

Yellow fever

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Key facts

- **Yellow fever is an acute viral haemorrhagic disease transmitted by infected mosquitoes. The "yellow" in the name refers to the jaundice that affects some patients.**
- **Symptoms of yellow fever include fever, headache, jaundice, muscle pain, nausea, vomiting and fatigue.**
- **A small proportion of patients who contract the virus develop severe symptoms and approximately half of those die within 7 to 10 days.**
- **The virus is endemic in tropical areas of Africa and Central and South America.**
- **Large epidemics of yellow fever occur when infected people introduce the virus into heavily populated areas with high mosquito density and where most people have little or no immunity, due to lack of vaccination. In these conditions, infected mosquitoes of the *Aedes aegypti* specie transmit the virus from person to person.**
- **Yellow fever is prevented by an extremely effective vaccine, which is safe and affordable. A single dose of yellow fever vaccine is sufficient to confer sustained immunity and life-long protection against yellow fever disease and a booster dose of the vaccine is not needed. The vaccine provides effective immunity within 30 days for 99% of persons vaccinated.**
- **Good supportive treatment in hospitals improves survival rates. There is currently no specific anti-viral drug for yellow fever.**
- **The Eliminate Yellow fever Epidemics (EYE) Strategy launched in 2017 is an unprecedented initiative. With more than 50 partners involved, the EYE partnership supports 40 at-risk countries in Africa and the Americas to prevent, detect, and respond to yellow fever suspected cases and outbreaks. The partnership aims at protecting at-risk populations, preventing international spread, and containing outbreaks rapidly. By 2026, it is expected that more than 1 billion people will be protected against the disease.**

Signs and symptoms

Once contracted, the yellow fever virus incubates in the body for 3 to 6 days. Many people do not experience symptoms, but when these do occur, the most common are fever, muscle pain with prominent backache, headache, loss of appetite, and nausea or vomiting. In most cases, symptoms disappear after 3 to 4 days.

A small percentage of patients, however, enter a second, more toxic phase within 24 hours of recovering from initial symptoms. High fever returns and several body systems are affected, usually the liver and the kidneys. In this phase people are likely to develop jaundice (yellowing of the skin and eyes, hence the name 'yellow fever'), dark urine and abdominal pain with vomiting. Bleeding can occur from the mouth, nose, eyes or stomach. Half of the patients who enter the toxic phase die within 7 - 10 days.

Diagnosis

Yellow fever is difficult to diagnose, especially during the early stages. A more severe case can be confused with severe malaria, leptospirosis, viral hepatitis (especially fulminant forms), other haemorrhagic fevers, infection with other flaviviruses (such as dengue haemorrhagic fever), and poisoning.

Polymerase chain reaction (PCR) testing in blood and urine can sometimes detect the virus in early stages of the disease. In later stages, testing to identify antibodies is needed.

Populations at risk

Forty seven countries in Africa (34) and Central and South America (13) are either endemic for, or have regions that are endemic for, yellow fever. A modelling study based on African data sources estimated the burden of yellow fever during 2013 was 84 000–170 000 severe cases and 29 000–60 000 deaths.

Occasionally travellers who visit yellow fever endemic countries may bring the disease to countries free from yellow fever. In order to prevent such importation of the disease, many countries require proof of vaccination against yellow fever before they will issue a visa, particularly if travellers come from, or have visited yellow fever endemic areas.

In past centuries (17th to 19th), yellow fever was transported to North America and Europe, causing large outbreaks that disrupted economies, development and in some cases decimated populations.

Transmission

The yellow fever virus is an arbovirus of the flavivirus genus and is transmitted by mosquitoes, belonging to the *Aedes* and *Haemogogus* species. The different mosquito species live in different habitats - some breed around houses (domestic), others in the jungle (wild), and some in both habitats (semi-domestic). There are 3 types of transmission cycles:

- Sylvatic (or jungle) yellow fever: In tropical rainforests, monkeys, which are the primary reservoir of yellow fever, are bitten by wild mosquitoes which pass the virus on to other monkeys. Occasionally humans working or travelling in the forest are bitten by infected mosquitoes and develop yellow fever.
- Intermediate yellow fever: In this type of transmission, semi-domestic mosquitoes (those that breed both in the wild and around households) infect both monkeys and people. Increased contact between people and infected mosquitoes leads to increased transmission and many separate villages in an area can develop outbreaks at the same time. This is the most common type of outbreak in Africa.
- Urban yellow fever: Large epidemics occur when infected people introduce the virus into heavily populated areas with high mosquito density and where most people have little or no immunity, due to lack of vaccination. In these conditions, infected mosquitoes transmit the virus from person to person.

Treatment

Good and early supportive treatment in hospitals improves survival rates. There is currently no specific anti-viral drug for yellow fever but specific care to treat dehydration, liver and kidney failure, and fever improves outcomes. Associated bacterial infections can be treated with antibiotics.

Prevention

1. Vaccination

Vaccination is the most important means of preventing yellow fever. In high-risk areas where vaccination coverage is low, prompt recognition and control of outbreaks using mass immunization is critical for preventing epidemics. It is important to vaccinate most

(80 % or more) of the population at risk to prevent transmission in a region with a yellow fever outbreak.

