Why Here? Why Now? Travel, Trade, and Emergence of Infectious Diseases

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November 9-12, 2018

UNIVERSITY OF TORONTO

Unprecedented Volume and Speed of Travel

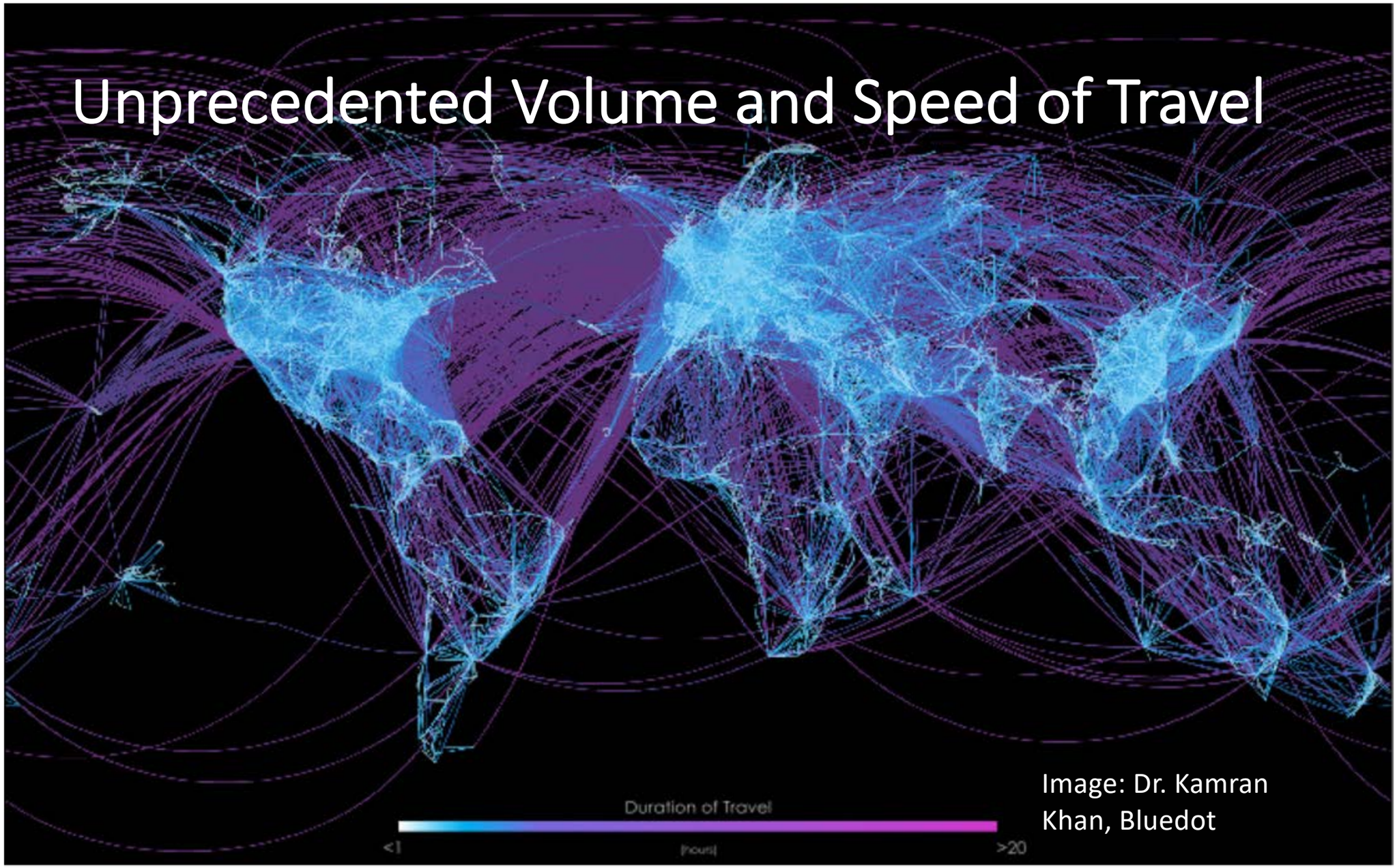
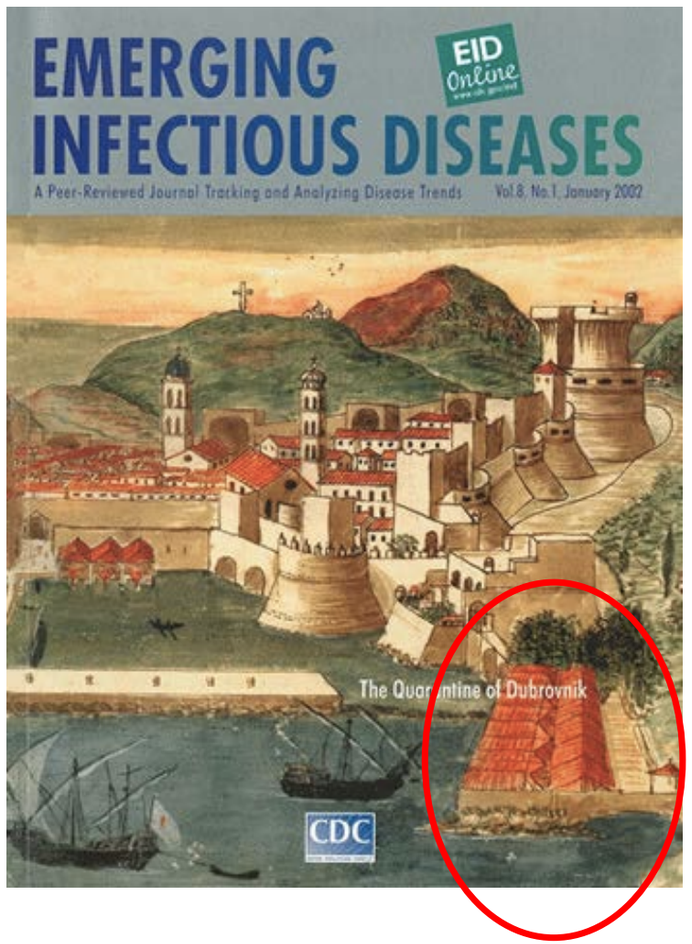


Image: Dr. Kamran Khan, Bluedot

Origins of Quarantine



- Dubrovnik (Ragusa) emerged as a trading center in Middle Ages.
- 1377: Great Council of Dubrovnik introduces 30 day quarantine of newcomers to avoid importing plague (trentina).
- Subsequently adopted by other cities, and extended to 40 days (”quaranti giorni”→”quarantine”).

[Sources: Mackowiak and Sehdev, Clin Infect Dis 2002; Emerg Infect Dis 2002]

Politics

Donald J. Trump
@realDonaldTrump

The U.S. cannot allow
people back. People
places to help out are
the consequences!

