

OBSERVATION: BRIEF RESEARCH REPORT

Epizootic Outbreak of Yellow Fever Virus and Risk for Human Disease in Salvador, Brazil

Background: Yellow fever virus (YFV) is an RNA virus maintained in an enzootic, sylvatic cycle involving nonhuman primates (NHPs) and sylvatic mosquito vectors primarily of the genus *Haemagogus* and *Sabethes*. Transmission occasionally spills over to humans entering forested regions. In the Americas, urban transmission of YFV to humans has not occurred since the mid-1900s because of vaccination and near-elimination of the anthropophilic *Aedes aegypti*, the urban vector (1). However, concerns about reemergence of urban YFV have recently increased because of the reappearance and rapid spread of *A. aegypti* in the urban environment. Furthermore, immunization coverage for YFV is insufficient because vaccination is generally indicated only for higher-risk populations, such as those living in or travelling to areas with sylvatic transmission.

Objective: To investigate the 2017 epizootic outbreak of YFV and the risk for human disease in Salvador, Brazil.

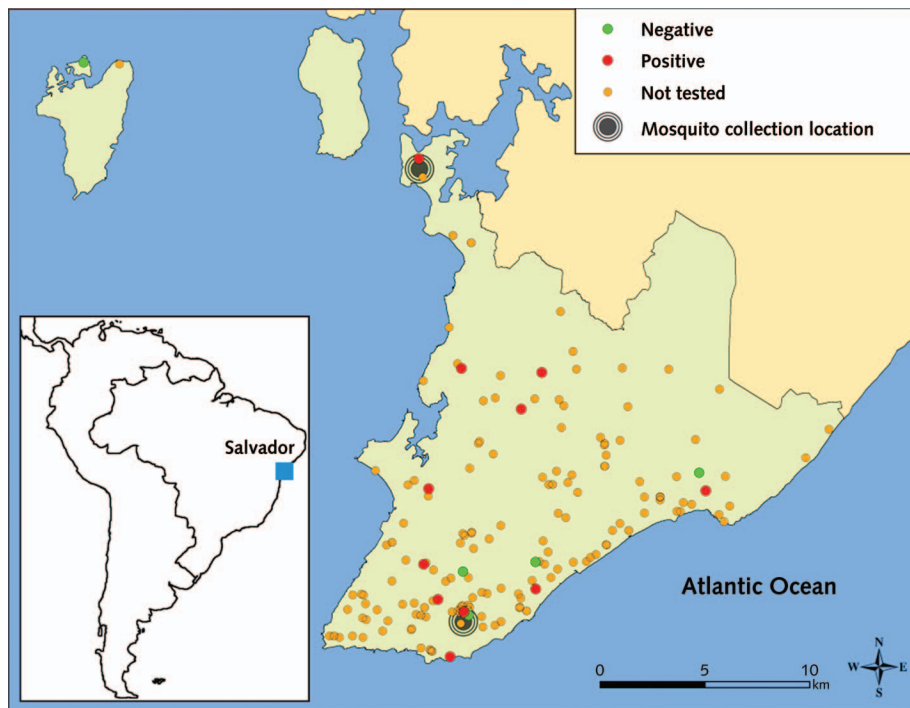
Methods and Findings: Since November 2016, deaths of NHPs due to YFV in Brazil have been reported in the state of São Paulo. Beginning in December 2016, human cases were also reported in the states of São Paulo and Minas Gerais. By the end of May 2017, the YFV outbreak in humans had spread

to 9 Brazilian states, with more than 130 municipalities reporting confirmed cases (Appendix Figure 1, available at www.annals.org), all deemed of sylvatic origin (rather than via urban *A. aegypti* transmission). Of 3240 suspected reported human cases, 792 were laboratory-confirmed. Among all reported patients, 435 died and 274 of these had laboratory-confirmed infection with YFV (case-fatality ratio for laboratory-confirmed cases, 34.6%) (2).

Reports of deaths of NHPs due to YFV also simultaneously increased. By the end of May 2017, a total of 3850 NHPs was suspected to have died of YFV infection, 642 of which were confirmed from 12 states (2). Since the beginning of the outbreak, the Brazilian Ministry of Health has distributed more than 25 million YFV vaccine doses to persons in areas with confirmed human or NHP cases, likely reducing incidence (2).

