

## Introduction

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Yellow fever is an acute viral haemorrhagic disease, found in tropical regions of Africa and the Americas. It principally affects humans and monkeys, and is transmitted via the bite of *Aedes* mosquitoes. It can produce devastating outbreaks, which can be prevented and controlled by mass vaccination campaigns.

The number of yellow fever cases has increased over the past two decades due to declining population immunity to infection, deforestation, urbanization, population movements and climate change.

Yellow fever can be recognized from historic texts stretching back 400 years. Infection causes a wide spectrum of disease, from mild symptoms to severe illness and death. The "yellow" in the name is explained by the jaundice that affects some patients, causing yellow eyes and yellow skin.

## Virology

Yellow fever virus is classified in genus *Flavivirus* which is in the family *Flaviviridae*. The yellow fever virus is small (35 to 45 nm) and consists of a core containing single-stranded RNA surrounded by a lipid envelope.

## Mode of transmission

Exposure of susceptible persons to bites from infected mosquitoes is the only significant mode of yellow fever transmission. An urban and a jungle (forest, sylvatic) form of yellow fever can be distinguished by differences in their respective transmission cycles. Urban yellow fever, which frequently occurs as large outbreaks, is transmitted from infected to susceptible humans by *Aedes aegypti*, a mosquito species that breeds in the proximity of human habitats. The urban form of transmission is found mainly in Africa. The sylvatic form of yellow fever is primarily an enzootic viral disease of non-human primates, but the various mosquito vectors involved may occasionally cause individual cases or small outbreaks of yellow fever among humans in the forested savanna of Africa and in jungle areas of South America.

## Clinical Features

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Once contracted, the virus incubates in the body for 3 to 6 days, followed by infection 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. Most patients improve and their symptoms disappear after 3 to 4 days.

However, 15% of patients enter a second, more toxic phase within 24 hours of the initial remission. High fever returns and several body systems are affected.

The patient rapidly develops jaundice and complains of abdominal pain with vomiting. Bleeding can occur from the mouth, nose, eyes or stomach. Once this happens, blood appears in the vomit and faeces. Kidney function deteriorates. Half of the patients who enter the toxic phase die within 10 to 14 days, the rest recover without significant organ damage.

There is no specific treatment for yellow fever. Treatment is symptomatic, aimed at reducing the symptoms for the comfort of the patient.

## Epidemiology

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### Global Situation

Forty-five endemic countries in Africa and Latin America, with a combined population of over 900 million, are at risk. In Africa, an estimated 508 million people living in 32 countries are at risk. The remaining population at risk is in 13 countries in Latin America.

There are an estimated 200,000 cases of yellow fever (causing 30,000 deaths) worldwide each year. Small numbers of imported cases occur in countries free of yellow fever. Although the disease has never been reported in Asia, the region is at risk because the conditions required for transmission are present there.

Millions of travellers to risk areas are also at risk of yellow fever infection. For unvaccinated individuals entering into endemic areas in Africa, the risks of yellow fever illness and death have been estimated at 1:267 and 1:1333, respectively, for a two week trip, although the risks vary considerably according to the season. The corresponding figures for South America are likely to be 10 times lower.

### Situation in Sri Lanka

Yellow fever is a notifiable disease in Sri Lanka and all cases of yellow fever should be notified immediately to the local Medical Officer of Health and WHO. Although the vector *Aedes aegypti* mosquito is found in Sri Lanka, yellow fever cases have not been reported.

### Yellow fever vaccine

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Vaccination is the single most important measure for preventing yellow fever. In high risk areas where vaccination coverage is low, prompt recognition and control of outbreaks through immunization is critical to prevent epidemics.

Preventive vaccination can be offered through routine infant immunization and one-time mass campaigns to increase vaccination coverage in countries at risk, as well as for travellers to yellow fever endemic areas.

WHO strongly recommends routine yellow fever vaccination for children in areas at risk for the disease.

For decades, a safe and effective 17D vaccine has been available and is recommended by WHO for large-scale use by residents of and visitors to at risk countries. The yellow fever vaccine is safe and affordable, providing effective immunity against yellow fever within one week for 95% of those vaccinated. A single dose provides protection for 30–35 years or more, and probably for life. Serious side effects are extremely rare.

## Characteristics of yellow fever vaccine

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The yellow fever 17D vaccine is the only commercially available vaccine against yellow fever. It is a lyophilized live attenuated vaccine. The vaccine is based on a wild type yellow fever virus (the Asibi strain) isolated in Ghana in 1927 and attenuated by serial passages, principally in chicken embryo tissue culture.

