current information on cholera-vaccination requirements of individual countries is published annually in *Health Information for International Travel.* All state health departments and many county and city health departments receive this publication. Travelers to countries with cholera-vaccination requirements should have an International Certificate of Vaccination filled in, dated, signed, and validated showing receipt of the vaccine 6 days to 6 months before entry into the country. Most city, county, and state health departments can validate certificates. Failure to secure validation may cause travelers to be revaccinated or quarantined.

- **Vaccine indications**

Cholera vaccine is indicated only for travelers to countries requiring evidence of cholera vaccination for entry. Boosters may be given every 6 months if required by a country.

- **Vaccine side effects and adverse reactions**

Vaccination often results in 1-2 days of pain, erythema, and induration at the site of injection. The local reaction may be accompanied by fever, malaise, and headache. Serious reactions, including neurologic reactions, following cholera vaccination are extremely rare.

- **Vaccine precautions and contraindications**

No specific information is available on the safety of cholera vaccine during pregnancy. Because cholera disease during pregnancy is a serious illness, whether to use cholera vaccine should be determined in individual circumstances based on the actual risk of disease and the probable benefits of the vaccine.

The only contraindication to cholera vaccine is a history of a severe reaction following a previous dose. Most governments will permit an unvaccinated traveler to enter the country if

he or she carries a physician's statement of medical contraindication. However, some countries may quarantine such unvaccinated persons or place them under surveillance if they come from areas with cholera.

Some data have indicated that persons given yellow fever and cholera vaccines simultaneously or 1-3 weeks apart had lower-than-normal antibody responses to both vaccines. Unless there are time constraints, cholera and yellow fever vaccines should be administered at a minimal interval of 3 weeks. If the vaccines cannot be administered at least 3 weeks apart, then they should preferably be given simultaneously.

Meningococcal Disease

Meningococcal disease is endemic throughout the world but may also occur in epidemics. Among U.S. civilians, meningococcal disease occurs primarily as single, isolated cases or, infrequently, in small, localized clusters. A third of all cases of meningococcal disease occur in patients 20 years old or older. Serogroup B strains cause the majority of U.S. cases, with serogroups C and W135 strains accounting for most of the remainder.

- **Meningococcal polysaccharide vaccine**

Two meningococcal polysaccharide vaccines, bivalent A-C and quadrivalent A, C, Y, and W135 vaccines, are available for use in the United States. Each is given as a single dose, and each induces specific serogroup immunity. The duration of immunity conferred by the vaccines is not known.

- **Vaccine indications**

Vaccine may be of benefit as an adjunct to antibiotic chemoprophylaxis for household and other close contacts of persons with meningococcal disease caused by serogroups A, C, Y, and W135 and for travelers to areas with epidemic meningococcal disease. The need for booster doses has not been established.

Routine vaccination of U.S. civilians with meningococcal polysaccharide vaccine is *not* recommended because of the lack of availability of a group B vaccine and the low risk of infection in the United States.

- **Vaccine side effects and adverse reactions**

Adverse reactions to meningococcal polysaccharide vaccines are infrequent and mild, consisting principally of localized erythema lasting 1-2 days.

- **Vaccine precautions and contraindications**

The safety of meningococcal polysaccharide vaccines for pregnant women has not been established. On theoretical grounds, it is prudent not to use them unless there is a substantial risk of infection.

Plague

Plague is a natural infection of rodents and their fleas. In the United States a few human cases occur yearly in humans exposed in the Western states to infected animals, primarily rodents, and their fleas. Other countries currently reporting plague infections are noted in the biweekly publication *Summary of Health Information for International Travel.* All state health departments and many county and city health departments receive this publication. A number of countries in Africa, Asia, and South America continue to report sporadic, epidemic, and epizootic infection. In most of these countries, the risk of exposure exists primarily in rural or semirural areas.

- **Plague vaccine**

A primary series of plague vaccine consists of three IM doses. The first dose, 1 ml, is followed in 4 weeks by a second dose of 0.2 ml. The third dose, also 0.2 ml, is administered 5

months after the second. The effectiveness of a primary series of plague vaccine has never been measured precisely. Field experience indicates that vaccination with plague vaccine reduces the incidence and severity of disease resulting from the bite of infected fleas. The degree of protection offered against primary pneumonic infection is unknown. Since plague vaccination may only ameliorate illness, prophylactic antibiotics may be indicated whenever a person, vaccinated or not, has a definite exposure.

- **Vaccine indications**

Vaccination is indicated for certain vocational groups. These include all laboratory and field personnel working with *Yersinia pestis* organisms that may be resistant to antimicrobials, persons engaged in aerosol experiments with *Y. pestis*, and field personnel engaged in operations in areas with enzootic or epidemic plague where preventing exposure to rodents and fleas is impossible. Plague vaccination should be considered for laboratory personnel regularly working with *Y. pestis* or plague-infected rodents and for persons whose vocation regularly exposes them to wild rodents or rabbits in areas with enzootic plague.

Vaccine may also be considered for travelers to areas known to have endemic plague in countries reporting plague, particularly if travel will not be limited to urban areas with tourist-hotel accommodations.

For persons with continuing exposure, three booster doses, each 0.1-0.2 ml, should be given at approximately 6-month intervals. Thereafter, booster doses at 1- to 2-year intervals should provide good protection.

- **Vaccine side effects and adverse reactions**

For about 10% of recipients, primary vaccination may result in general malaise, headache, fever, mild lymphadenopathy, and/or erythema and induration at the injection site. These reactions occur more commonly with repeated injections. Sterile abscesses occur rarely. Sensitivity reactions manifested by urticarial and asthmatic phenomena have occasionally been reported.

- **Vaccine precautions and contraindications**

Neither the safety nor efficacy of vaccination with plague vaccine during pregnancy has been determined; therefore, it should not be used unless there is a substantial risk of infection.

Plague vaccine should not be administered to anyone with a known hypersensitivity to any of its constituents (beef protein, soy, casein, and phenol). Patients who have had severe local or systemic reactions to plague vaccine should not be revaccinated.

Pneumococcal Disease

Precise data on the occurrence of serious pneumococcal disease in the United States are not available: however, the annual incidence rate of pneumococcal pneumonia is estimated to be 68 cases to 260 cases per 100,000 population, and of bacteremia, 7-25/100,000. The incidence of pneumococcal pneumonia, which causes a substantial number of deaths annually, increases in those over 40 years old, and shows a twofold increase in those over 60 years of age. Mortality from pneumococcal disease is highest among patients who have bacteremia or meningitis, patients with underlying medical conditions, and older persons.

Patients with certain underlying conditions are clearly at increased risk both of contracting pneumococcal infection and of experiencing more severe pneumococcal illness. These conditions include sickle cell anemia, multiple myeloma, cirrhosis, alcoholism, nephrotic syndrome, renal failure, splenic dysfunction, anatomic asplenia, and organ transplant. Persons suffering from diabetes mellitus, chronic pulmonary disease, cardiovascular disease, or conditions associated with immunosuppression may be at increased risk of contracting pneumococcal infection or of having more severe illness.

- **Pneumococcal polysaccharide vaccine**

The pneumococcal polysaccharide vaccine currently available contains purified capsular materials of the 23 types of *Streptococcus pneumoniae* responsible for 87% of recent bacteremic pneumococcal disease in the United States. Most healthy adults show a twofold rise in type-specific antibody 2-3 weeks after administration of a single dose of vaccine. The titer of antibody that is protective against each serotype has not been determined.

The duration of vaccine-induced immunity is unknown. Studies of persistence of vaccine-induced antibody show elevated titers 3-5 years after immunization. Booster doses are not recommended because of increased adverse reactions to subsequent doses.

Patients who have received the earlier pneumococcal polysaccharide vaccine containing capsular material from only 14 types of *S. pneumoniae* should not receive a dose of the 23-valent pneumococcal polysaccharide vaccine since the modest increase in coverage does not warrant the increased risk of adverse reactions.

- **Vaccine indications**

Newly available data regarding vaccine efficacy support the broader use of pneumococcal polysaccharide vaccine in the United States. Vaccination is particularly recommended for the following:

1) Adults with chronic illnesses, especially those with cardiovascular disease and chronic pulmonary disease, who sustain increased morbidity with respiratory infections.
2) Adults with chronic illnesses specifically associated with an increased risk of pneumococcal disease or its complications. These include splenic dysfunction or anatomic asplenia, Hodgkins' disease, multiple myeloma, cirrhosis, alcoholism, renal failure (including those on chronic dialysis), cerebrospinal-fluid leaks, and conditions associated with immunosuppression.
3) Older adults, especially those age 65 and over, who are healthy.

Programs for vaccine delivery in the recommended high-risk groups need to be developed further. Specifically, more effective programs are needed for giving vaccine in physicians' offices, in hospitals, and in nursing homes and other chronic-care facilities.

Since two-thirds of persons with serious pneumococcal disease have been hospitalized within 5 years before the pneumococcal illness (*14*), vaccine should be given to hospitalized patients in the high-risk groups before discharge, in order to prevent future admissions for pneumococcal disease. In addition, persons with chronic conditions who visit physicians frequently are probably at higher risk of pneumococcal infection than those who require infrequent visits. Office-based programs to identify and immunize patients requiring frequent medical care should help prevent pneumococcal illness. Furthermore, pneumococcal polysaccharide vaccine and influenza vaccine can be given at different sites at the same time without an increase in side effects (*15*).

Medicare has partially reimbursed the cost of pneumococcal polysaccharide vaccination since 1981. It has been determined that hospitals may be reimbursed for pneumococcal immunization of Medicare recipients independent of reimbursement based on systems of prospective payments.

- **Vaccine side effects and adverse reactions**

About half of the persons given pneumococcal polysaccharide vaccine experience mild side effects such as erythema and pain at the site of injection. Fever and myalgias have been reported by fewer than 1% of those given pneumococcal polysaccharide vaccine (*16*). Severe adverse effects such as anaphylactic reactions have rarely been reported—about five cases per million doses administered.

Arthus reactions and systemic reactions have been common among adults given second

doses (*17*). They are thought to result from localized antigen-antibody reactions involving antibody induced by previous vaccination. Therefore, second, or "booster," doses are *not* recommended.

- **Vaccine precautions and contraindications**

The safety of pneumococcal polysaccharide vaccine in pregnant women has not been evaluated. It should not be given to healthy pregnant women. Women at high risk of pneumococcal disease ideally should be vaccinated before pregnancy.