6:22 PM - 1 Aug 2014

5,851 Retweets **2,903** Likes

2.6K 5.9K 2.9K

Source: Howard Markel, When Germs Travel, Random House 2004.

bout Disease and

Travel Restrictions: Research and Policy


RESEARCH

Border Screening for SARS

Ronald K. St. John * Arlene King * Dick de Jong * Margaret Bodie-Collins *

OPEN ACCESS Freely available online

Lam et al. Theoretical Biology and Medical Modelling 2011, 8:44
http://www.tbiomed.com/content/8/1/44

THEORETICAL BIOLOGY AND MEDICAL MODELLING

RESEARCH Open Access

RESEARCH ARTICLE Open Access

Modeling the impact of air, sea, and land travel restrictions supplemented by other interventions on the emergence of a new influenza pandemic virus

Ka Chun Chong* and Benny Chung Ying Zee

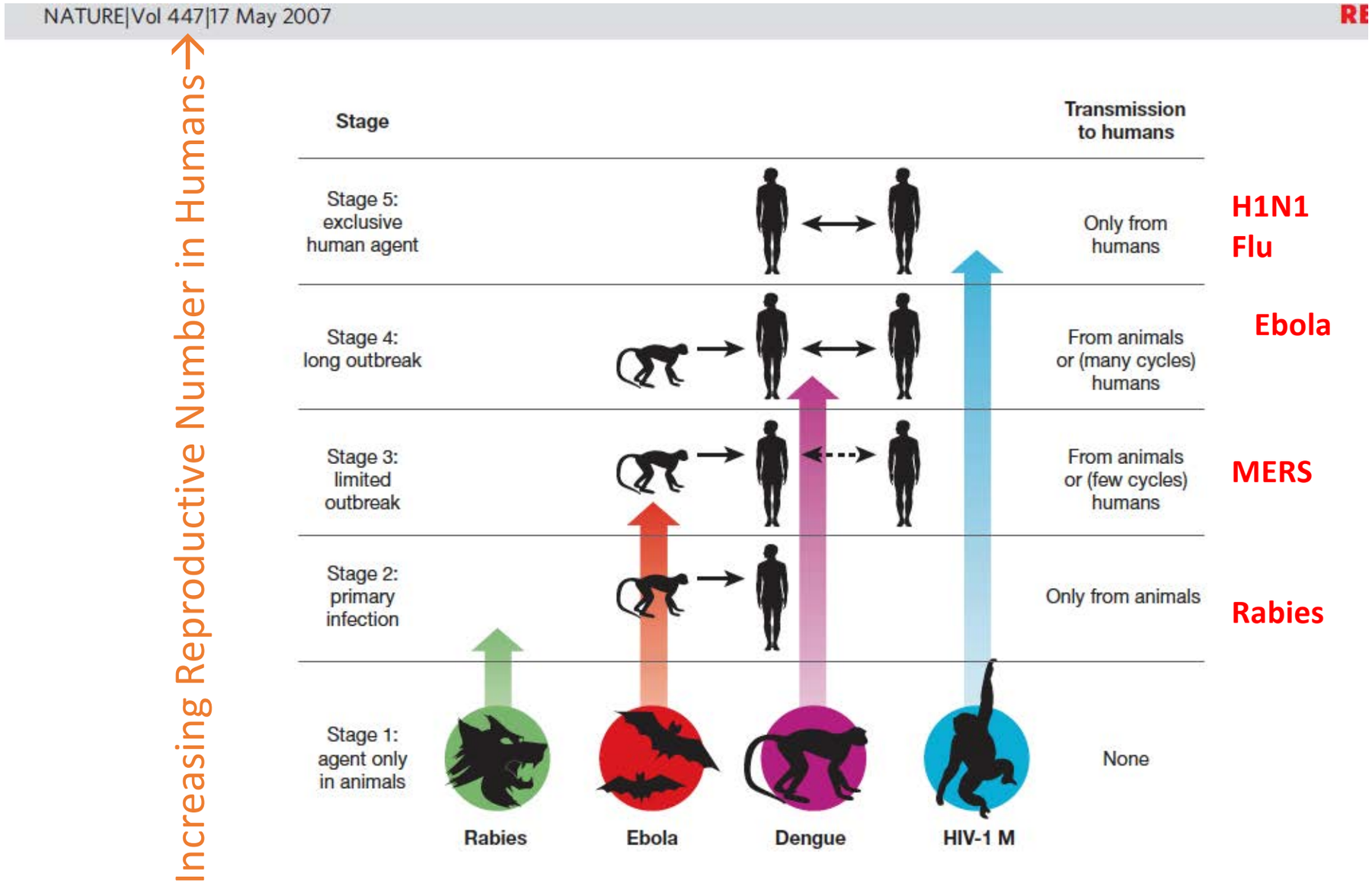
nt of the potential for international dissemination irus via commercial air travel during the 2014 west tbreak

reatore, Martin S Cetron, John S Brownstein, Nicki Pesik, Jennifer Miniota, Theresa Tam, Wei Hu, Adriano Nicolucci, oon, Isha Berry, Simon I Hay, Aranka Anema, Andrew J Tatem, Derek MacFadden, Matthew German, Kamran Khan

- **Limitations of travel restriction/travel screening:** economic consequences, prolonged incubation, alternate modes of travel, third country travel, ethical considerations (stigma, privation), impedance of outbreak response, poor sensitivity/specificity, others.

Factors Driving Disease Emergence

- **How** do diseases emerge and spread?
  - Need a "seed" (novel pathogen, opportunity for human infection).
  - Need "soil" (environmental conditions for introduction, ongoing reintroduction, or person-to-person transmission).
    - R can be < 1 (clusters) or > 1 (outbreaks and epidemics).



[Source: Wolfe, Dunavan, and Diamond, Nature 2007]

Outline: A Tale of Two Emergences

- **Cholera, North America, 1832.**
  - Importation followed by epidemics, likely high R_0.
  - Communicability dismissed as implausible (prior experience, culture).
    - Contrast with importations in 2010-2011.
- **Arboviral emergences/resurgences, South America, 2013-present.**
  - Focus on travel and trade as “reason” for Zika epidemic.
  - Ignores longstanding movements of people and goods.
  - Focus on dynamic R_0 for Zika and chikungunya viruses?
    - Climate change?