## Indications

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All persons aged 9 months or older and living in yellow fever at-risk areas should receive yellow fever vaccine.

Immigrants who are above 9 months of age to endemic regions from non-endemic areas should also be vaccinated against yellow fever. Travellers should be vaccinated at least 10 days before arrival in the at risk area.

## Efficacy

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Protective levels of neutralizing antibodies (log neutralization index of at least 0.7) are found in 90% of vaccinees within 10 days and in 99% within 30 days. In most cases, protection appears to last for 30 - 35 years or more.

## Immunization Schedule

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In countries at risk for yellow fever, vaccine is recommended for use in all children aged at least 9 - 12 months of age. Vaccination for yellow fever is also recommended for travellers aged above 9 months who plan to visit areas at risk for yellow fever e.g: Africa and South America.

## Dosage & Administration

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Yellow fever vaccine is a lyophilized vaccine and is provided with a vaccine specific diluent (sterile water for injection). It should be reconstituted only with the diluent supplied using a sterile syringe and needle.

A single dose of 0.5 ml is recommended for both children more than 9 months of age and adults. Reconstituted vaccine can be administered by either intramuscular or subcutaneous injection, although the subcutaneous route is preferred.

The vaccine can be administered concurrently with other vaccines, but in a separate syringe and at a different site. If not administered concurrently, the vaccine must be separated from other live vaccines (e.g. measles, mumps and rubella – MMR) by at least one month.

## Storage

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The vaccine and diluent should be stored at +2°C to +8°C. Do not freeze. Protect from light. The vaccine should be used within 1 hour of reconstitution.

## Cautions and contraindications

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The following conditions are considered as contraindications for the use of yellow fever vaccine.

- ◆ Presence of one of the general contraindications for any vaccine.
- ◆ Children aged under 6 months and is not recommended for those aged 6 - 8 months, except during epidemics when the risk of yellow fever virus transmission may be very high.
- ◆ History of a severe allergy to egg or any other vaccine components.
- ◆ Anyone who has experienced anaphylaxis to a previous dose of yellow fever vaccine.
- ◆ Persons who are severely immunocompromised as a result of congenital disease, HIV infection, advanced leukaemia or lymphoma, serious malignant disease, or treatment with high-dose steroids or in persons who are receiving immunosuppressive therapeutic radiation.
- ◆ Pregnancy (However, pregnant women may be vaccinated during epidemics when the risk of yellow fever virus transmission may be very high).

## Adverse Events

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Mild systemic reactions such as headache, myalgia, malaise and weakness occur during the first few days after vaccination in 10 - 30% of vaccinees. Severe adverse reactions like Post-vaccine encephalitis is an extremely rare event seen among infants.

## Yellow fever certificate

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A valid certificate of yellow fever vaccination is required under the International health regulations for entry into most yellow fever-endemic countries or for travel from yellow fever endemic countries to countries at risk for introduction of yellow fever virus. Country requirements are published annually by WHO in *International travel health* (available at [www.who.int/ith](http://www.who.int/ith)). The International Certificate of yellow fever vaccination is valid for ten years beginning from the tenth day after primary immunization; a booster dose of yellow fever vaccine is required in every 10 years.

The authorized yellow fever vaccination centre in Sri Lanka for travellers to high-risk areas is held at the office of the Assistant Port Health Officer situated at the Medical Research Institute (MRI), Colombo 08.

Travellers, arriving to Sri Lanka from African or Latin American yellow fever endemic countries must have a valid certificate of vaccination against yellow fever.

## Sources

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Department of Health and Ageing, Australia, 2008. *The Australian Immunization Handbook*, 9<sup>th</sup> ed. Australia, p.222 – 328.

CDC, 2001- 2002. Adverse events associated with 17D-derived yellow fever vaccination. *Morbidity and Mortality Weekly Report*, 51,p. 989-93.

Heymann, DL, 2008. *Control of Communicable Diseases Manual*, 19th ed. American Public Health Association: Washington DC, p. 685 - 690.

World Health Organisation, 2004. *International Travel and Health. Vaccination Requirements and Health Advice*. Geneva: World Health Organisation, p. 210.

World Health Organization, 2003. Yellow fever vaccine: WHO Position Paper. *Weekly Epidemiological Record*, 78 (40), p.349-360. ([www.who.int/wer](http://www.who.int/wer))