Because of a marked increase in adverse reactions with second injections of pneumococcal polysaccharide vaccine, second, or "booster," doses should not be given. However, when there is doubt or no information on whether a person in one of the high-risk groups has ever received pneumococcal polysaccharide vaccine, vaccine should be given. Complete records of vaccination can help to avoid repeat doses.

Typhoid

The occurrence of typhoid fever remained constant in the period 1972-1982, with an average of 486 cases reported annually. During the years 1978-1982, 57% of cases for which the patient's age was known occurred in patients 20 years of age or older. Approximately 62% of typhoid cases reported in the United States during 1977-1979 were acquired by travelers to other countries, and an additional 27% occurred in contacts of typhoid carriers.

- **Typhoid vaccine**

A primary series of two 0.5-ml doses of typhoid vaccine given SC 4 weeks apart has been shown to protect 70%-90% of recipients.

- **Vaccine indications**

Immunization is indicated for travelers to areas where a recognized risk of exposure to typhoid exists. It should be emphasized that even after typhoid vaccination, food and water should be selected carefully in these areas. Typhoid vaccination is not recommended in the United States or in areas of natural disaster. Booster doses should be given at least every 3 years to persons with continued or repeated exposure; these may be given SC (0.5 ml) or ID (0.1 ml). The acetone-killed and -dried vaccine should not be given ID. This preparation is available only to the U.S. Armed Forces.

- **Vaccine side effects and adverse reactions**

Typhoid vaccination often results in 1-2 days of discomfort at the site of injection. The local reaction may be accompanied by fever, malaise, and headache.

- **Vaccine precautions and contraindications**

The only contraindication to typhoid vaccine is a history of a severe local or systemic reaction following a previous dose.

Live-Bacteria Vaccines

Tuberculosis

The number of tuberculosis cases in the United States has declined steadily since reporting began in the 19th century. Between 1972 and 1982, the annual incidence of tuberculosis declined from 15.8 cases per 100,000 population to 11.0/100,000, a decrease of 30%. In 1982, approximately 92% of 25,059 reported cases with patient ages known occurred in persons 20 years of age or older. Reported cases usually are typical postprimary pulmonary disease. The risk of infection is greatest for those who have repeated exposure to persons with unrecognized or untreated sputum-positive pulmonary tuberculosis. In the United States, efforts to control tuberculosis are directed toward early identification and treatment of cases,

preventive therapy with isoniazid for infected persons at high risk of developing disease, and prevention of transmission to others.

- **BCG vaccine**

Although BCG vaccine is widely used in many areas of the world, results of a recent large-scale field trial in India have raised questions about its efficacy (*18*). BCG vaccines currently available in the United States differ from the products used in the published field trials, and their efficacy has not been demonstrated directly. In the United States, vaccines for ID and for percutaneous administration are licensed. (For percutaneous administration, one drop of vaccine is placed on the skin and introduced through the skin by multiple punctures with a bifurcated or other needle.) Vaccination should be only by the route indicated on the package labeling.

- **Vaccine indications**

In the United States the only situations in which BCG might be considered are 1) for individuals in prolonged close contact with patients with active tuberculosis that is untreated, ineffectually treated, or resistant to treatment; 2) for health-worker groups, such as hospital staffs, with an annual new-infection rate of 1% or higher in spite of other tuberculosis control measures; and 3) for other groups in which an excessive rate of new infection can be demonstrated and the usual surveillance and treatment programs have failed or are not feasible.

- **Vaccine side effects and adverse reactions**

BCG has been associated with severe or prolonged ulceration at the vaccination site, regional adenitis, disseminated BCG infection, and osteitis. Severe ulceration and adenitis occur in approximately 1%-10% of vaccinees, and disseminated infections and osteitis are quite rare (1-10 per million doses).

- **Vaccine precautions and contraindications**

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

Since BCG is a live-bacteria vaccine, it should not be given to persons immunocompromised as a result of immune deficiency diseases, leukemia, lymphoma, or generalized malignancy or to persons immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. (See "Conditions That Compromise the Immune System," page 8S.)

Other Licensed Vaccines

Adenovirus and Adenovirus Vaccine

Adenovirus types 4 and 7 have frequently been the cause of outbreaks of acute, febrile, respiratory-tract disease in young adults during military training. Live, oral adenovirus vaccines for types 4 and 7 are available for immunization of military populations. Use of the vaccines in other populations is not recommended.

Anthrax and Anthrax Vaccine

Anthrax is infrequently encountered. Anthrax vaccine is recommended only for individuals who come in contact with imported animal hides, furs, bonemeal, wool, animal hair (especially goat hair), and bristles in the workplace and for individuals undertaking investigational studies involving *Bacillus anthracis*.

Primary immunization consists of six SC 0.5-ml injections, the first three at 2-week intervals and the other three at 6-month intervals. Booster doses of 0.5-ml SC are recommended at 1-year intervals. The vaccine is only available from the Biologic Products Program, Michi-

gan Department of Public Health. Details on reactions and vaccine contraindications are found in the package insert.

Pertussis and Pertussis Vaccine

Pertussis disease in adults is generally milder than in children and is not known to result in death. Pertussis can be transmitted from adult patients to close contacts, especially unimmunized children. Such transmission may occur in the household and in hospitals, where chains of transmission have involved patients and staff.

In general, pertussis vaccine is not recommended for adults because both local and systemic reactions are thought to be more frequent and severe than in children under 7 years of age and because the disease itself is less severe in adults. In specific situations, such as documented transmission to and from personnel in a hospital, single-antigen pertussis vaccine in a 0.2-ml IM dose has been given as a part of control efforts. Single-antigen pertussis vaccine, adsorbed, is available only from the Biologic Products Program, Michigan Department of Public Health.

Immune Globulins

IG and specific immune globulins, i.e., HBIG, TIG, HRIG, and varicella zoster immune globulin (VZIG), are indicated for use in order to prevent or modify certain diseases in specific circumstances.

Immune Globulin for Intramuscular Use

IG is given IM for preexposure prophylaxis against hepatitis A to travelers in areas where contact with potentially contaminated food and water is unavoidable. For travelers at risk for 2-3 months, a single IM dose of 0.02 ml/kg is recommended. For more prolonged travel 0.06 ml/kg should be given every 5 months. IG is also indicated for postexposure prophylaxis for close household and sexual contacts of persons with hepatitis A, staff and attendees of day-care centers and household contacts of diapered children in day-care centers in which hepatitis A transmission is occurring, selected staff and clients of custodial institutions in which an outbreak is occurring, and co-workers of food handlers with hepatitis A. For such contacts a single dose of 0.02 ml/kg of IG is recommended as soon as possible after exposure. IG should be given within 2 weeks after exposure.

IG can be used to prevent or modify measles disease in susceptible contacts of persons with measles, especially those for whom measles vaccine is contraindicated, if given within 6 days after exposure. The recommended dose is 0.25 ml/kg (maximum dose = 15 ml). IG should not be used to control measles outbreaks.

Immune Globulin for Intravenous Use

IG modified for IV administration may be given to prevent acute infections in patients with defective antibody synthesis or as prophylaxis against hepatitis A for patients for whom the IM preparation is contraindicated because of thrombocytopenia or disorders that can cause IM hemorrhage. ONLY IG MODIFIED FOR INTRAVENOUS USE CAN BE GIVEN INTRAVENOUSLY. The IV dose is 100 mg/kg, given slowly. The IV preparation is supplied in 50-ml vials containing 2.5 g of IG.

Hepatitis B Immune Globulin

HBIG, alone or in combination with HB vaccine, is used for postexposure prophylaxis of HBV infection. For percutaneous or mucous membrane exposure to blood known to be HBsAg

positive or from a bite by an HBV carrier, a single dose of HBIG (0.06 ml/kg or 5 ml for adults) should be given as soon as possible, and a series of three doses of HB vaccine begun within 1 week after exposure. Vaccine and HBIG may be given simultaneously, but in different sites. For those who choose not to take HB vaccine, a second identical dose of HBIG should be given 1 month later.

Following percutaneous exposure to blood from individuals at high risk of being HBsAg positive (such as persons with acute, unconfirmed viral hepatitis) or from patients at high risk of being infected with hepatitis B (such as male homosexuals, users of illicit IV drugs, and hemodialysis patients), IG should be given immediately to the exposed person as an IM dose of 0.06 ml/kg. Then serologic confirmation of the HBsAg status of the suspected high-risk patient should be obtained as soon as possible, and certainly within 7 days. If the suspected high-risk patient is HBsAg positive, the exposed person should immediately receive HBIG and hepatitis B vaccine according to the schedule above. The value of HBIG given beyond 7 days after exposure is unclear.

For homosexual exposure to HBsAg-positive males (known carriers or persons with acute cases), a single dose of HBIG should be given to susceptible contacts within 14 days after the last sexual exposure. Since HB vaccine is routinely recommended for male homosexuals, an HB vaccine series should be started within 7 days after HBIG administration.

For heterosexual exposures to persons with acute cases of hepatitis B, a single dose of HBIG (0.06 ml/kg or 5 ml for adults) should be given within 14 days of the last sexual contact. If the index case remains HBsAg positive at 3 months and exposure continues, the contact should be given a second dose of HBIG. If the index case becomes an HBV carrier (HGsAg positive for 6 months), the HB vaccine series should be given to the contact.

Tetanus Immune Globulin

TIG is indicated in tetanus prophylaxis as part of the management of wounds other than clean, minor wounds in persons 1) whose previous tetanus toxoid immunization status is unknown or uncertain, 2) who have received fewer than two previous tetanus toxoid doses, or 3) who have received only two previous tetanus toxoid doses and whose wound is more than 24 hours old. The currently recommended prophylactic dose for wounds of average severity is 250 units IM. Td should be given at the same time but at a separate site.

A summary of the indications for active and passive immunization in the management of wounds is provided in Table 5.

Human Rabies Immune Globulin

Postexposure prophylaxis for rabies should always include HRIG with one exception: persons who have been previously immunized with the recommended preexposure or postexposure regimens of HDCV or have been immunized with other types of rabies vaccines and have a history of documented adequate rabies antibody titer should not receive HRIG (Table 4). The recommended dose of HRIG is 20 IU/kg body weight. If anatomically feasible, up to one-half the dose of HRIG should be thoroughly infiltrated in the area around the wound, the rest should be administered IM.

