Drivers of spread of *Aedes aegypti*-borne infections in Latin America

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World's Most Dangerous Animals.
(As per number of annual kills)

01 MOSQUITO
- Dengue, Zika, Chikungunya or Yellow Fever, that is the question...

02 SNAKES
- 50,000

03 BOX JELLYFISH
- 5,000

04 GREAT WHITE SHARK
- 3,500

05 AFRICAN LION
- 2900

06 SALTWATER CROCODILES
- 200

Areas of the world at risk of diseases transmitted by the Aedes aegypti mosquito.
Are some of us tastier than others...?

Why Do Some People Get Bitten More Than Others?

- How attractive you are to mosquitoes may be genetically based (about 85%, through gene control of body odor)
- Identical twins experience a similar number of mosquito bites while non-identical twins have a large disparity
- Movement and heat attract mosquitoes. Other factors include:

<table>
<thead>
<tr>
<th>People with high concentrations of steroids or cholesterol on their skin surface</th>
<th>People who produce excess amounts of uric acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>People who give off more carbon dioxide, including pregnant women and those who are larger or overweight</td>
<td>People with Type O blood²</td>
</tr>
<tr>
<td>People who are exercising, as this increases sweat, heat, lactic acid, and movement, all factors that lure in mosquitoes</td>
<td>Beer drinkers (for reasons that remain a mystery, drinking alcohol stimulates mosquito attraction)³</td>
</tr>
</tbody>
</table>
Wyeomyia smithii

Evolutionary transition from blood feeding to obligate nonbiting in a mosquito

Bradshaw et al. PNAS, Nov 2017

DGE: differential gene expression

If there is no bite, there is no disease transmission...

- Identification of key genes responsible for the evolution of an obligate nonbiting lifestyle, provides the potential to mitigate mosquito-borne diseases
- At the genetic level, it might lead to the identification of universal nonbiting genes or to universal target genetic pathways in mosquitoes
ZIKA, CHIK, DENGUE AEDES COINFECTIONS

Susceptibility of Aedes aegypti to arbovirus infection after single and dual exposure.

From: Impact of simultaneous exposure to arboviruses on infection and transmission by Aedes aegypti mosquitoes

Ae. aegypti mosquitoes were exposed to CHIKV, DENV-2 or ZIKV either individually or in combination by infectious bloodmeal. Infection rates for individual viruses after single exposure (yellow triangle) with CHIKV (a,b), DENV-2 (a,c) or ZIKV (b,c), and parallel co-exposures (blue square) with CHIKV/DENV-2 (a), CHIKV/ZIKV (b) and DENV-2/ZIKV (c).

Evaluation of Simultaneous Transmission of Chikungunya Virus and Dengue Virus Type 2 in Infected Aedes aegypti and Aedes albopictus (Diptera: Culicidae)

Zika virus alters the microRNA expression profile and elicits an RNAi response in *Aedes aegypti* mosquitoes

C. L. Campbell, T. Harrison, A. M. Hess, G. D. Ebel

First published: 15 November 2013

Arbovirus Research Branch, Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases, U.S. Centers for Disease Control and Prevention, Fort Collins, Colorado, USA

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**Figure 2.1** Diagram depicting the interaction between the vector, virus, and environmental factors. Area in the center of the diagram depicts concordance of all three of these factors that would hypothetically lead to enhanced interactions for optimal transmissibility of arboviral agents.
OTHER FACTORS INVOLVED IN SPREAD OF Aedes aegypti-BORNE DISEASES

First evidence of Zika virus venereal transmission in Aedes aegypti mosquitoes

Martin Grunnill1,2 and Michael Boots3

Vertical transmission of Zika virus in Aedes aegypti mosquitoes

Jakkravee Chompoochart, Sangkliporn, and Paredes S
AEDES DISPERSAL BY VEHICLES

- **Argentina**: average vector passive dispersal of >60 km a year by automotive vehicles
GLOBALIZATION AND VECTOR-BORNE DISEASES

> 1.3 billion international travelers, globally
World Bank, 2017

- Modern contributing factors to the rapid expansion of vector-borne disease include globalization of travel and trade, associated with vector accommodating trends in modern human settlement and suitable climate conditions.

- The contributions of increased mobility, both of vector and human populations, may be the most important variable to explain the recent increase in dengue transmission.
Historically, the increase in the number of cases of DH/DF has been correlated closely with the growth of urban human population. In addition, complacency by health authorities, as well as lack of public health resources for research, surveillance, prevention and control programs.

The increased epidemic activity caused by several viral serotypes increases the rate of genetic variation of the virus, thus increasing the probability of emergence of strains of viruses or genotypes with greater potential for epidemic or virulence, an important risk factor for severe dengue.

Gubler and Meltzer, Adv Virus Res 1990, 53, 35–70
Population growth and uncontrolled/unplanned urbanization

Percentage of urban population in Latin America

Social and economical drivers:
Lack of access to drinking water and drainage system

Dengue incidence in the Americas according to sanitation coverage, 2011 and 2013
Dengue incidence in The Americas according to % of urban population with access to an improved source of drinking water

Dengue incidence in countries in the Americas region, according to per capita, NGP in US$

Figure 8B. Dengue incidence in the Americas according to literacy level, 2011 and 2013

