

# LIVESAY EXPEDITIONS & ADVENTURES

## Yellow Fever

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### Infectious Agent

Yellow fever virus (YFV) is a single-stranded RNA virus that belongs to the genus *Flavivirus*.

### Mode of Transmission

- Vector-borne transmission occurs via the bite of an infected mosquito, primarily *Aedes* or *Haemagogus* spp.
- Nonhuman and human primates are the main reservoirs of the virus, with anthroponotic (human-to-vector-to-human) transmission occurring.
- There are three transmission cycles for yellow fever: sylvatic (jungle), intermediate (savannah), and urban.
  - The sylvatic (jungle) transmission cycle involves transmission of the virus between nonhuman primates and mosquito species found in the forest canopy. The virus is transmitted via mosquitoes from monkeys to humans when the humans encroach into the jungle during occupational or recreational activities.
  - In Africa, an intermediate (savannah) cycle involves transmission of YFV from tree hole-breeding *Aedes* spp. to humans living or working in jungle border areas. In this cycle, the virus may be transmitted from monkeys to humans or from human to human via these mosquitoes.
  - The urban transmission cycle involves transmission of the virus between humans and urban mosquitoes, primarily *Ae. aegypti*.
- Humans infected with YFV experience the highest levels of viremia and can transmit the virus to mosquitoes shortly before onset of fever and for the first 3–5 days of illness.
- Given the high level of viremia attained in humans, bloodborne transmission can also occur (via transfusion, needlestick, and intravenous drug abuse).

### Occurrence

- Yellow fever occurs in sub-Saharan Africa and tropical South America (Maps 2-3 and 2-4), where it is endemic and intermittently epidemic (see Table 2-12 for a list of countries with risk of yellow fever transmission).
- In Africa, natural immunity accumulates with age, and thus infants and children are at greatest risk for disease.
- In South America, yellow fever occurs most frequently in unimmunized young men who are exposed to mosquito vectors through their work in forested or transitional areas.
- Most yellow fever disease in humans is due to sylvatic or intermediate transmission cycles. However, urban yellow fever does occur periodically in Africa and sporadically in the Americas.

## Risk for Travelers

### General

A traveler's risk for acquiring yellow fever is determined by various factors, including immunization status, location of travel, season, duration of exposure, occupational and recreational activities while traveling, and local rate of virus transmission at the time of travel. Although reported cases of human disease are the principal indicator of disease risk, case reports may be absent because of a low level of transmission, a high level of immunity in the population (e.g., due to vaccination), or failure of local surveillance systems to detect cases. This "epidemiologic silence" does not equate to absence of risk and should not lead to travel without the protection provided by vaccination.

### Africa

YFV transmission in rural West Africa is seasonal, with an elevated risk during the end of the rainy season and the beginning of the dry season (usually July–October). However, YFV may be episodically transmitted by *Ae. aegypti* even during the dry season in both rural and densely settled urban areas.

### South America

- The risk for infection for South America is highest during the rainy season (January–May, with a peak incidence in February and March).
- Given the high level of viremia in humans and the widespread distribution of *Ae. aegypti* in many towns and cities, South America is at risk for a large-scale urban epidemic.

### Yellow Fever Cases in Travelers

- During 1970–2002, a total of nine cases of yellow fever were reported in unvaccinated travelers from the United States and Europe who traveled to West Africa (five cases) or South America (four cases). Eight of these nine travelers died.
- Only one documented case of yellow fever has occurred, which was in a vaccinated traveler from Spain, who visited several West African countries during 1988.

### Risk Estimates for Travelers

- The risk of acquiring yellow fever is difficult to predict because of variations in ecologic determinants of virus transmission. For a 2-week stay, the risks for illness and death due to yellow fever for an unvaccinated traveler traveling to an endemic area of
  - West Africa are 50 per 100,000 and 10 per 100,000, respectively
  - South America are 5 per 100,000 and 1 per 100,000, respectively
- These estimates are a rough guideline based on the risk to indigenous populations, often during peak transmission season. Thus, these risk estimates may not accurately reflect the true risk to travelers, who may have a different immunity profile, take precautions against getting bitten by mosquitoes, and have less outdoor exposure.
- The risk of acquiring yellow fever in South America is lower than that in Africa because the mosquitoes that transmit the virus between monkeys in the forest canopy do not often come in contact with humans, and there is a relatively high level of immunity in local residents secondary to vaccine use.