Varicella-Zoster Immune Globulin

Most adults (85%-95%) with negative or unknown histories of varicella disease (chickenpox) are likely to be immune. (Susceptibility rates for adults raised in some tropical areas, particularly remote areas, may be somewhat higher.) Rates of complications and death for immunocompromised adults who contract varicella are likely to be substantially greater than for

normal adults. After careful, individual evaluation, an immunocompromised patient who is believed to be susceptible and who has had significant exposure to varicella should receive VZIG to prevent complications.

Significant exposure to a person with varicella includes household contact, close contact indoors of longer than 1 hour, sharing the same two- to four-bed hospital room, or prolonged, direct, face-to-face contact such as occurs with nurses or doctors who take care of the patient.

Chickenpox can be more severe in adults than in normal children. The decision to administer VZIG to a normal adult should be made on an individual basis. The objective of VZIG use for normal adults is to modify rather than prevent illness in hopes of inducing lifelong immunity. When deciding whether to administer VZIG, the clinician should consider the patient's health status, the type of exposure, and the likelihood of previous infection. It is likely that adults who were older siblings in large families or whose children have had varicella are immune. If, after careful evaluation, a normal adult with significant exposure to varicella is believed to be susceptible, VZIG may be administered. Pregnant women and potentially susceptible hospital personnel should be evaluated in the same way as other adults. Supplies of VZIG are limited, and indiscriminate administration of VZIG to normal adults would quickly exhaust supplies and prevent prophylaxis for known high-risk individuals. The cost of a five-vial adult dose is approximately $375.

VZIG, available through some American Red Cross distribution centers (Appendix 5), is supplied in vials containing 125 units. Whereas 125 units/10 kg of body weight up to a maximum of 625 units generally is considered likely to prevent or modify varicella in normal adults, higher doses may be necessary for the immunocompromised adult. However, the appropriate dose for immunocompromised adults has not been determined. VZIG should be administered IM as directed by the manufacturer. While the duration of protection is unknown, it seems reasonable that protection should last for at least one half-life of the immune globulin, that is, approximately 3 weeks.

Immune Globulin Side Effects and Adverse Reactions

Serious adverse effects have been rare from immune globulins administered as recommended.

Immune Globulin Precautions and Contraindications

Immune globulins, if needed, are not contraindicated for pregnant women. Except for the IV preparation of IG, immune globulins are prepared for IM use and should *not* be given IV. The various preparations intended for IM use should not be given to patients with severe thrombocytopenia or other coagulation disorders that would ordinarily contraindicate IM injections unless the expected benefits outweigh the risks.

Parenterally administered live-virus vaccines (e.g., MMR or other combinations) should be given at least 14 days before or at least 6 weeks, and preferably 3 months, after the administration of immune globulins. If an immune globulin must be administered within 14 days after the administration of most live-virus vaccines, the vaccine should be administered again 3 months after the immune globulin is given. If the interval between vaccine receipt and immune globulin receipt is longer, the vaccine need not be readministered.

Preliminary data indicate that immune globulins do not interfere with the immune response to either OPV or yellow fever vaccine.

In July 1983, a WHO Consultative Group reviewed data on both normal and specific immune globulins prepared from plasma collected mainly in the United States, including dona-

tions from homosexuals. The data indicated that although about 19.5 million 2-ml to 10-ml doses of immune globulin had been prepared during the preceding 4 years, no transmission of hepatitis B or any other infectious agents and no cases of AIDS had been reported in persons observed for 1-4 years after receiving immune globulin. Therefore, the Consultative Group confirmed that, at present, there is no evidence of risk attached to the use of normal or specific immune globulins prepared by the universally accepted methods (*19*).

References

1. Immunization Practices Advisory Committee, General recommendations on immunizations. MMWR 1983;32:1-8, 13-7.
2. CDC. Rubella in hospitals—California. MMWR 1983;32:37-9.
3. Amler RW, Bloch AB, Orenstein WA, Bart KJ, Turner PM Jr, Hinman AR. Imported measles in the United States. JAMA 1982;248:2129-33.
4. Weiss BP, Strassburg MA, Feeley JC. Tetanus and diphtheria immunity in an elderly population in Los Angeles County, Am J Pub Health 1983;73:802-4.
5. Crossley K, Irvine P, Warren JB, Lee BK, Mead K. Tetanus and diphtheria immunity in urban Minnesota adults. JAMA 1979;242:2298-3000.
6. Ruben FL, Nagel J, Fireman P. Antitoxin responses in the elderly to tetanus-diphtheria (Td) immunization. Am J Epidemiol 1978;108:145-9.
7. Jacobs RL, Lowe RS, Lanier BQ. Adverse reactions to tetanus toxoid. JAMA 1982;247:40-2.
8. Herman JJ, Radin R, Schneiderman R. Allergic reactions to measles (rubeola) vaccine in patients hypersensitive to egg protein. J Pediatr 1983;102:196-9.
9. CDC. Postexposure prophylaxis of hepatitis B. MMWR 1984;33:285-90.
10. Turner GS, Nicholson KG, Tyrrell DAJ, Akoi FY. Evaluation of a human diploid cell strain rabies vaccine: final report of a three year study of pre-exposure immunization. J Hyg 1982;89:101-10.
11. CDC. Field evaluations of pre-exposure use of human diploid cell rabies vaccine. MMWR 1983;32:601-3.
12. CDC. Systemic allergic reactions following immunization with human diploid cell rabies vaccine. MMWR 1984;33:185-7.
13. Bernard KW, Smith PW, Kader FJ, Moran MJ. Neuroparalytic illness and human diploid cell rabies vaccine. JAMA 1982;248:3136-8
14. Fedson DS, Chiarello LA. Previous hospital care and pneumococcal bacteremia: importance for pneumococcal immunization. Arch Intern Med 1983;143:885-9.
15. DeStefano F, Goodman RA, Noble GR, et al. Simultaneous administration of influenza and pneumococcal vaccines. JAMA 1982;247:2551-4.
16. Semel JD, Seskind C. Severe febrile reaction to pneumococcal vaccine. JAMA 1979;241:1792.
17. Borgono JM, McLean AA, Vella PP, Woodhour AF, et al. Vaccination and revaccination with polyvalent pneumococcal polysaccharide vaccines in adults and infants (40010). Proc Soc Exp Biol Med 1978;157:148-54.
18. Clemens JD, Chuong JJH, Feinstein AR. The BCG controversy: a methodological and statistical reappraisal. JAMA 1983;249:2362-9.
19. World Health Organization. Viral hepatitis: the use of normal and specific immunoglobulin. Weekly Epidemiological Record 1983;58(31):237.

TABLE 1. Vaccines and toxoids recommended for adults in general, by age groups

	Vaccine or toxoid					
Age group	Td*	Measles	Mumps	Rubella	Influenza	Pneumococcal polysaccharide
18-24 years	X	X	X§	X		
25-64 years	X	X†	X§	X¶		
≥65 years	X				X	X

NOTE: Refer to text on specific vaccines or toxoids for indications, contraindications, precautions, dosages, side effects and adverse reactions, and special considerations.

*Diphtheria and tetanus toxoids adsorbed (for adult use), Td, a combined preparation containing less than 2 Lf of diphtheria toxoid.

†Indicated for persons born after 1956.

§Indicated especially for susceptible males.

¶Principally recommended for females up to 45 years of age.

TABLE 2. Immunobiologics recommended for special occupations, lifestyles, environmental circumstances, travel, foreign students, immigrants, and refugees*

Indication	Immunobiologic(s)
Occupation	
Hospital, laboratory, and other health care personnel	Hepatitis B Polio Influenza
Staff of institutions for the mentally retarded	Hepatitis B
Veterinarians and animal handlers	Rabies
Selected field workers	Plague
Lifestyles	
Homosexual males	Hepatitis B
Illicit drug users	Hepatitis B
Environmental situation	
Inmates of long-term correctional facilities	Hepatitis B
Residents of institutions for the mentally retarded	Hepatitis B
Travel	Measles Rubella Polio Yellow fever Hepatitis B Rabies Meningococcal polysaccharide Typhoid Cholera Plague Immune globulin
Foreign students, immigrants, and refugees	Measles Rubella Diphtheria Tetanus

NOTE: Refer to text on specific vaccines or toxoids for use by specific risk groups, details on indications, contraindications, precautions, dosages, side effects and adverse reactions, and special considerations.

*Unless specifically contraindicated, the vaccine or toxoids generally recommended for adults are also indicated. Table 1 shows vaccines and toxoids appropriate for age for most adults.

TABLE 3. Vaccines and toxoids indicated or specifically contraindicated for special health status situations*

Health situations	Vaccines or toxoids	
	Indicated	**Contraindicated**
Pregnancy	Diphtheria and tetanus toxoids (Td)	Live-virus vaccines
Immunocompromised	Influenza Pneumococcal polysaccharide	Live-virus vaccines
Splenic dysfunction, anatomic asplenia	Influenza Pneumococcal polysaccharide	
Hemodialysis	Hepatitis B (double dose) Influenza Pneumococcal polysaccharide	
Deficiencies of factors VIII or IX	Hepatitis B	
Chronic alcoholism	Pneumococcal polysaccharide	
Diabetes and other high-risk diseases	Influenza Pneumococcal polysaccharide	

NOTE: Refer to text on specific vaccines or toxoids for details on indications, contraindications, precautions, dosages, side effects and adverse reactions, and special considerations.

*Unless specifically contraindicated, the vaccines and toxoids generally recommended for adults are also indicated. Table 1 shows vaccines and toxoids appropriate for age for most adults.