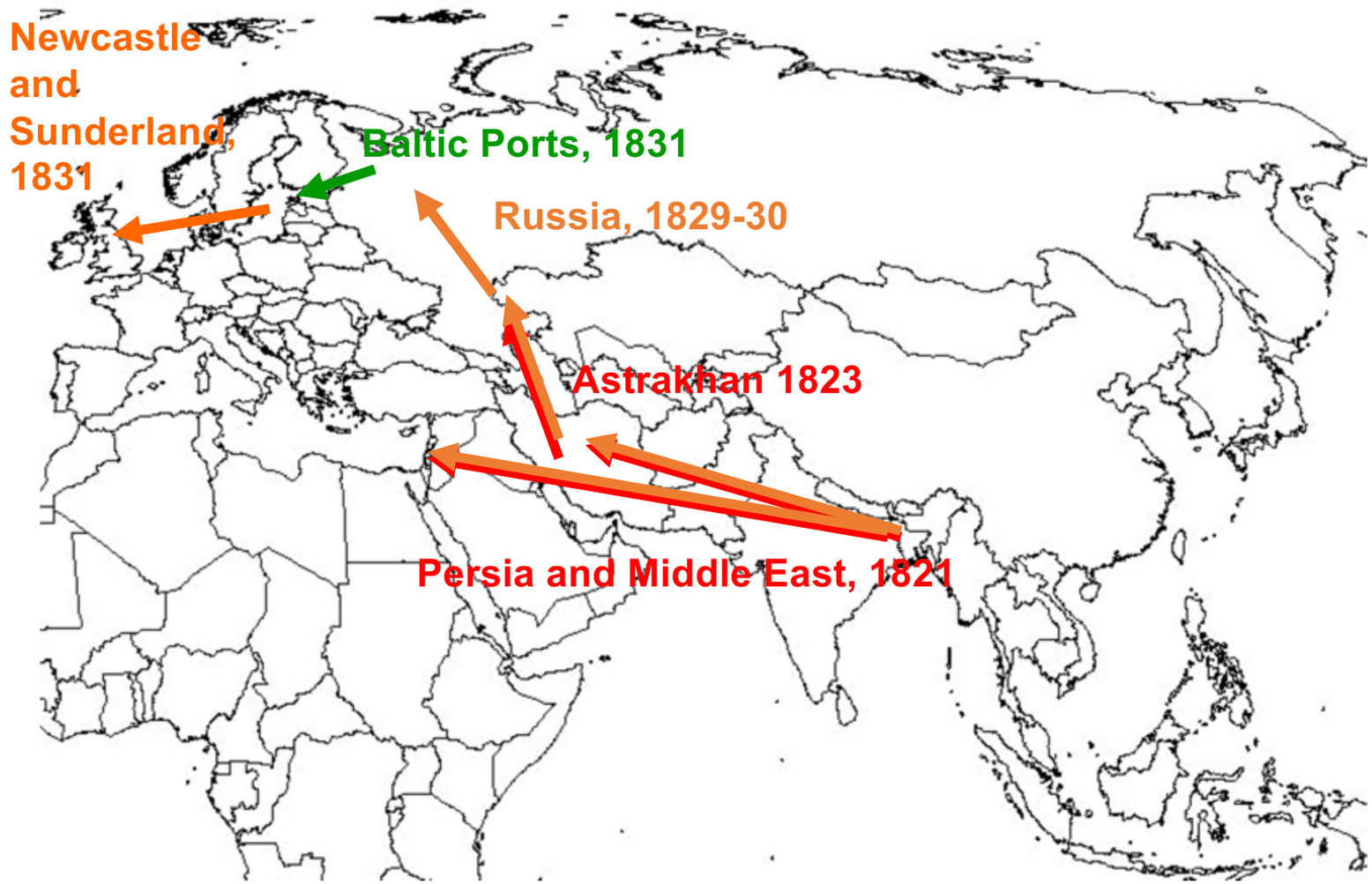
Part I: Cholera, Commerce and Contagion

Rediscovering Dr. Beck's Report. [Ashleigh Tuite, Christina Chan and David Fisman, J Public Health Policy 2011]

Cholera and Empire

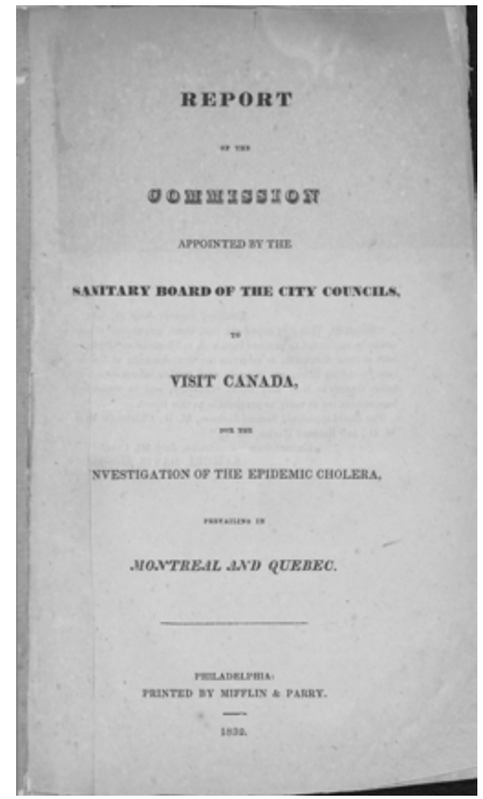
- First western description by East India Company physicians, 1817.
- East Bengal hub of jute industry (manufacture in Dundee, Scotland).
- Timing of introduction of cholera to U.K. corresponds with expansion of British Raj (1755-1856).

First (Recognized?) Cholera Pandemic



Cholera in North America, 1832

- Initial appearance in Great Britain in 1831.
- First reports in North America:
  - **Quebec** and **Montreal** in June 1832 in Irish immigrants.
  - Philadelphia delegation visit Canada (Drs. Meigs, Harlan, and Jackson).
  - Cholera moves south and west along waterways, including Northern and Western (Erie) Canals.



REPORT

OF THE

COMMISSION

APPOINTED BY THE

SANITARY BOARD OF THE CITY COUNCILS,

TO

VISIT CANADA,

FOR THE

NVESTIGATION OF THE EPIDEMIC CHOLERA,

PREVAILING IN

MONTREAL AND QUEBEC.

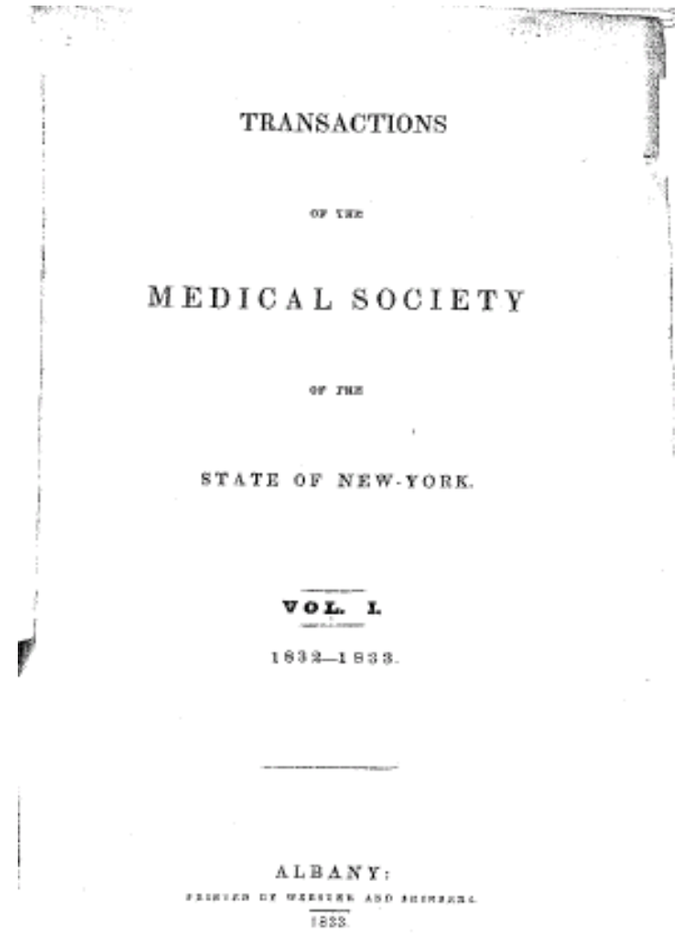
PHILADELPHIA:
PRINTED BY MIFFLIN & PARRY.

