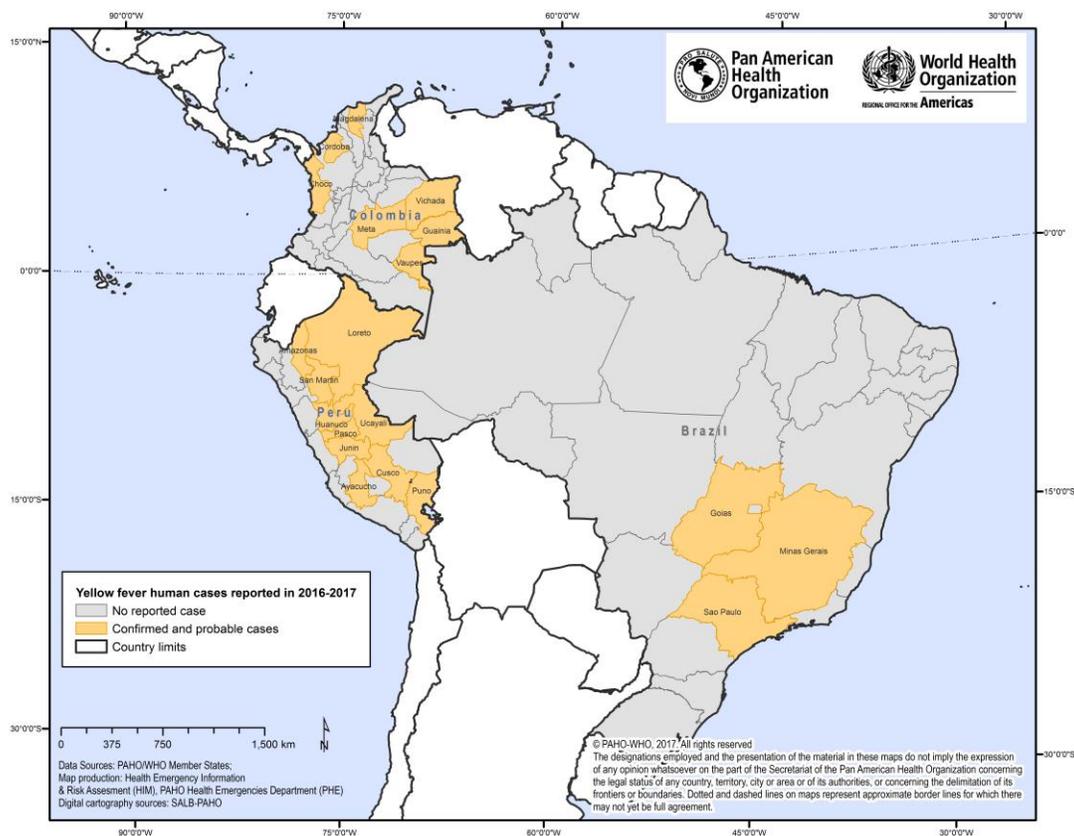


Situation summary in the Americas

In 2016, Brazil, Colombia, and Peru reported confirmed cases of yellow fever (**Figure 1**).

Figure 1. Geographic location of probable and confirmed cases of yellow fever reported in the Americas during 2016 and 2017



Brazil confirmed six human yellow fever cases in 2016¹ and the number of epizootics, especially in the state of São Paulo, increased considerably during 2016 in comparison to previous years. From the beginning of 2016 until 12 December 2016 the state of São Paulo reported 163 epizootics in non-human primates (NHP) with a total of 227 affected animals. To date, a total of 16 epizootics (corresponding to 24 NHPs) were confirmed and 35 were discarded. The remaining epizootics are under investigation.