TABLE 4. Immunobiologics and schedules for adults (18 years of age and older)*†

Immunobiologic generic name	Primary schedule and booster(s)	Indications	Major precautions and contraindications§	Special considerations
TOXOIDS				
Tetanus-diphtheria toxoid (Td)	2 doses intramuscularly (IM) 4 weeks apart; 3rd dose 6-12 months after 2nd dose; booster every 10 years	All adults	Except in the first trimester, pregnancy is not a contraindication. History of a neurologic reaction or immediate hypersensitivity reaction following a previous dose. History of severe local reaction (Arthus-type) following previous dose. Such individuals should not be given further routine or emergency doses of Td for 10 years.	Tetanus prophylaxis in wound management (summarized in text on page 11S and in Table 5)
LIVE-VIRUS VACCINES				
Measles live-virus vaccine	1 dose subcutaneously (SC); no booster	All adults born after 1956 without documentation of live vaccine on or after 1st birthday or physician-diagnosed measles or laboratory evidence of immunity; persons born before 1957 are generally considered immune. Susceptible travelers	Pregnancy; immunocompromised persons¶; history of anaphylactic reactions following egg ingestion or receipt of neomycin (see text)	Measles, mumps, rubella vaccine (MMR) is the vaccine of choice if recipients are likely to be susceptible to rubella and/or mumps as well as to measles. Persons vaccinated between 1963 and 1967 with a killed-measles vaccine, followed by live vaccine within 3 months or with a vaccine of unknown type should be revaccinated with live-measles-virus vaccine.
Mumps live-virus vaccine	1 dose SC; no booster	All adults, particularly males, believed to be susceptible can be vaccinated. Most adults can be considered immune.	Pregnancy; immunocompromised persons¶; history of anaphylactic reaction following egg ingestion or receipt of neomycin (see text)	MMR is the vaccine of choice if recipients are likely to be susceptible to measles and rubella as well as to mumps.

Rubella live-virus vaccine	1 dose SC, no booster	Indicated for adults, both male and female, lacking documentation of live vaccine on or after 1st birthday or laboratory evidence of immunity, particularly women of childbearing age and young adults who work or congregate in places such as hospitals, colleges, and the military. Susceptible travelers	Pregnancy; immunocompromised persons[¶]; history of anaphylactic reaction following receipt of neomycin	Women pregnant when vaccinated or who become pregnant within 3 months of vaccination should be counseled on the theoretical risks to the fetus. The risk of rubella vaccine-associated malformations in these women is so small as to be negligible. MMR is vaccine of choice if recipients are likely to be susceptible to measles or mumps as well as to rubella.
Smallpox vaccine (vaccinia virus)	THERE ARE NO INDICATIONS FOR THE USE OF SMALLPOX VACCINE IN THE GENERAL CIVILIAN POPULATION.			Laboratory workers involved with orthopox virus or in the production and testing of smallpox vaccines should receive regular smallpox vaccinations. For advice on vaccine administration and contraindications, contact the International Health Program Office, CDC, Atlanta, Georgia 30333.
Yellow fever live, attenuated virus (17D strain)	1 dose SC 6 days to 10 years before travel; booster every 10 years	Selected persons traveling or living in areas where yellow fever infection exists.	Although specific information is not available concerning adverse effects on the developing fetus,	Some countries require a valid International Certification of Vaccination showing receipt of vaccine.

*Several other vaccines, toxoids, and immune globulins are licensed and available. These are noted in Appendix 3. In addition, the following antitoxins are licensed and available: (1) botulism antitoxin, trivalent (ABE) equine (distributed by CDC only), (2) tetanus antitoxin (equine), (3) diphtheria antitoxin (equine), and (4) rabies antitoxin (equine).

†Several vaccines and toxoids are in "Investigation of New Drug" (IND) status and available only through the Division of Host Factors, Center for Infectious Disease, CDC. These are: (1) pentavalent (ABCDE) botulinum toxoid, (2) eastern equine encephalitis (EEE) vaccine, (3) Venezualan equine encephalitis (VEE) vaccine, and (4) tularemia vaccine

§When any vaccine or toxoid is indicated during pregnancy, waiting until the second or the third trimester, when possible, is a reasonable precaution that minimizes concern about teratogenicity.

¶Persons immunocompromised because of immune deficiency diseases, leukemia, lymphoma or generalized malignancy or immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites or radiation.

TABLE 4. Immunobiologics and schedules for adults (18 years of age and older)*† — Continued

Immunobiologic generic name	Primary schedule and booster(s)	Indications	Major precautions and contraindications§	Special considerations
			it is prudent on theoretical grounds to avoid vaccinating pregnant women unless the individual must travel to areas where the risk of yellow fever is high. Immunocompromised persons;¶ history of hypersensitivity to egg ingestion	If the only reason to vaccinate a pregnant woman is an international requirement, efforts should be made to obtain a waiver letter (see page 19S).
LIVE-VIRUS AND INACTIVATED-VIRUS VACCINES				
Polio vaccines: Killed-poliovirus vaccine (IPV) Live-poliovirus vaccine (OPV)	IPV preferred for primary vaccination; 3 doses SC 4 weeks apart; a 4th dose 6-12 months after 3rd; for adults with a completed primary series and for whom a booster is indicated, either OPV or IPV can be given. If immediate protection is needed, OPV is recommended.	Persons traveling to areas where wild poliovirus is epidemic or endemic and certain health-care personnel (see text for recommendations for incompletely immunized adults and adults in households of children to be immunized).	Although there is no convincing evidence documenting adverse effects of either OPV or IPV on the pregnant woman or developing fetus, it is prudent on theoretical grounds to avoid vaccinating pregnant women. However, if immediate protection against poliomyelitis is needed, OPV is recommended. OPV should not be given to immunocompromised individuals or to persons with known or possibly immunocompromised family members.¶ IPV is recommended in such situations.	Although a protective immune response to IPV in the immunocompromised individual cannot be assured, the vaccine is safe and some protection may result from its administration.
INACTIVATED-VIRUS VACCINES				
Hepatitis B (HB) inactivated-virus vaccine	2 doses IM 4 weeks apart; 3rd dose 5 months after 2nd; need for boosters unknown	Adults at increased risk of occupational, environmental, social, or family exposure	Data are not available on the safety of the vaccine for the developing fetus. Because the vaccine	The vaccine produces neither therapeutic nor adverse effects on HBV-infected persons. Prevaccination serologic

			contains only noninfectious hepatitis B surface antigen particles, the risk should be negligible. Pregnancy should *not* be considered a vaccine contraindication if the woman is otherwise eligible.	screening for susceptibility before vaccination may or may not be cost effective depending on costs of vaccination and testing and on the prevalence of immune individuals in the group.
Influenza vaccine (inactivated whole-virus and split-virus) vaccine	Annual vaccination with current vaccine. Either whole- or split-virus vaccine may be used.	Adults with high-risk conditions, residents of nursing homes or other chronic-care facilities, medical-care personnel, healthy persons over 65.	Although no evidence exists of maternal or fetal risk when vaccine is given in pregnancy because of an underlying high-risk condition in a pregnant woman, waiting until the second or third trimester, if possible, is reasonable. History of anaphylactic hypersensitivity to egg ingestion	
Human diploid cell rabies vaccine (HDCV) (inactivated, whole-virion and subvirion)	Preexposure prophylaxis: 2 doses 1 week apart; 3rd dose 3 weeks after 2nd; if exposure continues, booster doses every 2 years, or an antibody titer determined	Veterinarians, animal handlers, certain laboratory workers, and persons living in or visiting countries for > 1 month where rabies is a constant	If there is substantial risk of exposure to rabies, preexposure vaccination may be indicated during pregnancy. Corticosteroids and immunosuppressive agents can interfere with	Complete preexposure prophylaxis does not eliminate the need for additional therapy with rabies vaccine after a rabies exposure. The Food and Drug Administration has not approved the intradermal (ID) use of HDCV.

*Several other vaccines, toxoids, and immune globulins are licensed and available. These are noted in Appendix 3. In addition, the following antitoxins are licensed and available: (1) botulism antitoxin, trivalent (ABE) equine (distributed by CDC only), (2) tetanus antitoxin (equine), (3) diphtheria antitoxin (equine), and (4) rabies antitoxin (equine).

†Several vaccines and toxoids are in "Investigation of New Drug" (IND) status and available only through the Division of Host Factors, Center for Infectious Disease, CDC. These are: (1) pentavalent (ABCDE) botulinum toxoid, (2) eastern equine encephalitis (EEE) vaccine, (3) Venezualan equine encephalitis (VEE) vaccine, and (4) tularemia vaccine

§When any vaccine or toxoid is indicated during pregnancy, waiting until the second or the third trimester, when possible, is a reasonable precaution that minimizes concern about teratogenicity.

¶Persons immunocompromised because of immune deficiency diseases, leukemia, lymphoma or generalized malignancy or immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites or radiation.

TABLE 4. Immunobiologics and schedules for adults (18 years of age and older)*† — Continued

Immunobiologic generic name	Primary schedule and booster(s)	Indications	Major precautions and contraindications§	Special considerations
	and a booster dose given if titer inadequate (< 5) Postexposure prophylaxis: All postexposure treatment should begin with immediate cleansing of the wound with soap and water. (1) Persons who have a) previously received postexposure prophylaxis with HDCV, b) received recommended IM preexposure series of HDCV, c) received recommended ID preexposure series of HDCV in the U.S., or d) have a previously documented rabies antibody titer considered adequate: 2 doses of HDCV, 1.0 ml IM, one each on days 0 and 3 (2) Persons not previously immunized as above: HRIG 20 international units (IU)/kg body weight, half infiltrated at bite site if possible, remainder IM; and 5 doses of HDCV, 1.0 ml-IM, one each on days 0, 3, 7, 14, 28	threat	the development of active immunity; history of anaphylactic or Type III hypersensitivity reaction to previous dose of HDCV (See text).	Recommendations for the ID use of HDCV are currently being discussed. Suggestions concerning ID use of HDCV for preexposure prophylaxis are found on page 26S and in CDC. Rabies Prevention—United States, 1984. MMWR 1984;33: 393-402,407-8. The decision for postexposure use of HDCV depends on the species of biting animal, the circumstances of biting incident, and the type of exposure (i.e. bite,saliva contamination of wound, etc.). The type of and schedule for post-exposure prophylaxis depends upon the person's previous rabies vaccination status, or the result of a previous or current serologic test for rabies antibody. For post-exposure prophylaxis, HDCV should always be administered IM, *not* ID.

