Immunizations for Foreign Travel

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One of the most important aspects of preparing travelers for destinations throughout the world is providing them with immunizations. Before administering any vaccines, however, a careful health and immunization history and travel itinerary should be obtained in order to determine vaccine indications and contraindications. There are three categories of immunizations for foreign travel. The first category includes immunizations which are routinely recommended whether or not the individual is traveling. Many travelers are due for primary vaccination or boosting against tetanus-diphtheria, measles-mumps-rubella, pneumococcal pneumonia, and influenza, for example, and the pre-travel visit is an ideal time to administer these. The second category are immunizations which might be required by a country as a condition for entry; these are yellow fever and cholera. The final category contains immunizations which are recommended because there is a risk of acquiring a particular disease during travel. Typhoid fever, meningococcal disease, rabies, and hepatitis are some examples. Travelers who are pregnant or who are infected with the human immunodeficiency virus require special consideration. Provision of appropriate immunizations for foreign travel is an important aspect of preventing illness in travelers.

The need to get "travel shots" is probably the most frequent reason for which an individual visits a physician's office prior to foreign travel. This visit provides an ideal opportunity to update immunizations routinely recommended for those individuals residing in the United States, in addition to providing those immunizations which should be given for a trip. The pre-travel visit is also the time to discuss other preventive measures, such as those against malaria and traveler's diarrhea, which are applicable to travel in the developing world [1,2]. Although internists, pediatricians, and family physicians are able to administer most travel immunizations in their offices, changing disease patterns and international health requirements, as well as complex itineraries, make it a difficult task to remain up to date. In addition, the administration of yellow fever vaccine is restricted by state health authorities, and other vaccines such as those against rabies or meningococcal meningitis may be too costly to maintain routinely in an office setting. Many areas now have travel clinics, run by specialists in tropical or travel medicine (emporiatries), which can provide the necessary immunizations, advice, and post-travel care at one site. Several excellent resources discuss immunizations; this review will put their use into the context of foreign travel [2-7].

Abbreviations:  BCG: bacillus of Calmette and Guérin  eIPV: inactivated polio vaccine of enhanced potency  HDCV: human diploid cell rabies vaccine  HIV: human immunodeficiency virus  IG: immune globulin  OPV: oral polio vaccine

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GENERAL CONSIDERATIONS

For each traveler, it is important that a detailed travel itinerary, including the areas to be visited within each country, duration of stay, and medical and immunization history be obtained before any immunizations are given. A trip to Nairobi, Kenya, for a week's business conference does not present the same level of health risk as does prolonged travel for a malaria research project on the shores of Lake Victoria, even though both trips are to Kenya.

Vaccinations can be divided into those which are routinely recommended whether or not a person is traveling, such as tetanus-diphtheria, those which are required by countries as a condition for entry, such as yellow fever, and those which are recommended because of potential risk during travel, such as typhoid fever. Each immunization and its schedule for administration is listed in Table 1.

It is important to distinguish between required and recommended vaccines. Required vaccines are those which one must have prior to being allowed to enter a country. Recommended vaccines are those which may be needed because infection could be acquired in the country of destination or in a particular location within that country. As an example, epidemic meningococcal disease only occurs in certain geographic areas of the world, and, if the traveler does not visit these areas, there is no need for that person to receive vaccine. On the other hand, typhoid fever occurs throughout the developing world but will be a risk to travelers only if they ingest untreated liquids or foods in areas of poor sanitation, such as may occur in rural areas and small villages. For those diseases which are transmitted by fecal contamination of the food and water supply, such as travelers' diarrhea, typhoid, poliomyelitis, cholera, hepatitis A, and giardiasis, the best prevention may be careful selection of food and liquids. If, however, there is unavoidable exposure to poor sanitation for more than two to three weeks, then it is reasonable to administer vaccines. For each of the potentially recommended vaccines, the physician must weigh the risk of disease acquisition with vaccine efficacy and side effects.

Vaccines are either inactivated viral or bacterial products, such as tetanus toxoid, typhoid, and rabies, or they are live, but attenuated, bacteria or viruses, such as yellow fever, oral poliomyelitis, and the new oral typhoid vaccine. Most parenteral vaccines, whether they are killed or attenuated, can be administered simultaneously at different sites, although cumulative side effects may preclude this procedure. If attenuated live viral vaccines cannot be given simultaneously, they should be given separated by one month. The administration of live vaccines may be contraindicated in certain groups of travelers, such as pregnant women [8] or immunocompromised hosts, including those with human immunodeficiency virus (HIV) infection [9-12]. These issues will be discussed in the sections which follow, and specific contraindications are also listed in Table 1. Tables 2 and 3 give general guidelines for the administration of vaccines to pregnant or HIV-infected travelers, respectively. Infants and small children can be considered for the same immunizations as adults; however, the schedule and the administration may need to be altered [2,5,6].

