Yellow Fever Resurgence

Charles Mosler, RPh, PharmD, BCGP

The University of Findlay College of Pharmacy

Global Missions Health Conference

November 14, 2026

Learning Objectives

- Analyze the epidemiological factors driving yellow fever's 2025 resurgence in the Americas and implications for endemic zones
- Appraise current yellow fever vaccine options, effectiveness data in pediatric populations, and booster recommendations
- Evaluate pharmacotherapy and supportive care approaches for confirmed yellow fever cases in resource-limited settings

Current Numbers

Numbers Behind the Resurgence

346	**143**	**41%**	**5.6×**
confirmed cases in 2025	deaths in 2025	2025 case fatality rate	increase vs 2024

79	**6**	**44%**
cases Jan 1–May 26, 2026	Americas countries reporting	CFR through EW7 of 2026

*WHO June 2026 global update reports 79 confirmed infections in the Americas through May 26; CFR is only through EW7 (mid-Feb 2026)

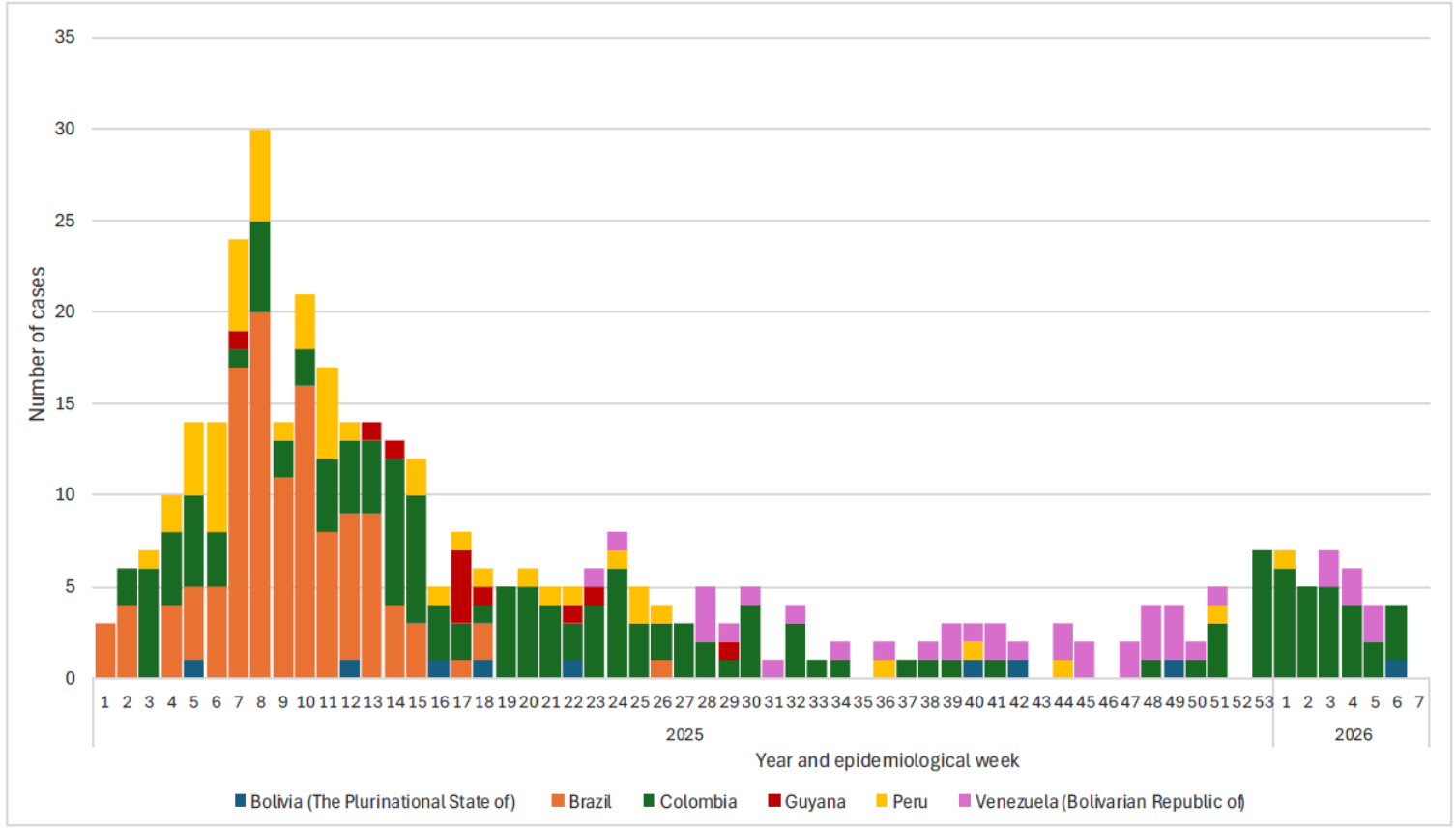
PAHO/WHO Epidemiological Alert, 13 Mar 2026
WHO Disease Outbreak News, 24 Jun 2026

