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Yellow Fever Vaccine Recommendations of the Immunization Practices Advisory Committee (ACIP)

These revised Immunization Practices Advisory Committee (ACIP) recommendations on yellow fever vaccine update previous recommendations (MMWR 1984;32:679-88). Changes have been made to clarify 1) the risks of acquiring yellow fever associated with travel to endemic areas, 2) the precautions necessary for vaccination of special groups (immunosuppressed individuals, infants, pregnant women), and 3) simultaneous administration of cholera vaccine and other vaccines. INTRODUCTION

Yellow fever presently occurs only in Africa and South America. Two forms of yellow fever--urban and jungle--are epidemiologically distinguishable. Clinically and etiologically they are identical (1,2).

Urban yellow fever is an epidemic viral disease of humans transmitted from infected to susceptible persons by Aedes aegypti mosquitoes, which breed in domestic and peridomestic containers (e.g., water jars, barrels, drums, tires, tin cans) and thus in close association with humans. In areas where Ae. aegypti has been eliminated or suppressed, urban yellow fever has disappeared. In the early 1900s, eradication of Ae. aegypti in a number of countries, notably Panama, Brazil, Ecuador, Peru, Bolivia, Paraguay, Uruguay, and Argentina, led to the disappearance of urban yellow fever. The last documented Ae. aegypti-borne yellow fever epidemic in the western hemisphere occurred in Trinidad in 1954. Ae. aegypti is suspected to have played a role in transmission in outbreaks occurring in Bolivia in 1989 and 1990, but that role was not proven. However, periodic reinfestations of some countries have occurred in recent years (Brazil, Bolivia, Ecuador, Panama). Other countries remain infested, including areas of Venezuela, Colombia, and the Guyanas, which include enzootic areas for jungle yellow fever. In West Africa, Ae. aegypti-transmitted epidemics continue to occur and involve human populations both in towns and in rural villages (3).

Jungle yellow fever is an enzootic viral disease transmitted among nonhuman primate hosts by various mosquito vectors. It is currently observed only in forest-savannah zones of tropical Africa and in forested areas of South America but occasionally extends into parts of Central America and the island of Trinidad. In South America, approximately 100-300 cases are reported annually, mainly among men with occupational exposures in forested areas; however, the disease is believed to be greatly underreported. In Africa, epidemics involving tree-hole-breeding mosquito vectors affect tens of thousands of persons at intervals of a few years, but few cases are officially reported. Sometimes the disease is not detected in an area for years but then will reappear. Delineation of affected areas depends on surveillance of animal reservoirs and vectors, accurate diagnosis, and prompt reporting of all human cases. The jungle yellow fever cycle may be active but unrecognized in forested areas of countries within the yellow fever endemic zone (Figure 1).

Urban yellow fever can be prevented by eradicating Ae. aegypti mosquitoes or by suppressing their numbers to the point that they no longer perpetuate infection. Jungle yellow fever can most effectively be prevented by vaccination of human populations at risk of exposure. YELLOW FEVER VACCINE

Yellow fever vaccine is a live, attenuated virus preparation made from the 17D yellow fever virus strain (4). The 17D vaccine is safe and effective (5). The virus is grown in chick embryos inoculated with a seed virus of a fixed-passage level. The vaccine is a freeze-dried supernate of centrifuged embryo homogenate, packaged in 1-dose and 5-dose vials for domestic use.