Prior to the administration of any biologic product, the manufacturer's full prescribing information should be consulted. For each vaccination, the type of vaccine, date of administration, dose, site, manufacturer, and lot number, as well as any untoward effects, should be recorded in the patient's record [13].
| Vaccine                  | Type                                      | Schedule<sup>a,b</sup> | Indications | Precautions and Contraindications<sup>c</sup> | Side Effects<sup>c</sup> |
|--------------------------|-------------------------------------------|-------------------------|-------------|-----------------------------------------------|-------------------------|
| **Tetanus-Diphtheria (Td)** | Adsorbed toxoids                          | Primary:                |             |                                               |                         |
|                          |                                           | Two doses (0.5 ml)      | All adults  | First trimester of pregnancy                  | Local reactions         |
|                          |                                           | IM, 4–8 weeks apart;    |             | Hypersensitivity or neurologic reaction to     | Occasional fever,       |
|                          |                                           | third dose 6–12 months  |             | previous doses                                | systemic symptoms       |
|                          |                                           | later                    |             | Severe local reaction                         | Arthus-like reactions in |
|                          |                                           | Booster:                 |             |                                               | persons with multiple   |
|                          |                                           | Every ten years          |             |                                               | previous boosters       |
|                          |                                           |                         |             |                                               | Rare—systemic allergy   |
| **Cholera**              | Phenol-killed *Vibrio cholera* (4 × 10<sup>9</sup>/ml) | Primary:                |             | Safety in pregnancy is unknown                | Local reaction of pain, |
|                          |                                           | 0.5 ml IM or SC, or     |             | Previous severe local or systemic reaction    | erythema, and indura-    |
|                          |                                           | 0.2 ml ID; give two     |             | Should not be administered                     | tion lasting 1–2         |
|                          |                                           | doses one week to        |             | simultaneously with yellow fever vaccine      | days                    |
|                          |                                           | one month apart, at     |             |                                               | Occasional fever,        |
|                          |                                           | least six days before    |             |                                               | malaise                 |
|                          |                                           | travel                   |             |                                               |                         |
|                          |                                           | Booster:                 |             |                                               |                         |
|                          |                                           | 0.5 ml IM or SC          |             |                                               |                         |
|                          |                                           | or                       |             |                                               |                         |
|                          |                                           | 0.2 ml ID given          |             |                                               |                         |
|                          |                                           | every six months         |             |                                               |                         |
| **Hemophilus influenzae** | HbOC—Polysaccharide conjugated to *Coryne- | Primary<sup>d</sup>:    | Children two months of age | Hypersensitivity to any | Mild local reactions in |
| Type b                   | bacterium diphtheriae toxoid              | Three doses (0.5 ml)    |             | of the vaccine components                     | approximately 10 per-   |
|                          |                                           | IM at two-month intervals|             |                                               | cent of patients        |
|                          |                                           | Booster<sup>d</sup>:     |             |                                               |                         |
|                          |                                           | One dose at 15 months    |             |                                               |                         |
| Vaccine                      | Type                                                                 | Schedule<sup>a,b</sup>                                                                 | Indications                        | Precautions and Contraindications<sup>c</sup> | Side Effects<sup>c</sup> |
|------------------------------|---------------------------------------------------------------------|----------------------------------------------------------------------------------------|------------------------------------|-----------------------------------------------|--------------------------|
| *Hemophilus influenzae*      | PRP-OMP—polysaccharide conjugated to *Neisseria meningitidis* outer membrane protein | Primary<sup>d</sup>: Two doses at a two-month interval Booster<sup>d</sup>: One dose at 12 months | Children two months of age          | Hypersensitivity to any of the vaccine components | Mild local reactions in approximately 10 percent of patients |
| Type b                       |                                                                     |                                                                                        |                                    |                                               |                          |
| *Hemophilus influenzae*      | PRP-D—polysaccharide conjugated to diphtheria toxoid                 | Primary: One dose (0.5 ml) IM Booster: None                                             | Children 15 months to five years   | Hypersensitivity to any of the vaccine components | Mild local reactions in approximately 10 percent of patients |
| Type b                       |                                                                     |                                                                                        |                                    |                                               |                          |
| *Streptococcus pneumoniae*   | Polysaccharide containing 23 serotypes                               | Primary: One dose (0.5 ml) SC or IM Booster: Recommended for some patients at high risk | Persons ≥ 2 years at increased risk of pneumococcal disease and its complications [see text] Healthy adults 65 years or older | Safety in pregnancy is unknown Previous pneumococcal vaccination | Approximately 50 percent of patients have mild erythema and pain at injection site Systemic reaction in < 1 percent of patients Arthus-like reaction with booster doses |
| *Neisseria meningitidis*     | Polysaccharide containing four serotypes (A, C, Y, W-135)           | Primary: One dose (0.5 ml) SC Booster: Not officially recommended; may be given after five years | Travelers to areas with epidemic meningococcal disease [see text] Asplenia or certain complement deficiency states | Safety in pregnancy is unknown | Infrequent, mild local reactions |
| Typhoid                      | Heat-phenol-inactivated *Salmonella typhi* (10<sup>9</sup>/ml)       | Primary: Two doses (0.5 ml) SC, given four or more weeks apart Booster: 0.5 ml SC or 0.1 ml ID, every three years | Risk for exposure to typhoid fever [see text] | Previous severe local or systemic reaction lasting 1–2 days Acetone-killed vaccines should not be given ID | Frequent local reaction of pain, swelling, and induration Occasional systemic reaction |
| Vaccine  | Type                              | Schedule<sup>a,b</sup>                      | Indications                                      | Precautions and Contraindications<sup>c</sup>                                                                 | Side Effects<sup>c</sup>                                      |
|---------|----------------------------------|--------------------------------------------|-------------------------------------------------|-------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| **Typhoid** | Attenuated Ty 21a strain of *Salmonella typhi* | Primary: One capsule orally given on alternate days for four doses | Risk for exposure to typhoid fever [see text] | Safety in pregnancy is unknown | Infrequent gastrointestinal upset, rash |
|         |                                  | Booster: Every five years                   |                                                 | Immunocompromised host<sup>c</sup> Children &lt; 6 years Persons with an acute febrile or gastrointestinal illness Persons taking antibiotics Refrigerate capsules |                                                 |
| **Measles** | Attenuated live virus (available in monovalent form or combined with rubella [MR] ± mumps [MMR]) | Primary: Two doses (0.5 ml) SC; see text for interval between doses | Persons born after 1956 who have not had documented measles infection or received two doses of live measles vaccine | Pregnancy Immunocompromised host<sup>c</sup> (HIV-infected persons may be vaccinated) History of anaphylaxis to eggs or neomycin Should not be administered with immune globulin [see text] | Temperature of ≥ 39.4°C, 5–21 days after vaccination in 5–15 percent Transient rash in 5 percent Of persons previously immunized with killed vaccine (1963–1967), 4–55 percent have a local reaction |
| **Mumps** | Attenuated live virus            | Primary: One dose (0.5 ml) SC (usually given as part of MMR vaccine) | Persons born after 1956 who have not had documented mumps | Pregnancy Immunocompromised host<sup>c</sup> History of anaphylaxis to eggs or neomycin Should not be administered with immune globulin [see text] | Mild allergic reactions uncommon Rare—parotitis |
| Vaccine   | Type                                     | Schedule<sup>a,b</sup>                                                                 | Indications                                      | Precautions and Contraindications<sup>c</sup> | Side Effects<sup>c</sup> |
|-----------|------------------------------------------|-----------------------------------------------------------------------------------------|-------------------------------------------------|-----------------------------------------------|-------------------------|
| Poliomyelitis | Attenuated live virus, trivalent | Primary: Three oral doses, the first two given at a six- to eight-week interval, the third, eight to 12 months later | Children and adolescents < 18 years of age | Immunocompromised host<sup>c</sup> or immunocompromised contacts of recipients | Rare paralysis [see text] |
|           |                                          | Booser: One oral dose                                                                  |                                                 | Not used for primary immunization in persons ≥ 18 years |                         |
|           |                                          | Boost previously immunized persons; complete series in partially immunized adults; alternative to inactivated poliomyelitis vaccine in previously unimmunized adults when there is < 1 month before travel |                                                 |                                                               |                         |
| Rubella   | Attenuated live virus                    | Primary: One dose (0.5 ml) SC (usually given as part of MR or MMR) | All persons, particularly women of childbearing age, without documented illness or live vaccine on or after first birthday | Pregnancy | Up to 40 percent of post-pubertal females have joint pains, transient arthritis, beginning 3–25 days after vaccination, persisting 1–11 days |                         |
|           |                                          | Booster: None                                                                          |                                                 | Immunocompromised host<sup>c</sup> | Frank arthritis in < 2 percent |                         |
|           |                                          |                                                                                       |                                                 | History of anaphylaxis to neomycin |                         |                         |
|           |                                          |                                                                                       |                                                 | Should not be administered with immune globulin [see text] |                         |
| Vaccine            | Type                              | Schedule<sup>a,b</sup>                                      | Indications                                                                 | Precautions and Contraindications<sup>c</sup>                                                                 | Side Effects<sup>c</sup> |
|-------------------|-----------------------------------|-------------------------------------------------------------|-----------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|------------------------|
| Yellow Fever      | Attenuated live virus             | Primary: One dose (0.5 ml) SC, ten days to ten years before travel; Booster: Every ten years | As required by individual countries                                          | Avoid in pregnant women, unless high-risk travel; Prudent to avoid vaccinating infants < 9 months; Immunocompromised host; Hypersensitivity to eggs; Should not be administered simultaneously with cholera vaccine | 2–5 percent—mild headache, myalgia, fever, 5–10 days after vaccination; Rare—immediate hypersensitivity |
|                   |                                   |                                                             |                                                                             |                                                                                                                 |                        |
| Hepatitis B       | Yeast-derived recombinant hepatitis B surface antigen | Primary<sup>f</sup>: Three doses (1.0 ml), IM in deltoid, at 0, 1, and 6 months; Booster: Not routinely recommended | Health care workers in contact with blood persons residing for > 6 months in areas of high endemicity for hepatitis B surface antigen; Others at risk for contact with blood, body fluids, or potentially contaminated medical or dental instruments | Although safety to fetus is not known, pregnancy is not a contraindication in high-risk women | Mild local reactions in 10–20 percent |
|                   |                                   |                                                             |                                                                             |                                                                                                                 |                        |
| Poliomyelitis     | Killed poliomyelitis virus, trivalent; enhanced potency | Primary: Two doses (0.5 ml) SC at a 4- to 8-week interval; third dose 6–12 months after second; Booster: One lifetime dose (0.5 ml) SC | Preferred for persons 18 years and older, and for immunocompromised hosts<sup>e</sup> | Safety in pregnancy is unknown; Anaphylactic reactions to streptomycin or neomycin | Mild local reaction    |
TABLE 1—Continued