2025 Yellow Fever Burden By Country

Country	Cases	Deaths	CFR
Bolivia	8	2	25%
Brazil	120	48	40%
Colombia	125	46	37%
Ecuador	11	8	73%
Guyana	1	1	100%
Peru	49	19	39%
Venezuela	32	19	59%

PAHO/WHO Epidemiological Alert, 13 Mar 2026

Confirmed cases of yellow fever in humans by country and epidemiological week (EW) of symptom onset in the Americas Region, EW 1 of 2025 to EW 7 of 2026.



PAHO/WHO Epidemiological Alert, 13 Mar 2026

https://shiny.paho-phe.org/yellowfever/?tab=country

Unofficial 2026 Numbers As of 11/11/26

111
Confirmed cases[3]

48
Fatal cases

6
Countries/territories reporting cases

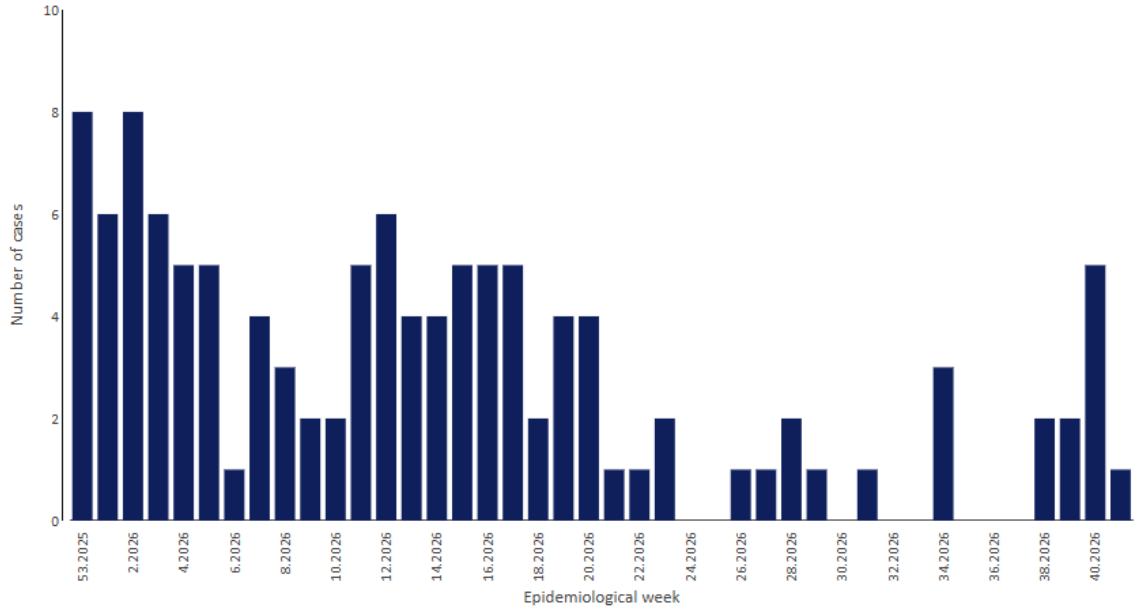
Epicurve | Table

Classification
(•) Cases ( ) Fatal cases

Stratification
(•) General ( ) Country

Period
( ) Year ( ) Month (•) Epiweek

Human cases of yellow fever in the region of the Americas by epidemiological week (EW) of symptom onset, 2026