Vaccine should be stored at temperatures between 5 C (41 F) and -30 C (-22 F)--preferably frozen, below 0 C (32 F)--until it is reconstituted by the addition of diluent sterile, physiologic saline supplied by the manufacturer. Multiple-dose vials of reconstituted vaccine should be held at 5 C-10 C (41 F-50 F); unused vaccine should be discarded within 1 hour after reconstitution. VACCINE USAGE

A. Persons living or traveling in endemic areas

1. Persons greater than or equal to 9 months of age traveling

to or living in areas of South America and Africa where yellow fever infection is officially reported should be vaccinated. These areas are listed in the "Bi-Weekly Summary of Countries with Areas Infected with Quarantinable Diseases," available in state and local health departments. Information on known or probably infected areas is also available from the World Health Organization (WHO) and Pan American Health Organization offices or the Division of Vector-Borne Infectious Diseases, Center for Infectious Diseases, CDC, Fort Collins, Colorado, telephone (303) 221-6400. Vaccination is also recommended for travel outside the urban areas of countries that do not officially report the disease but that lie in the yellow fever endemic zone (shaded area, Figure 1). The actual areas of yellow fever virus activity far exceed the infected zones officially reported; in recent years, fatal cases of yellow fever have occurred among unvaccinated tourists visiting rural areas within the yellow fever endemic zone (6).

2. Infants less than 9 months of age and pregnant women should be considered for vaccination if traveling to areas experiencing ongoing epidemic yellow fever when travel cannot be postponed and a high level of prevention against mosquito exposure is not feasible. However, in no instance should infants less than 4 months of age receive yellow fever vaccine because of the risk of encephalitis (see Precautions and Contraindications).

3. Laboratory personnel who might be exposed to virulent yellow fever virus by direct or indirect contact or by aerosols should also be vaccinated. B. Vaccination for international travel.

For purposes of international travel, yellow fever vaccines produced by different manufacturers worldwide must be approved by WHO and administered at an approved Yellow Fever Vaccination Center. State and territorial health departments have the authority to designate nonfederal vaccination centers; these can be identified by contacting state or local health departments. Vaccinees should receive an International Certificate of Vaccination completed, signed, and validated with the center's stamp where the vaccine is given. Vaccination for international travel may be required under circumstances other than those specified herein. Some countries in Africa require evidence of vaccination from all entering travelers. Some countries may waive the requirements for travelers coming from noninfected areas and staying less than 2 weeks. Because requirements may change, all travelers should seek current information from health departments. Travel agencies, international airlines, and/or shipping lines should also have up-to-date information. Some countries require an individual, even if only in transit, to have a valid International Certificate of Vaccination if s/he has been in countries either known or thought to harbor yellow fever virus. Such requirements may be strictly enforced, particularly for persons traveling from Africa or South America to Asia. Travelers should consult Health Information for International Travel 1989 (7) to determine requirements and regulations for vaccination. C. Primary vaccination.

For persons of all ages, a single subcutaneous injection of 0.5 ml of reconstituted vaccine is used. D. Booster doses.

The International Health Regulations require revaccination at intervals of 10 years. Revaccination boosts antibody titer; however, evidence from several studies (8-10) suggests that yellow fever vaccine immunity persists for at least 30-35 years and probably for life. REACTIONS

Reactions to 17D yellow fever vaccine are generally mild. After vaccination, 2%-5% of vaccinees have mild headaches, myalgia, low-grade fevers, or other minor symptoms for 5-10 days. Fewer than 0.2% of the vaccinees curtail regular activities. Immediate hypersensitivity reactions, characterized by rash, urticaria, and/or asthma, are uncommon (incidence less than 1/1,000,000) and occur principally among persons with histories of egg allergy. Although greater than 34 million doses of vaccine 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. PRECAUTIONS AND CONTRAINDICATIONS

A. Age. Infants less than 4 months of age are more susceptible to serious adverse reactions (encephalitis) than older children. The risk of this complication appears to be age-related; whenever possible, vaccination should be delayed until age 9 months.

B. Pregnancy. Although specific information is not available concerning adverse effects of yellow fever vaccine on the developing fetus, pregnant women theoretically should not be vaccinated, and travel to areas where yellow fever is present should be postponed until after delivery. If international travel requirements constitute the only reason to vaccinate a pregnant woman, rather than an increased risk of infection, efforts should be made to obtain a waiver letter from the traveler's physician (see section D. Hypersensitivity). Pregnant women who must travel to areas where the risk of yellow fever is high should be vaccinated. Under these circumstances, for both mother and fetus, the small theoretical risk from vaccination is far outweighed by the risk of yellow fever infection.