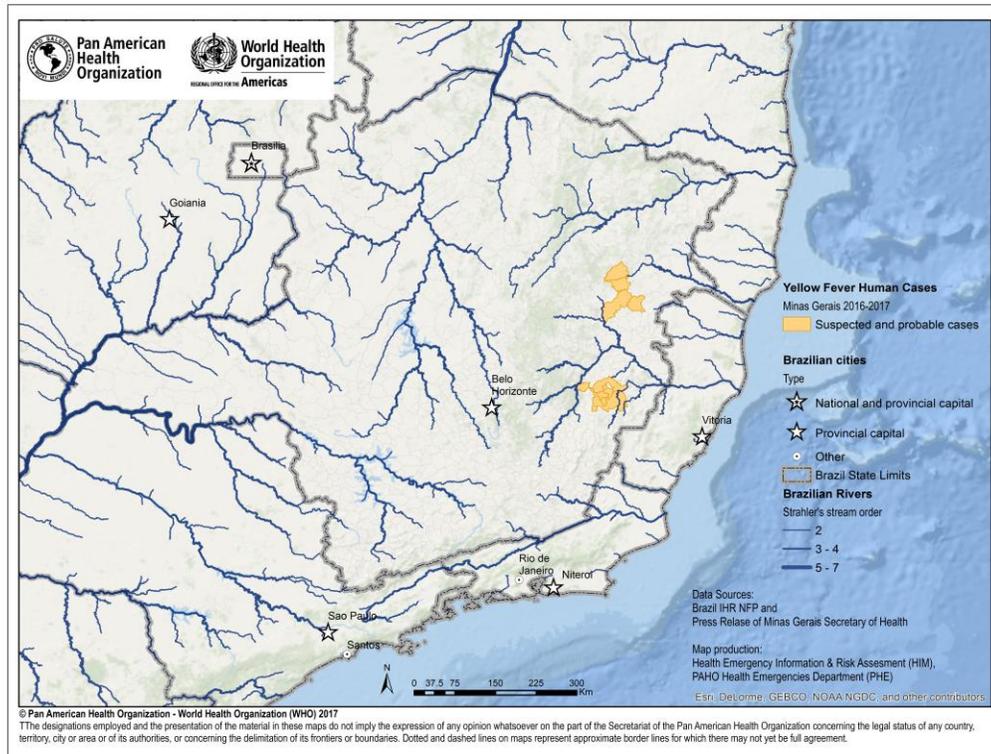
¹ This includes one imported case from Angola.

Suggested citation: Pan American Health Organization / World Health Organization. Epidemiological Update: Yellow Fever. 9 January, Washington, D.C.: PAHO/WHO; 2017

The São Paulo municipalities with confirmed epizootics for yellow fever are Ribeirão Preto (Jaboticabal, Monte Alto, and Ribeirão Preto); Barretos (Cajobi and Severínea), and São José do Rio Preto (Pindorama, Potirendaba, Catanduva, Ibira, Adolfo, Catiguá, and São José do Rio Preto).² In addition, on 4 January 2017, the Fernandópolis Secretary of Health, also in the state of São Paulo, confirmed the death of a NHP infected by yellow fever. The animal was found on 8 December in an area located between São Vicente de Paulo and Recanto do Tamburi.

On 6 January 2017, the Brazil International Health Regulations (IHR) National Focal Point (NFP) notified the Pan American Health Organization, Regional Office of the World Health Organization (PAHO/WHO) of the occurrence of 23 suspected and probable cases of yellow fever, including 14 deaths, from 10 municipalities in the state of Minas Gerais (**Figure 2**). The onset of symptoms of the first case was 18 December 2016. All 12 cases for which the information is available are male, rural residents, with a median age of 36.6 years (range from 7 to 53 years). The investigation is ongoing.

Figure 2. Geographic location of suspected and probable cases of yellow fever reported in Minas Gerais, 2016 – 2017



In **Colombia**, from EW 1 to EW 52 of 2016, 12 cases of jungle yellow fever were reported, 7 laboratory confirmed and 5 probable.

The confirmed cases were reported by the departments of Antioquia, Amazonas, Guainía, Meta, Vaupés, and Vichada.

² *São Paulo intensifies prevention against Yellow fever.* Press release from the São Paulo State Secretary of Health, available at: <http://www.saude.sp.gov.br/ses/perfil/cidadao/homepage/destaques/sp-intensifica-prevencao-contr-a-febre-amarela>.

The 7 confirmed cases are male, 57% of them are between 20 and 29 years of age. Out of the 7 confirmed cases, six died (case fatality rate of 85.7%).

As indicated in the [Yellow Fever Epidemiological Update of 14 December 216](#), the confirmation of cases in Vichada Department (border with Venezuela), in Chocó Department (border with Panama), and in Guainía Department (border with Venezuela and Brazil), represents a risk of circulation of the virus to those bordering countries, especially in areas where they share the same ecosystem.

Table 1. Distribution of probable and confirmed yellow fever cases by department in Colombia. EW 1 to EW 52 of 2016

Reporting territorial entity	Territorial entity of origin	Probable cases	Confirmed cases	Total
Meta	Meta	0	2	2
Córdoba	Córdoba	1	0	1
Vichada	Vichada	2	1	3
Vaupés	Vaupés	1	1	2
Antioquia	Chocó	0	1	1
Amazonas	Imported*	0	1	1
Santa Marta	Santa Marta	1	0	1
Guainía	Guainía	0	1	1
Total		5	7	12

*Caballococha municipality, Peru

Source: Data published in the Colombia National Institute of Health Epidemiological Bulletin of EW 52 of 2016 and reproduced by PAHO/WHO.