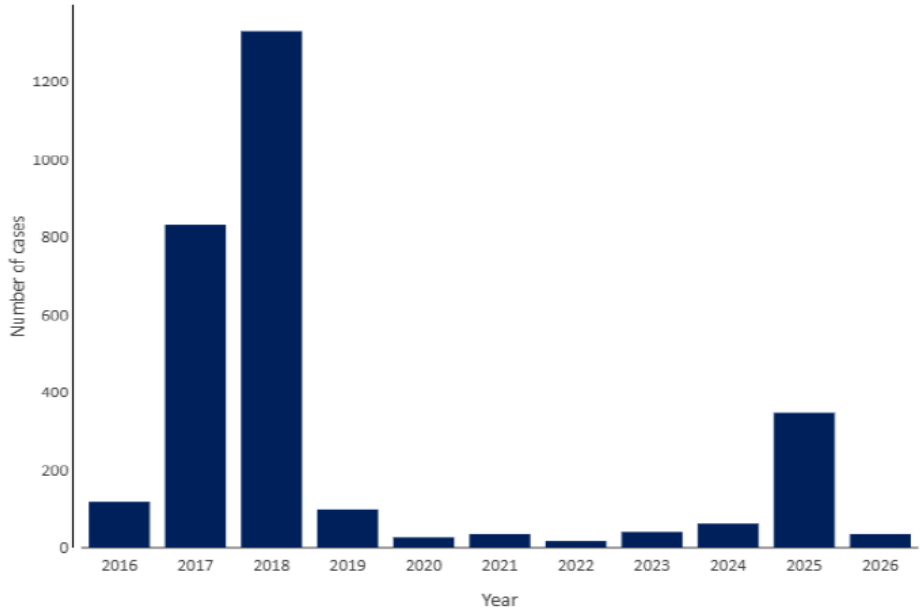
Note: 2 cases are not shown in the graph as they were reported only on an annual basis (Colombia=2)

Geographic distribution of human cases and fatal cases of yellow fever in the region of the Americas, 2026



To Be Fair…

Figure 1. Confirmed cases of yellow fever in humans by year in the Americas Region, between 2016 and 2026.



Source: Pan American Health Organization. Yellow Fever Dashboard in the Americas Region. Washington, D.C.: PAHO; 2025 [cited 5 March 2026]. Available from: https://shiny.paho-phe.org/yellowfever/. *(11)*.

PAHO/WHO Epidemiological Alert, 13 Mar 2026

But What About Africa?

- Persistent endemic and outbreak transmission
- 67 confirmed cases / 18 deaths through Oct. 12, 2026
- 9 countries affected
- Recent concentration in West Africa
- Vaccination gaps + occupational/forest exposure + cross-border movement
- Regional risk currently moderate

Potential Causes of Recent Increase

A Convergence of Factors

- Ecology
  - Rainfall, temperature, mosquito abundance, sylvatic epizootics
- Immunity Gaps
  - Uneven routine coverage; most reported cases were unvaccinated
- Mobility
  - Forest work, travel, migration, cross-border movement
- Urban Interface
  - Expansion into forest edges with Aedes capable cities nearby

WHO Disease Outbreak News, 24 Jun 2026
CDC Yellow Book 2026

From Forest Spillover to Urban Amplification

Sylvatic cycle

Nonhuman primate ↔ Haemagogus/Sabethes

→

Spillover

Unvaccinated human enters forest-edge transmission

→

Viremic window

Highest near onset and first 3–5 illness days

→

Urban risk

Aedes aegypti + low immunity + delayed detection

Bed-net or screened-room isolation during viremia is both patient care and outbreak control.