| Vaccine                  | Type                                      | Schedule<sup>a,b</sup>                                                                 | Indications                                                                 | Precautions and Contraindications<sup>c</sup>                                  | Side Effects<sup>c</sup>                                                                 |
|-------------------------|------------------------------------------|----------------------------------------------------------------------------------------|------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| Influenza               | Inactivated whole and split influenza A and B virus | Annual vaccination with current vaccine                                                   | Persons ≥ 6 months of age at increased risk of complications from influenza [see text] | First trimester of pregnancy is a relative contraindication Anaphylaxis to eggs          | Mild local reactions in < one-third of recipients Occasional systemic reaction of malaise, myalgia, beginning 6–12 hours after vaccination and lasting 1–2 days Rare allergic reaction |
| Japanese B Encephalitis | Inactivated virus                         | Primary: Three doses SC at weekly intervals Booster: One dose at 12–18 months and then every four years | Travelers to areas of risk [see text] with rural exposure or prolonged residence | Pregnancy Allergy to mice or rodents Immunocompromised host<sup>c</sup>                   | Local mild reactions lasting 1–3 days Occasional systemic symptoms of malaise, myalgias, and fever |
| Rabies                  | Inactivated virus grown in human diploid cells | Pre-exposure: 1 ml IM in deltoid or 0.1 ml ID on days 0, 7, and 21 or 28 Booster: Depends upon risk category and is based upon serologic testing; dose is 1.0 ml IM or 0.1 ml ID | Travel to areas for > 1 month where rabies is a constant threat | Allergy to previous doses May be given in pregnancy if indicated ID route should be completed ≥ 30 days before travel ID route should not be used with concurrent chloroquine or mefloquine administration | Approximately 30 percent have local reactions Approximately 20 percent have mild systemic reactions of headache, nausea, aches, and dizziness Rare neurologic illness Occasional (6 percent) immune-complex reactions with booster doses occurring 2–21 days after vaccination |
**TABLE 1—Continued**

| Vaccine       | Type                                   | Schedule<sup>a,b</sup>            | Indications                        | Precautions and Contraindications<sup>c</sup> | Side Effects<sup>c</sup>     |
|---------------|----------------------------------------|-----------------------------------|------------------------------------|-----------------------------------------------|-------------------------------|
| Immune globulin | Fractionated immuno-globulins (primarily IgG) | Travel of < 3 months duration: 0.02 ml/kg Travel > 3 months: 0.06 ml/kg every 4–6 months | For prevention of hepatitis A Some travelers may benefit from pre-travel hepatitis A antibody testing [see text] | —                              | Transient local discomfort Rare systemic reaction |

<sup>a</sup>Manufacturer's full prescribing information should be consulted.

<sup>b</sup>Abbreviations: IM, intramuscularly; SC, subcutaneously; ID, intradermally

<sup>c</sup>Only major precautions, contraindications, and side effects listed

<sup>d</sup>Schedule of administration will vary if child does not start vaccination at two months of age.

<sup>e</sup>Persons immunocompromised because of immunodeficiency diseases, leukemia, lymphoma, generalized malignancy, or AIDS, or immunosuppressed from therapy with corticosteroids, alkylating agents, antimetabolites, or radiation

<sup>f</sup>One vaccine (Engerix-B<sup>®</sup>) can be given in an alternative four-dose schedule of 0, 1, 2, and 12 months.

*Source: Adapted, with permission, from [1]*
IMMUNIZATIONS

Routinely Recommended Immunizations

The pre-travel visit is an ideal time to update routinely recommended immunizations for both children and adults. The vaccine coverage for many travelers may be inadequate, putting them at risk for vaccine-preventable disease [14,15]. At the International Traveler’s Medical Service at the University of Connecticut Health Center, 43 percent of travelers were due for boosting against tetanus-diphtheria, 55 percent of those born in 1957 and later for a primary series or booster for measles, and 70 percent for poliomyelitis if their travel itinerary included a polio risk [14]. In addition, the wide age range of this group (4 percent were 12 years old and younger, and 13 percent were 65 years and older) provides the opportunity to bring children up to date on childhood immunizations and the elderly on influenza and pneumococcal vaccine. The immunizations listed below can be considered as routinely recommended. Although there has been a recent recommendation to include protection against hepatitis B as part of routine childhood immunizations, this vaccine will be discussed in the later section on immunizations recommended because of exposure [16].

1. Tetanus-Diphtheria Toxoids: Adults over the age of 50 constitute nearly 70 percent of tetanus cases in the United States. Most of these occurred in persons who were never immunized, received an incomplete primary series, or, rarely, had gone longer than ten years since their last booster [17,18]. In addition, recent antibody studies also indicate that over 50 percent of adults may be susceptible to diphtheria [19]. For these reasons, all adults should have completed a primary series of tetanus-diptheria and received boosters with the combined toxoids at ten-year intervals. Children under seven should receive the combined tetanus-diphtheria-pertussis vaccine.

Some adult travelers may benefit from a booster of tetanus-diphtheria at a five- to ten-year interval, because they will not need either tetanus immune globulin or a booster if they sustain a tetanus-prone wound and have been boosted within five years [17]. Obtaining immunization before travel may be easier and safer than receiving an injection in a developing area, where the sterility of needles and vaccine storage conditions may be inadequate.

2. Measles: In the last few years, recommendations for measles immunization have been changed to include a two-dose schedule for the primary immunization of children and revaccination of selected older children and young adults [20,21]. The reason for this change has been the dramatic increase in measles cases in the United States in 1989 and 1990, when the number of annual cases rose nearly tenfold to over 27,000 cases [22]. These cases primarily occurred in unvaccinated, inner-city children ≤ 5 years of age, and in previously vaccinated school and college age individuals (five to 19 years). Measles which occurs in persons previously vaccinated is thought to be due to primary vaccine failure rather than to waning immunity.

Travel overseas may also constitute a substantial measles exposure to the unprotected traveler. From 1983 to 1988, 4 to 22 percent of measles cases (1,478 cases) were epidemiologically linked within two generations to international travel [23,24], and about half of the initial cases were in returning Americans. In addition, during this period, 8 percent of all outbreaks of measles in the United States could be traced to an imported case [23,25].
All international travelers should be immune to measles [26]. Children traveling to high-risk areas where they are likely to be exposed at a young age can be vaccinated from six to 12 months with single-antigen (monovalent) measles vaccine, and from 12 to 15 months with the trivalent, measles-mumps-rubella vaccine. These children should be reimmunized at 15 months with the trivalent vaccine and should receive an additional dose at entry to school [20].

Travelers born in 1957 and later who have not had physician-documented measles, laboratory evidence of immunity, or two doses of live vaccine, with the second dose administered after 1980, should be given a one-time dose of measles vaccine. If they have never been immunized, they should receive two doses of vaccine, separated by at least one month. Those born before 1957 can be considered immune secondary to natural infection.

3. Rubella, Mumps: Women travelers who are of childbearing age should be immune to rubella. If they are susceptible, they should be vaccinated to prevent congenital rubella syndrome [27]. Most adults have been naturally infected with mumps virus; however, if an adult is susceptible, vaccination may be considered [28]. Many physicians will give the trivalent, measles-mumps-rubella vaccine if immunity to one or more of the three viruses is lacking. The side effects are not increased if a traveler receives a vaccine to which he or she is already immune. Immune globulin should not be given less than three months before or two weeks after measles, mumps, or rubella vaccine so that there is no interference with vaccine immunogenicity because of the passive transfer of antibodies.

4. Pneumococcal Vaccine: With approximately 13 percent of a travel population age 65 years and older, both pneumococcal and influenza immunization become particularly important. While the efficacy of pneumococcal vaccine in elderly or chronically ill populations may be limited, it is still recommended for well-defined risk groups. These risk groups include healthy persons 65 years of age and older and adults or children ≥ 2 years old with chronic illness or immunosuppression, which predisposes them to a higher risk for complications from bacteremic or pulmonary infection with the pneumococcus. The vaccine consists of antigenic polysaccharides from 23 serotypes of *Streptococcus pneumoniae* and has replaced the older 14-valent vaccine [29].

