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 NHPs were found positive for YFV.

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

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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 *Ae. 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 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.

Igor Adolfo Dexheimer Paploski, DVM, MSc, DPH*
Universidade Federal da Bahia and Instituto GoñçaL Moniz, Fundação Oswaldo Cruz
Salvador, Brazil

Raquel Lima Souza, BS, MSc*
Laura Beatriz Tauro, BS, PhD
Instituto GoñçaL Moniz, Fundação Oswaldo Cruz
Salvador, Brazil

Cristiane Wanderley Cardoso, BS, MSc, PhD
Secretaria Municipal de Saúde de Salvador
Salvador, Brazil

Vânia André Mugabe, BS, MPH
Universidade Federal da Bahia
Salvador, Brazil

Anna Beatriz Pereira Simões Alves
Joice de Jesus Gomes
Instituto GoñçaL Moniz, Fundação Oswaldo Cruz
Salvador, Brazil

Mariana Kikutí, DVM, MPH
Universidade Federal da Bahia and Instituto GoñçaL Moniz, Fundação Oswaldo Cruz
Salvador, Brazil

Guilio Soares Campos, PharmD, PhD
Silvia Sardi, DVM, PhD
Universidade Federal da Bahia
Salvador, Brazil

Scott C. Weaver, BS, MS, PhD
University of Texas Medical Branch
Galveston, Texas

Mittemayer Galvão Reis, MD, MSc, PhD
Universidade Federal da Bahia and Instituto GoñçaL Moniz, Fundação Oswaldo Cruz
Salvador, Brazil

Uriel Kitron, BS, MPH, PhD
Emory University
Atlanta, Georgia

Guilherme Sousa Ribeiro, MD, MSc, PhD
Universidade Federal da Bahia and Instituto GoñçaL Moniz, Fundação Oswaldo Cruz
Salvador, Brazil

* Dr. Paploski and Ms. Souza contributed equally to this work.

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

<table>
<thead>
<tr>
<th>Species</th>
<th>Total</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Aedes albopictus</em></td>
<td>139</td>
<td>87</td>
</tr>
<tr>
<td><em>Ae. aegypti</em></td>
<td>49</td>
<td>13</td>
</tr>
<tr>
<td><em>Ae. serratus</em></td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td><em>Ae. scapularis</em></td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td><em>Ae. species</em></td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Wyeomyia species</td>
<td>149</td>
<td>149</td>
</tr>
<tr>
<td>Culex quinquefasciatus</td>
<td>58</td>
<td>18</td>
</tr>
<tr>
<td>Limatus species</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>Psorophora ferox</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>435</td>
<td>307</td>
</tr>
</tbody>
</table>

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.
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References
**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.