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

These revised Immunization Practices Advisory Committee (ACIP) recommendations on yellow fever vaccine update the previous recommendations (MMWR 1978:27:268-70). Changes have been made to clarify (1) the risks of acquiring yellow fever associated with travel to endemic areas; (2) the precautions necessary for immunization of special groups (infants, pregnant women); (3) procedures for immunization of persons with histories of possible egg allergy; and (4) simultaneous administration of 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 a vector, the Aedes aegypti mosquito. In areas where Ae. aegypti has been eliminated or suppressed, urban yellow fever has disappeared; eradication of Ae. aegypti in a number of countries, notably Panama, Brazil, Ecuador, Peru, Bolivia, Paraguay, Uruguay, and Argentina, achieved in the early 1900s, led to the disappearance of urban yellow fever. The last Ae. aegypti- borne yellow fever epidemic occurred in Trinidad in 1954. However, periodic reinfestations of some countries have occurred in recent years, and other countries remain infested, including areas of Venezuela, Colombia, and Guiana, which border on the enzootic zone for jungle yellow fever. In West Africa, Ae. aegypti-transmitted epidemics continue to occur at frequent intervals and involve human populations in both towns and rural villages (3).

Jungle yellow fever is an enzootic viral disease transmitted among nonhuman primate hosts by a variety of 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 200-400 cases are recognized annually, mainly among persons with occupational exposures in forested areas; the disease is, however, believed to be greatly underreported. In Africa, epidemics involving forest mosquito vectors affect tens of thousands of persons at intervals of a few years, but few cases are officially reported. The disease may sometimes not be detected in an area for some years and then reappear. Delineation of affected areas depends on surveillance of animal reservoirs and vectors, accurate diagnosis, and prompt reporting of all cases. The jungle yellow fever cycle may be active but unrecognized in forested areas of countries within the yellow fever endemic zone (Figure 2).

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. At the present time, jungle yellow fever can most effectively be prevented in humans by immunization.

YELLOW FEVER VACCINE

Yellow fever vaccine * is a live, attenuated virus preparation made from the 17D yellow fever virus strain (4). The 17D vaccine has proven to be extremely safe and effective (5).

The 17D strain is grown in chick embryo inoculated with a seed virus of a fixed-passage level. The vaccine is freeze-dried supernate of centrifuged embryo homogenate, packaged in one-dose and five-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 reconsitituted 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

1. Persons living or traveling in endemic areas:

2. Persons 6 months of age or older traveling or living in areas where yellow fever infection exists -- currently parts of Africa and South America -- should be vaccinated. (These 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 probable infected areas is also available from the World Health Organization (WHO) and Pan American Health Organization offices or the Division of Vector- Borne Viral Diseases, Center for Infectious Diseases, CDC, Fort Collins, Colorado.)

   Vaccination is also recommended for travel outside the urban areas of countries in the yellow fever endemic zone (Figure 1). It should be emphasized that the actual areas of yellow fever virus activity far exceed the infected zones officially reported and that, in recent years, fatal cases of yellow fever have occurred in unvaccinated tourists (6).

3. Infants under 6 months of age and pregnant women should be considered for vaccination if traveling to high-risk areas when travel cannot be postponed and a high level of prevention against mosquito exposures is not feasible.

4. Laboratory personnel who might be exposed to virulent yellow fever virus should also be vaccinated.

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 have an International Certificate of Vaccination filled in, 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. These requirements may change, so 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 he or she 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.

Primary immunization: For persons of all ages, a single subcutaneous injection of 0.5 ml of reconstituted vaccine is used.

Booster doses: Yellow fever immunity following vaccination with 17D strain virus persists for more than 10 years (7-9); the International Health Regulations do not require vaccination more often than every 10 years.

REACTIONS

Reactions to 17D yellow fever vaccine are generally mild. Two percent to 5% of vaccinees have mild headaches, myalgia, low-grade fevers, 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 (incidence less than 1/1,000,000) and occur principally in persons with histories 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.

PRECAUTIONS AND CONTRAINDICATIONS

1. Age: Infants under 6 months of age are theoretically more susceptible to serious adverse reactions (encephalitis) than older children.

2. Pregnancy: Although specific information is not available concerning adverse effects of yellow fever vaccine on the developing fetus, it is prudent on theoretical grounds to avoid vaccinating pregnant women and to postpone travel to areas where yellow fever is present 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 below). 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 small theoretical risk for mother and fetus from vaccination is far outweighed by the risk of yellow fever infection.

