Assessing the threat of establishing a sylvatic Zika virus cycle in South America

Ben Althouse

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How likely is it that Zika virus will establish a sylvatic cycle in South America?
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3. What is the probability of establishment?
4. What else do we need to know?
0. Zika Virus

- Isolated in 1947 in the Zika forest of Uganda
- Flavivirus – ssRNA virus
- Transmitted by *Aedes* mosquitoes
- WHO PHEIC
- Mostly asymptomatic
- Rash, conjunctivitis, fever, arthralgia
- Emerging evidence for teratogenic effects and neurovirulence
Transmission cycles: human/endemic

Aedes aegypti subsp. aegypti (tropics)
Aedes albopictus (tropics)
Aedes polynesiensis (Polynesia)

TOT

Human cycle

Vasilakis et al., Nature Reviews Microbio, 2011
Transmission cycles: human/endemic
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SPECIAL REPORT

Zika Virus and Birth Defects — Reviewing the Evidence for Causality

Sonja A. Rasmussen, M.D., Denise J. Jamieson, M.D., M.P.H.,
Margaret A. Honein, Ph.D., M.P.H., and Lyle R. Petersen, M.D., M.P.H.
Transmission cycles: sylvatic/enzOOTic

Aedes africanus
Aedes luteocephalus (West Africa)
Aedes furcifer (West Africa)
Aedes niveus spp. (Southeast Asia)

Aedes aegypti subsp. aegypti (tropics)
Aedes albopictus (tropics)
Aedes polynesiensis (Polynesia)

Vasilakis et al., Nature Reviews Microbio, 2011
Sylvatic cycles in Africa

- Routine arbovirus surveillance by Institute Pasteur de Dakar
- 50 years of data
- Mosquito virus isolation
- Opportunistic primate isolation
- Expanded primate and mosquito sampling 2010-2012
Sylvatic cycles in Africa

Dengue

Yellow Fever

Chikungunya

Zika
### Sylvatic cycles in Africa

#### Dengue

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#### Yellow Fever

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#### Chikungunya

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#### Zika

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**Period (years)**
- 2
- 4
- 8
- 16
- 32
Sylvatic Zika in 2011

- 2011 saw an outbreak of Zika in Kedougou
- Zika isolated from 10 species of *Aedes*
  - *Ae. hirsutus, Ae. unilineatus, Ae. metallicus, and Ae. africanus* had highest infection rates
- Previous isolations in African green monkeys (*Chlorocebus sabaeus*) and patas monkeys (*Erythrocebus patas*)
- Isolated in rhesus macaque in Uganda
- ZEST team currently investigating Zika in rhesus macaque ([https://zika.labkey.com/project/OConnor/ZIKV-001/ begin.view](https://zika.labkey.com/project/OConnor/ZIKV-001/ begin.view))
Why do we think a sylvatic cycle is possible?

- Old World monkeys are susceptible to Zika virus infection
- Multiple mosquito species are susceptible to Zika virus infection
- *Both host and vector are present in South America*
Yellow fever has an established sylvatic cycle

What is the probability of establishment?

- Stochastic sylvatic transmission model (Gillespie)
- Parameterized using dengue virus transmission
- Single infectious introduction, no importation
- Multiple runs, find proportion that do not go extinct
- Key parameters:
  - Primate birthrate (lifespan)
  - Zika virus force of infection (infectious bites per day)
The diagram illustrates a model of disease spread between mosquito and primate populations. The states are:

- **Sm**: Mosquito susceptible
- **Im**: Mosquito infected
- **Sp**: Primate susceptible
- **Ip**: Primate infected
- **Rp**: Primate recovered

The transitions between states are governed by:

- **Mosquito Death Rate**: Sm to Im
- **Primate Death Rate**: Sp, Ip, Rp to Sm, Im, Sp
- **Primate Birth Rate**: Sm to Sp
- **Mosquito Birth Rate**: Sm to Im
- **Transmission (m to p)**: Sm → Ip
- **Transmission (p to m)**: Sp → Im
- **Recovery Rate**: Ip to Rp

The diagram uses arrows to indicate the direction of these transitions.
Single introduction
out$data[, "Ip1"] + out$data[, "Ip2"]

- Single introduction
- Established cycles
- Extinctions
Number of primates (1000s)

Number of mosquitoes (1000s)

Lifespan\(^{-1}\) = 5 years

Lifespan\(^{-1}\) = 15 years

Lifespan\(^{-1}\) = 25 years

Force of Infection = 0.15

Force of Infection = 0.3

Force of Infection = 0.45
Number of mosquitoes

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<th>Lifespan⁻¹</th>
<th>0.25</th>
<th>0.5</th>
<th>0.75</th>
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Lifespan$^{-1}$ = 5 years

Number mosquitoes

0.25 0.5 0.75 0.95

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Force of Infection = 0.45

Lifespan$^{-1}$ = 25 years

Number mosquitoes

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Number of primates (1000s)

Number of mosquitoes (1000s)
What is the probability of establishment?

- High for a range of biologically realistic parameters
  - Higher birthrates -> higher probability (susceptible turnover)
- Need more mosquitoes than primates
- But…
What else do we need to know?
What else do we need to know?

- Susceptibility of New World primates to Zika
  - Viremia

- Susceptibility of other small mammals to Zika

- Rapidly reproducing hosts

- Susceptibility of New World mosquitoes to Zika
  - Ae. albopictus, potentially Sabethes or Haemagogus spp which transmit YFV

- Ranges of both these novel hosts and vectors

- The extent of a sylvatic dengue virus cycle (increased surveillance)
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- The extent of a sylvatic dengue virus cycle (increased surveillance)
Outlook?

- Establishment of a sylvatic Zika virus cycle would make future elimination efforts impossible
- Requiring intensive surveillance and reactive mass vaccination in response to outbreaks
Thank you!

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http://biorxiv.org/content/early/2016/04/05/047175

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