

## Yellow Fever



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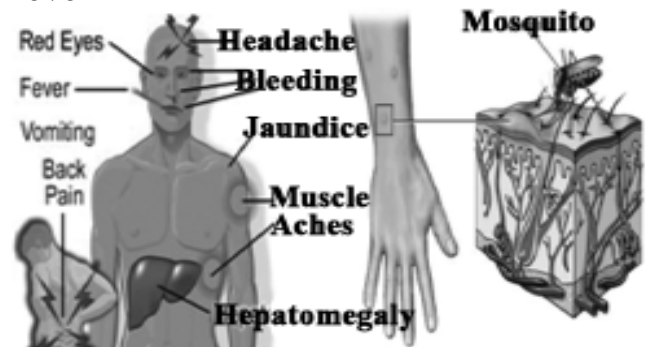
Yellow Fever is a viral infection caused by RNA viruses belonging to the Flavivirus genus. It is a zoonosis (an animal disease that can spread to humans) primarily transmitted by daytime biting *Aedes Aegypti* female mosquitoes, but also by mosquitoes belonging to the *Haemagogus* genus. Yellow fever, also known as Yellow Jack or "Yellow Rainer" and other names,[1] is an acute viral hemorrhagic disease.[2] The virus is a 40 to 50 nm enveloped positive-sense RNA virus, the first human virus discovered and the namesake of the Flavivirus genus.

**Risk:** Travellers are at risk when going to endemic areas of Africa and South America.

**Transmission:** In the sylvatic cycle, Yellow Fever is transmitted by mosquitoes that bite infected monkeys passing the infection to humans living in or visiting jungle areas. Yellow Fever is endemic in the sylvatic setting in sub-Saharan Africa and the tropical regions of South America. In the intermediate or savannah cycle, the infection is transmitted to humans via mosquitoes that bite infected monkeys or other humans living or working in jungle border areas in Africa. In the urban cycle, infected mosquitoes transmit Yellow Fever from person to person that can cause large outbreaks in cities and suburbs. Yellow Fever outbreaks occur periodically in Africa and have occurred sporadically in South America.

**Pathogenesis:** After transmission of the virus from a mosquito, the viruses replicate in the lymph nodes and infect dendritic cells in particular. From there they reach the liver and infect hepatocytes (probably indirectly via Kupffer cells), which leads to eosinophilic degradation of these cells and to the release of cytokines. Necrotic masses (Councilman bodies) appear in the cytoplasm of hepatocytes.[9][21]

When the disease takes a deadly course, a cardiovascular shock and multi-organ failure, with strongly increased cytokine levels (cytokine storm), follow.[14]



**Symptoms:** Yellow fever has three stages:

❖ **Stage 1 (infection):** Headache, muscle and joint aches, fever, flushing, loss of appetite, vomiting, and jaundice are common. Symptoms often go away briefly after about 3-4 days.

**Stage 2 (remission):** Fever and other symptoms go away. Most people will recover at this stage, but others may get worse within 24 hours.

**Stage 3(intoxication):**Problems with many organs occur. This may include heart, liver, and kidney failure, bleeding disorders, seizures, coma, and delirium.

**Symptoms may include:** Irregular heart beats (arrhythmias), Bleeding (may progress to hemorrhage), Coma, Decreased urination, Delirium, Fever, Headache, Yellow skin and eyes (jaundice), Muscle aches, Red eyes, face, tongue, Seizures

**Diagnosis:** Yellow fever is a clinical diagnosis, which often relies on the whereabouts of the diseased person during the incubation time. Mild courses of the disease can only be confirmed virologically. Since mild courses of yellow fever can also contribute significantly to regional outbreaks, every suspected case of yellow fever (involving symptoms of fever, pain, nausea and vomiting six to ten days after leaving the affected area) has to be treated seriously.

If yellow fever is suspected, the virus cannot be confirmed until six to ten days after the illness. A direct confirmation can be obtained by reverse transcription polymerase chain reaction where the genome of the virus is amplified.[8] Another direct approach is the isolation of the virus and its growth in cell culture using blood plasma; this can take one to four weeks.

Serologically, an enzyme linked immunosorbent assay during the acute phase of the disease using specific IgM against yellow fever or an increase in specific IgG-titer (compared to an earlier sample) can confirm yellow fever. Together with clinical symptoms, the detection of IgM or a fourfold increase in IgG-titer is considered sufficient indication for yellow fever. Since these tests can cross-react with other flaviviruses, like Dengue virus, these



indirect methods can never prove yellow fever infection.