Several vaccination strategies are used to protect against outbreaks: routine infant immunization; mass vaccination campaigns designed to increase coverage in countries at risk; and vaccination of travellers going to yellow fever endemic areas.

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There have been rare reports of serious side-effects from the yellow fever vaccine. The rates for these severe 'adverse events following immunization' (AEFI), when the vaccine provokes an attack on the liver, the kidneys or on the nervous system, leading to hospitalization, are between 0.4 and 0.8 per 100 000 people vaccinated.

The risk is higher for people over 60 years of age and anyone with severe immunodeficiency due to symptomatic HIV/AIDS or other causes, or who have a thymus disorder. People over 60 years of age should be given the vaccine after a careful risk-benefit assessment.

People who are usually excluded from vaccination include:

- infants aged less than 9 months, except during an epidemic when infants aged 6-9 months, in areas where the risk of infection is high, should also receive the vaccine;
- pregnant women – except during a yellow fever outbreak when the risk of infection is high;
- people with severe allergies to egg protein; and
- people with severe immunodeficiency due to symptomatic HIV/AIDS or other causes, or who have a thymus disorder.

In accordance with the International Health Regulations (IHR), countries have the right to require travellers to provide a certificate of yellow fever vaccination. If there are medical grounds for not getting vaccinated, this must be certified by the appropriate authorities. The IHR are a legally binding framework to stop the spread of infectious diseases and other health threats. Requiring the certificate of vaccination from travellers is at the discretion of each State Party, and it is not currently required by all countries.

2. Vector control

The risk of yellow fever transmission in urban areas can be reduced by eliminating potential mosquito breeding sites by applying larvicides to water storage containers and other places where standing water collects.

Both vector surveillance and control are components of the prevention and control of vector-borne diseases, especially for transmission control in epidemic situations. For yellow fever, vector surveillance targeting *Aedes aegypti* and other *Aedes* species will help inform where there is a risk of an urban outbreak.

Understanding the distribution of these mosquitoes within a country can allow a country to prioritize areas to strengthen their human disease surveillance and testing, and consider vector control activities. There is currently a limited public health arsenal of safe, efficient and cost-effective insecticides that can be used against adult vectors. This is mainly due to the resistance of major vectors to common insecticides and the withdrawal or abandonment of certain pesticides for reasons of safety or the high cost of re-registration.

Historically, mosquito control campaigns successfully eliminated *Aedes aegypti*, the urban yellow fever vector, from most of Central and South America. However, *Aedes aegypti* has re-colonized urban areas in the region, raising a renewed risk of urban yellow fever. Mosquito control programmes targeting wild mosquitoes in forested areas are not practical for preventing jungle (or sylvatic) yellow fever transmission.

Personal preventive measures such as clothing minimizing skin exposure and repellents are recommended to avoid mosquito bites. The use of insecticide-treated bed nets is limited by the fact that *Aedes* mosquitoes bite during the daytime.

3. Epidemic preparedness and response

Prompt detection of yellow fever 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 to 250 times what is now being reported.

WHO recommends that every at-risk country have at least one national laboratory where basic yellow fever blood tests can be performed. One laboratory-confirmed case of yellow fever in an unvaccinated population is considered an outbreak. A confirmed case in any context must be fully investigated, particularly in an 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.

WHO response

In 2016, two linked urban yellow fever outbreaks – in Luanda (Angola) and Kinshasa (Democratic Republic of the Congo), with wider international exportation from Angola to other countries, including China – have shown that yellow fever poses a serious global threat requiring new strategic thinking. The Eliminate Yellow Fever Epidemics (EYE)

Strategy was developed to respond to the increased threat of yellow fever urban outbreaks with international spread. Steered by WHO, UNICEF, and Gavi, the Vaccine Alliance, EYE supports 40 countries and involves more than 50 partners.

The global EYE Strategy is guided by three strategic objectives:

1. protect at-risk populations
2. prevent international spread of yellow fever
3. contain outbreaks rapidly.

These objectives are underpinned by five competencies of success:

1. affordable vaccines and sustained vaccine market
2. strong political commitment at global, regional and country levels
3. high-level governance with long-term partnerships
4. synergies with other health programmes and sectors
5. research and development for better tools and practices.

The EYE strategy is comprehensive, multi-component and multi-partner. In addition to recommending vaccination activities, it calls for building resilient urban centres, planning for urban readiness, and strengthening the application of the International Health Regulations (2005).

The EYE partnership supports yellow fever high and moderate risk countries in Africa and the Americas by strengthening their surveillance and laboratory capacity to respond to yellow fever cases and outbreaks. EYE partners also support the implementation and sustainability of routine immunization programmes and vaccination campaigns (preventive, pre-emptive, reactive) whenever and wherever needed.

To guarantee a rapid and effective response to outbreaks, an emergency stockpile of 6 million doses of yellow fever vaccine, funded by Gavi, is continually replenished. This emergency stockpile is managed by the International Coordinating Group for Vaccine Provision, for which WHO serves as secretariat.

It is expected that by the end of 2026, more than 1 billion people will be protected against yellow fever through vaccination.