- CDC Yellow Book 2026
- WHO Disease Outbreak News, 24 Jun 2026

Clinical Presentation and Management

Clinical Course

- **Incubation**: 3–6 days post-mosquito bite
- **Infection Phase (Days 1–3/5)**: Abrupt high fever, severe backache/myalgia, headache, nausea/vomiting, facial flushing, Faget's sign (relative bradycardia).
- **Remission Phase (2–24 Hours)**: Temporary defervescence in ~85% of cases and ~15% progress to toxemic phase; albuminuria present
- **Toxemic Phase (Days 4–10)**: Jaundice, black vomit (hematemesis), petechiae/epistaxis, acute kidney injury, encephalopathy, and shock
- **High Fatality**: 20%–50% CFR in toxic phase; 37%–52% CFR observed in recent Americas outbreaks

CDC Yellow Book 2026
WHO Arboviral Guidelines 2025

Diagnostics

Diagnostic Assay	Optimal Window	Clinical Role & Interpretation
RT-PCR (Serum / Whole Blood)	**Days 1–5** (up to Day 10 in severe cases)	**Gold standard** during acute viremia; detects viral RNA directly. *Urine RT-PCR* may remain positive longer into the convalescent phase.
IgM Capture ELISA (MAC-ELISA)	**≥ Day 5** post-symptom onset	Primary serologic screen once viremia clears; presumptive positive requires confirmation due to flavivirus cross-reactivity.
Plaque Reduction Neutralization Test (PRNT)	**≥ Day 7–10** (paired acute/convalescent sera)	**Confirmatory gold standard** for serology; a **≥4-fold rise** in neutralizing titers distinguishes YFV from Dengue, Zika, and West Nile.

- WHO Guidelines for clinical management of arboviral diseases, 2025
- CDC Yellow Book 2026

Supportive Laboratory Findings

- Hematology: Early leukopenia with neutropenia (Days 1–4), followed by progressive thrombocytopenia (often less than 50,000/mm^3) in the toxemic phase.
- Hepatic & Renal Panels: Marked transaminitis (AST typically greater than ALT, often exceeding 1,000 IU/L), rising direct bilirubin, elevated BUN/creatinine, and proteinuria/albuminuria (helps distinguish YF from viral hepatitis).
- Coagulation: Prolonged PT/INR and aPTT, reduced fibrinogen, and elevated D-dimer consistent with hepatic synthetic failure.

Treatments

- Fluid & Hemodynamic Resuscitation: Isotonic crystalloids (Lactated Ringer's or 0.9% NaCl) guided by urine output and lactate; add norepinephrine for refractory vasodilatory shock.
- Analgesia & Antipyresis (Strict Contraindications):
  - AVOID NSAIDs and Aspirin: Contraindicated due to platelet dysfunction, GI mucosal injury, and severe hemorrhagic risk.
  - Cautious Acetaminophen: Use only in mild/early stages; discontinue immediately upon rising transaminases or jaundice (max ≤2 g/day if hepatic function is intact).

- WHO Guidelines for clinical management of arboviral diseases, 2025
- CDC Yellow Book 2026

Treatments

- Gastrointestinal & Coagulopathy Management:
  - Stress Ulcer Prophylaxis: Intravenous proton pump inhibitors (omeprazole/pantoprazole) to prevent upper GI hemorrhage.
  - Hemorrhage & DIC: Vitamin K (10 mg IV) for prolonged INR; fresh frozen plasma (FFP) or platelets for active bleeding.
- Metabolic & Organ Support: Frequent dextrose monitoring (prevent hypoglycemia from hepatic glycogen depletion), lactulose/rifaximin for hepatic encephalopathy, and early renal replacement therapy for refractory acidosis or hyperkalemia.