5. Influenza: Influenza occurs throughout the world and is a risk for persons traveling to the tropics at any time of the year or to the Southern Hemisphere during April to September. The composition of the influenza vaccine is determined annually and includes the viral subtypes of influenza A and B which are projected to cause disease in the United States [30]. The influenza viruses which are active in the developing world may or may not, however, be included in the U.S. vaccine [31]. Vaccination is recommended for adults and children who are likely to experience complications from influenza and for persons such as health care workers, who have an increased risk of influenza because of exposure [30]. Persons who may have complications from influenza are those with chronic disorders of the cardiovascular or pulmonary system, persons with other chronic medical conditions, nursing home residents, healthy persons age 65 and older, and children (age six months to 18 years) on chronic aspirin therapy.

6. Haemophilus influenzae Type b: There are now three conjugate vaccines using the polysaccharide capsule of *Hemophilus influenzae* type b for the prevention of invasive *H. influenzae* disease [32]. Two of these, HibTITER® and PedvaxHIB®,
are licensed for use in children beginning at two months of age, and one, ProHIB-IT®, is licensed for use at age 15 months and older. Each vaccine differs in the conjugated protein carrier used to stimulate T-cell responses, the size of the polysaccharide, the method of chemical conjugation, and the schedule of administration. All children, beginning at age two months, should receive protection against H. influenzae as part of their routine childhood immunizations. Those children older than two months and up to five years of age should receive the vaccine in a modified dosing schedule [32]. Immunization with the conjugate vaccines does not protect against the carrier protein, nor does it preclude immunizations with the other standard vaccines, such as diphtheria and tetanus toxoids and pertussis vaccine.

Required Immunizations

The vaccinations which may be required by a country prior to allowing the traveler to enter are yellow fever and cholera. A list of vaccine requirements by country is published annually by the Centers for Disease Control in Health Information for International Travel [2]. According to international health regulations, required vaccinations must be recorded in the document “International Certificate of Vaccination” [33], and validated by a stamp issued by state health departments. No vaccinations are required to re-enter the United States by returning U.S. residents. In 1980, the World Health Organization declared the world free of smallpox. Accordingly, in 1982, smallpox vaccination was no longer required for international travel and should not be given for this purpose [34].

1. Yellow Fever: Yellow fever is a viral disease transmitted by mosquitoes. Areas where cases of yellow fever are occurring are called “infected” areas. These lie primarily in equatorial South America and in Africa, for approximately 15 degrees on either side of the equator [35], and can be determined specifically by consulting the Summary of Health Information for International Travel, published every two weeks by the Centers for Disease Control [36]. In recent years, jungle yellow fever in non-human primates has been reported from Trinidad and Tobago [37]. Areas in Africa and South America where infection could occur, but where cases are not being reported, are called “endemic zones.”

The yellow fever vaccine should be given to persons who are traveling to or living in “infected” areas, and to persons who visit rural areas of countries in the “endemic zones” for yellow fever [38]. Some countries which do not lie in the endemic zones, particularly those in Asia, may require immunization for persons entering from an area where yellow fever is occurring. The vaccine is given only in approved vaccination centers because of its requirement for cold storage and viability for only 60 minutes after reconstitution. One can call state or local health departments to identify these centers. If cholera and yellow fever vaccines are both given, they should ideally be separated by a minimum of three weeks, since simultaneous administration may interfere with the antibody response to each vaccine [39]. Immune globulin does not interfere with the response to yellow fever vaccine.

2. Cholera: The outbreak of cholera which began in January of 1991 in western South America and has spread to Mexico, Central America, and other areas of South America, has captured world attention [40]. This outbreak emphasizes what can happen when an infectious agent such as Vibrio cholerae is introduced into a susceptible population. Although a few cases have occurred in tourists to these areas, the overall risk of cholera remains extremely low for those who exercise caution in
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food and water sanitation [41,42]. The poor vaccine efficacy, combined with its uncomfortable side effects, make vaccination infrequently indicated [43]. In accordance with this information, in 1988 the World Health Organization no longer recommended cholera immunization for international travel. No country requires administration of cholera vaccine before direct travel from the United States, and fewer than ten countries require vaccination before entry from a country reporting cholera, such as entering Pakistan from India or Tanzania from Kenya [2].

Persons who may be considered for vaccination are those who will work and live in highly endemic areas with poor sanitary conditions and persons with impaired gastrointestinal defense mechanisms. One dose, properly recorded and given at least six days before travel, is satisfactory for entry into countries requiring vaccination. A letter of medical contraindication should suffice for those travelers who either cannot or do not wish to receive vaccine. Studies continue on new oral preparations of vaccine [44].

**Immunizations Recommended Because of Exposure**

1. **Typhoid:** The risk of typhoid fever varies by destination. In a retrospective review of typhoid cases in the United States, it was estimated that 0.1 per one million travelers to Northern Europe compared with over 100 per one million travelers to India, Pakistan, or Peru will acquire typhoid fever [45]. Two vaccines are currently available in the United States for protection: the older inactivated vaccine and a recently released attenuated oral vaccine [46]. A third vaccine, which has not yet been licensed in the United States, contains purified Vi capsular polysaccharide of *S. typhi* and has approximately 70 percent efficacy over one to two years [47,48].

   The attenuated oral vaccine uses the Ty 21a mutant of *S. typhi* that produces enough lipopolysaccharide to be immunogenic but does not undergo sustained replication [49]. In a large-scale field trial in Chilean school children, it had an efficacy of 67 percent [50], which is similar to that of the older heat-phenol-inactivated parenteral vaccine (50 percent to 70 percent). The attenuated vaccine, however, is easier to give because of its oral route of administration, is better tolerated by the patient, and can be completed within a week of starting the procedure. Strict instructions need to be given to recipients to assure vaccine refrigeration and compliance with each dose given on alternate days for a total of four doses [51].

   Typhoid vaccine should be given to travelers visiting areas endemic for typhoid fever, where fecally contaminated food and water are likely to be ingested [52]. Travelers to areas where *Salmonella typhi* is resistant to antimicrobial agents should also be considered for vaccination. Although it is not stated in the product insert, the oral typhoid vaccine may interfere with the response to oral polio vaccine, suggesting that their administration should be separated by at least two weeks [53]. It may also be best to delay initiation of anti-malarial prophylaxis until a week after completing oral typhoid vaccine because of the theoretical antimicrobial effect of anti-malarials [53].

2. **Meningococcal Disease:** Several areas of the world have epidemic meningococcal disease, which poses a low, but potential, risk to international travelers [54]. Trekkers in Nepal, travelers to the New Delhi region of India, to Kenya or Tanzania, religious pilgrims to Saudi Arabia, and long-term visitors to sub-Saharan Africa should be considered at potential risk and vaccinated [54,55]. The epidemic serotype
is usually type A, which is contained in the current quadrivalent vaccine (groups A, C, Y, and W-135). The vaccine is available in single-dose vials.

3. **Plague:** The efficacy of plague vaccine has not been demonstrated in any controlled trial. The vaccine is not required by any country, and the risk to an individual traveler is extremely small; therefore, vaccination is rarely recommended for international travel [56]. Prophylactic antibiotics may be indicated for the traveler with a definite exposure.

4. **Tuberculosis prevention:** A traveler to the developing world is at risk for tuberculosis if that person has prolonged contact with respiratory droplets from infected persons in a closed setting. The approach to these travelers should not be vaccination with the bacillus of Calmette and Guérin (BCG) vaccine, but pre- and post-travel tuberculin skin testing [57]. For those rare children who will have unavoidable exposure to tuberculosis and for whom other preventive measures such as prophylactic isoniazid have failed or cannot be used, BCG vaccine may be considered.

5. **Poliomyelitis:** The decade of the 1990s holds the hope of elimination of polio from the Americas [58]. Already 30 percent of the world’s population lives in polio-free areas. Polio virus remains endemic throughout many areas of the developing world, however, particularly in Asia and Africa, and, if vaccine coverage falls, poliomyelitis can occur in the developed world as well [59]. The risk for poliomyelitis for an international traveler is extremely small [60]. In the United States, of 138 cases of paralytic polio from 1973 to 1984, only 13 cases were imported [61]. Nevertheless, all travelers to areas of risk with exposure to poor food and water sanitation should be immunized to polio.