1832.

[U.S. National Library of Medicine, "Cholera Online" http://www.nlm.nih.gov/exhibition/cholera/

Beck's Report

- Cholera popularly perceived to be communicable.
  - Medical opinion: "miasma" acting on susceptible ("corrupt") constitutions.
- New York State: should government restrict trade and travel?
  - Newly completed Erie Canal (1825).
- Dr. Lewis Beck (1798-1853) commissioned by Legislature and Gov. Throop to report on cholera.
- Documents dates and locales of outbreaks from June to late July 1832.
  - Circumstances surrounding outbreak (presence of immigrants, importation of cases, habits of stricken individuals, case-fatality).



TRANSACTIONS

OF THE

MEDICAL SOCIETY

OF THE

STATE OF NEW-YORK.

VOL. I.

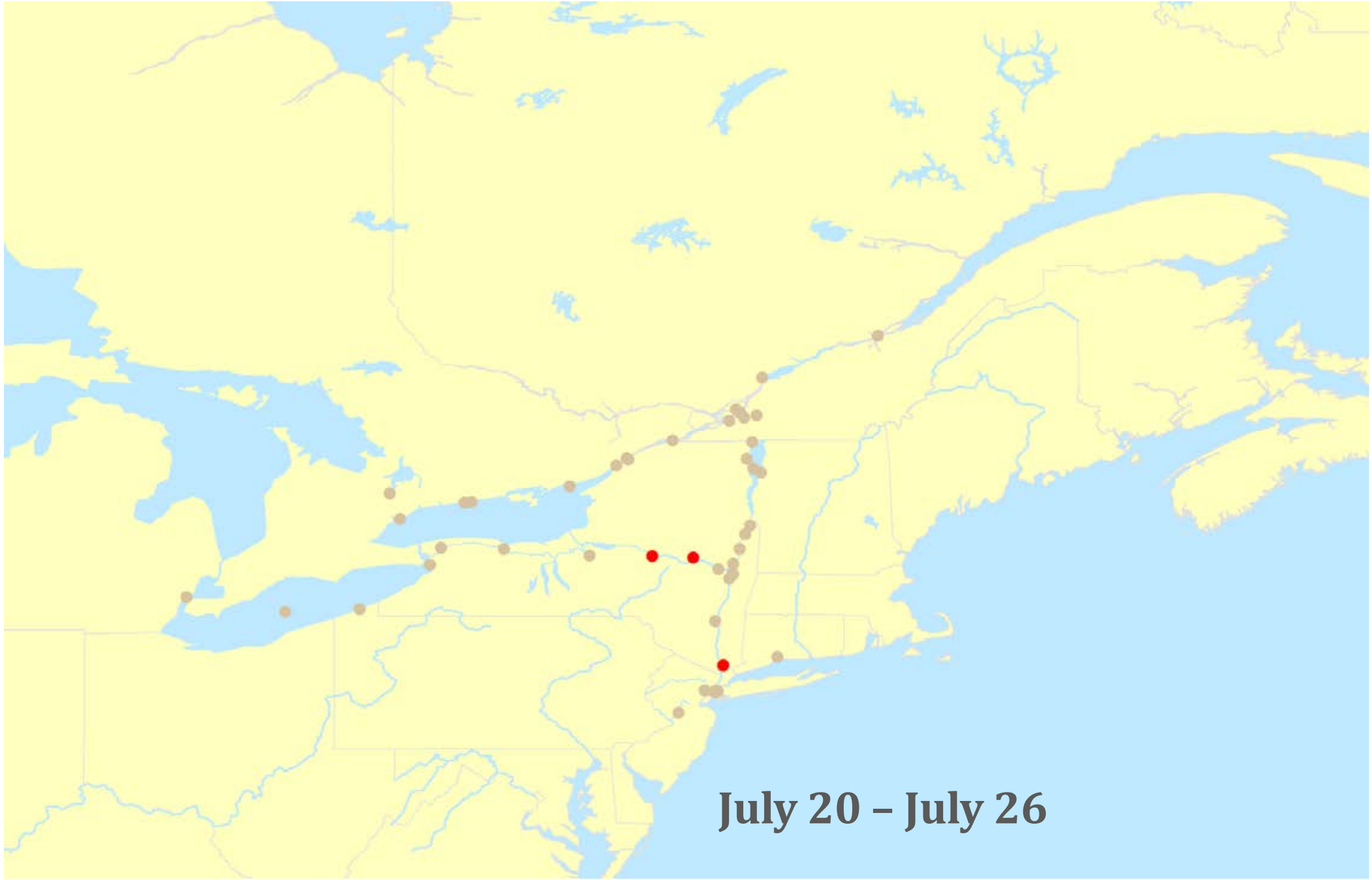
1832—1833.

ALBANY:

PRINTED BY WEBSTER AND SKINNER.

1833.

[New York Historical Society]


July 20 – July 26

Beck's Interpretation

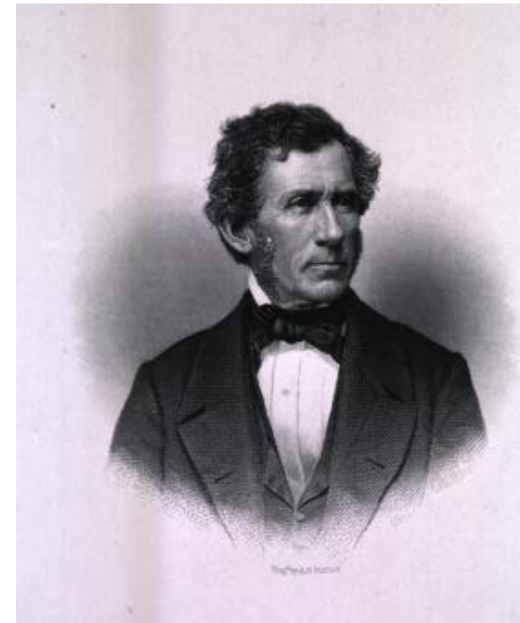
- Having documented epidemics that follow movement of (potentially infectious) individuals, Beck concedes cholera ***looks*** contagious:
  - "[This pattern] seem[s] at first sight to favor the idea that cholera is contagious, or directly communicable from man to man…[but] that cholera is not contagious can be proved by a multitude of facts."
- (Spoiler: his arguments are unconvincing).