On 14 January 2017, deaths of NHPs suspected of having YFV were first reported in Salvador, the fourth largest Brazilian city, which had not been considered a risk area for transmission (Appendix Figure 1, available at www.annals.org). The number of NHPs found dead throughout the city rapidly increased, and by 24 August, 205 NHPs of the genus *Callithrix* suspected of having infection with YFV had been collected (Appendix Figure 2, available at www.annals.org). Reverse transcriptase polymerase chain reaction testing for the virus was done on tissue samples of 21 dead animals at the Oswaldo Cruz Foundation in Rio de Janeiro; samples from 13

Figure. Spatial distribution of locations of NHP collections according to YFV status and of sites of mosquito collections in Salvador, Brazil*.



NHP = nonhuman primate; YFV = yellow fever virus.

* Distribution of 7 of the 8 YFV-negative NHPs, all 13 of the YFV-positive NHPs, and 173 of the 184 NHPs that were not tested is shown.

This article was published at www.annals.org on 7 November 2017.

Table. Number of Mosquitos Collected at Ground Level in Salvador, Brazil*

| Species | Total | Female |
|-------------------------------|-------|--------|
| <i>Aedes albopictus</i> | 139 | 87 |
| <i>A aegypti</i> | 49 | 13 |
| <i>A serratus</i> | 10 | 10 |
| <i>A scapularis</i> | 4 | 4 |
| <i>A species</i> | 2 | 2 |
| <i>Wyeomyia species</i> | 149 | 149 |
| <i>Culex quinquefasciatus</i> | 58 | 18 |
| <i>Limatus species</i> | 21 | 21 |
| <i>Psorophora ferox</i> | 3 | 3 |
| Total | 435 | 307 |

YFV = yellow fever virus.

* Pools of all female mosquitoes from the same species were tested for YFV by reverse transcriptase polymerase chain reaction; none was positive. Values are numbers.

animals (61.9%) tested positive. Animals suspected of being infected were found throughout Salvador, with a cluster (3 of the 13 YFV-positive animals) around a city park, a 0.66-km² recreational area of residual Atlantic forest with trees less than 10 m high (Figure).

To investigate potential vectors involved in YFV transmission among NHPs in Salvador, we initiated ground-level mosquito collections within and around the city park and at the naval base, another preserved Atlantic forest area where dead, YFV-positive NHPs were found. During 10 days of fieldwork in 26 sites between 10 April and 7 June 2017, a total of 435 adult mosquitoes (307 females) was captured using human landing catches (Table). Most females captured were *Wyeomyia* species and *A albopictus*. Although we did not capture *Haemagogus* or *Sabethes* species, *Haemagogus* mosquitoes were identified in Salvador in January 2017 in a suburban, forested area. Pools of captured female mosquitoes from each species were tested for YFV by reverse transcriptase polymerase chain reaction (primers CAG and YF7) (3) and cell culture (C6/36, *A albopictus*), and none was positive.

Discussion: To date, urban *Aedes* mosquitoes have not been associated with YFV transmission to humans in Brazil. However, cases of YFV in NHPs in densely urbanized areas pose a considerable risk for resurgence of *A aegypti*-mediated YFV transmission to humans. Salvador has long been an epicenter of dengue transmission and more recently of Zika (4) and chikungunya (5) viruses, all with *A aegypti* as the main vector. In addition, *A albopictus*, which is susceptible to YFV infection in laboratory settings, is commonly found here, particularly in peridomestic and green areas. Although never implicated in natural YFV transmission, this species was only introduced into the Americas in the 1980s.

Continuous entomologic and veterinary surveillance of mosquitoes and NHP deaths, accompanied by laboratory testing for YFV, is the cornerstone of assessing the risk that this virus will establish an urban transmission cycle. In parallel, scaling up vaccination coverage is critical to prevent additional human cases of this disease.

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Acknowledgment: The authors thank Roberto Fonseca dos Santos for his advice during identification of mosquito specimens and the Health Surveillance Directory, Salvador Secretary of Health, especially the Center for Zoonosis Control.