There are two vaccines for protection against polio: the oral polio vaccine (OPV; Sabin, live attenuated trivalent vaccine), and the inactivated polio vaccine of enhanced potency (eIPV). The eIPV has replaced the conventional inactivated polio virus vaccine (Salk vaccine). Primary immunization of children in the United States is accomplished with OPV [62]. Because rare cases of paralytic polio are associated with OPV, it is usually not given as primary vaccination in adults. The risk of paralysis in first-time recipients of OPV and contacts of recipients is approximately one case per 520,000 doses, and, for all subsequent doses, one case per 12.3 million doses [61]. Contacts of vaccine recipients accounted for nearly 60 percent of cases. These contacts were usually unimmunized or inadequately immunized parents or relatives of a child who received OPV.

Primary vaccination for persons 18 years or older should be done with eIPV [63]. If at least two doses of eIPV cannot be given before protection is required (less than four weeks before departure), a single dose of either oral polio vaccine or eIPV can be given. If a person has completed or started a primary series with either OPV or an inactivated polio vaccine, either oral polio vaccine or eIPV may be used to complete the series or to boost the patient’s response. It is recommended that persons who have completed a primary series receive a one-time booster if traveling to an area of risk. Both oral polio vaccine and eIPV provide long-term immunity and may be given with immune globulin.

6. **Japanese B Encephalitis:** The risk of Japanese B encephalitis to the international traveler is extremely low; however, rare fatalities have occurred and have prompted interest in vaccination [64]. Japanese B encephalitis is a mosquito-transmitted flavivirus infection of the central nervous system, and occurs in temper-
ate zones (China, Japan [little to no risk], Korea, the lowlands of Nepal, Burma, Bangladesh, Kampuchea, Laos, northern India, and Thailand, and the eastern part of the former Union of Soviet Socialist Republics) from June through September, and in tropical zones (southern India and Thailand, Taiwan, Indonesia, the Philippines, Malaysia, Sri Lanka, and Singapore), throughout the entire year [65]. Over 98 percent of infections are unapparent, but among those patients with symptomatic disease, the fatality rate is approximately 20 percent, with a high morbidity in survivors [66,67]. Clinical disease occurs primarily in young children and adults more than 65 years of age.

Beginning in May 1983, a monovalent inactivated vaccine, purified from mouse brain (BIKEN, The Research Foundation for Microbial Diseases, Osaka University, Japan), was studied under an investigational new drug exemption in the United States. The vaccine was immunogenic and well-tolerated in a three-dose schedule [68], and in the Far East it has been safe and effective, based on years of use [69]. Nevertheless, because of concern about liability protection, the vaccine was withdrawn from the United States in July of 1987. Efforts are under way, by the Centers for Disease Control, Connaught Laboratories, Inc., the Food and Drug Administration, and the U.S. Army, to obtain a product license.

Persons are at risk for Japanese B encephalitis if they are traveling in endemic areas for more than three weeks and will have rural exposure in areas of rice and pig farming during the summer months [66–68]. If they will not have such exposure, but are planning prolonged residence in endemic countries, they should also be vaccinated. Until the vaccine is licensed in the United States, travelers should obtain vaccine in the country of destination. All travelers should exercise prevention measures against the Culex mosquito, the vector for transmission.

7. Rabies: Although the risk of rabies during travel is very low, all travelers should be informed about it because animal rabies remains endemic in many areas of Latin America, the Far East, and Africa. Those countries which report no cases of rabies are listed in Health Information for International Travel [2]. Dog rabies continues to be the major reservoir for transmission to humans, with eight of ten cases of rabies in travelers from 1975 to 1984 associated with dog bites [70]. Some of the dogs had been vaccinated against rabies in the foreign country, raising important questions about the type and method of delivery of vaccine.

The first step after being bitten by a potentially rabid animal is thorough cleansing of the wound with soap and water. If the traveler has not received pre-exposure rabies prophylaxis, the individual should then seek immediate post-exposure prophylaxis. Pre-exposure prophylaxis does not eliminate the need for prophylaxis after exposure, but does make the treatment easier by requiring fewer doses of vaccine and eliminating the need for human rabies immune globulin.

Travelers who should be considered for rabies vaccine are those who will live for one month or more in an area where rabies is a constant threat [71]. The primary vaccine available in the United States is the human diploid cell rabies vaccine (HDCV). An absorbed vaccine adapted to fetal rhesus lung tissue is available to residents of Michigan from the Michigan Department of Public Health. HDCV can be administered either intradermally or intramuscularly [71]. If vaccination cannot be completed before initiating malaria chemoprophylaxis, then the intramuscular route is necessary. The simultaneous administration of chloroquine for malaria prophylaxis has been shown to decrease the immune response to intradermally
administered vaccine [72]. Although this phenomenon has not been studied with mefloquine, it would seem prudent to avoid the intradermal route when mefloquine is being given. As with other intramuscular vaccines for adults, intramuscular rabies vaccine should be given in the deltidoid muscle in order to assure adequate absorption.

8. **Hepatitis Prophylaxis:**

**Hepatitis A:** The highest risk for hepatitis A occurs with travel to rural areas with poor hygiene, outside the usual tourist routes [73]. Because hepatitis A has occurred in travelers on standard tourist itineraries, however, most travelers should be offered protection. Hepatitis A in travelers who have not received prophylaxis occurs from one to ten times per 1,000 travelers for a two- to three-week stay in the developing world [74].

Prevention of hepatitis A is achieved with immune globulin (IG), a sterile preparation of purified antibodies, primarily of IgG type, which contains high titers against hepatitis A. IG prepared in the United States has not transmitted any viral infections, including hepatitis B or HIV [75]. The protection conferred by IG is short-lived, two to three months for the standard dose (0.02 ml/kg) and four to six months for the higher dose (0.06 ml/kg). For those travelers who remain overseas for more than six months, regular administration (at four- to six-month intervals) is necessary. Pre-travel anti-hepatitis A IgG antibody screening may be helpful for travelers who are frequent visitors to the developing world, or who are likely to have acquired hepatitis A in the past, and would prefer not to get the intermittent injections of IG. Persons who may have acquired hepatitis A previously are those over the age of 50, those who were born or lived for a prolonged time in the developing world, and those with a history of hepatitis [76]. Human trials are currently under way with whole-cell inactivated hepatitis A vaccines, and preliminary studies have examined live, attenuated, and recombinant vaccines [77,78]. Killed, whole-cell vaccines seem most promising [79].

**Hepatitis B:** Hepatitis B is a risk for short- or long-term travelers with exposure to blood or body fluids, and for long-term travelers (≥6 months) to countries with a high seroprevalence of hepatitis B surface antigen carriage. Those who are at risk because of exposure are usually physicians, nurses, other health care workers, and laboratory technicians, and those who are likely to have sexual exposure [73]. Regions with a high prevalence (5 percent to 20 percent) of hepatitis B carriage include China, southeast Asia, sub-Sahara Africa, the Amazon basin, and parts of the Middle East.

Vaccines which contain recombinant hepatitis B surface antigen have replaced the original plasma-derived vaccine in the United States. Hepatitis B vaccines should be administered intramuscularly in the deltidoid in order to assure an optimal response. One vaccine can be given in a four-dose schedule, with the first three doses given over two months (Table 1). This timing can allow a more rapid achievement of immunity prior to travel for those who might require it. To date, vaccine boosting has not been recommended for the non-compromised host [16,73]. Vaccination against hepatitis B will protect the traveler against delta hepatitis, since this agent requires active hepatitis B replication [80].