INACTIVATED-BACTERIA VACCINES				
Cholera vaccine	Two 0.5-ml doses SC or IM or two 0.2-ml doses ID 1 week to 1 month apart; booster doses (0.5 ml IM or 0.2 ml ID) every 6 months	Travelers to countries requiring evidence of cholera vaccination for entry	No specific information on vaccine safety during pregnancy. Use in pregnancy should reflect actual increased risk. Persons who have had severe local or systemic reactions to a previous dose	One dose generally satisfies International Health Regulations. Some countries may require evidence of a complete primary series or a booster dose given within 6 months before arrival. Vaccination should not be considered as an alternative to continued careful selection of foods and water.
Meningococcal polysaccharide vaccines (bivalent A and C and tetravalent A, C, W135, and Y)	1 dose in volume and by route specified by manufacturer; need for boosters unknown	Travelers visiting areas of a country that are recognized as having epidemic meningococcal disease	Pregnancy, unless there is substantial risk of of infection	
Plague vaccine	3 IM doses; first dose 1.0 ml; 2nd dose 0.2 ml 1 month later; 3rd dose 0.2 ml 5 months after 2nd; booster doses (0.2 ml) at 1-2 year intervals if exposure continues	Selected travelers to countries reporting cases, for whom avoidance of rodents and fleas is impossible; all laboratory and field personnel working with *Yersinia pestis* organisms possibly resistant to antimicrobials; those engaged in *Y. pestis* aerosol experiments or in field operations in areas with enzootic	Pregnancy, unless there is substantial and unavoidable risk of exposure; persons with known hypersensitivity to any of the vaccine constituents (see manufacturer's label); patients who have had severe local or systemic reactions to a previous dose	Prophylactic antibiotics may be recommended for definite exposure whether or not the exposed persons has been vaccinated.

*Several other vaccines, toxoids, and immune globulins are licensed and available. These are noted in Appendix 3. In addition, the following antitoxins are licensed and available: (1) botulism antitoxin, trivalent (ABE) equine (distributed by CDC only), (2) tetanus antitoxin (equine), (3) diphtheria antitoxin (equine), and (4) rabies antitoxin (equine).

†Several vaccines and toxoids are in "Investigation of New Drug" (IND) status and available only through the Division of Host Factors, Center for Infectious Disease, CDC. These are: (1) pentavalent (ABCDE) botulinum toxoid, (2) eastern equine encephalitis (EEE) vaccine, (3) Venezualan equine encephalitis (VEE) vaccine, and (4) tularemia vaccine

§When any vaccine or toxoid is indicated during pregnancy, waiting until the second or the third trimester, when possible, is a reasonable precaution that minimizes concern about teratogenicity.

TABLE 4. Immunobiologics and schedules for adults (18 years of age and older)*†—Continued

Immunobiologic generic name	Primary schedule and booster(s)	Indications	Major precautions and contraindications§	Special considerations
		plague where regular exposure to potentially infected wild rodents, rabbits, or their fleas cannot be prevented		
Pneumococcal polysaccharide vaccine (23 valent)	1 dose, booster not recommended	Adults who are at increased risk of pneumococcal disease and its complications because of underlying health conditions; older adults, especially those age 65 and over, who are healthy	The safety of vaccine in pregnant women has not been evaluated; it should not be given during pregnancy unless the risk of infection is high. Previous recipients of any type of pneumococcal polysaccharide vaccine should not receive another dose of vaccine	
Typhoid vaccine	Two 0.5-ml doses SC 4 or more weeks apart, booster 0.5 ml SQ or 0.1 ml ID every 3 years if exposure continues	Travelers to areas where there is a recognized risk of exposure to typhoid	Severe local or systemic reaction to a previous dose. Acetone killed and dried vaccines should not be given ID.	Vaccination should not be considered as an alternative to continued careful selection of foods and water.
LIVE-BACTERIA VACCINE				
BCG	1 ID or SC dose (see package label)	Prolonged close contact with untreated or ineffectively treated active tuberculosis patients; groups with excessive rates of new infection in which other control measures have not been successful	Pregnancy, unless there is unavoidable exposure to infective tuberculosis; immunocompromised patients¶	In the United States tuberculosis control efforts are directed toward early identification, treatment of cases and preventive therapy with isoniazid.
IMMUNE GLOBULINS				
Immune globulin (IG)	Hepatitis A prophylaxis: **Preexposure**-1 IM dose	Household and sexual contacts of persons with		For travelers IG is not an alternative to continued

	of 0.02 ml/kg for anticipated risk of 2-3 months; IM dose of 0.06 ml/kg for anticipated risk of 5 months; repeat appropriate dose at above intervals if exposure continues. **Postexposure**-1 IM dose of 0.02 ml/kg given within 2 weeks of exposure	hepatitis A; travelers to high-risk areas outside tourist routes; staff, attendees, and parents of diapered attendees in day-care-center outbreaks		careful selection of foods and water. Frequent travelers should be tested for hepatitis antibody.
	Measles prophylaxis: 0.25 ml/kg IM (maximum 15 ml) given within 6 days after exposure	Exposed susceptible contacts of measles cases	IG should *not* be used to control measles	IG given within 6 days after exposure can prevent or modify measles. Recipients of IG for measles prophylaxis should receive live-measles vaccine 3 months later.
Hepatitis B immune globulin (HBIG)	0.06 ml/kg IM as soon as possible after exposure followed by a second dose 1 month later except when HB vaccine is given	Following percutaneous or mucous membrane exposure to blood known to be HBsAg positive; following sexual exposure to or a bite from a person with acute HBV or an HBV carrier.		IG (0.06 ml/kg) may be used if HBIG is not available.

*Several other vaccines, toxoids, and immune globulins are licensed and available. These are noted in Appendix 3. In addition, the following antitoxins are licensed and available: (1) botulism antitoxin, trivalent (ABE) equine (distributed by CDC only), (2) tetanus antitoxin (equine), (3) diphtheria antitoxin (equine), and (4) rabies antitoxin (equine).

†Several vaccines and toxoids are in "Investigation of New Drug" (IND) status and available only through the Division of Host Factors, Center for Infectious Disease, CDC. These are: (1) pentavalent (ABCDE) botulinum toxoid, (2) eastern equine encephalitis (EEE) vaccine, (3) Venezualan equine encephalitis (VEE) vaccine, and (4) tularemia vaccine

§When any vaccine or toxoid is indicated during pregnancy, waiting until the second or the third trimester, when possible, is a reasonable precaution that minimizes concern about teratogenicity.

¶Persons immunocompromised because of immune deficiency diseases, leukemia, lymphoma or generalized malignancy or immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites or radiation

TABLE 4. Immunobiologics and schedules for adults (18 years of age and older)*†—Continued

Immunobiologic generic name	Primary schedule and booster(s)	Indications	Major precautions and contraindications§	Special considerations
Tetanus immune globulin (TIG)	250 units IM	Part of management of nonclean, nonminor wound in a person with unknown tetanus toxoid status, with less than two previous doses, or with two previous doses and a wound more than 24 hours old.		
Rabies immune globulin, human (HRIG)	20 IU/kg, up to half infiltrated around wound, remainder IM	Part of management of rabies exposure in persons lacking a history of recommended preexposure or postexposure prophylaxis with HDCV		Although preferable to be given with the 1st dose of vaccine, can be given up to the 8th day after the 1st dose of vaccine.
Varicella-zoster immune globulin (VZIG)	Persons ≤ 50 kg: 125 units/10kg IM; persons > 50 kg: 625 units**	Immunocompromised patients known or likely to be susceptible with close and prolonged exposure to a household contact case or to an infectious hospital staff member or hospital roommate.¶		

NOTE: Refer to text on specific vaccines or toxoids for further details on indications, contraindications, precautions, dosages, side effects, and adverse reactions, and special considerations and individual ACIP statements (see list of published ACIP statements in Appendix 2).

*Several other vaccines, toxoids, and immune globulins are licensed and available. These are noted in Appendix 3. In addition, the following antitoxins are licensed and available: (1) botulism antitoxin, trivalent (ABE) equine (distributed by CDC only), (2) tetanus antitoxin (equine), (3) diphtheria antitoxin (equine), and (4) rabies antitoxin (equine).

†Several vaccines and toxoids are in "Investigation of New Drug" (IND) status and available only through the Division of Host Factors, Center for Infectious Disease, CDC. These are: (1) pentavalent (ABCDE) botulinum toxoid, (2) eastern equine encephalitis (EEE) vaccine, (3) Venezualan equine encephalitis (VEE) vaccine, and (4) tularemia vaccine

§When any vaccine or toxoid is indicated during pregnancy, waiting until the second or the third trimester, when possible, is a reasonable precaution that minimizes concern about teratogenicity.

¶Persons immunocompromised because of immune deficiency diseases, leukemia, lymphoma or generalized malignancy or immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites or radiation.

**Some persons have recommended 125 units/10 kg regardless of total body weight.

TABLE 5. Summary guide to tetanus prophylaxis in routine 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§
3 or more	No¶	No	No**	No

NOTE: Refer to text on specific vaccines or toxoids for contraindications, precautions, dosages, side effects and adverse reactions, and special considerations. Important details are in the text and ACIP recommendation (MMWR 1981; 30:392-407).

*The combined preparations Td, containing both tetanus and diphtheria toxoids, is preferred to tetanus toxoid alone.

†Tetanus immune globulin.

§Yes, if wound more than 24 hours old.

¶Yes, if more than 10 years since last dose.

**Yes, if more than 5 years since last dose (more frequent boosters are not needed and can accentuate side effects.)

APPENDIX 1. Suggested immunization record form

Name _____ Sex _____ Birthdate _____

VACCINE	VACCINE TYPE	DATE GIVEN MO/DAY/YR	VACCINE LOT #	DOCTOR OR CLINIC	DATE DOSE DUE
POLIO OPV or IPV (specify type used)					
DTP (diphtheria tetanus pertussis) DT (Pediatric) or Td (Adult) (specify type used)					
MEASLES MUMPS RUBELLA or Combinations (MMR, measles-rubella, rubella-mumps) (specify type used)					
OTHER vaccines or immune globulins (specify type used)					
TUBERCULIN TEST					

NOTES:

APPENDIX 2. Published ACIP statements* (as of June 30, 1984)

Title of ACIP Statement	MMWR Publication
General recommendations on immunizations	1983;32:1-8,13-7
Diphtheria, tetanus, and pertussis: guidelines for vaccine prophylaxis and other preventive measures	1981;30:392-96,401-7 Erratum. 1981;30:420
Measles prevention	1982;31:217-24,229-31
Mumps vaccine	1982;31:617-20,625
Rubella prevention	1984;33:301-10,315-8
Yellow fever vaccine	1984;32:679-82,687-8
Poliomyelitis prevention	1982;31:22-6,31-4
Prevention and control of influenza†	1984;33:253-60,265-6
Inactivated hepatitis B virus vaccine	1982;31:317-22,327-8
Postexposure prophylaxis of hepatitis B	1984;33:285-90
Rabies prevention Supplementary statement on rabies vaccine and serologic testing	1981;30:535-6
Rabies	1984;33:393-402,407-8
Supplementary statement on pre-exposure rabies prophylaxis by the intradermal route	1982;31:279-80,285
Cholera vaccine	1978;27:173-4
Meningococcal polysaccharide vaccine	1978;27:327-9
Plague vaccine	1982;31:301-4
Update: Pneumococcal polysaccharide vaccine usage—United States	1984;33:273-6,81
Typhoid vaccine	1978;27:231-3
BCG vaccines	1979;28:241-4
Immune globulins for protection against viral hepatitis	1981;30:423-8,433-5
Varicella-zoster immune globulin for the prevention of chickenpox	1984;33:84-90,95-100

*The Immunization Practices Advisory Committee (ACIP) periodically reviews recommendations on vaccination and prophylaxis. When recommendations are revised, they are published individually in the MMWR.