Financial Support: By the Brazilian National Council for Scientific and Technological Development (grants 400830/2013-2 and 440891/2016-7 to Dr. Ribeiro and scholarships to Drs. Paploski, Reis, Kitron, and Ribeiro and Mr. Mugabe), the Brazilian Coordination for the Improvement of Higher Education (grant 440891/2016-7 to Dr. Ribeiro and scholarship to Dr. Kikuti), the Bahia Foundation for Research Support (grant PET0022/2016 to Dr. Ribeiro), the University of Texas Medical Branch Institute for Human Infections and Immunity, and National Institutes of Health (grant R24AI120942 to Dr. Weaver). The funding sources had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Disclosures: Authors have disclosed no conflicts of interest. Forms can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M17-1949.

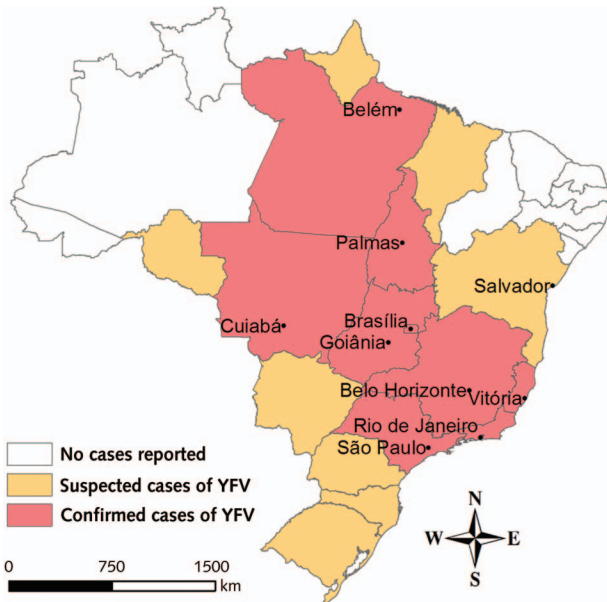
Reproducible Research Statement: *Study protocol and statistical code:* Not Available. *Data set:* Available from Dr. Ribeiro (e-mail, guilherme.ribeiro@bahia.fiocruz.br).

doi:10.7326/M17-1949

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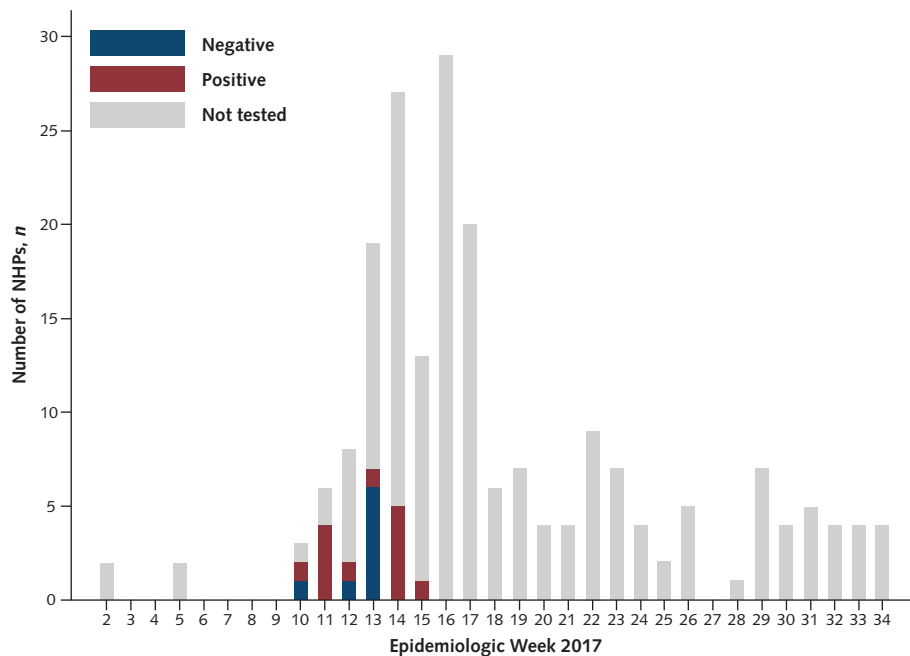
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Appendix Figure 1. Brazilian states where human cases of YFV were reported between December 2016 and May 2017, according to laboratory confirmation status.



YFV = yellow fever virus.

Appendix Figure 2. Temporal distribution of NHPs collected in Salvador, Brazil, by epidemiologic week in 2017.



NHP = nonhuman primate.