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Yellow fever vaccine

An effective vaccine for travelers

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Yellow fever (YF) is an acute viral communicable disease transmitted by an arbovirus of the *Flavivirus* genus. It is primarily a zoonotic disease, especially the monkeys. Worldwide, an estimated 200 000 cases of yellow fever occurred each year, and the case-fatality rate is ~15%. Forty-five endemic countries in Africa and Latin America, with a population of close to 1 billion, are at risk. Up to 50% of severely affected persons from YF die without treatment. During 2009, 55 cases and 18 deaths were reported from Brazil, Colombia, and Peru. Brazil reported the maximum number of cases and death, i.e., 42 cases with 11 deaths. From January 2010 to March 2011, outbreaks of YF were reported to the WHO by Cameroon, Democratic Republic of Congo, Cote d'Ivoire, Guinea, Sierra Leone, Senegal, and Uganda. Cases were also reported in three northern districts of Abim, Agago, and Kitugun near the border with South Sudan. YF usually causes fever, muscle pain with prominent backache, headache, shivers, loss of appetite, and nausea or vomiting. Most patients improve, and their symptoms disappear after 3 to 4 d. Half of the patients who enter the toxic phase die within 10–14 d, while the rest recover without significant organ damage. Vaccination has been the single most important measure for preventing YF. The 17D-204 YF vaccine is a freeze-dried, live attenuated, highly effective vaccine. It is available in single-dose or multi-dose vials and should be stored at 2 –8 °C. It is reconstituted with normal saline and should be used within 1 h of reconstitution. The 0.5 mL dose is delivered subcutaneously. Revaccination is recommended every 10 y for people at continued risk of exposure to yellow fever virus (YFV). This vaccine is available worldwide. Travelers, especially to Africa or Latin America from Asia, must have a certificate documenting YF vaccination, which is required by certain countries for entry under the International Health Regulations (IHR) of the WHO.

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Yellow fever (YF) is an acute viral hemorrhagic disease caused by an arbovirus in the flavivirus genus that is transmitted by mosquitoes among monkeys and humans. Several different species of the Aedes and Hemogogus mosquitoes that transmit the arbovirus breed around houses (domestic), in the jungle (wild), or in both habitats (semi-domestic).[1] Worldwide, ~200 000 cases of YF occurred annually with a case-fatality rate of ~15%.[2,3] Forty-five endemic countries are at risk in Africa and Latin America, with a population of close to 1 billion. Over 500 million people live at risk in 32 African countries: Angola, Benin, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Congo, Democratic Republic of the Congo, Ivory Coast, Equatorial Guinea, Ethiopia, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Liberia, Mali, Mauritania, Niger, Nigeria, Rwanda, Senegal, Sierra Leone, South Sudan, Sudan, Togo, and Uganda. The remaining at-risk populations are in 13 countries in Latin America, with Bolivia, Brazil, Colombia, Ecuador and Peru at greatest risk, plus Argentina (Misiones Province), Bolivia, Brazil, Colombia, and Ecuador

excluding Galapagos Islands, French Guiana, Guyana, Panama, Paraguay, Peru, Suriname, Trinidad, and Venezuela.[4]

The WHO region of the America experienced an increase in number of cases of YF in late 2007 and early 2008. In particular, an outbreak of jungle YF occurred in the monkey population (epizootic) in the south eastern regions of Brazil including the state of Rio Grande do Sul (the first outbreak of the jungle YF in the state since 1966). The outbreak spread to Paraguay (the first monkey and human case since 1974) and the provinces of Misiones and Corrientes, Argentina (the first human case in Corrientes since 1966).[5] YF was also identified in monkeys in Trinidad and Venezuela during this epizootic. In the year 2008, 102 cases including 52 deaths were reported by Argentina, Bolivia, Brazil, Colombia, Paraguay, and Peru.[5] In 2008–9, intense YFV circulation occurred in West Africa with outbreaks reported in Burkina Faso, Cameroon, Central Africa Republic, Chad, Congo, Cote d'Ivoire, Guinea, Liberia, and Sierra Leone.[6]

Up to 50% of severely affected persons from YF die without treatment. During 2009, 55 cases and 18 deaths were reported from Brazil, Colombia, and Peru. Brazil reported the largest number of cases and death, i.e., 42 cases with 11 deaths.[6] From January 2010 to March 2011, outbreaks were reported by Cameroon, Democratic Republic of Congo, Cote d'Ivoire, Guinea, Sierra Leone, Senegal, and Uganda. Cases were also reported in three northern districts of Abim, Agago, and Kitugun near the border with South Sudan.[7] In 2010, there were only two confirmed cases of YF reported in Brazil.[8] In 2010, no other countries in the America region reported YF outbreak to the WHO. Although the disease has never been reported in Asia, the region is at risk because the conditions required for transmission are present there. The number of YF cases has increased over the past two decades due to declining population immunity to infection, deforestation, urbanization, population movements, and climate change.

Once contracted, YFV incubates for 3–6 d, followed by disease that can occur in one or two phases. The first "acute" phase usually causes fever, muscle pain with prominent backache, headache, shivers, loss of appetite, and nausea or vomiting. Symptoms disappear in most patients after 3–4 d.[1] However, 15% of patients enter a second more toxic phase within 24 h of the initial remission. High fever returns, and several body systems are affected. The patient rapidly develops jaundice and reports abdominal pain with vomiting. Bleeding can occur from the mouth, nose, eyes or stomach, and blood appears in the vomit and feces. Kidney function deteriorates. Half of the patients who enter this toxic phase die within 10–14 d, while the rest recover without significant organ damage.