Factors Contributing to Mischaracterization of Cholera

- Medical dogma ("ignorant public" disparaged by physicians [Rosenberg, *The Cholera Years*, 1962]).
- High attack rates among impoverished: equation of prosperity and morality.
  - Interaction between corrupted atmosphere **("miasma")** and predisposed (**"corrupted")** individual, (with **"contingent contagion").**
  - Ruth Richardson: "hardly regarded as a biological entity but a means of retribution upon the morally suspect".
- Observed failure of quarantine and *cordon sanitaire* in Russia (and subsequent rioting).
- Low attack rates/case fatality in care providers, spatial heterogeneity (villages unaffected), "hardy" boatmen (constitutions).

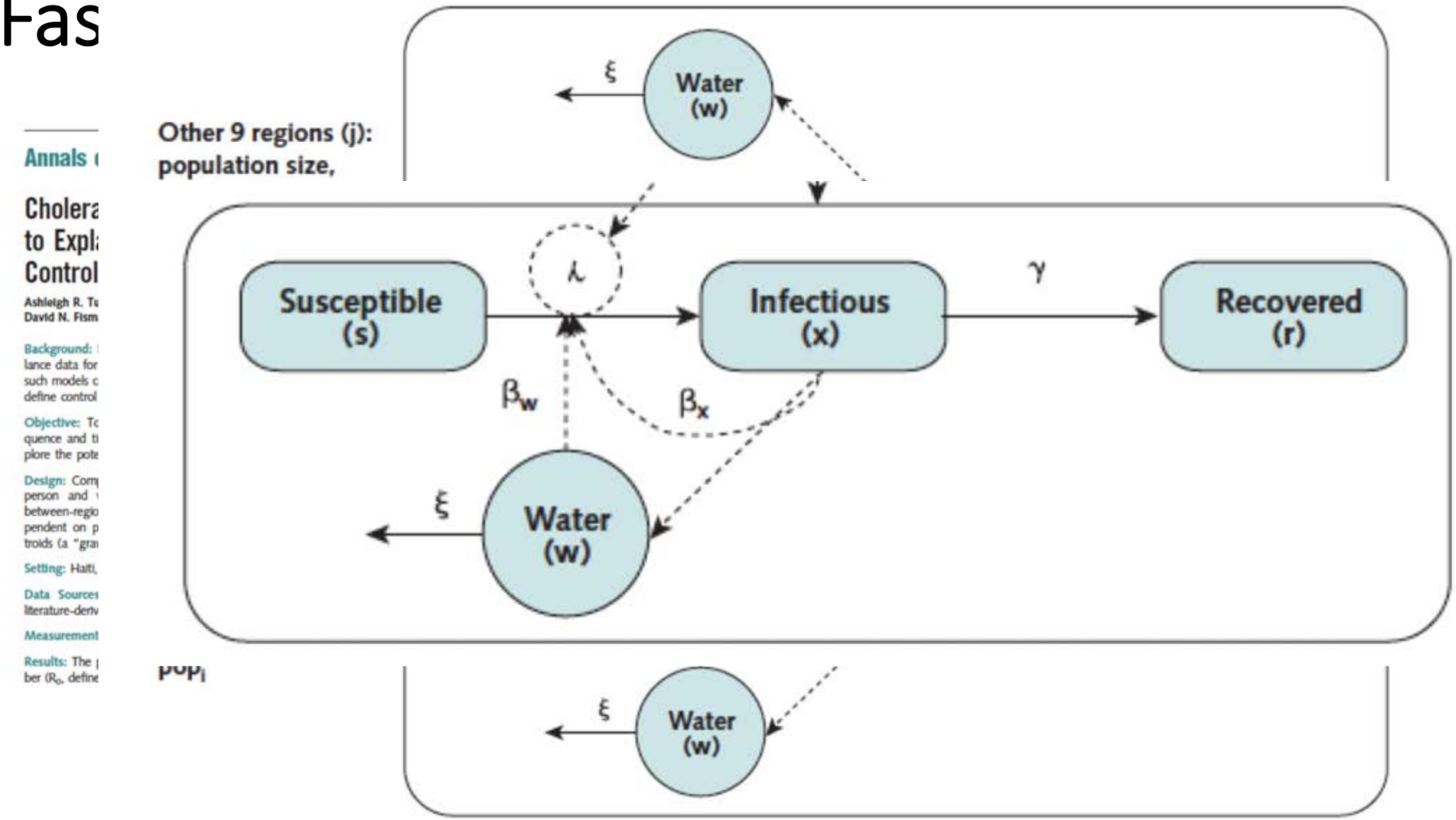
Daniel Drake: A Dissenting Voice

- Contemporaries (e.g., Daniel Drake) able to recognize importance of marine commerce to spread.
  - Attribution to “a poisonous, invisible, aerial insects, of the same or similar habits with the gnat” as this explains movement with ships, outbreaks at sea.



[Dr. Daniel Drake, 1785-1852] Engd. by A.H. Ritchie. Source: IHM collection, National Library of Medicine

Fas



[Source: Tulle A et al., Annals of Internal Medicine 2011]

R_0 for Cholera (Tien SIWR Model)

$$R_0 \sim \frac{\beta_H + \beta_w}{\gamma}$$

Appendix Table 2. **Best-Fit Parameter Values Based on Model Fit to MSPP Hospitalization Data**

Parameter	Description	Plausible Range	Best-Fit Value
β_I	Transmissibility, case	0.010 to 0.100	0.010
β_w	Transmissibility, water	0.789 to 0.945	0.944
ξ^{-1}	Mean survival of pathogen in water (weeks)	2.743 to 5.949	5.910
γ^{-1}	Mean duration of infectiousness (days)	2.376 to 3.013	2.913
κ	Gravity constant	6.76×10^{-13} to 8.92×10^{-12}	6.83×10^{-12}
R_0	Basic reproductive number	2.07 to 2.78	2.78

MSPP = Ministère de la Santé Publique et de la Population.

[References: Tien and Earn, Bull Math Biol 2010; Tuite et al., Annals of Internal Medicine, 2011]

Connec

Published Date: 2010-11-17 22:00:03
Subject: PRO/EDR> Cholera - Haiti (21): USA (FL)
Archive Number: 20101117.4171

CHOLERA - HAITI (21): USA (FLORIDA)
****
A ProMED-mail post
<http://www.promedmail.org>
ProMED-mail is a program of the
International Society for Infectious Diseases
<http://www.isid.org>