**Table 2-12. Countries with risk of yellow fever transmission<sup>1</sup>**

| <b>Africa</b>                    |                         |                       | <b>Central and South America</b> |
|----------------------------------|-------------------------|-----------------------|----------------------------------|
| Angola                           | Ethiopia                | Nigeria               | Argentina <sup>2</sup>           |
| Benin                            | Gabon                   | Rwanda                | Bolivia <sup>2</sup>             |
| Burkina Faso                     | The Gambia              | Sierra Leone          | Brazil <sup>2</sup>              |
| Burundi                          | Ghana                   | São Tomé and Príncipe | Colombia                         |
| Cameroon                         | Guinea                  | Senegal               | Ecuador <sup>2</sup>             |
| Central African Republic         | Guinea-Bissau           | Somalia               | French Guiana                    |
| Chad <sup>2</sup>                | Kenya                   | Sudan <sup>2</sup>    | Guyana                           |
| Congo, Republic of the           | Liberia                 | Tanzania              | Panama <sup>2</sup>              |
| Côte d'Ivoire                    | Mali <sup>2</sup>       | Togo                  | Paraguay                         |
| Democratic Republic of the Congo | Mauritania <sup>2</sup> | Uganda                | Peru <sup>2</sup>                |
| Equatorial Guinea                | Niger <sup>2</sup>      |                       | Suriname                         |
|                                  |                         |                       | Trinidad and Tobago <sup>2</sup> |
|                                  |                         |                       | Venezuela <sup>2</sup>           |

<sup>1</sup>Countries/areas where “a risk of yellow fever transmission is present,” as defined by the World Health Organization, are countries or areas where “yellow fever has been reported currently or in the past, plus vectors and animal reservoirs currently exist” (see [www.who.int/ith/countries/2008\\_country\\_list.pdf](http://www.who.int/ith/countries/2008_country_list.pdf) (PDF)).

<sup>2</sup>These countries are not holoendemic (i.e., only a portion of the country has risk of yellow fever transmission). Please see Maps 2-3 and 2-4 and yellow fever vaccine recommendations (Table 2-14) for details.

**Map 2-3. Yellow fever-endemic zones in Africa, 2009**



**Map 2-4. Yellow fever-endemic zones in the Americas, 2009**



## Clinical Presentation

- Asymptomatic or clinically inapparent infection is believed to occur in the majority of persons infected with YFV.
- The incubation period is typically 3–6 days.
- The initial illness presents as a nonspecific influenza-like syndrome with sudden onset of fever, chills, headache, backache, myalgias, prostration, nausea, and vomiting. Most patients improve after the initial presentation.
- After a brief remission of hours to a day, approximately 15% of cases progress to develop a more serious or toxic form of the disease characterized by jaundice, hemorrhagic symptoms, and eventually shock and multisystem organ failure.
- The overall case–fatality ratio for cases with jaundice is 20%–50%.

## Diagnosis

- The preliminary diagnosis is based on the patient’s clinical features, places and dates of travel, and activities.
- Laboratory diagnosis is generally accomplished by testing serum to detect virus-specific IgM and IgG antibodies by serologic assays. Due to cross-reactivity between antibodies raised against other flaviviruses, more specific antibody testing, such as a neutralization test, should be done to confirm the infection.
- Early in the illness, YFV or yellow fever viral RNA can often be detected in serum samples by virus isolation or nucleic acid amplification tests (NAAT). However, by the time more overt symptoms are recognized, the virus or viral RNA is usually undetectable. Therefore, virus isolation and NAAT should not be used for ruling out a diagnosis of yellow fever.
- Health-care providers should contact their state or local health department or call 800-CDC-INFO (800-232-4636) for assistance with diagnostic testing for yellow fever infections and for questions about antibody response to vaccination.

## Treatment

- No specific treatments have been found to benefit patients with yellow fever.
- Treatment is symptomatic. Rest, fluids, and use of analgesics and antipyretics may relieve symptoms of fever and aching. Care should be taken to avoid certain medications, such as aspirin or other nonsteroidal anti-inflammatory drugs, which may increase the risk for bleeding.
- Infected persons should be protected from further mosquito exposure (staying indoors and/or under a mosquito net) during the first few days of illness, so they do not contribute to the transmission cycle.