†Each year influenza vaccine recommendations are reviewed and amended to reflect updated information on influenza activity in the United States for the preceding influenza season and to provide information on the vaccine available for the upcoming influenza season. These recommendations are published in the MMWR annually, usually during June or July.

APPENDIX 3. Immunobiologics available as of June 30, 1984, by manufacturer and product name

Immunobiologic	Manufacturer	Product Name
Adenovirus vaccine	Wyeth Labs, Inc	Adenovirus, Live, Oral, Type 4* Adenovirus, Live, Oral, Type 7*
Anthrax vaccine	Biol Prods Program, Michigan Dept of Public Health	Anthrax Vaccine Adsorbed
BCG vaccine	Glaxo Operations UK Limited	BCG Vaccine
	Inst Tuberculosis Research, Univ Of Illinois at Chicago	BCG Vaccine
Cholera vaccine	Lederle Laboratories, Div American Cyanamid Co	Cholera Vaccine (strains Ogawa-Inaba)
	Wyeth Labs, Inc	Cholera Vaccine
	Sclavo SpA†	Cholera Vaccine
Diphtheria and tetanus toxoids adsorbed	Lederle Laboratories, Div American Cyanamid Co	Diphtheria Tetanus Toxoids Adsorbed (Purogenated for Pediatric Use)
	Massachusetts Public Health Biol Labs	Diphtheria and Tetanus Toxoids Adsorbed
	Biol Prods Program, Michigan Dept of Public Health	Diphtheria and Tetanus Toxoids Adsorbed (Pediatric)§
	Sclavo SpA†	Diphtheria and Tetanus Toxoids Adsorbed (For Pediatric Use)
	Wyeth Labs, Inc	Diphtheria and Tetanus Toxoids Adsorbed ([pediatric] Aluminum Phosphate Adsorbed, Ultrafined)
Diphtheria and tetanus toxoids and pertussis vaccine adsorbed	Connaught Labs, Inc†	Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed
	Lederle Laboratories, Div American Cyanamid Co	Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed (Tri Immunol®)
	Massachusetts Public Health Biol Labs	Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed

*Available *only* to the U.S. Armed Forces.

†Connaught Laboratories, Inc., products distributed in the United States by E. R. Squibb and Sons, Inc. Sclavo SpA products distributed in United States by Sclavo, Inc. Institut Merieux products distributed in United States by Merieux Institute, Inc.

APPENDIX 3. Immunobiologics available as of June 30, 1984, by manufacturer and product name — Continued

Immunobiologic	Manufacturer	Product Name
	Biol Prods Program, Michigan Dept of Public Health	Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed[§]
	Wyeth Labs, Inc	Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed (Aluminum Phosphate Adsorbed, Ultrafined, Triple Antigen)
Diphtheria toxoid adsorbed	Sclavo SpA[†]	Diphtheria Toxoid Adsorbed (Pediatric)
Hepatitis B immune globulin	Alpha Therapeutic Corp Produces for Abbott Laboratories	Hepatitis B Immune Globulin (Human) (H-BIG®)
	Merck Sharp & Dohme Div of Merck & Co, Inc	Hepatitis B Immune Globulin (Human) (MSD, HEP-B-GAMMEE®)
	Cutter Biological Div of Miles Labs, Inc	Hepatitis B Immune Globulin (HYPER-HEP™)
Hepatitis B vaccine	Merck Sharp & Dohme Div of Merck & Co, Inc	Hepatitis B Vaccine (MSD, HEPTAVAX-B™)
Immune globulin	Alpha Therapeutic Corp	Immune Serum Globulin (Human)
	Armour Pharmaceutical Co	Immune Serum Globulin (Human) (GAMMAR®)
	Central Laboratory Blood Transfusion Service, Swiss Red Cross	Immune Globulin Intravenous (SANDOGLOBULIN®)
	Cutter Biological Div of Miles Labs, Inc	Immune Serum Globulin (Human) (GAMASTAN®)
		Immune Globulin Intravenous [5% in 10% Maltose (GAMIMUNE®)]
	Hyland Therapeutics Div Travenol Labs, Inc also produces for Savage Labs	Immune Serum Globulin (Human)
		Immune Serum Globulin (Human) (IMMUGLOBULIN®)
	Massachusetts Public Health Biol Labs	Immune Serum Globulin (Human)

[†]Connaught Laboratories, Inc., products distributed in the United States by E. R. Squibb and Sons, Inc. Sclavo SpA products distributed in United States by Sclavo, Inc. Institut Merieux products distributed in United States by Merieux Institute, Inc.

[§]Outside of Michigan, available only to health departments.

APPENDIX 3. Immunobiologics available as of June 30, 1984, by manufacturer and product name — Continued

Immunobiologic	Manufacturer	Product Name
	Biol Prods Program, Michigan Dept of Public Health	Immune Serum Globulin (Human)
	Wyeth Labs, Inc	Immune Serum Globulin (Human)
	New York Blood Ctr, Inc	Immune Serum Globulin (Human)
Influenza vaccine	Connaught Labs, Inc†	Influenza Virus Vaccine ([Zonal Purified]), Whole Virion (FLUZONE®)
		Influenza Virus Vaccine ([Zonal Purified]), Split Virion (FLUZONE®)
	Parke-Davis, Div of Warner-Lambert Co	Influenza Virus Vaccine (Split Virion [FLUOGEN®])
	Wyeth Labs, Inc	Influenza Virus Vaccine Trivalent Types A and B (Chromatograph), Subvirion Antigen
Measles and mumps vaccine, live	Merck Sharp & Dohme Div of Merck & Co, Inc	Measles and Mumps Virus Vaccine, Live (MSD, M-M-VAX®)
Measles, mumps and rubella vaccine	Merck Sharp & Dohme Div of Merck & Co, Inc	Measles, Mumps and Rubella Virus Vaccine, Live (MSD, MMR II®)
Measles and rubella vaccine	Merck Sharp & Dohme Div of Merck & Co, Inc	Measles and Rubella Virus Vaccine, Live (MSD, M-R-VAX II®)
Measles vaccine	Merck Sharp & Dohme Div of Merck & Co, Inc	Measles Virus Vaccine, Live (Attenuated [MSD,] ATTENUVAX®])
Meningococcal polysaccharide vaccine		
A and C	Connaught Labs, Inc†	Meningococcal Polysaccharide Vaccine (MENOMUNE-A/C®)
A, C, Y, and W 135	Connaught Labs, Inc†	Meningococcal Polysaccaride Vaccine (MENOMUNE-A/CY/W-135®)

†Connaught Laboratories, Inc., products distributed in the United States by E. R. Squibb and Sons, Inc. Sclavo SpA products distributed in United States by Sclavo, Inc. Institut Merieux products distributed in United States by Merieux Institute, Inc.

APPENDIX 3. Immunobiologics available as of June 30, 1984, by manufacturer and product name — Continued

Immunobiologic	Manufacturer	Product Name
Mumps vaccine	Merck Sharp & Dohme Div of Merck & Co, Inc	Mumps Virus Vaccine, Live (MSD, MUMPSVAX®)
Pertussis immune globulin	Cutter Biological Div of Miles Labs, Inc	Pertussis Immune Globulin (Human) (HYPERTUSSIS®)
Pertussis vaccine adsorbed	Biol Prods Program, Michigan Dept of Public Health	Pertussis Vaccine Adsorbed
Plague vaccine	Cutter Biological Div of Miles Labs, Inc	Plague Vaccine
Pneumococcal polysaccharide	Lederle Laboratories, Div American Cyanamid Co	Pneumococcal Vaccine, Polyvalent (PNEU-IMUNE23®)
	Merck Sharp & Dohme Div of Merck & Co, Inc	Pneumococcal Vaccine, Polyvalent (MSD, PNEUMOVAX 23®)
Poliovirus vaccine		
Inactivated	Connaught Labs, Ltd† (Purified-Salk)	Poliomyelitis Vaccine
Oral	Lederle Laboratories, Div American Cyanamid Co	Poliovirus Vaccine, Live, Oral Trivalent (ORIMUNE®)
Rabies immune globulin	Cutter Biological Div of Miles Labs, Inc	Rabies Immune Globulin (Human) (HYPERAB®)
	Institut Merieux†	Rabies Immune Globulin (Human) (IMOGAMRABIES®)
Rabies vaccine	Institut Merieux†	Rabies Vaccine (Human Diploid Cell [IMOVAX®])
	Wyeth Labs, Inc	Rabies Vaccine (Human Diploid Cell Strain, Subvirion Antigen [WYVAC®])
Rubella vaccine	Merck Sharp & Dohme Div of Merck & Co, Inc	Rubella Virus Vaccine, Live (MSD, MERUVAX®II)
Rubella and mumps vaccine	Merck Sharp & Dohme Div of Merck & Co, Inc	Rubella and Mumps Virus Vaccine, Live (MSD, BIAVAX®II)
Tetanus immune globulin	Alpha Therapeutic Corp	Tetanus Immune Globulin (Human)

†Connaught Laboratories, Inc., products distributed in the United States by E. R. Squibb and Sons, Inc. Sclavo SpA products distributed in United States by Sclavo, Inc. Institut Merieux products distributed in United States by Merieux Institute, Inc.