Social drivers involved in the transmission of dengue
Level of inequity

Dengue incidence in The Americas according to GINI index, 2013

IG:
0 = absolute equity in income
100 = absolute inequity

<table>
<thead>
<tr>
<th>País</th>
<th>IG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Honduras</td>
<td>57,0</td>
</tr>
<tr>
<td>Colombia</td>
<td>55,9</td>
</tr>
<tr>
<td>Brasil</td>
<td>54,7</td>
</tr>
<tr>
<td>Paraguay</td>
<td>52,4</td>
</tr>
<tr>
<td>Chile</td>
<td>52,1</td>
</tr>
<tr>
<td>Panamá</td>
<td>51,9</td>
</tr>
<tr>
<td>Costa Rica</td>
<td>50,7</td>
</tr>
<tr>
<td>Ecuador</td>
<td>49,3</td>
</tr>
<tr>
<td>El Salvador</td>
<td>48,3</td>
</tr>
<tr>
<td>Perú</td>
<td>48,1</td>
</tr>
<tr>
<td>México</td>
<td>47,2</td>
</tr>
<tr>
<td>República</td>
<td>47,2</td>
</tr>
<tr>
<td>Dominicana</td>
<td>45,3</td>
</tr>
<tr>
<td>Uruguay</td>
<td>44,5</td>
</tr>
</tbody>
</table>

Dengue incidence x100,000 hab
### Table 5. Multivariate logistic regression model of risk factors associated with living in a hot spot household.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>OR</th>
<th>CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Domestic worker/housewife</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2.86</td>
<td>1.45–5.64</td>
<td>0.002</td>
</tr>
<tr>
<td>Type of housing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>House/Apartment/ other</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rancho&lt;sup&gt;a&lt;/sup&gt;</td>
<td>13.55</td>
<td>5.40–34.02</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of persons per household</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–6</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥7</td>
<td>0.42</td>
<td>0.24–0.76</td>
<td>0.004</td>
</tr>
<tr>
<td>Water storage in containers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.95</td>
<td>1.09–3.52</td>
<td>0.024</td>
</tr>
<tr>
<td>Litter outdoors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2.37</td>
<td>1.38–4.08</td>
<td>0.002</td>
</tr>
<tr>
<td>Use of repellent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2.03</td>
<td>1.17–3.51</td>
<td>0.011</td>
</tr>
</tbody>
</table>

<sup>a</sup> In Venezuela, the word “rancho” is used to define a “shack”, an informal substandard type of housing typical of slum areas.

Other drivers involved

- Technical failures of the national vector control programs (i.e., lack of proper training and/or human and material resources)
- Absence of national policies (or inadequate application) in the correct use of insecticides
- Lag in availability of new molecules (insecticides) for the health sector
Dengue endemicity and seroprevalence between neighboring border cities in Northern Mexico and Southern Texas, where climatic suitability is similar, in 2005, n=276 participants

- Socioeconomic and behavioral factors including income, water storage, usage of air-conditioning, waste disposal, and cross-border travel differed sustainably, as did dengue prevalence

32% Incidence 77% seroprevalence

4% Incidence 39% seroprevalence
DENV-infection risk among contacts. Diagrams A and B show two clusters plotted in relative space (index house is at the center). Each segment represents one participant, color indicates serological status.. (A) DENV+ cluster ($\sigma = 1.1$). (B) DENV− cluster ($\sigma = -0.71$). Both clusters were initiated in the same neighborhood, in the same week of the second season of transmission in Iquitos, Peru.

Highly focal patterns of DENV transmission around the home (<100 m) indicating that transmission occurs among multiple, fine-scale foci connected by the movements of infected and susceptible people. At these short distances from the home, the relative contribution of mosquitoes versus humans to pathogen dispersal is still uncertain, but clearly both are important.

Stoddard et al. *PNAS* 2013, 110: 995-1003
Rainfall appears to precede ZIKV and CHIKV epidemics suggesting that an early warning system based on weather that predicts these outbreaks 3-4 weeks in advance would provide policy-makers and clinicians a warning to prepare countermeasures, which could lead to improved prognoses for ZIKV patients.

The incubation period of CHIKV in *Aedes aegypti* is 2–4 days whereas that of ZIKV is at least 10 days.

Proportion of *Ae. aegypti* with a detectable infection after being held at low temperatures

- Increased infection and transmission rates at higher temperatures, as well as altered infection rates and extrinsic incubation period (EIP) in response to fluctuating temperatures and diurnal temperature range (DTR)
- DTRs have been shown to enhance DENV infection rates and reduce EIPs at low temperatures, but decrease infection rates (and not affect DENV EIP) at higher temperatures

*Carrington L, et al. PLOS Neglected Tropical Diseases, April 25, 2013*
Hierarchy of factors that influence ZIKV transmission, illness, and social consequences.

Climate suitability, mosquito abundance & human–mosquito contact partly determine rates of ZIKV transmission, which causes illness in some cases. Social consequences depend on both actual and perceived risks of illness.

Figure 1. Quantification of ZIKV in Ae. aegypti and Cx. quinquefasciatus saliva expectorated onto FTA cards 9–12 days post infection (dpi). Green and red bars show the Ae. aegypti (RecLab) and Cx. quinquefasciatus populations blood-fed with ZIKV at 10^6 PFU/mL, respectively. The hashed pattern gray and black bars show the Ae. aegypti (RecLab) and Cx. quinquefasciatus populations, respectively, blood-fed with ZIKV at 10^4 PFU/mL. Parallel dashed lines indicate variations of ZIKV viremia in humans.
GENERAL CONCLUSIONS

• The individual role played by climate change in the resurgence of *Aedes aegyti*-transmitted infections remains uncertain

• The contributions of increased mobility, both of vector and human populations due to globalization factors, such as travel and trade, associated with vector accommodating trends in modern human settlements, may be the most important variable to explain the recent increase in *Aedes*-borne diseases

• To better understand the likely impact of climate change on VBDs, it is important to view climate-driven disease systems as complex socio-ecological dynamical systems
THANKS....GRACIAS!

TRUST ME, I'M NOT EVIL....

I JUST REALLY WANT TO HAVE KIDS AND MAKE SURE THEY'RE HEALTHY.