## Preventive Measures for Travelers

### Personal Protection Measures

- No drugs for preventing infection are available.
- The best way to prevent mosquito-borne diseases, including yellow fever, is to avoid mosquito bites (see the [Protection Against Mosquitoes, Ticks, and Other Insects and Arthropods](#) section later in this chapter):
  - Use insect repellent containing DEET, Picaridin, oil of lemon eucalyptus, or IR3535 on

exposed skin. Always follow the directions on the package.

- Wear long sleeves, pants, and socks. If possible, treat clothes with permethrin.
- Stay in screened or air-conditioned accommodations to keep mosquitoes out.
- Get rid of mosquito sources by emptying standing water from flowerpots, buckets, car tires and barrels.

## **Yellow Fever Vaccine**

- Yellow fever is preventable by a relatively safe, effective vaccine.
- All yellow fever vaccines currently manufactured are live attenuated viral vaccines.
- YF-VAX, the only yellow fever vaccine approved for use in the United States, is manufactured by sanofi pasteur.
- Studies comparing the reactogenicity and immunogenicity of various yellow fever vaccines, including those manufactured outside of the United States, suggest that there is no significant difference in the reactogenicity or immune response generated by the various vaccines. Thus, individuals who receive yellow fever vaccines in other countries should be considered protected against yellow fever.

## **Recommendations for the Use of Yellow Fever Vaccine for Travelers**

- Persons aged  $\geq 9$  months of age who are traveling to or living in areas with risk of yellow fever transmission in South America and Africa should be vaccinated. In addition, some countries require proof of yellow fever vaccination for entry. See the following section in this chapter ([Yellow Fever Vaccine Requirements and Recommendations, by Country](#)) for more detailed information on the requirements and recommendations for yellow fever vaccination for specific countries.
- However, because severe adverse events (see below) can follow yellow fever vaccination, physicians should be careful to administer the vaccine only to persons truly at risk of exposure to YFV.
- Refer to Yellow Fever Vaccine Recommendations of the Advisory Committee on Immunization Practices (ACIP) for additional information at [www.cdc.gov/vaccines/pubs/ACIP-list.htm](http://www.cdc.gov/vaccines/pubs/ACIP-list.htm).

## **Vaccine Dose and Administration**

- For all eligible persons, a single injection of 0.5 mL of reconstituted vaccine should be administered subcutaneously.
- The International Health Regulations (IHR) published by WHO require revaccination at 10-year intervals.

## **Vaccine Safety and Adverse Reactions**

### **Common Adverse Events**

- Reactions to yellow fever vaccine are generally mild, with 10%–30% of vaccinees reporting mild systemic adverse events.
- Reported events typically include low-grade fever, headache, and myalgias that begin within days after vaccination and last 5–10 days.
- Approximately 1% of vaccinees temporarily curtail their regular activities because of these reactions.

## Severe Adverse Events

### Hypersensitivity

Immediate hypersensitivity reactions, characterized by rash, urticaria, or asthma or a combination of these, are uncommon. Anaphylaxis following yellow fever vaccine is reported to occur at a rate of 1.8 cases per 100,000 doses administered.

### Yellow Fever Vaccine-Associated Neurologic Disease (YEL-AND)

- YEL-AND represents a conglomerate of different clinical syndromes, including meningoencephalitis, Guillain–Barré syndrome (GBS), acute disseminated encephalomyelitis (ADEM), bulbar palsy, and Bell’s palsy.
- Historically, YEL-AND was seen primarily among infants as encephalitis, but more recent reports have been among persons of all ages.
- The onset of illness for documented cases ranges 3–28 days after vaccination, and almost all cases were in first-time vaccine recipients.
- YEL-AND is rarely fatal.
- The incidence of YEL-AND in the United States is 0.8 per 100,000 doses administered. The rate is higher in persons  $\geq 60$  years of age, with a rate of 1.6 per 100,000 doses in persons 60–69 years of age and 2.3 per 100,000 doses in persons  $\geq 70$  years of age.