In **Peru**, up to EW 51 of 2016, 80 cases of jungle yellow fever were reported, of which 62 were confirmed, and 18 classified as probable, including 26 deaths. Of the 25 departments in Peru, cases were reported in 10, with Junín being the department that reported the highest number of confirmed and probable cases (52 cases).

The number of confirmed and probable cases reported in Peru between EW 1 to EW 51 of 2016, exceeds the number of cases (confirmed and probable) reported in the previous 9 years.

Recommendations

In the light of the increase in confirmed cases of yellow fever in countries of the Americas Region as well as the increase of epizootic due to yellow fever, PAHO / WHO recommends that Member States continue their efforts to detect, confirm and manage cases of yellow fever in a context of circulation of several arboviruses. To this end, health personnel should be kept up-to-date and trained to detect and treat cases especially in known areas of virus circulation.

PAHO/WHO urges Member States to implement necessary actions to properly inform and vaccinate travelers heading to areas where certification of yellow fever vaccine is mandatory.

PAHO/WHO does not recommend any restrictions on travel or trade to countries with ongoing outbreaks of yellow fever.

The recommendations issued in the [Yellow Fever Epidemiological Alert of 31 December 2015](#) remain in effect and are highlighted below.

Surveillance

Yellow fever epidemiological surveillance must be aimed at (i) achieving early detection of virus circulation to enable timely adoption of appropriate control measures to keep new cases from appearing, (ii) interrupting outbreaks, and (iii) preventing the reurbanization of the disease.

The method of surveillance should be a combination of:

- Surveillance of clinical compatibility with the classic form of the disease, based on WHO case definitions
- Surveillance of febrile jaundice syndrome
- Surveillance of epizootics
- Monitoring post-vaccination events allegedly attributable to yellow fever vaccination

The surveillance of febrile jaundice syndrome usually conducted through sentinel sites, uses a more sensitive case definition and rules out cases through laboratory testing.

Laboratory Diagnostics

Laboratory diagnosis of yellow fever is conducted by detecting the genetic material of the virus in blood or tissue using the polymerase chain reaction (PCR), and through serological tests for IgM antibodies detection.

Virologic test

In the acute phase (viremia period) viral RNA can be detected in serum by using molecular techniques, such as conventional or real time RT-PCR. A positive result obtained with appropriate controls, confirms the diagnosis.

Viral isolation can be performed by intracerebral inoculation in mice or in cell culture, but due to its complexity it is rarely used as a diagnostic method and is recommended for research studies only as a complement to public health surveillance.

Serologic test

Serology (detection of specific antibodies) is useful for diagnosis of yellow fever during the acute and convalescent phase of the disease (i.e., after day 6 after the onset of symptoms).

A positive IgM reaction by ELISA (MAC-ELISA or other immunoassay) in a sample taken after the 6th day of onset, is presumptive of recent yellow fever infection. Moreover the diagnostic confirmation can only be made by demonstrating an increase in antibody titer (four times or

more) in two serum samples (one from the acute phase and one from the convalescent phase) by using quantitative techniques.

Serological tests could have cross-reactions, especially in areas where different flavivirus are circulating. Therefore, in those places serological confirmation should be made with other more specific serologic techniques such as plaque neutralization test (PRNT) and once infections by other causal agents have been ruled out as part of the differential diagnosis. In any case, the results of serological tests should be interpreted carefully, and taking into account the patient's vaccination history.

Post-mortem test

Histopathology in liver tissue is the "gold standard" for the diagnosis of suspected yellow fever fatal cases. The analysis includes the typical microscopic description of yellow fever lesions (midzonal necrosis, fatty change, among others), detection of Councilman bodies (pathognomonic), and immunohistochemistry which reveal viral proteins inside the hepatocytes. While immunohistochemistry for yellow fever is specific, given the possibility of cross reaction with other antigenically related flaviviruses, it is nonetheless recommended to confirm cases by using the polymerase chain reaction (PCR) technique on fresh tissue samples or those preserved in paraffin.

Biosafety

Serum samples from acute phase are considered infectious. All laboratory personnel who manage yellow fever samples in a laboratory setting must be vaccinated against yellow fever. The use of Class II certified biosafety cabinets, for the handling of samples, is also recommended to exercise caution and avoid puncture accidents.

Given the differential diagnosis of yellow fever that includes hemorrhagic fevers caused by arenaviruses, samples should be handled under BSL3 containment conditions, and a risk assessment and analysis of the medical history should be conducted before handling of samples in the laboratory setting.