- WHO Guidelines for clinical management of arboviral diseases, 2025
- CDC Yellow Book 2026

Resource Limited Treatments

- **Clinical Endpoints Over Invasive Monitoring:** Titrate oral rehydration salts (ORS) and isotonic crystalloids to urine output (≥0.5 mL/kg/hr) and capillary refill rather than arterial lines or lactates.
- **Scheduled Glucose Checks:** Perform bedside capillary glucose checks every 4–6 hours with 10%–50% IV dextrose boluses to prevent hepatic hypoglycemia.
- **Low-Tech Bleeding & Ulcer Bundles:** Give Vitamin K 10 mg IV/PO (3 days) and omeprazole 40 mg IV/PO; use whole blood if component therapy is unavailable, and eliminate all IM injections.
- **Deprescribing & Physical Cooling:** Rely on tepid sponging and immediately stop OTC NSAIDs, aspirin, and high-dose acetaminophen to prevent GI hemorrhage and liver failure.

- WHO Guidelines for clinical management of arboviral diseases, 2025
- CDC Yellow Book 2026

N-acetylcysteine

- Mechanism & Rationale: Replenishes depleted hepatic glutathione stores, scavenges reactive oxygen species, and improves hepatic microcirculatory blood flow to mitigate midzonal hepatocyte necrosis.
- Clinical Evidence:
  - No Randomized Controlled Trials: Lacks definitive RCT data specific to yellow fever; extrapolated from non-acetaminophen acute liver failure (NA-ALF) guidelines and observational case series from Brazilian yellow fever outbreaks (2017–2019).
  - Observational Outcomes: Used as adjuvant therapy in ICU patients with severe transaminitis (AST/ALT greater than 1,000 IU/L) or early hepatic encephalopathy, showing acceptable safety and potential improvement in transplant-free survival when started early.
- Dosing – same as acetaminophen overdose

What to Avoid

- Aspirin and NSAIDs
- Routine systemic corticosteroids
- IV immunoglobulin
- Prophylactic platelets solely for count <50,000/μL without bleeding
- Sofosbuvir or TY014 or other investigational products outside of research
- Unproven “liver tonics” or herbal products

- WHO Guidelines for clinical management of arboviral diseases, 2025
- CDC Yellow Book 2026

Antivirals and Investigational

- No FDA/WHO-Approved Specific Antivirals: Treatment relies entirely on early, aggressive supportive care.
- Investigational Agents: Direct-acting antivirals (e.g., sofosbuvir, galidesivir) and monoclonal antibodies (e.g., TY014) show in vitro/animal or early-phase activity, but remain restricted to clinical trials or compassionate-use protocols.

- WHO Guidelines for clinical management of arboviral diseases, 2025
- CDC Yellow Book 2026

Question

- A patient with suspected severe yellow fever is hypotensive, jaundiced, and has platelets 32,000/μL but no active bleeding. Which order is least appropriate?

A. IV 0.9% sodium chloride

B. Platelets

C. N-acetylcysteine

The Vaccine

Vaccine Essentials

- Eligible Age - ≥9 months for most travelers/residents at risk
- Protection - ~90-95% immune within 10 days and up to 99% by 1 month
- Documentation – ICVP valid beginning 10 days post vaccine and good for life for most
- Vaccinate only when exposure risk or entry requirement

- CDC Yellow Book 2026
- WHO Yellow Fever vaccines page, updated 8 Jun 2026

To Vaccinate or Not

CONTRAINDICATIONS

- Age <6 months
- Severe allergy to component
- Symptomatic HIV or CD4 <200/mm³
- Primary immunodeficiency
- Immunosuppressive therapy / malignancy
- Thymus disorder with immune dysfunction
- Transplantation

PRECAUTIONS

- Age 6–8 months
- Age ≥60 years
- Pregnancy
- Breastfeeding
- Asymptomatic HIV, CD4 200–499/mm³