### Yellow Fever Vaccine-Associated Viscerotropic Disease (YEL-AVD)

- YEL-AVD is a severe illness similar to wild-type disease, with vaccine virus proliferating in multiple organs and often leading to multisystem organ failure and death.
- Since the initial cases of YEL-AVD were published in 2001, more than 40 confirmed and suspected cases have been reported throughout the world.
- The onset of illness for YEL-AVD cases averaged 3.5 days (range: 1–8 days) after vaccination. YEL-AVD appears to occur after the first dose of yellow fever vaccine rather than with booster doses.
- The case–fatality ratio for reported YEL-AVD cases is 53%.
- The incidence of YEL-AVD in the United States is 0.4 cases per 100,000 doses of vaccine administered. The rate is higher for persons  $\geq 60$  years of age, with a rate of 1 per 100,000 doses in persons 60–69 years of age and 2.3 per 100,000 doses in persons aged  $\geq 70$  years of age.

## Contraindications

### Infants <9 Months of Age

- The vaccine is contraindicated for routine use in infants <9 months of age by the manufacturer and the FDA because of the increased risk of postvaccine encephalitis. However, ACIP and WHO recognize that situations occur in which vaccination of an infant 6–8 months of age might be considered, such as residence in or unavoidable travel to a yellow fever endemic or epidemic zone. The decision to immunize infants who are 6–8 months of age must balance the infant’s risk for exposure with the risk for vaccine-associated encephalitis. **YF vaccine should never be administered to infants <6 months of age.**
- Physicians considering vaccinating infants aged <9 months of age should contact their state health department or call 800-CDC-INFO (800-232-4636) for further advice.

### Hypersensitivity

- Yellow fever vaccine is contraindicated in anyone with a history of acute hypersensitivity

reaction to any of the vaccine components, including gelatin. Because the yellow fever vaccine is produced in chicken embryos, vaccine should not be administered to anyone with a history of acute hypersensitivity to egg or chicken proteins.

- If vaccination of a person with a questionable history of hypersensitivity to one of the vaccine components is considered essential because of a high risk for acquiring yellow fever, desensitizing and vaccinating procedures are described in the vaccine package insert and should be performed under close medical supervision.

#### Immunosuppression

- The vaccine is contraindicated in persons with immunocompromising conditions, including symptomatic HIV infection or AIDS, malignancy, or diseases of the thymus (e.g., thymectomy) or those receiving immunosuppressant therapy (e.g., corticosteroids, alkylating agents, antimetabolites) or radiation therapy.
- Immunosuppressed persons should not be immunized, and travel to yellow fever-endemic areas should be postponed or avoided.
- If travel to yellow fever endemic areas is unavoidable, persons who cannot be immunized because of their immunosuppressive condition should be advised of the risk for acquiring yellow fever disease, instructed in methods for avoiding vector mosquitoes, and, if warranted, issued a medical waiver to fulfill international health regulations (see information in Exemption from Vaccination and Waiver Letters in this section).
- Physicians considering vaccinating an immunosuppressed individual can contact their state health department or call for more information.
- Family members of immunosuppressed or HIV-infected persons who themselves have no contraindications can receive yellow fever vaccine.

#### AIDS or Symptomatic HIV

No large-scale trials have been done to evaluate the safety of the yellow fever vaccine in individuals with HIV or AIDS. However, because yellow fever vaccine is a live, viral vaccine, it is contraindicated in persons with symptomatic HIV infection or AIDS. (For persons with asymptomatic HIV infection, see Precautions below.)

#### History of Thymus Disease

- A history of thymus disease is a contraindication to yellow fever vaccine.
- Four persons with a history of thymectomy for a thymoma were noted among the first 23 cases of YEL-AVD, suggesting that compromised thymus function is an independent risk factor for YEL-AVD.
- Health-care providers should be careful to ask about a history of thymus disorder, including myasthenia gravis, thymoma, or prior thymectomy, when screening a patient before administering yellow fever vaccine.

#### Immunosuppressive Medication

- Although no studies have been done to evaluate the safety of yellow fever vaccine in persons receiving immunosuppressive or immunomodulating medicines, the vaccine is contraindicated in those receiving medications that alter the ability to resist viral infections. The vaccine should not be given to individuals who are taking medications with a warning in the package insert against the use of live viral vaccines.
- Low-dose (i.e., 20 mg or less of prednisone or equivalent/day); short-term (i.e., <2 weeks) systemic corticosteroid therapy or intra-articular, bursal, or tendon injections with

corticosteroids; and intranasal corticosteroids are not thought to be sufficiently immunosuppressive to constitute an increased hazard to recipients of yellow fever vaccine (see [The Immunocompromised Traveler](#) section in Chapter 8).