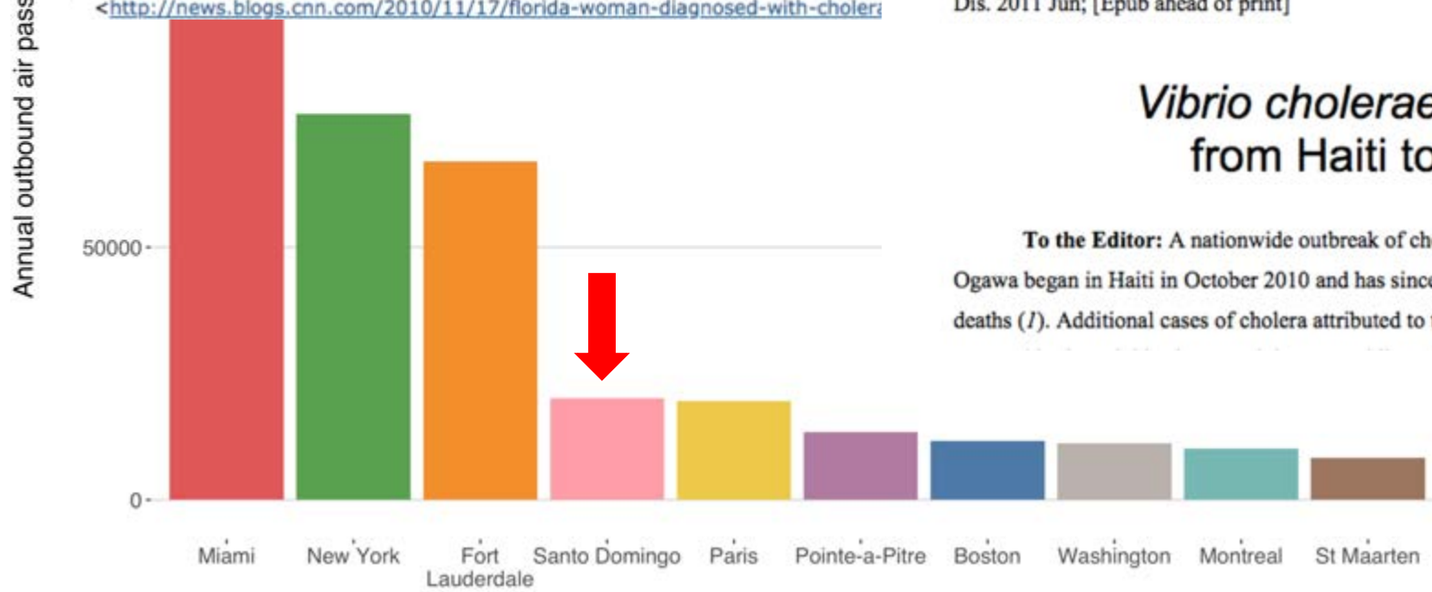
Date: 17 Nov 2010
Source: CNN [edited]
<http://news.blogs.cnn.com/2010/11/17/florida-woman-diagnosed-with-choler

DOI: 10.3201/eid1706.110161

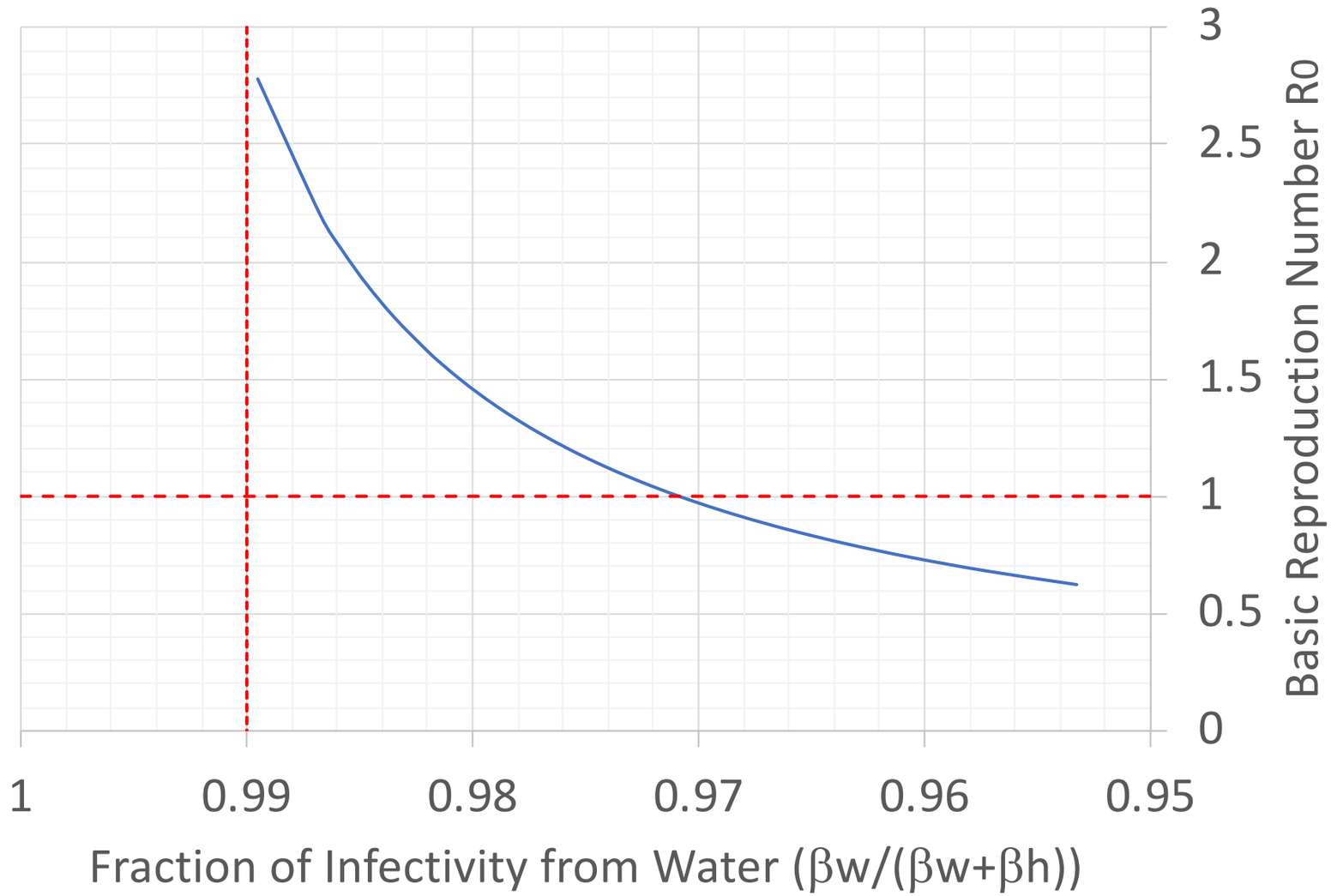
Suggested citation for this article: Gilmour MW, Martel-Laferrière V, Lévesque S, Gaudreau C, Bekal S, Nadon C, et al. *Vibrio cholerae* in traveler from Haiti to Canada [letter]. Emerg Infect Dis. 2011 Jun; [Epub ahead of print]

Vibrio cholerae in Traveler from Haiti to Canada

To the Editor: A nationwide outbreak of cholera caused by *Vibrio cholerae* O1 serotype Ogawa began in Haiti in October 2010 and has since resulted in >200,000 illnesses and 4,000 deaths (*1*). Additional cases of cholera attributed to the outbreak strain have subsequently been



[Figure by Dr. Ashleigh Tuite]