**Enterically Transmitted Hepatitis:** A new form of enterically transmitted non-A, non-B hepatitis has been recognized in Mexico, the Indian subcontinent, and Africa over the past decade [81]. Several outbreaks [82] have been linked to a fecally contaminated water source, often after heavy rains [83]. Pregnant women have had a
TABLE 2
Immunization of the Pregnant Traveler

| Vaccine                             | Safety |
|-------------------------------------|--------|
| **Bacterial**                       |        |
| Tetanus-Diphtheria                  | Yes\*  |
| Pneumococcal                        | Yes\*  |
| Meningococcal                       | Yes\*  |
| Typhoid                             |        |
| Killed                              | No     |
| Live, Attenuated                    | Unknown\* |
| Cholera                             | No     |
| **Viral**                           |        |
| Poliomyelitis                       |        |
| Inactivated                         | Yes    |
| Live, Attenuated                    | Yes    |
| Yellow Fever                        | Yes\*  |
| Measles, Mumps, Rubella             | No     |
| Influenza                           | Yes\*  |
| Rabies                              | Yes    |
| Japanese B Encephalitis             | Unknown\* |
| Hepatitis B                         | Yes    |
| Immune Globulin                     | Yes    |

*Should ideally wait until after the first trimester
\*Probably safe, but has not been studied conclusively
\*Safety is unknown, and vaccination should be avoided until further study.
\*Should generally be avoided, but may be given with high-risk exposure

particularly high mortality rate. Immune globulin preparations manufactured in the United States are not expected to prevent this form of hepatitis [83], and proper food and liquid sanitation will be the most important mode of prevention.

IMMUNIZATION OF SPECIAL GROUPS

The Pregnant Traveler

During the pre-travel evaluation of the pregnant traveler, one needs to consider the likelihood of acquiring a vaccine-preventable disease during the trip, the consequences of this disease to the mother and her unborn child, and the potential risks and benefits of vaccination to both mother and child. There are several sources which help to assess these factors [2–4,7,8]. While many vaccines may be safely tolerated during pregnancy, it is best to avoid vaccination altogether, if possible, or at least to delay it until after the first trimester. Table 2 lists recommendations for vaccine administration to pregnant travelers.

1. Bacterial Vaccines: If tetanus-diphtheria boosting is needed, it can be given safely, although one should ideally wait until after the first trimester has been completed. The polysaccharide vaccines, pneumococcal and meningococcal vaccines, may be given to high-risk women, although their safety during pregnancy has not been conclusively studied. The whole-cell, killed bacteria vaccines, typhoid and cholera, can cause systemic febrile reactions and may put the fetus at risk. They should, therefore, be avoided. If cholera vaccination is required, a letter of medical contraindication to the vaccine should be sufficient. There is no information on the
use of the new attenuated, live, oral typhoid vaccine. Unless there is a strong indication, vaccination with this type should probably be avoided. For prevention of cholera and typhoid fever, emphasis should be placed on food and liquid sanitation.

2. Viral Vaccines: In general, live viral vaccines should be avoided during pregnancy. If, however, there is substantial risk for poliomyelitis during travel, either OPV or eIPV can be given. Travel to areas where yellow fever epidemics are occurring should be postponed until after pregnancy. If travel cannot be avoided, however, the pregnant traveler may be vaccinated. For those going to an area where the actual risk of disease from yellow fever is minimal, but vaccine is required, a letter of medical contraindication may be given. Vaccination against measles, rubella, or mumps should be deferred until after pregnancy.

Women who are at high risk for complications from influenza may be immunized. Pre-exposure rabies vaccine is also considered safe for women at risk. Because of the potentially severe consequences of hepatitis B in children born to women with hepatitis B infection, vaccination may be considered. There is no information on the safety of Japanese B encephalitis vaccine in pregnant women, and it should be avoided until further information is gained. Administration of immune globulin for the passive prophylaxis of hepatitis A is safe.

The HIV-Infected Traveler

The high prevalence of HIV infection emphasizes the need to assess a traveler’s risk factors for HIV. If a traveler is found to be infected with HIV, there are several important issues to consider when counseling such an HIV-infected traveler. First, many countries have instituted HIV testing for long-term travelers, which could result in an individual being barred from entry or residence within a country [84,85]. Second, many diseases such as salmonellosis, cryptosporidium, tuberculosis, and leishmaniasis are more prevalent in the developing world and may have more severe or prolonged clinical courses in HIV-infected or AIDS travelers [12,86–89]. Finally, access to sophisticated medical care may be limited, increasing the potential morbidity from an HIV-associated illness such as Pneumocystis carinii pneumonia.

The two issues of efficacy and safety also apply to immunizing HIV-infected travelers [9–12]. Many vaccines are less immunogenic in HIV-positive individuals, and response rates decline as HIV infection advances [90]. Moreover, there are theoretical risks of progressive, disseminated infections with attenuated live vaccines, as has occurred with BCG and vaccinia virus [91,92]. In contrast, the morbidity from measles outweighs the theoretical risk of vaccine toxicity [93,94]. Each of these issues needs to be considered and discussed with the HIV-infected traveler prior to vaccine administration. Table 3 provides guidelines for the immunization of asymptomatic HIV-infected travelers and those with symptomatic infection and AIDS. It may be reasonable to determine the CD4 lymphocyte count prior to vaccine administration, both to predict the potential response to vaccination and to assess the potential risk of the vaccine [12].

1. Bacterial Vaccines: The inactivated bacterial vaccines can be given safely. Tetanus-diphtheria should be given by the routine schedule. Because HIV-infected persons are at increased risk from infections with encapsulated bacteria, they should be protected with both pneumococcal and Hemophilus influenzae vaccines. Meningococcal vaccine should be given to those who travel to areas of risk. Although there is no data on the safety of the live, attenuated vaccine against S. typhi, it would be
prudent to avoid this type and to give the killed, whole-cell preparation. The minimal risk for cholera and poor vaccine efficacy do not justify routine vaccination. Some AIDS patients may be at higher risk for enteric organisms because of lowered gastric acidity, however, and for these travelers at risk for cholera, vaccination may be considered [95]. BCG vaccination is unnecessary, may be dangerous, and should be avoided.

2. **Viral Vaccines:** Inactivated viral vaccines should be used for protection against viral illness. Influenza immunization should be given annually to HIV-infected patients. Protection against polio should be achieved with eIPV rather than with OPV because of the risk of vaccine-associated paralysis. Because of the high incidence of hepatitis B infection in the HIV-infected population, pre-vaccination screening for hepatitis B antigen and antibody should be done. If rabies prevention is needed, the intramuscular route of administration should be used in order to assure the maximum immune response. There is no information on safety or efficacy of Japanese B encephalitis vaccine in immunocompromised hosts. Immune globulin may be administered safely.

Although yellow fever vaccine has been demonstrated to be very safe after millions of doses, rare cases of vaccine-associated encephalitis have occurred. Because of the theoretical risk of encephalitis in immunosuppressed patients, vaccination should be
avoided in symptomatic HIV-infected patients. These travelers should also avoid areas of the world where outbreaks of yellow fever are occurring [36,38]. If exposure is unavoidable for the symptomatically infected traveler, a letter of medical contraindication should be provided, and the individual should be instructed on rigorous avoidance of mosquitoes. For the asymptomatic HIV-infected traveler, vaccination can be offered after the risks are explained. Because the immune response may be diminished, it may be wise to check post-vaccination titers.

The consequences of measles in unprotected HIV-infected persons may be severe [94]. Because of the severity of the illness and the safety of vaccination, HIV-infected travelers at risk for measles should be immunized. This precaution should be done routinely for asymptomatic patients and considered for at-risk patients with symptomatic HIV infection.