## Precautions

### Adults 60 Years of Age or Older

- Analysis of adverse events passively reported to the Vaccine Adverse Event Reporting System (VAERS) indicate that persons 60 years of age or older may be at increased risk for systemic adverse events following vaccination compared with younger persons.
- The rate of any serious adverse event following vaccination is 1.5 times higher than the average rate for persons 60–69 years of age and 3 times higher for persons 70 years or older.
- To determine if vaccination should be administered to travelers 60 years of age or older, the risks and benefits of vaccination should be weighed against their destination-specific risk for exposure to YFV.

### Asymptomatic HIV

- Persons who are HIV-infected but who do not have AIDS or other symptomatic manifestations of HIV infection, who have established laboratory verification of adequate immune system function (e.g., CD4+ T cell counts  $>200/\text{mm}^3$ ), and who cannot avoid potential exposure to YFV should be offered the choice of vaccination.
- If international travel requirements are the only reason to vaccinate an asymptomatic HIV-infected person, rather than an increased risk for acquiring yellow fever, the person should be excused from immunization and issued a medical waiver to fulfill health regulations (see information in Exemption from Vaccination and Waiver Letters in this section).
- Data are limited regarding seroconversion rates after yellow fever vaccination among asymptomatic HIV-infected persons, but indicate that the seroconversion rate among such persons may be reduced. Because vaccination of asymptomatic HIV-infected persons might be less effective than that of persons not infected with HIV, measurement of the neutralizing antibody response to vaccination should be considered before travel.

### Pregnancy

- The safety of yellow fever vaccination during pregnancy has not been studied in a large prospective trial. However, a recent study of women who were vaccinated with yellow fever vaccine early in their pregnancies found no major malformations in their infants. There was slight increased risk noted for minor, mostly skin, malformations.
- In a similar study, a higher rate of spontaneous abortions in pregnant women receiving the vaccine was reported but not substantiated.
- The proportion of women vaccinated during pregnancy who develop YF IgG-specific antibodies is variable depending on the study (38.6% or 98.2%) and may be correlated with the trimester in which they received the vaccine. Because pregnancy may affect immunologic function, serologic testing can be considered to document a protective immune response to the vaccine.
- For pregnant women, if travel is unavoidable and the vaccination risks are felt to outweigh the risks of YF exposure, these women should be excused from immunization and, if applicable, issued a medical waiver to fulfill international health regulations (see information in Exemption from Vaccination and Waiver Letters in this section). Pregnant women who must travel to areas where the risk of yellow fever infection is high should be vaccinated, and their infants should be

monitored after birth for evidence of congenital infection and other possible adverse effects resulting from yellow fever vaccination.

- Although there are no specific data, it is recommended that a woman wait 4 weeks after receiving the live virus yellow fever vaccine before conceiving.

#### **Breastfeeding**

- Whether the yellow fever vaccine is excreted in breast milk is not known.
- One suspect case of YEL-AND has been reported in a 1-month old infant whose mother was vaccinated with yellow fever vaccine and the infant was exclusively breastfed. Testing was unable to determine if the breast milk was the mode of transmission.
- It is recommended that vaccination of nursing mothers should be avoided. However, when travel of nursing mothers to high-risk yellow fever-endemic areas cannot be avoided or postponed, these women should be vaccinated.

#### **Simultaneous Administration of Other Vaccines and Drugs**

- One study suggested that the immune response to yellow fever vaccine is not inhibited by administration of measles vaccine (also a live, attenuated vaccine) given concurrently or at various intervals of a few days to 1 month prior. However, to minimize the potential risk for interference, injectable or nasally administered live vaccines not administered on the same day should be given at least 4 weeks apart.
- A prospective study of persons given yellow fever vaccine along with 5 mL of commercially available IG showed no alteration of the immunologic response to yellow fever vaccine when compared with controls.

## **International Certificate of Vaccination or Prophylaxis (ICVP)**

### **Background**

- The International Health Regulations (IHR) allow countries to require proof of yellow fever vaccination for entry and from travelers arriving from certain countries, even if only in transit, to prevent importation and indigenous transmission of YFV.
- Some countries require evidence of vaccination from all entering travelers, which includes direct travel from the United States (Table 2-13).
- Travelers who arrive in a country with a yellow fever vaccination entry requirement without proof of yellow fever vaccination may be quarantined up to 6 days.
- Travelers with a specific contraindication to yellow fever vaccine should request a waiver from a physician before traveling to countries requiring vaccination (see below).