YF is difficult to diagnose, especially during the early stages. It can be confused with severe malaria, dengue hemorrhagic fever, leptospirosis, viral hepatitis (especially the fulminating forms of hepatitis B and D), other hemorrhagic fevers (Bolivian, Argentine, Venezuelan hemorrhagic fevers, and others flaviviruses such as West Nile and Zika) and other diseases, as well as poisoning. Blood tests can detect YF-specific antibodies produced in response to infection. Several other techniques are used to identify the virus in blood specimens or liver tissue collected after death.[1] There is no cure for YF. Treatment is symptomatic only, especially for dehydration and fever. Associated bacterial infections can be treated with antibiotics. Supportive care may improve outcomes for seriously ill patients, but is rarely available in poorer areas.

Strategies to Control Yellow Fever

1. Vaccines

Vaccination is the single most important measure for preventing YF. In high-risk areas where YF vaccination coverage is low, prompt recognition and control of outbreaks through vaccination is important to prevent epidemics. To prevent outbreaks throughout affected regions, vaccination coverage must reach at least 60–80% of the at-risk population. Few endemic countries in Africa benefited from the recent mass vaccination campaign. YF vaccination is offered through routine infant immunization or through mass vaccination campaigns to increase coverage in countries at risk, as well as for travelers to endemic areas. WHO strongly recommends routine vaccination for children in high-risk areas. Vaccine is indicated for susceptible adults and children aged nine months or older who need primary or booster vaccination for personal protection or in order to comply with International Health Regulation (IHR; 2005), or both (the requirement for vaccination is not always related to the risk of exposure). YF vaccine is also indicated in laboratory workers handling infective material

YF vaccines have been available for >60 years. Two 17D substrain vaccines are manufactured, namely the 17DD and 17D-204 YF vaccines. The 17DD YF vaccine is manufactured in Brazil and is used in Brazil and many other South American countries. The 17D-204 YF vaccine is a freeze-dried, live attenuated, highly effective vaccine. It is available worldwide in single- or multi-dose vials and should be stored at 2–8 °C. It should be used within 1 h of reconstitution with normal saline. The 0.5 mL dose is injected subcutaneously. Revaccination is recommended every 10 y for people at continued risk of exposure to YFV.

The YF vaccine is safe and affordable, providing effective immunity within one week for 95% of vaccinees. A single dose provides protection for 30^{+} years and probably for life. Serious side effects are extremely rare and have been reported in a few endemic areas and among some vaccinated travelers. The risk of death from YF is far greater than risks related to vaccinations.

Contraindication of YF vaccine

- Children aged <9 mo for routine immunization (or <6 mo during an epidemic);
- Pregnant women—except during a YF outbreak when the risk of infection is high;
- People with severe allergies to egg protein; and
- People with severe immunodeficiency due to symptomatic HIV or other causes, or in the presence of a thymus disorder.

International certificate of YF vaccination

Travelers, especially to Africa or Latin America from Asia, must have a certificate of YF vaccination for entry to certain

countries under the International Health Regulations (IHR) of WHO.[9] The countries that require proof of vaccination from all arriving travelers are Angola, Benin, Burkina Faso, Burundi, Cameroon, Central African Republic Congo Republic of the Côte d'Ivoire, Democratic Republic of Congo, French Guiana, Gabon, Ghana, Guinea-Bissau, Liberia, Mali, Niger, Rwanda,, São Tomé, and Príncipe Sierra Leone, and Togo.[10] Such travelers arriving without proof of vaccination may be quarantined for up to 6 d, refused entry, or vaccinated on site. A traveler with a specific contraindication to YF vaccine or other medical grounds for not getting vaccinated and who cannot avoid travel to a country requiring vaccination should request a waiver from a physician before embarking on travel. Most countries will accept a medical waiver for persons with a medical reason not to receive the vaccine. A physician's letter clearly stating the medical reason not to receive the vaccine might be acceptable to some governments. It should be written on letterhead stationery and bear the stamp used by a health department or official immunization center to validate the International Certificate of Vaccination (ICV). After immunization an ICV is issued and is valid from 10 d after vaccination to meet entry and exit requirements of all countries for up to 10 y.[11]

The IHR directs countries to ask for proof of YF vaccination as a condition of entry for travelers arriving from certain countries, even if only in transit to prevent importation and indigenous transmission of YFV. Under the revised IHR (2005), which was effective from December 2007, all countries are required to issue a new ICV or Prophylaxis (ICVP). This is intended to replace the former ICV against Yellow Fever (ICVYF). People vaccinated after December 2007 must provide proof of vaccination on the new ICVP. If one was vaccinated before December 2007, the original ICV card is still valid, provided that vaccination had been given <10 y previously. An ICVP must be complete in every detail; if incomplete or inaccurate, it is invalid. Failure to secure validations can cause denied entry, or possibly require revaccination at the point of entry to a country; the latter is not a recommended option for the traveler.

2. Control strategies for mosquito

The risk of YF transmission in urban areas can be reduced by checking on breeding sites and applying insecticides to water where they develop. Spray insecticides can be used to kill adult mosquitoes during urban epidemics, combined with emergency vaccination campaigns. It can reduce or halt YF transmission, "buying time" for vaccinated populations to build immunity. Mosquito control strategies for mosquitoes in forested areas are not practical for preventing jungle (or sylvatic) YF transmission.

3. Rapid response during outbreak

Prompt detection of YF and rapid response through emergency vaccination campaigns are essential for controlling outbreaks. However, underreporting is a concern. The true number of cases is estimated to be 10–250 times what is being reported. WHO recommends that every at-risk country have at least one national laboratory where basic YFV blood tests can be performed. Even one confirmed case of YF in an unvaccinated population should be considered an outbreak, and a confirmed case in any context must be fully investigated (particularly in any area where most of the population has been vaccinated). Investigation teams must assess and respond to the outbreak with both emergency measures and longer-term immunization plans.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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