3
2.5
2
1.5
1
0.5
0
Basic Reproduction Number R0
1
0.99
0.98
0.97
0.96
0.95
Fraction of Infectivity from Water (βw/(βw+βh))

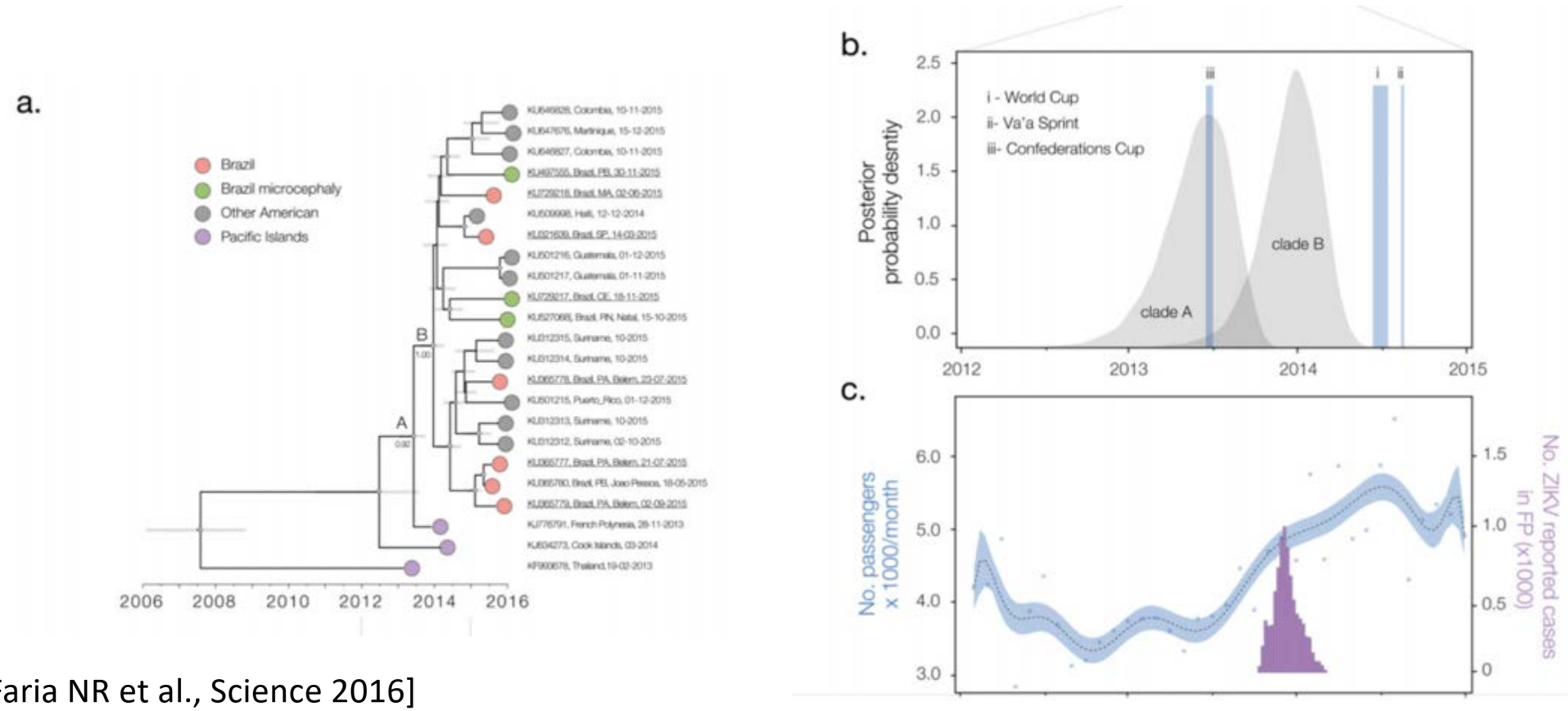
Part II: Recent Arboviral Emergences

Trade and Travel Are Not Enough

2000-2015: The Era of Arboviral Emergence and Resurgence?

- Introduction, resurgence, or *de novo* recognition of numerous arboviral pathogens in the Western hemisphere since 2000.
  - Chikungunya, Zika, Mayaro, Oropouche, Itaqui, Heartland, Cache Valley, Powassan, West Nile, Bourbon, West Nile viruses.
- ~150% increase in dengue incidence 2005-2015 (GBDS).

Zika Emergence in South America: Emphasis on Introduction via Travel



[Source: Faria NR et al., Science 2016]

Anticipating the International Spread of Zika

Bogoch I.B. et al. Lancet 2016; 387(10016): 335-6

Brazil and Sub-Saharan Africa: Historical Linkages

Voyage Pittoresque et Historique au Brésil, ou Séjour d'un Artiste Français au Brésil, Jean-Baptiste Debret (1834-39)

Brazilian slave trade evolved primarily to support sugar production (1533 onwards). Authorized by Portuguese crown, Papal blessing (1452).
4 million slaves imported to Brazil from sub-Saharan Africa (~40% of trans-Atlantic slave trade) (USA ~ 3.5%). Last western country to abolish slavery (1888).

[Images: Wikimedia commons, https://www.quora.com/profile/John-Dewar-Gleissner]

P. falciparum Malaria Importation

PNAS

Multiple independent introductions of *Plasmodiu falciparum* in South America

Erhan Yalcindag[a,1,2], Eric Elguero[a,1,2], Céline Arnathau[a], Patrick Durand[a], Jean Akiana[b], Timothy J. Anderso
Agnes Aubouy[d], François Balloux[e], Patrick Besnard[f], Hervé Bogreau[g], Pierre Carnevale[h], Umberto D'Alessa
Didier Fontenille[a], Dionicia Gamboa[j], Thibaut Jombart[e], Jacques Le Mire[f], Eric Leroy[a,k], Amanda Maestre[l],
Mayfong Mayxay[m], Didier Ménard[n], Lise Musset[o], Paul N. Newton[m], Dieudonné Nkoghé[k], Oscar Noya[p],
Benjamin Ollomo[k], Christophe Rogier[g], Vincent Veron[q], Albina Wide[p], Sedigheh Zakeri[r], Bernard Carme[q],
Eric Legrand[o], Christine Chevillon[a], Francisco J. Ayala[s,2], François Renaud[a,2,3], and Franck Prugnolle[a,2,3]