### **Authorization to Provide Vaccinations and to Validate the ICVP**

- Under the revised IHR (2005), effective December 15, 2007, all state parties (countries) are required to issue a new ICVP. This is intended to replace the former International Certificate of Vaccination against Yellow Fever (ICV).
  - Persons who received a yellow fever vaccination after December 15, 2007, must provide proof of vaccination on an ICVP.
  - If the person received the vaccine before December 15, 2007, the original ICV is still valid, provided that the vaccination was given less than 10 years previously.

- Vaccinees should receive a completed ICVP (Figure 2-1), validated (stamped and signed) with the center’s stamp where the vaccine was given (see below).
  - An ICVP must be complete in every detail; if incomplete or inaccurate, it is not valid.
  - Failure to secure validations can cause a traveler to be quarantined, denied entry, or possibly revaccinated at the point of entry to a country. This is not a recommended option for the traveler.
- A copy of the ICVP, CDC 731 (formerly PHS 731) may be purchased from the U.S. Government Printing Office, Washington, D.C., <http://bookstore.gpo.gov/>, telephone 866-512-1800. The stock number is 017-001-00567-3 for 25 copies and 017-001-00566-5 for 100 copies.
- This certificate of vaccination is valid for a period of 10 years, beginning 10 days after vaccination. With booster doses of the vaccine, the certificate is considered valid from the day of vaccination.

### **Persons Authorized to Sign the Certificate and Designated Yellow Fever Vaccination Centers**

- The ICVP must be signed by a licensed physician or by a health-care worker designated by the physician supervising the administration of the vaccine (Figure 2-1). A signature stamp is not acceptable.
- Yellow fever vaccination must be given at a certified center in possession of an official “Uniform Stamp,” which can be used to validate the ICVP.
- State health departments are responsible for designating nonfederal yellow fever vaccination centers and issuing Uniform Stamps to physicians.
- Information about the location and hours of yellow fever vaccination centers may be obtained by visiting CDC’s Travelers’ Health website at [wwwn.cdc.gov/travel/yellowfever.aspx](http://wwwn.cdc.gov/travel/yellowfever.aspx).

### **Exemption from Vaccination and Waiver Letters**

- Some countries do not require an ICVP for infants younger than a certain age (e.g., <6 months, <9 months, or <1 year of age, depending on the country). Age requirements for vaccination for individual countries can be found in the Yellow Fever Vaccine Requirements and Recommendations section in this chapter.
- For medical contraindications, a physician who has decided to issue a waiver should fill out and sign the Medical Contraindications to Vaccination section of the ICVP (Figure 2-2). The physician should also—
  - Give the traveler a signed and dated exemption letter on the physician’s letterhead stationery, clearly stating the contraindications to vaccination and bearing the stamp used by the yellow fever vaccination centers to validate the ICVP.
  - Inform the traveler of any increased risk of yellow fever infection associated with nonvaccination and how to minimize this risk by using mosquito protection measures.
- Reasons other than medical contraindications are not acceptable for exemption from vaccination.
- The traveler should be advised that issuance of a waiver does not guarantee its acceptance by the destination country. On arrival at the destination, the traveler may be faced with quarantine, refusal of entry, or vaccination on site.
- To potentially improve the likelihood of acceptance of a waiver upon arrival at the destination country, the provider can suggest that the traveler take the following additional measures before initiating travel:
  - Obtain specific and authoritative advice from the embassy or consulate of the country or

countries he or she plans to visit.

- Request documentation of requirements for waivers from embassies or consulates and retain these along with the completed Medical Contraindication to Vaccination section of the ICVP.