Liver biopsy can verify inflammation and necrosis of hepatocytes and detect viral antigens. Because of the bleeding tendency of yellow fever patients, a biopsy is only advisable post mortem to confirm the cause of death.

In a differential diagnosis, infections with yellow fever have to be distinguished from other feverish illnesses like malaria. Other viral hemorrhagic fevers, such as Ebola virus, Lassa virus, Marburg virus and Junin virus, have to be excluded as cause.

**Prevention:** Yellow Fever is a vaccine preventable disease. Vaccination is recommended for persons over 9 months of age travelling to or living in endemic areas. The vaccine affords long term protection.

Note that some countries require a valid Yellow Fever Vaccination Certificate for entry" vaccination administered at least 10 days before travel and no longer than 10 years ago" under International Health Regulations. Listed below are the countries requiring proof of Yellow Fever vaccination certificates.

If going to low risk Yellow Fever areas, travellers should take measures to prevent mosquito bites both indoors and outdoors, especially during the daytime. Insect-bite prevention measures include applying a DEET-containing repellent to exposed skin, applying permethrin spray (or solution) to clothing and gear, wearing long sleeves and pants, getting rid of water containers around dwellings and ensuring that door and window screens work properly.

**Vaccination precautions:** Children between the ages of 6 to 8 months, persons over 60 years, those with asymptomatic HIV, pregnant, or breastfeeding. Vaccination should only be given if travel to endemic area cannot be delayed or avoided.

**Vaccination contraindications:** Children under 6 months of age, persons with immune deficiencies or on immunosuppressive therapies, allergies to egg proteins, transplant recipients, and persons with symptomatic HIV infection. If vaccination is contraindicated for medical reasons an exemption letter or waiver should be issued to the traveller. However, acceptance of such a letter is at the discretion of the destination country, and entry might be denied.

**Special issues:** International health regulations: A yellow fever vaccination certificate is now the only vaccination certificate that should be required in international travel, and then only for a limited number of persons. Many countries require a valid international certificate of vaccination from travellers, including those in transit, arriving from infected areas or from countries with infected areas. Some countries require a certificate from all entering travellers, even those arriving from countries where there is no risk of yellow fever. Although this exceeds the provisions of International Health

Regulations, travellers may find that it is strictly enforced, particularly for people arriving in Asia from Africa or South America. Vaccination is strongly advised for travellers outside urban areas of countries in zones where yellow fever is endemic, even if these countries have not officially reported the disease and do not require evidence of vaccination on entry. The actual areas of yellow fever virus activity far exceed the officially reported infected zones.

**Administration summary**

Type of vaccine	Live viral
Number of doses	One dose of 0.5 ml subcutaneously
Schedule	Routine immunization with measles vaccine at nine months of age
Booster	International health regulations require a booster every 10 years
Contraindications	Egg allergy; immune deficiency from medication or disease; symptomatic HIV infection; hypersensitivity to previous dose; pregnancy*
Adverse reactions	Hypersensitivity to egg; rarely, encephalitis in the very young; hepatic failure. Rare reports of death from massive organ failure (see above).
Special precautions	Do not give before six months of age; avoid during pregnancy

**For the Consumer:** Check with your doctor or nurse immediately if any of the following side effects occur while taking yellow fever vaccine:

**Rare:** Confusion, Convulsions (seizures), Coughing, Difficulty with breathing or swallowing, Fast heartbeat, Feeling of burning, crawling, or tingling of the skin, Nervousness or irritability, Reddening of the skin, Severe headache, Skin rash or itching, Sneezing, Stiff neck, Throbbing in the ears, Unusual tiredness or weakness, Vomiting.

Some side effects of yellow fever vaccine may occur that usually do not need medical attention. These side effects may go away during treatment as your body adjusts to the medicine. Also, your health care professional may be able to tell you about ways to prevent or reduce some of these side effects. Check with your health care professional if any of the following side effects continue or are bothersome or if you have any questions about them:  
Less common

Difficulty with moving, Joint pain, Low fever, Mild headache, Muscle aching or cramping, Muscle pains or stiffness, Pain at the injection site, Swollen joints

**References**

01. Weir, E (October 2001). "Yellow fever vaccination: be sure the patient needs it". CMAJ : Canadian Medical Association 165 (7): 941. PMC 81520. PMID 11599337.  
02. Mark Gershman, Betsy Schroeder, and J. Erin Staples. "Yellow Fever". Yellow Book. Center for Disease Control (Canada). Retrieved 1 July 2011.