APPENDIX 3. Immunobiologics available as of June 30, 1984, by manufacturer and product name — Continued

Immunobiologic	Manufacturer	Product Name
	Cutter Biological Div of Miles Labs, Inc	Tetanus Immune Globulin (Human) (HYPER-TET®)
	Hyland Therapeutics Div Travenol Labs, Inc	Tetanus Immune Globulin (Human) (HU-TET®)
	Hyland Therapeutics Div Travenol Labs, Inc also produces for Savage Labs	Tetanus Immune Globulin (Human) (HOMO-TET®)
	Wyeth Labs, Inc	Tetanus Immune Globulin (Human)
	Massachusetts Public Health Biol Labs	Tetanus Immune Globulin (Human)
Tetanus and diphtheria toxoids adsorbed	Connaught Labs, Inc†	Tetanus and Diphtheria Toxoids Adsorbed (For Adult Use)
	Lederle Laboratories, Div American Cyanamid Co	Tetanus and Diphtheria Toxoids Adsorbed (For Adult Use) (Purogenated Parenteral)
	Massachusetts Public Health Biol Labs	Tetanus and Diphtheria Toxoids Adsorbed (For Adult Use)
	Biol Prods Program, Michigan Dept of Public Health	Tetanus and Diphtheria Toxoids Adsorbed (For Adult Use) (not available to health departments outside Michigan)
	Sclavo SpA†	Tetanus and Diphtheria Toxoids Adsorbed (For Adult Use)
	Wyeth Labs, Inc	Tetanus and Diphtheria Toxoids Adsorbed (For Adult Use) [Aluminum Phosphate, Ultrafined]
Tetanus toxoid adsorbed	Connaught Labs, Inc†	Tetanus Toxoid Adsorbed
	Lederle Laboratories, Div American Cyanamid Co	Tetanus Toxoid Adsorbed (Purogenated [Aluminum Phosphate Adsorbed])
	Massachusetts Public Health Biol Labs	Tetanus Toxoid Adsorbed

†Connaught Laboratories, Inc., products distributed in the United States by E. R. Squibb and Sons, Inc. Sclavo SpA products distributed in United States by Sclavo, Inc. Institut Merieux products distributed in United States by Merieux Institute, Inc.

APPENDIX 3. Immunobiologics available as of June 30, 1984, by manufacturer and product name — Continued

Immunobiologic	Manufacturer	Product Name
	Biol Prods Program, Michigan Dept of Public Health	Tetanus Toxoid Adsorbed
	Sclavo SpA†	Tetanus Toxoid Adsorbed
	Wyeth Labs, Inc	Tetanus Toxoid Adsorbed (Aluminum Phosphate Adsorbed, Ultrafined)
Tetanus toxoid, fluid	Connaught Labs, Inc†	Tetanus Toxoid (Fluid)
	Lederle Laboratories, Div American Cyanamid Co	Tetanus Toxoid (Purogenated, Tetanus Toxoid Fluid)
	Wyeth Labs, Inc	Tetanus Toxoid (Fluid, Purified, Ultrafined)
Typhoid vaccine	Wyeth Labs, Inc	Typhoid Vaccine¶
Varicella-zoster immune globulin	Massachusetts Public Health Biol Labs	Varicella-Zoster Immune Globulin (Human)
Yellow fever vaccine	Connaught Labs, Inc†	Yellow Fever Vaccine (Live, 17D Virus, ALV-Free [YF-VAX®])

NOTE: In the preparation of this appendix every effort was made to assure its completeness and accuracy. This appendix was compiled from information obtained from manufacturers, the Division of Product Certification, Food and Drug Administration, and the Physicians Desk Reference, 37th Edition, 1983, and to the best of our knowledge is an accurate and complete listing as of June 30, 1984. However, omissions and errors may have occurred inadvertently. This appendix is intended to be a resource and does not replace the provider's obligation to remain otherwise current on the availability of vaccines, toxoids, and immune globulins.

†Connaught Laboratories, Inc., products distributed in the United States by E. R. Squibb and Sons, Inc. Sclavo SpA products distributed in United States by Sclavo, Inc. Institut Merieux products distributed in United States by Merieux Institute, Inc.

¶The acetone-killed and -dried form of this vaccine is available only to the U.S. Armed Forces.

APPENDIX 4. Use of immunobiologics in pregnancy*†

Immunizing agent	Risk from disease to pregnant female	Risk from disease to fetus or neonate	Type of immunizing agent
LIVE-VIRUS VACCINES			
Measles	Significant morbidity, low mortality; not altered by pregnancy	Significant increase in abortion rate; may cause malformations	Live, attenuated virus vaccine
Mumps	Low morbidity and mortality; not altered by pregnancy	Probable increased rate of abortion in 1st trimester. Questionable association of fibroelastosis in neonates	Live, attenuated virus vaccine
Poliomyelitis	No increased incidence in pregnancy, but may be more severe if it does occur	Anoxic fetal damage reported; 50% mortality in neonatal disease	Live, attenuated virus (OPV) and inactivated virus (IPV) vaccine§

Risk from immunizing agent to fetus	Indications for immunization during pregnancy	Dose schedule	Comments
None confirmed	Contraindicated (See immune globulins)	Single dose	Vaccination of susceptible women should be part of post-partum care
None confirmed	Contraindicated	Single dose	
None confirmed	Not routinely recommended for adults in U.S., except persons at increased risk of exposure	Primary: 3 doses of IPV at 4-8 week intervals and a 4th dose 6-12 months after the 3rd dose; 2 doses of OPV with a 6-8 week interval and a 3rd dose at least 6 weeks later, customarily 8-12 months later. Booster: Every 5 years until 18 years of age for IPV	Vaccine indicated for susceptible pregnant women traveling in endemic areas or in other high-risk situations

Rubella	*Low morbidity and mortality; not altered by pregnancy*	*High rate of abortion and congenital rubella syndrome*	*Live, attenuated virus vaccine*	*None confirmed*	*Contraindicated*	*Single dose*	*Teratogenicity of vaccine is theoretical, not confirmed to date; vaccination of susceptible women should be part of postpartum care*
Yellow fever	Significant morbidity and mortality; not altered by pregnancy	Unknown	Live, attenuated virus vaccine	Unknown	Contraindicated except if exposure unavoidable	Single dose	Postponement of travel preferable to vaccination, if possible
TOXOIDS							
Tetanus-Diphtheria	Severe morbidity; tetanus mortality 60%, diphtheria mortality 10%; unaltered by pregnancy	Neonatal tetanus mortality 60%	Combined tetanus-diphtheria toxoids preferred; adult tetanus-diphtheria formulation	None confirmed	Lack of primary series, or no booster within past 10 years	Primary: 2 doses at 1- to 2-month interval with a 3rd dose 6-12 months after the second; Booster: single dose every 10 years, after completion of the primary series	Updating of immune status should be part of antepartum care
IMMUNE GLOBULINS: HYPERIMMUNE							
Hepatitis B	Possible increased severity during 3rd trimester	Possible increase in abortion rate and prematurity. Perinatal trans-	Hepatitis B immune globulin (HBIG)	None reported	Postexposure prophylaxis	0.06 ml/kg or 5 ml immediately, plus hepatitis B (HB) vaccine series, if indicated	Infants born to HBsAg-positive mothers should receive 0.5 ml HBIG as soon as

*Reproduced from: American College of Obstetrics and Gynecologists. Immunization during pregnancy (ACOG Technical Bulletin #64), Washington, D.C. ACOG. May 1982.

†The Appendix, Immunization During Pregnancy, describes methods and techniques of clinical practice that are currently acceptable and used by recognized authorities. However, it does not represent official policy or recommendations of the American College of Obstetricians and Gynecologists. Its publication should not be construed as excluding other acceptable methods of handling similar problems.

§IPV recommmended for unimmunized adults at increase risk.

APPENDIX 4. Use of immunobiologics in pregnancy*† — Continued

Immunizing agent	Risk from disease to pregnant female	Risk from disease to fetus or neonate	Type of immunizing agent
		mission may occur if mother is a chronic carrier or is acutely infected	
Rabies	Near 100% fatality; not altered by pregnancy	Determined by maternal disease	Rabies immune globulin (RIG)
Tetanus	Severe morbidity; mortality 60%	Neonatal tetanus mortality 60%	Tetanus immune globulin (TIG)
Varicella	Possible increase in severe varicella pneumonia	Can cause congenital varicella with increased mortality in neonatal period; very rarely causes congenital defects	Varicella-zoster immune globulin (VZIG)
INACTIVATED-VIRUS VACCINES			
Hepatitis B	Possible increased severity during 3rd trimester	Possible increase in abortion rate and prematurity.	Inactivated HB vaccine

Risk from immunizing agent to fetus	Indications for immunization during pregnancy	Dose schedule	Comments
			possible after birth, plus 0.5 ml HB vaccine within 1 week of birth. Vaccine should be repeated at 1 and 6 months
None reported	Postexposure prophylaxis	20 IU/kg in one dose of RIG	Used in conjunction with rabies killed-virus vaccine
None reported	Postexposure prophylaxis	250 units in one dose of TIG	Used in conjunction with tetanus toxoid
None reported	Not routinely indicated in healthy pregnant women exposed to varicella	1 vial/kg in one dose of VZIG, up to 5 vials	Only indicated for newborns of mothers who developed varicella within 4 days prior to delivery or 2 days following delivery. Approximately 90%-95% of adults are immune to varicella
None reported	Indications for prophylaxis not altered by pregnancy	1.0 ml (20 μg) IM at time, 0, 1, and 6 months	Infants born to HBsAg-positive mothers should receive 0 5 ml

		Perinatal transmission may occur if mother is a chronic carrier or is acutely infected					HBIG as soon as possible after birth, plus 0.5 ml HB vaccine within 1 week of birth. Vaccine should be repeated at 1 and 6 months
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; public health authorities to be consulted for current recommendation	Consult with public health authorities since recommendations change each year	Criteria for vaccination of pregnant women same as for all adults
Rabies	Near 100% fatality; not altered by pregnancy	Determined by maternal disease	Killed-virus vaccine	Unknown	Indications for prophylaxis not altered by pregnancy; each case considered individually	Public health authorities to be consulted for indications and dosage	
INACTIVATED-BACTERIA VACCINES							
Cholera	Significant morbidity and mortality; more severe during 3rd trimester	Increased risk of fetal death during 3rd trimester maternal illness	Killed-bacteria vaccine	Unknown	Only to meet international travel requirements	2 injections, 4-8 weeks apart	Vaccine of low efficacy

*Reproduced from: American College of Obstetrics and Gynecologists. Immunization during pregnancy (ACOG Technical Bulletin #64), Washington, D.C. ACOG. May 1982.