Clinical Management

There is no specific antiviral treatment for yellow fever; therefore, supportive therapy is critical. Severe cases should be treated in intensive care units. General supportive therapy with administration of oxygen, intravenous fluids, and vasopressors is indicated to treat hypotension and metabolic acidosis. Gastric protectors should be included to reduce the risk of gastrointestinal bleeding.

Treatment in severe cases includes mechanical ventilation, treatment of disseminated intravascular coagulation, use of frozen fresh plasma to treat hemorrhage, treatment of secondary infections with antibiotics, and management of liver and kidney failure. Other supportive measures include the use of nasogastric tube for nutritional support or prevention of gastric distention, and dialysis for renal failure or patient with refractory acidosis.

In mild cases the symptoms are treated. Salicylates should not be used as they can produce hemorrhage.

Differential diagnosis

The different clinical forms of yellow fever must be differentiated from other febrile diseases that progress with jaundice, hemorrhagic manifestations, or both. In the Americas, the following diseases should be considered in the differential diagnosis of yellow fever:

- Leptospirosis
- Severe malaria
- Viral hepatitis, especially the fulminating form of hepatitis B and D
- Viral hemorrhagic fevers³
- Dengue
- Typhoid and typhus fever
- Hepatotoxicity or fulminating secondary hepatitis due to drugs or toxics.

Patient Isolation

To prevent infection of other persons, a patient infected with yellow fever virus should avoid being bitten by *Aedes* mosquito for at least for the first 5 days of illness (viremic phase). The patient is recommended to stay under a bed net (treated or without insecticide), or stay in a place with intact window/door screen. In addition, health care personnel attending patients with yellow fever should be protected from mosquito bites by using repellents and wearing long sleeves and pants.

Prevention and control measures

Vaccination

Vaccination is the single and key measure for preventing yellow fever. Preventive vaccination can be performed by routine vaccination schedule for children and one-time mass campaigns to increase the vaccination coverage in at risk areas, as well as for travelers to yellow fever risk areas.

The yellow fever vaccine is safe and affordable, providing effective immunity against yellow fever within 10 days for 80-100% of people and 99% immunity within 30 days. **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 yellow fever vaccine is not needed.** Serious adverse events have been reported rarely following immunization.

Given the limited availability of the vaccines it is recommended that national authorities carry out an assessment of vaccination coverage against yellow fever in at risk areas in order to target the distribution of vaccines. Additionally, a national reserve of the vaccines should be maintained to respond to potential outbreaks.

³ Infection Prevention Control (IPC) measures corresponding to the suspected hemorrhagic fever should be implemented.

The yellow fever vaccine should not be administered to:

- People with acute febrile disease, whose general health status is compromised
- People with a history of hypersensitivity to chicken eggs and/or their derivatives
- Pregnant women, except in an epidemiological emergency and at the express recommendations from health authorities
- People with severe drug related or disease related (e.g., cancer, leukemia, AIDS, etc.) immunosuppression
- Children under 6 months old (consult the vaccine's laboratory insert)
- People of any age with a disease involving the thymus

Note: It is recommended to individually assess the epidemiological risk of contracting the disease against the risk of an adverse reaction in persons over 60 years that have not previously been vaccinated.

Vector Control

The risk of transmission of yellow fever in urban areas can be reduced through effective vector control strategy. Combined with emergency vaccination campaigns, the application of insecticide spray to kill adult mosquitoes during urban epidemics can reduce or halt yellow fever transmission, while populations are vaccinated to acquire immunity.

Mosquito control programs targeting wild mosquitos in forested areas are not practical for preventing jungle yellow fever transmission.

References

1. Epidemiological situation in Brazil. Brazil Ministry of Health site. Available at: <http://portalsaude.saude.gov.br/index.php/situacao-epidemiologica-dados-febre-amarela>
2. Updated on the investigation of suspected yellow fever cases in Minas Gerais. News. Minas Gerais State Secretary of Health. Available at: <http://saude.mg.gov.br/component/gmg/story/8933-atualizacao-sobre-a-investigacao-de-casos-suspeitos-de-febre-amarela-em-minas-gerais>
3. National Center for Epidemiology, Prevention and Control of Diseases - MINSA of the Ministry of Health of Peru; Situational Room for Health Situation Analysis - EW 51 of 2016: Yellow Fever. Available at: http://www.dge.gob.pe/portal/index.php?option=com_content&view=article&id=14&Itemid=121
4. Epidemiological Bulletin Week 52. Colombia National Institute of Health. Available at: <http://www.ins.gov.co/boletin-epidemiologico/Boletn%20Epidemiol%20gico/2016%20Boletn%20epidemiol%20gico%20semana%2052.pdf>
5. PAHO/WHO. Control of Yellow Fever. Practical Guide. 2005. Scientific and Technical Publication No. 603.