### Requirements Versus Recommendations

- Country entry **requirements** for proof of yellow fever vaccination under the IHRs are different from CDC's **recommendations**.
- Yellow fever vaccine entry **requirements** are established by countries in order to prevent the importation and transmission of YFV, and are allowed under the IHRs. Travelers must comply with these to enter the country, unless they have been issued a medical waiver. Certain countries require vaccination from travelers arriving from all countries, while some countries require vaccination only for travelers coming from "a country with risk of yellow fever transmission" (Table 2-14). WHO defines those areas "at risk of yellow fever transmission" as countries or areas where yellow fever has been reported currently or in the past, plus where vectors and animal reservoirs currently exist. Country requirements are subject to change at any time; therefore, CDC encourages travelers to check with the appropriate embassy or consulate before departure.
- The information in the section on yellow fever vaccine **recommendations** is advice given by CDC to prevent yellow fever infections among travelers. **Recommendations** are subject to change at any time if disease conditions change; therefore, CDC encourages travelers to check for relevant travel notices on the CDC website [www.cdc.gov/travel](http://www.cdc.gov/travel) before departure.

### Vaccination for Travel on Military Orders

Because military requirements may exceed those indicated in this publication, any person who plans to travel on military orders (civilians and military personnel) should be advised to contact the nearest military medical facility to determine the requirements for the trip.

### Table 2-13. Countries that require proof of yellow fever vaccination for all arriving travelers<sup>1</sup>

|   |                       |
|---|-----------------------|
| Angola  | French Guiana         |
| Benin   | Gabon                 |
| Bolivia (or signed affidavit at point of entry) | Ghana                 |
| Burkina Faso                                    | Liberia               |
| Burundi   | Mali                  |
| Cameroon  | Niger                 |
| Central African Republic                        | Rwanda                |
| Congo, Republic of the                          | São Tomé and Príncipe |
| Côte d'Ivoire                                   | Sierra Leone          |
| Democratic Republic of Congo                    | Togo                  |

<sup>1</sup> Country requirements for yellow fever vaccination are subject to change at any time; therefore, CDC encourages travelers to check with the destination country's embassy or consulate before departure.

**Figure 2-1. Example International Certificate of Vaccination or Prophylaxis (ICVP)**

**INTERNATIONAL CERTIFICATE OF VACCINATION OR PROPHYLAXIS**  
**Certificat international de vaccination ou de prophylaxie**

This is to certify that \_\_\_\_\_  
 Nous certifions que \_\_\_\_\_  
(name – nom) (date of birth – née) le (sex – de sexe) (nationality – et de nationalité)

\_\_\_\_\_ whose signature follows  
 \_\_\_\_\_ dont la signature suit

(national identification document, if applicable – document d'identification nationale, le cas échéant)

has on the date indicated been vaccinated or received prophylaxis against \_\_\_\_\_ in accordance with the International Health Regulations  
 a été vacciné(e) ou a reçu une prophylaxie à la date indiquée \_\_\_\_\_ conformément au Règlement sanitaire international.  
(name of disease or condition – nom de la maladie ou de l'affection)

| Vaccine or prophylaxis<br>Vaccin ou agent prophylactique | Date | Signature and professional status of supervising clinician<br>Signature et titre du professionnel de santé responsable | Manufacturer and batch no. of vaccine or prophylaxis<br>Fabricant du vaccin ou de l'agent prophylactique et numéro du lot | Certificate valid from: until:<br>Certificat valable à partir du: jusqu'au: | Official stamp of administering center<br>Cachet officiel du centre habilité |
|--|------|--|---|---|--|
|  |      |  |   |   |  |
|  |      |  |   |   |  |

**Figure 2-2. Example International Certificate of Vaccination or Prophylaxis (ICVP) medical contraindication to vaccination**

**MEDICAL CONTRAINDICATION TO VACCINATION**  
**Contre-indication médicale à la vaccination**

This is to certify that immunization against \_\_\_\_\_  
 Je soussigné(e) certifie que la vaccination contre \_\_\_\_\_  
(Name of disease – Nom de la maladie)

\_\_\_\_\_ for \_\_\_\_\_  
 \_\_\_\_\_ est médicalement \_\_\_\_\_  
(Name of traveler – Nom du voyageur)

contraindicated because of the following conditions:  
 contre-indiquée pour les raisons suivantes:

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_ (Signature and address of physician)  
 \_\_\_\_\_ (Signature et adresse du médecin)