C. Altered immune states. Infection with yellow fever vaccine virus poses a theoretical risk of encephalitis to patients with immunosuppression in association with acquired immunodeficiency syndrome (AIDS) or other manifestations of human immunodeficiency virus (HIV) infection, leukemia, lymphoma, generalized malignancy, or to those whose immunologic responses are suppressed by corticosteroids, alkylating drugs, antimetabolites, or radiation. Such patients should not be vaccinated. If travel to a yellow fever-infected zone is necessary, patients should be advised of the risk, instructed in methods for avoiding vector mosquitoes, and supplied with vaccination waiver letters by their physicians. Low-dose (10 mg prednisone or equivalent) or short-term (less than 2 weeks) corticosteroid therapy or intra-articular, bursal, or tendon injections with corticosteroids should not be immunosuppressive and constitute no increased hazard to recipients of yellow fever vaccine. Persons who have had previously diagnosed asymptomatic HIV infections and who cannot avoid potential exposure to yellow fever virus should be offered the choice of vaccination. Vaccinees should be monitored for possible adverse effects. Since the vaccination of such persons may be less effective than that for non-HIV-infected persons, their neutralizing antibody response to vaccination may be desired before travel. For such determinations, the appropriate state health department or CDC ((303) 221-6400) may be contacted. Family members of immunosuppressed persons, who themselves have no contraindications, may receive yellow fever vaccine.

D. Hypersensitivity. Live yellow fever vaccine is produced in chick embryos and should not be given to persons hypersensitive to eggs; generally, persons who are able to eat eggs or egg products may receive the vaccine. If international travel regulations are the only reason to vaccinate a patient hypersensitive to eggs, efforts should be made to obtain a waiver. A physician's letter stating the contraindication to vaccination has been acceptable to some governments. (Ideally, it should be written on letterhead stationary and bear the stamp used by health department and official

immunization centers to validate the International Certificate of Vaccination.) Under these conditions, the traveler should also obtain specific and authoritative advice from the embassy or consulate of the country or countries s/he plans to visit. Waivers of requirements obtained from embassies or consulates should be documented by appropriate letters and retained for presentation with the International Health Certificate. If vaccination of an individual with a questionable history of egg hypersensitivity is considered essential because of a high risk of exposure, an intradermal test dose may be administered under close medical supervision. Specific directions for skin testing are found in the package insert. SIMULTANEOUS ADMINISTRATION OF OTHER VACCINES

Determination of whether to administer yellow fever vaccine and other immunobiologics simultaneously should be made on the basis of convenience to the traveler in completing the desired vaccinations before travel and on information regarding possible interference. The following will help guide these decisions.

Studies have shown that the serologic response to yellow fever vaccine is not inhibited by the administration of certain other vaccines concurrently or at various intervals of a few days to 1 month. Measles and yellow fever vaccines have been administered in combination with full efficacy of each of the components; Bacillus Calmette Guerin (BCG) and yellow fever vaccines have been administered simultaneously without interference. Additionally, severity of reactions to vaccination has not been amplified by the concurrent administration of yellow fever and other live virus vaccines (11). If live virus vaccines are not given concurrently, 4 weeks should elapse between sequential vaccinations.

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 (12,13). 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, the vaccines can be given simultaneously or at any time within the 3-week interval.

Hepatitis B and yellow fever vaccine may be given concurrently (14). No data exist on possible interference between yellow fever and typhoid, paratyphoid, typhus, plague, rabies, or Japanese encephalitis vaccines.

In a prospective study of persons given yellow fever vaccine and 5 cc of commercially available immune globulin, no alteration of the immunologic response to yellow fever vaccine was detected when compared with controls (15). Although chloroquine inhibits replication of yellow fever virus in vitro, it does not adversely affect antibody responses to yellow fever vaccine in humans receiving antimalaria prophylaxis (16).

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