REFERENCES

1. Hill DR, Pearson RD: Health advice for international travel. Ann Intern Med 108:839–852, 1988
2. Health Information for International Travel, 1991. HHS Publication No. (CDC) 91-8280. Atlanta, GA, U.S. Department of Health and Human Services, Public Health Service, 1991
3. Task Force on Adult Immunization, American College of Physicians and the Infectious Diseases Society of America: Guide for Adult Immunization. Philadelphia, PA, American College of Physicians, 1990
4. Immunization Practices Advisory Committee (ACIP): General recommendations on immunization. MMWR 38:205–214, 1989
5. Preblud SR, Tsai TF, Brink EW, Nahalen BL, Parsonnet J: International travel and the child younger than two years: I. Recommendations for immunization. Pediatr Infect Dis J 8:416–425, 1989
6. Wolfe MS: Vaccines for foreign travel. Pediatr Clin N Amer 37:757–769, 1990
7. Centers for Disease Control: Update on adult immunization: Recommendations of the immunization practices advisory committee (ACIP). MMWR 40 (No. RR-12):1–94, 1991
8. Barry M, Bia F: Pregnancy and travel. JAMA 261:728–731, 1989
9. Centers for Disease Control: Immunization of children infected with human T-lymphotropic virus type III/lymphadenopathy-associated virus. Recommendations of the immunization practices advisory committee (ACIP). MMWR 35:595–605, 1986
10. von Reyn CF, Clements CJ, Mann JM: Human immunodeficiency virus infection and routine childhood immunisation. Lancet ii:669–672, 1987
11. Onorato IM, Markowitz LE, Oxtoby MJ: Childhood immunization, vaccine preventable diseases and infection with human immunodeficiency virus. Pediatr Infect Dis J 6:588–595, 1988
12. Wilson ME, von Reyn CF, Fineberg HV: Infections in HIV-infected travelers: Risks and prevention. Ann Intern Med 114:582–592, 1991
13. National childhood vaccine injury act: Requirements for permanent vaccination records and for reporting of selected events after vaccination. MMWR 37:197–200, 1988
14. Hill DR: Pre-travel health, immunization status and demographics of travel of individuals visiting a travel medicine service. Amer J Trop Med Hyg 45:263–270, 1991
15. Hilton E, Singer C, Kozarsky P, Smith MA, Lardis MP, Borenstein MT: Status of immunity to tetanus, measles, mumps, rubella, and polio among U.S. travelers. Ann Intern Med 115:32–33, 1991
16. Centers for Disease Control: Hepatitis B virus: A comprehensive strategy for eliminating transmission in the United States through universal childhood vaccination: Recommendations of the immunization practices advisory committee (ACIP). MMWR 40 (No. RR-13):1–25, 1991
17. Immunization Practices Advisory Committee (ACIP): Diphtheria, tetanus, and pertussis: Guidelines for vaccine prophylaxis and other preventive measures. MMWR 40 (No. RR-10):1–28, 1991
18. Centers for Disease Control: Tetanus—United States, 1985–1986. MMWR 36:477–481, 1987
19. Karzon DT, Edwards KM: Diphtheria outbreaks in immunized populations. N Engl J Med 318:41–43, 1988
20. Centers for Disease Control: Measles prevention: Recommendations of the immunization practices advisory committee (ACIP). MMWR 38 (No. S-9):1–18, 1989
21. American Academy of Pediatrics, Committee on Infectious Diseases: Measles: Reassessment of the current immunization policy. American Academy of Pediatrics News 5:6, 1989
22. Centers for Disease Control: Measles—United States, 1990. MMWR 40:369–372, 1991
23. Centers for Disease Control: Measles—United States, 1988. MMWR 38:601–605, 1989
24. Markowitz LE, Tomasi A, Hawkins CE, Preblud SR, Orenstein WA, Hinman AR: International measles importations, 1980–1985. Internat J Epidemiol 17:187–192, 1988
25. Markowitz LE, Preblud SR, Orenstein WA, et al: Patterns of transmission in measles outbreaks in the United States, 1985–1986. N Engl J Med 320:75–81, 1989
26. Hill DR, Pearson RD: Measles prophylaxis for international travel (Editorial). Ann Int Med 111:699–701, 1989
27. Centers for Disease Control: Rubella prevention: Recommendations of the immunization practices advisory committee (ACIP). MMWR 39 (No. RR-15):1–18, 1990
28. Centers for Disease Control: Mumps vaccine. MMWR 38:388–400, 1989
29. Immunization Practices Advisory Committee (ACIP): Pneumococcal polysaccharide vaccine. MMWR 38:64–68,73–76, 1989
30. Centers for Disease Control: Prevention and control of influenza: Recommendations of the immunization practices advisory committee (ACIP). MMWR 39 (No. RR-7):1–15, 1990
31. Update: Influenza activity—Worldwide—and influenza vaccine availability—United States. MMWR 37:599–600, 1988
32. Centers for Disease Control: Haemophilus b conjugate vaccines for the prevention of Haemophilus influenzae Type b disease among infants and children two months of age and older: Recommendations of the immunization practices advisory committee (ACIP). MMWR 40 (No. RR-1):1–7, 1991
33. Public Health Service: International Certificates of Vaccination. PHS-731. Washington, DC, Superintendent of Documents, U.S. Government Printing Office, 1991
34. Immunization Practices Advisory Committee (ACIP): Smallpox vaccine. MMWR 34:341–342, 1985
35. Yellow fever in 1987. Bull WHO 67:451–453, 1989
36. Summary of Health Information for International Travel. HHS Publication No. 396. Atlanta, GA, U.S. Department of Health and Human Services, Public Health Service, 1991
37. Centers for Disease Control: Yellow fever activity—Trinidad and Tobago. MMWR 38:57–59, 1989
38. Centers for Disease Control: Yellow fever vaccine: Recommendations of the immunization practices advisory committee (ACIP). MMWR 39 (No. RR-6):1–6, 1990
39. Felsenfeld O, Wolf RH, Gyr K, Grant LS, Dutton NK, Zerifi AZ, Zafari Y: Simultaneous vaccination against cholera and yellow fever. Lancet i:457–458, 1973
40. Centers for Disease Control: Update: Cholera Western Hemisphere, 1991. MMWR 40:860, 1991
41. Snyder JD, Blake PA: Is cholera a problem for US travelers? JAMA 247:2268–2269, 1982
42. Centers for Disease Control: Importation of cholera from Peru. MMWR 40:258–259, 1991
43. Immunization Practices Advisory Committee (ACIP): Cholera vaccine. MMWR 37:617–618, 623–624, 1988
44. Clemens JD, Sack DA, Harris JR, van Loon F, Chakraborty J, Ahmed F, Rao MR, Khan MR, Yunus M, Huda N, Stanton BF, Kay BA, Walter S, Eeckels R, Svennerholm AM, Holmgren J: Field trials of oral cholera vaccines in Bangladesh: Results from three-year follow-up. Lancet i:270–273, 1990
45. Ryan CA, Hargrett-Bean NT, Blake PA: Salmonella typhi infections in the United States, 1975–1984: Increasing role of foreign travel. Rev Infect Dis 11:1–8, 1989
46. Woodruff BA, Pavia AT, Blake PA: A new look at typhoid vaccination. Information for the practicing physician. JAMA 265:756–759, 1991
47. Klugman KP, Gilbertson IT, Koornhof HJ, Robbins JB, Schneerson R, Schulz D, Cadoz M, Armand J, Vaccination Advisory Committee: Protective activity of Vi capsular polysaccharide vaccine against typhoid fever. Lancet ii:1165–1169, 1987
48. Acharya IL, Lowe CU, Thapa R, Gurubacharya VL, Shrestha MB, Cadoz M, Schulz D, Armand J, Bryla DA, Trollfors B, Cramton T, Schneerson R, Robbins JB: Prevention of typhoid fever in Nepal with the Vi capsular polysaccharide of Salmonella typhi. A preliminary report. N Engl J Med 317:1101–1104, 1987