## References

1. Monath TP, Teuwen D, Cetron MS. Yellow fever vaccine. In: Plotkin S, Orenstein WA, Offit PA, editors. *Vaccines*. 5th ed. Philadelphia: W.B. Saunders; 2008. p. 959–1055.
2. Monath TP, Cetron MS. Prevention of yellow fever in persons traveling to the tropics. *Clin Infect Dis*. 2002;34(10):1369–78.
3. Van der Stuyft P, Gianella A, Pirard M, et al. Urbanisation of yellow fever in Santa Cruz, Bolivia. *Lancet*. 1999;353(9164):1558–62.
4. Pan American Health Organization. EID Updates: Emerging and Reemerging Infectious Diseases, Region of the Americas. Vol. 5, No. 6 (25 Feb. 2008) Yellow fever in Paraguay: Mobilization continues. [cited 2008 Jun 8]. Available from: <http://www.paho.org/english/AD/DPC/CD/eid-eer-2008-02-25.htm>.
5. Tomori O. Yellow fever: The recurring plague. *Crit Rev Clin Lab Sci*. 2004;41(4):391–427.
6. World Health Organization. Yellow fever vaccine: WHO position paper. *Wkly Epidemiol Rec*. 2003;40:349–60.
7. Monath TP, Nichols R, Archambault WT, et al. Comparative safety and immunogenicity of two yellow fever 17D vaccines (Arlivax and YF-Vax) in a phase III multicenter, double-blind clinical trial. *Am J Trop Med Hyg*. 2002;66(5):553–41.
8. Pfsiter M, Kuersteiner O, Hilfiker H, et al. Immunogenicity and safety of Berna-YF compared with two other 17D yellow fever vaccines in a phase 3 clinical trial. *Am J Trop Med Hyg*. 2005;72(3):339–46.
9. Ripoll C, Ponce A, Wilson MM, et al. Evaluation of two yellow fever vaccines for routine immunization programs in Argentina. *Hum Vaccin*. 2008;4(2):121–6.
10. CDC. Yellow fever vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep*. 2002;51(RR-17):1–12.
11. World Health Organization. International Health Regulations. 2005. Geneva. [cited 2008 Jun 9]. Available from: <http://www.who.int/csr/ihr/en/index.html>.
12. Lindsey NP, Schroeder BA, Miller ER, et al. Adverse event reports following yellow fever vaccination. *Vaccine*. 2008;26(48):6077–82.
13. McMahon AW, Eidex RB, Marfin AA, et al. Neurologic disease associated with 17D-204 yellow fever vaccination: a report of 15 cases. *Vaccine*. 2007;25(10):1727–34.
14. CDC. Adverse events associated with 17D-derived yellow fever vaccination—United States, 2001–2002. *MMWR Morb Mortal Wkly Rep*. 2002;51(44):989–93.
15. Marfin AA, Eidex Barwick R, Monath TP. Yellow fever. In: Guerrant RL, Walker DH, Weller PF, editors. *Tropical infectious diseases: principles, pathogens, & practice*. 2nd ed. Philadelphia: Mosby Elsevier; 2005: p.797–812.
16. Hayes EB. Acute viscerotropic disease following vaccination against yellow fever. *Trans R Soc Trop Med Hyg*. 2007;101(10):967–71.
17. Muñoz J, Vilella A, Domingo C, et al. Yellow fever-associated viscerotropic disease in Barcelona, Spain. *J Travel Med*. 2008;15(3):202–5.
18. Barwick R. History of thymoma and yellow fever vaccination. *Lancet*. 2004;364(9438):936.
19. Cavalcanti DP, Salomao MA, Lopez-Camelo J, et al. Early exposure to yellow fever vaccine during pregnancy. *Trop Med Int Health*. 2007;12(7):833–7.
20. Nishioka Sde A, Nunes-Araujo FRF, Pires WP, et al. Yellow fever vaccination during pregnancy and spontaneous abortion: a case–control study. *Trop Med Int Health*. 1998;3(1):29–33.
21. Suzano CE, Amaral E, Sato HK, et al. The effects of yellow fever immunization (17DD) inadvertently used in early pregnancy during a mass campaign in Brazil. *Vaccine*. 2006;24(9):1421–6.
22. Nasidi A, Monath TP, Vandenberg J, et al. Yellow fever vaccination and pregnancy: a four-year

- prospective study. *Trans R Soc Trop Med Hyg.* 1993;87(3):337–9.
23. CDC. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2006;55(RR-15):1–48.
  24. Kaplan JE, Nelson DB, Schonberger LB, et al. The effect of immune globulin on the response to trivalent oral poliovirus and yellow fever vaccinations. *Bull World Health Organ.* 1984;62(4):585–90.