3. Altered immune states: Infection with yellow fever vaccine virus poses a theoretical risk to patients with leukemia, lymphoma, or generalized malignancy or to those whose immunologic responses are suppressed by corticosteroids, alkylating drugs, antimetabolites, or radiation. 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.

4. Hypersensitivity: Live yellow fever vaccine is produced in chick embryos and should not be given to persons clearly 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 clearly stating the contraindication to vaccination has been acceptable to some governments. (Ideally, it 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.) Under these conditions, it is also useful for the traveler to obtain specific and authoritative advice from the country or countries he or she plans to visit. Their embassies or consulates may be contacted. Subsequent waiver of requirements should be documented by appropriate letters.

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 immunizations 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 administration of certain other vaccines concurrently or at various intervals of a few days to 1 month. Measles, smallpox, 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 was not amplified by concurrent administration of yellow fever and other live virus vaccines (10). If live virus vaccines are not given concurrently, 4 weeks should be allowed to elapse between sequential vaccinations.

Other studies have indicated that persons given yellow fever and cholera vaccines simultaneously or 1-3 weeks apart showed reduced antibody responses to both vaccines (11, 12). When feasible, cholera and yellow fever vaccines should be administered at a minimal interval of 3 weeks, unless time constraints preclude this. If the vaccines cannot be administered at least 3 weeks apart, they should be given simultaneously. There are no data on possible interference between yellow fever and typhoid, paratyphoid, typhus, hepatitis B, plague, rabies, or Japanese encephalitis vaccines.

A recently completed prospective study of persons given yellow fever vaccine and 5 cc of commercially available immune globulin revealed no alteration of the immunologic response to yellow fever vaccine when compared to controls (13).

Acknowledge you have read and understand this protocol by signing below:

_____ _____

Signature Date

_____

Print Name

_____

Lab Affiliation

* Official name: Yellow Fever Vaccine.

References

1. Strode GK, ed. Yellow Fever. New York: McGraw Hill, 1951.

2. World Health Organization Expert Committee on Yellow Fever, 3rd Report WHO Tech Rep: Ser. No. 4791, 1971..

3. Monath TP, Craven RB, Adjukiewicz A, et al. Yellow fever in the Gambia, 1978-1979: epidemiologic aspects with observations on the occurrence of Orungo virus infections. Am J Trop Med Hyg 29:912-28, 1980.

4. Smithburn KC, Durieux C, Koerber R, et al. Yellow fever vaccination. WHO Monograph Series No. 30, Geneva, 1956.

5. Wisseman CL Jr, Sweet BH. Immunological studies with group B arthropod-borne viruses. III. Response of human subjects to revaccination with 17D strain yellow fever vaccine. Am J Trop Med 1962;11:570-5.

6. Rodhain F, Hannoun C, Jousset FX, Ravisse P. Isolement du virus de la fievre jaune a Paris a partir de deux cas humains importes. Bull Soc Pathol Exot 1979;72:411-5.

7. Groot H, Ribeiro RB. Neutralizing and haemagglutination-inhibiting antibodies to yellow fever 17 years after vaccination with 17D vaccine. Bull WHO 1962;27:699-707.

8. Poland JD, Calisher CH, Monath TP, Downs WG, Murphy K. Persistence of neutralizing antibody 30-35 years after immunization with 17D yellow fever vaccine. Bull WHO 1981;59:895-900.

9. Rosenzweig EC, Babione RW, Wisseman CL Jr. Immunological studies with group B arthropod-borne viruses. IV. Persistence of yellow fever antibodies following vaccination with 17D strain yellow fever vaccine. Am J Trop Med 1963;12:230-5.

10. Tauraso NM, Myers, MG, Nau EV, et al. Effect of interval between inoculation of live smallpox and yellow-fever vaccines on antigenicity in man. J Infect Dis 126:363-371,1972.

11. Felsenfeld O, Wolf RH, Gyr K, et al. Simultaneous vaccination against cholera and yellow fever. Lancet 1973;I:457-8.

12. Gateff C. Acquisitions recentes en matiere d'associations vaccinales. Bull Soc Pathol Exot 1972;65:784-96.

13. Kaplan JE, Nelson DB, Schonberger LB, et al. The effect of immune globulin on trivalent oral polio and yellow fever vaccinations. Bull WHO 1984 (in press).

14. Recommendations of the Immunization Practices Advisory Committee (ACIP) Yellow Fever Vaccine: Morbidity and Mortality Weekly Report January 06, 1984 / 32(52);679-82,687-8