49. Gilman RH, Hornick RB, Woodward WE, DuPont HL, Snyder MJ, Levine MM, Libonati JP: Evaluation of a UDP-glucose-4-epimeraseless mutant of Salmonella typhi as a live oral vaccine. J Infect Dis 136:717–723, 1977
50. Levine MM, Black RE, Ferreccio C, Germanier R: Large-scale field trial of Ty 21a live oral typhoid vaccine in enteric-coated capsule formulation. Lancet i:1049–1052, 1987
51. Kaplan DT, Hill DR: Compliance with live, oral typhoid vaccine (Letter). JAMA, 267:1074, 1992
52. Centers for Disease Control: Typhoid vaccine: Recommendations of the immunization practices advisory committee (ACIP). MMWR 39 (No. RR-10):1–5, 1990
53. Wolfe MS: Precautions with oral typhoid (Ty 21a) vaccine (Letter). Lancet ii:631–632, 1990
54. Immunization Practices Advisory Committee (ACIP): Meningococcal vaccines. MMWR 34:255–259, 1985
55. Centers for Disease Control: Epidemic meningococcal disease—Kenya and Tanzania: Recommendations for travelers, 1990. MMWR 39:13–14, 1990
56. Immunization Practices Advisory Committee (ACIP): Plague vaccine. MMWR 31:301–304, 1982
57. Immunization Practices Advisory Committee (ACIP): Use of BCG vaccines in the control of tuberculosis: A joint statement by the ACIP and the advisory committee for elimination of tuberculosis. MMWR 37:663–664,669–675, 1988
58. Centers for Disease Control: Update: Progress toward eradicating poliomyelitis from the Americas. MMWR 39:567–561, 1990
59. Centers for Disease Control: Poliomyelitis—Israel. MMWR 37:624–625, 1988
60. Kubli D, Steffen R, Schar M: Importation of poliomyelitis to industrialised nations between 1975 and 1984: Evaluation and conclusions for vaccination recommendations. Brit Med J 295:169–171, 1987
61. Nkowane BM, Wassilak SGF, Orenstein WA, Bart KJ, Schonberger LB, Hinman AR, Kew OM: Vaccine-associated paralytic poliomyelitis. United States: 1973 through 1984. JAMA 257:1335–1340, 1987
62. Immunization Practices Advisory Committee (ACIP): Poliomyelitis prevention. MMWR 31:22–26, 31–34, 1982
63. Immunization Practices Advisory Committee (ACIP): Poliomyelitis prevention: Enhanced-potency inactivated poliomyelitis vaccine—supplementary statement. MMWR 36:795–798, 1987
64. Trillin C: American chronicles—Zei-da-man. The New Yorker 61 (October 7):61–94, 1985
65. Umenai T, Krzyzko R, Bektimirov A, Assaad FA: Japanese encephalitis: Current worldwide status. Bull WHO 63:625–631, 1985
66. Japanese encephalitis: Report of a World Health Organization working group. MMWR 33:119–120,125, 1984
67. Monath TP: Japanese encephalitis—A plague of the orient. N Engl J Med 319:641–643, 1988
68. Poland JD, Cropp CB, Craven RB, Monath TP: Evaluation of the potency and safety of inactivated Japanese encephalitis vaccine in US inhabitants. J Infect Dis 161:878–882, 1990
69. Hoke CH, Nisalak A, Sangawhipa N, Jatanasen S, Laarakapongse T, Innis BL, Kotchasenee S, Gingrich JB, Latendresse J, Fukai K, Burke DS: Protection against Japanese encephalitis by inactivated vaccines. N Engl J Med 319:608–614, 1988
70. Human rabies acquired outside the United States. MMWR 34:235–236, 1985
71. Centers for Disease Control: Rabies prevention—United States, 1991: Recommendations of the immunization practices advisory committee (ACIP). MMWR 40 (No. RR-3):1–19, 1991
72. Pappaiouannou M, Fishbein DB, Dressen DW, Schwartz IK, Campbell GH, Sumner JW, Patchen LC, Brown WJ: Antibody response to preexposure human-diploid cell rabies vaccine given concurrently with chloroquine. N Engl J Med 314:280–284, 1986
73. Centers for Disease Control: Protection against viral hepatitis: Recommendations of the immunization practices advisory committee (ACIP). MMWR 39 (No. RR-2):1–26, 1990
74. Steffen R, Rickenbach M, Wilhelm U, Helmingera M, Schär M: Health problems after travel to developing countries. J Infect Dis 156:84–91, 1987
75. Safety of therapeutic immune globulin preparations with respect to transmission of human T-lymphotropic virus type III/lymphadenopathy-associated virus infection. MMWR 35:231–233, 1986
76. Parry JV, Perry KR, Mortimer PP, Farrington CP, Waight PA, Miller E: Rational programme for screening travellers for antibodies to hepatitis A virus. Lancet i:1447–1449, 1988
77. Sjogren MH, Hoke CH, Binn LN, Eckels KH, Dubois DR, Lyde L, Tsuchida A, Oaks S, Marchwicik R, Lednar W, Chloupek R, Ticehurst J, Bancroft WH: Immunogenicity of an inactivated hepatitis A vaccine. Ann Int Med 114:470–471, 1991
78. Flehmig B, Heinrich U, Pfister M: Prospects for a hepatitis A virus vaccine. Prog Med Virol 37:56–71, 1990
79. Hoffman M: Hepatitis A vaccine shows promise (News and Comment). Science 254:1581–1582, 1992
80. Hadler SC, De Monzon M, Ponzetto A, et al: Delta virus infection and severe hepatitis. An epidemic in the Yucpa indians of Venezuela. Ann Int Med 100:339–344, 1984
81. Purcell RH: Enterically transmitted non-A, non-B hepatitis. Prog Liv Dis 9:497–504, 1990
82. Gust ID, Purcell RH: Report of a workshop: Waterborne non-A, non-B hepatitis. J Infect Dis 156:630–635, 1987
83. Enterically transmitted non-A, non-B hepatitis Mexico. MMWR 36:597–602, 1987
84. Gostin LO, Cleary PD, Mayer KH, Brandt AM, Chittenden EH: Screening immigrants and international travelers for the human immunodeficiency virus. N Engl J Med 322:1743–1746, 1990
85. von Reyn CF, Mann JM, Chin J: International travel and HIV infection. Bull WHO 68:251–259, 1990
86. Glaser JB, Morton-Kute L, Berger SR, Weber J, Siegal FP, Lopez C, Robbins W, Landesman SH: Recurrent Salmonella typhimurium bacteremia associated with the acquired immunodeficiency syndrome. Ann Int Med 102:189–193, 1985
87. Ungar BLP, Mulligan M, Nutman TB: Serologic evidence of Cryptosporidium infection in US volunteers before and during Peace Corps service in Africa. Arch Int Med 149:894–897, 1989
88. Goodgame RW: AIDS in Uganda—Clinical and social features. N Engl J Med 323:383–389, 1990
89. Berenguer J, Moreno S, Cercendado E, Bernal de Quiros JC, Garcia de la Fuente A, Bouza E: Visceral leishmaniasis in patients infected with human immunodeficiency virus (HIV). Ann Int Med 111:129–132, 1989
90. Nelson KE, Clements ML, Miotti P, Cohn S, Polk BF: The influence of human immunodeficiency virus (HIV) infection on the antibody responses to influenza vaccines. Ann Int Med 109:383–388, 1988
91. Boudes P, Sobel A, Deforges L, Leblie E: Disseminated Mycobacterium bovis infection from BCG vaccination and HIV infection (Letter). JAMA 262:2386, 1989
92. Redfield RR, Wright DC, James WD, Jones TS, Brown C, Burke DS: Disseminated vaccinia in a military recruit with human immunodeficiency virus (HIV) disease. N Engl J Med 316:673–676, 1987
93. Krasinski K, Borkowsky W: Measles and measles immunity in children infected with human immunodeficiency virus. JAMA 261:2512–2516, 1989
94. Centers for Disease Control: Immunization of children with human immunodeficiency virus—supplementary ACIP statement: Recommendations of the immunization practices advisory committee (ACIP). MMWR 37:181–183, 1988
95. Lake-Bakaar G, Quadros E, Beidas S, et al: Gastric secretory failure in patients with the acquired immunodeficiency syndrome. Ann Int Med 109:502–504, 1988