†The Appendix, Immunization During Pregnancy, describes methods and techniques of clinical practice that are currently acceptable and used by recognized authorities. However, it does not represent official policy or recommendations of the American College of Obstetricians and Gynecologists. Its publication should not be construed as excluding other acceptable methods of handling similar problems.

APPENDIX 4. Use of immunobiologics in pregnancy*† — Continued

Immunizing agent	Risk from disease to pregnant female	Risk from disease to fetus or neonate	Type of immunizing agent
Meningo-coccus	No increased risk during pregnancy; no increase in severity of disease	Unknown	Killed-bacteria vaccine
Plague	Significant morbidity and mortality; not altered by pregnancy	Determined by maternal disease	Killed-bacteria vaccine
Pneumo-coccus	No increased risk during pregnancy; no increase in severity of disease	Unknown	Polyvalent polysaccharide vaccine
Typhoid	Significant morbidity and mortality; not altered by pregnancy	Unknown	Killed-bacteria vaccine
Hepatitis A	Possible increased severity during 3rd trimester	Probable increase in abortion rate and prematurity. Possible	Pooled immune globulin (IG)

Risk from immunizing agent to fetus	Indications for immunization during pregnancy	Dose schedule	Comments
No data available on use during pregnancy	Indications not altered by pregnancy; vaccination recommended only in unusual outbreak situations	Public health authorities to be consulted	
None reported	Very selective vaccination of exposed persons	Public health authorities to be consulted for indications and dosage	
No data available on use during pregnancy	Indications not altered by pregnancy; vaccine used only for high-risk individuals	In adults 1 dose only	
None confirmed	Not recommended routinely except for close, continued exposure or travel to endemic areas	Primary; 2 injections, 4 weeks apart; Booster; single dose	
None reported	Postexposure prophylaxis	0.02 ml/kg in 1 dose of IG	IG should be given as soon as possible and within 2 weeks of

		transmission to neonate at delivery if mother is incubating the virus or is acutely ill at that time					*exposure.* Infants born to mothers who are incubating the virus or are acutely ill at delivery should receive one dose of 0.5 ml as soon as possible after birth
Measles	Significant morbidity, low mortality; not altered by pregnancy	Significant increase in abortion rate; may cause malformations	Pooled immune globulin (IG)	None reported	Postexposure prophylaxis	0.25 ml/kg in 1 dose of IG, up to 15 ml	Unclear if it prevents abortion. Must be given within 6 days of exposure

*Reproduced from: American College of Obstetrics and Gynecologists. Immunization during pregnancy (ACOG Technical Bulletin #64), Washington, D.C. ACOG. May 1982.

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APPENDIX 5. Varicella-zoster immune globulin—regional distribution centers

Service area	Regional center and 24-hour telephone
Massachusetts	Massachusetts Public Health Biologics Laboratories 305 South St. Jamaica Plain, MA 02130 (617) 522-3700
Maine	American Red Cross Blood Services Northeast Region 812 Huntington Ave. Boston, MA 02115 (617) 731-2130
	American Red Cross Blood Services Northeast Region-Portland Location 524 Forest Ave. Portland, ME 04101 (207) 775-2367
Connecticut	American Red Cross Blood Services Connecticut Region 209 Farmington Ave. Farmington, CT 06032 (203) 678-2730
Vermont, New Hampshire	American Red Cross Blood Services Vermont-New Hampshire Region 32 N. Prospect St. Burlington, VT 05402 (802) 658-6400
Rhode Island	Rhode Island Blood Center 551 N. Main St. Providence, RI 02904 (401) 863-8368
New Jersey, New York	The Greater New York Blood Program 150 Amsterdam Ave. New York, NY 10023 (212) 570-3067 (212) 570-3068 (night)
New York	American Red Cross Blood Services Northeastern New York Region Hackett Blvd. at Clara Barton Dr. Albany, NY 12208 (518) 449-5020 (518) 462-7461 (518) 462-6964 (night)
	American Red Cross Blood Services Greater Buffalo Chapter 786 Delaware Ave. Buffalo, NY 14209 (716) 886-7500
	American Red Cross Blood Services Rochester Region 50 Prince St. Rochester, NY 14607 (716) 461-9800
	American Red Cross Blood Services Syracuse Region 636 S. Warren St. Syracuse, NY 13202 (315) 425-1647
Delaware, Pennsylvania, Southern New Jersey	American Red Cross Blood Services Penn-Jersey Region 23rd and Chestnut Philadelphia, PA 19103 (215) 299-4110
Maryland	American Red Cross Blood Services Baltimore Region 2701 N. Charles St. Baltimore, MD 21218 (301) 467-9905
Virginia	American Red Cross Blood Services Tidewater Region 611 W. Brambleton Ave. P.O. Box 1836 Norfolk, VA 23501 (804) 446-7708
	Richmond Metropolitan Blood Service 2201 Westwood Ave. Richmond, VA 23230 (804) 359-5100
Washington, D.C., Maryland, Virginia, West Virginia	American Red Cross Blood Services Washington Region 2025 E Street, N.W. Washington, DC 20006 (202) 728-6426
	American Red Cross Blood Services Tri-State Region 1111 Veterans Memorial Blvd P.O. Box 605 Huntington, WV 25710 (304) 522-0328

APPENDIX 5. Varicella-zoster immune globulin—regional distribution centers — Continued

Service area	Regional center and 24-hour telephone
Georgia	American Red Cross Blood Services Atlanta Region 1925 Monroe Dr., N.E. Atlanta, GA 30324 (404) 881-9800 (404) 881-6752 (night)
North Carolina	American Red Cross Blood Services Carolinas Region 2425 Park Rd. Charlotte, NC 28236 (704) 376-1661
South Carolina	American Red Cross Blood Services South Carolina Region 1100 Shirley St. Columbia, SC 29205 (803) 256-2301
Florida	South Florida Blood Service 1675 N.W. Ninth Ave. Miami, FL 33136 (305) 326-8888
	American Red Cross Blood Services Mid-Florida Region 341 White St. Daytona Beach, FL 32014 (904) 255-5444
Alabama, Mississippi	American Red Cross Blood Services Alabama Region 2225 Third Ave., N. Birmingham, AL 35203 (205) 322-5661
Indiana	American Red Cross Blood Services Fort Wayne Region 1212 E. California Rd. Fort Wayne, IN 46825 (219) 482-3781
Michigan	American Red Cross Blood Services Southeastern Michigan Region 100 Mack Ave. P.O. Box 351 Detroit, MI 48232 (313) 494-2715
	American Red Cross Blood Services Wolverine Region 202 E. Boulevard Dr. Flint, MI 48501 (313) 232-1176
	American Red Cross Blood Services Great Lakes Region 1800 E. Grand River Lansing, MI 48912 (517) 484-7461
Ohio	American Red Cross Blood Services Northern Ohio Region 3950 Chester Ave. Cleveland, OH 44114 (216) 781-1800
	American Red Cross Central Ohio Region 995 E. Broad St. Columbus, OH 43205 (614) 253-7981
Wisconsin, Iowa, North Dakota, South Dakota	The Blood Center of S.E. Wisconsin 1701 W. Wisconsin Ave. Milwaukee, WI 53233 (414) 933-5000
Wisconsin	American Red Cross Blood Services Badger Region 1202 Ann St. Madison, WI 53713 (608) 255-0021
Minnesota	American Red Cross Blood Services St. Paul Region 100 S. Robert St. St. Paul, MN 55107 (612) 291-6789 (612) 291-6767 (night)
Northern Illinois (Chicago)	American Red Cross Blood Services Mid-America Region 43 E. Ohio St. Chicago, IL 60611 (312) 440-2222

APPENDIX 5. Varicella-zoster immune globulin—regional distribution centers — Continued

Service area	Regional center and 24-hour telephone
Arkansas, Kansas, Kentucky, Missouri, Southern Illinois	American Red Cross Blood Services Missouri-Illinois Region 4050 Lindell Blvd. St. Louis, MO 63108 (314) 658-2000 (314) 658-2136 (night)
Nebraska	American Red Cross Blood Services Midwest Region 3838 Dewey Ave. Omaha, NE 68105 (402) 341-2723
Tennessee	American Red Cross Blood Services Nashville Region 321 22nd Ave., N. Nashville, TN 37203 (615) 327-1931, ext. 315
Louisiana, Oklahoma, Texas	Gulf Coast Regional Blood Center 1400 La Concha Houston, TX 77054-1802 (713) 791-6250
	American Red Cross Blood Services Central Texas Region McLennan County Chapter 4224 Cobbs Dr. Waco, TX 76710 (817) 776-8754
	American Red Cross Blood Services Red River Region 1809 Fifth St. Wichita Falls, TX 76301 (817) 322-8686
Colorado, New Mexico	United Blood Services 1515 University Blvd., N.E. P.O. Box 25445 Albuquerque, NM 87125 (505) 247-9831
Arizona	American Red Cross Blood Services Southern Arizona Region 222 South Cherry Ave. Tucson, AZ 85719 (602) 623-0541
Hawaii, Southern California	American Red Cross Blood Services L.A.-Orange Counties Region 1130 S. Vermont Ave. Los Angeles, CA 90006 (213) 739-5200
Nevada, Utah, Wyoming, Northern California	American Red Cross Blood Services Central California Region 333 McKendrie St. San Jose, CA 95110 (408) 292-1626
Alaska, Montana, Oregon	American Red Cross Blood Services Pacific Northwest Region 4200 S.W. Corbett St. Portland, OR 97201 (503) 243-5286
Idaho	American Red Cross Blood Services Snake River Region 5380 Franklin St. Boise, ID 83705 (208) 342-4500
Washington	Puget Sound Blood Center Terry at Madison Seattle, WA 98104 (206) 292-6525
Canada	Canadian Red Cross Blood Transfusion Service National Office 95 Wellesley St. E. Toronto, Ontario M4Y 1H6 (416) 923-6692
Puerto Rico	American Red Cross Servicio de Sangre Capitulo GPO Box 6046 San Juan, PR 00936 (809) 759-7979
Central and South America	South Florida Community Blood Center 1675 N.W. Ninth Ave. Miami, FL 33142 (305) 326-8888
All other countries	American Red Cross Blood Services Northeast Region 60 Kendrick St. Needham, MA 02194 (617) 449-0773
	American Red Cross Blood Services 812 Huntington Ave. Boston, MA 02115 (617) 731-2130

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