PROCEED

- Age ≥9 months
- Meaningful destination exposure or entry requirement
- No contraindication after medication and immune-status review
- Document consent and ICVP

- CDC Yellow Book 2026
- WHO Yellow Fever vaccines page, updated 8 Jun 2026

Serious Vaccine Complications

- **YEL-AND (Yellow Fever Vaccine-Associated Neurotropic Disease):** Incidence ~0.8 per 100,000 doses overall, rising to ~2.2 per 100,000 in adults ≥60 years; presents 2–56 days post-vaccination (encephalitis, Guillain-Barré, ADEM); usually resolves without sequelae.
- **YEL-AVD (Yellow Fever Vaccine-Associated Viscerotropic Disease):** Mimics wild-type fulminant yellow fever (multi-organ failure, >50% fatality); incidence ~0.3 per 100,000 overall, rising to ~1.2 per 100,000 in adults ≥60 years (and ~2.5+ in ≥70 years). Strongly linked to thymic disease/thymectomy (an absolute contraindication).

Booster or Not

- Every 10 year booster for all was phased out from 2013-2016
- **High-Priority Populations for Booster Dosing**
  - Children vaccinated under age 2, especially in high-endemic zones, experience significant antibody waning and can be considered for a booster dose to ensure durable immunity.
  - Pregnant Travelers: Individuals who received their initial dose while pregnant
  - Hematopoietic Stem Cell Transplant (HSCT) Recipients: Patients who were vaccinated prior to receiving a transplant require revaccination once immunocompetent (typically ≥24 months post-HSCT).
  - Persons Living with HIV: Individuals who were HIV-positive at the time of their primary vaccination
- **Occupational & High-Risk Exposure Groups**
  - Laboratory Personnel: Workers routinely handling wild-type yellow fever virus (measure neutralizing antibody titers every 10 years)
  - Prolonged Endemic/Outbreak Deployment: Travelers spending extended periods in active outbreak zones or high-transmission areas if ≥10 years have elapsed since primary vaccination.

- CDC Yellow Book 2026
- WHO Yellow Fever vaccines page, updated 8 Jun 2026

What is Fractional Dosing?

- Off-label, dose-sparing regimen administering 0.1ml of vaccine during an outbreak
- Why? Egg-grown vaccine that can take 12 months to manufacture
- Use in those ≥ 2 years old living in an outbreak
- Do not use in those < 2 years old, pregnant, or immunocompromised
- Fractional dosing does not satisfy ICVP requirements

- WHO position on fractional yellow fever vaccine doses, 2017
- Doshi et al. Lancet, 11 Sep 2026

Question

Which intervention most directly interrupts the risk of an urban outbreak after a sylvatic spillover?

A. Empiric antibiotics for all febrile patient
B. Rapid vaccination and mosquito protection of suspected cases
C. Routine booster vaccination for everyone every 10 years
D. Waiting for serology report before notifying public health

Question

A 34 year old male ecologist is planning to spend the next 4 months in the Amazon basin and there is currently an outbreak. He last had a yellow fever vaccine 12 years ago. Which of the following is the best recommendation for him?

A. A booster is not needed for anyone anymore
B. Routine booster is still required for anyone over the age of 18 every 10 years
C. Consider a booster due to prolonged exposure and high risk area

Summary

- The 2025–2026 Americas surge (**>40% CFR**) and ongoing West African activity are likely driven by sylvatic spillover into under-immunized populations.
- Vaccinate eligible residents and travelers (**≥9 months**) at least **10 days prior to departure**
- With no approved antivirals, survival depends on early **isotonic crystalloids (titrated to urine output ≥0.5 mL/kg/hr)**, **frequent glucose checks**, **stress ulcer prophylaxis (PPI)**, and **Vitamin K**.

Any Questions?



GMHC 2026 Breakout Block 7 Evaluation