[a]Laboratoire Maladies Infectieuses et Vecteurs, Ecologie, Génétique, Evolution et Contrôle, Unité Mixte de Recherche 5290-224, Centre National de la Recherche Scientifique-Institut de Recherche pour le Développement-Université de Montpellier I-Université de Montpellier II, 34394 Montpellier Cedex France; [b]Service Epidémiologie Moléculaire et Parasitaire, Département de la Médecine Préventive et des Essais Cliniques, Laboratoire National de San Publique, Brazzaville, 1 Kinshasa, Republic of the Congo; [c]Department of Genetics, Texas Biomedical Research Institute, San Antonio, TX 78245; [d]Institu Recherche pour le Développement–Unité Mixte de Recherche 152, Université Paul Sabatier, 31062 Toulouse, France; [e]Medical Research Council Centre Outbreak Analysis and Modelling, Department of Infectious Disease Epidemiology, Faculty of Medicine, Imperial College, London W2 1PG, United Kingc [f]Malaria Control Program, Société Nationale de Métallurgie (Sonamet), Lobito, Angola; [g]Institute for Biomedical Research of the French Army and Unit Recherche sur les Maladies Infectieuses et Tropicales Émergentes–Unité Mixte de Recherche 6236, Allée du Médecin Colonel Jamot, Marseille, Cedex 0 France; [h]Institut de Recherche pour le Développement, 34394 Montpellier, France; [i]Department of Parasitology, Institute of Tropical Medicine, 2000 Antw Belgiu
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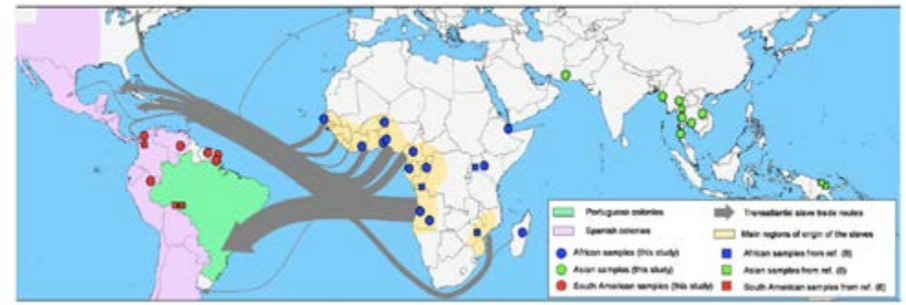
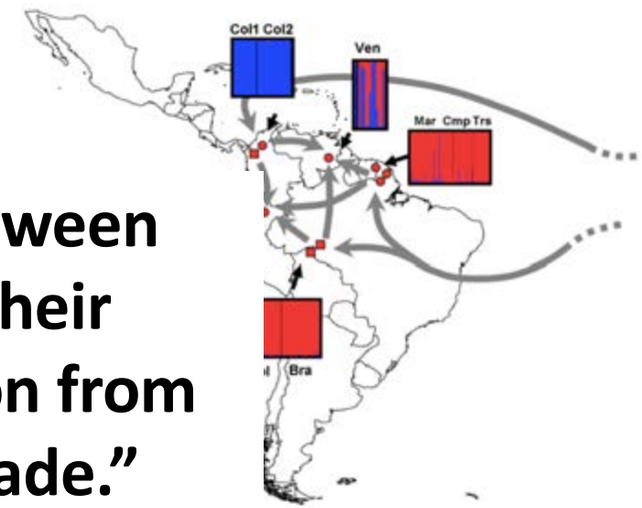




"Our estimates of divergence time between the South American populations and their likely sources favor a likely introduction from Africa during the transatlantic slave trade."

[Source: Yalcindaga E, et al., PNAS 2011]

Yellow Fever Importation

Table 2. Evolutionary Rates and Divergence Times of Yellow Fever Viruses

Data Set *(n)*	Demographic Model	Epidemic Doubling Time (Years)[a]	Substitution Rate ($\times 10^{-4}$ subs/site/year)[a]	Age (Years)[a]	d_N/d_S
Brazil (38)	Exponential	26 (12, 211)	6.7 (3.7, 9.6)	96 (65, 143)	0.130[b]
Peru (25)	Constant	NA	8 (3.4, 13.3)	58 (28, 107)	0.191[b]

"[E]stimated mean divergence time of the West African and South American clades was approximately 470 years ago [1537]…while the mean time of origin of both South American genotypes was 306 years ago [1701]. Taken together, these analyses…provide compelling support for an initial introduction during the period of the slave trade and first contact between the two continents."

[Source: Bryant JE et al., PLoS Pathogens 2007]

Chikungunya and Zika Endemic Ranges

Chikungunya local transmission (as of May, 2018)

Zika local transmission (as of September, 2018)

[Source: US CDC Yellow Book, available via the Internet at https://wwwnc.cdc.gov/travel/page/world-map-areas-with-zika and https://www.cdc.gov/chikungunya/geo/index.html]

What is R_0 in the Ross Model?

Humans infected by an infectious human

$$amb_H/r \quad x \quad ab_M/\mu$$

$$R_0 = a^2mb_Hb_M/r\mu$$

Climate Change in Brazil: Current Observations (1960-2010)

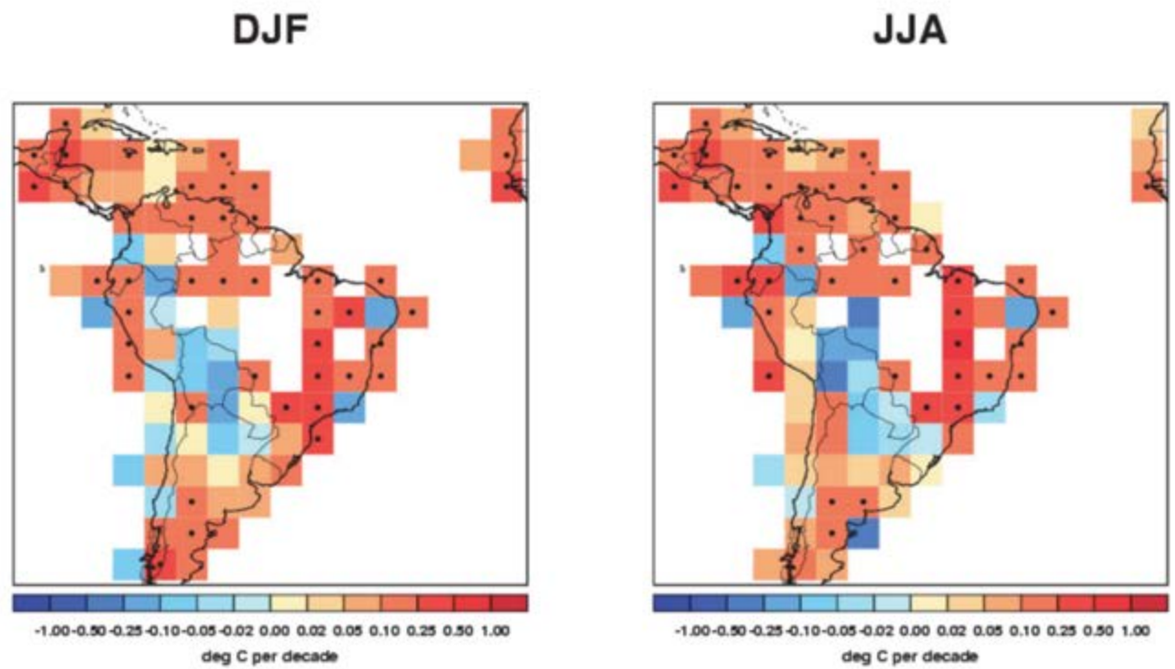
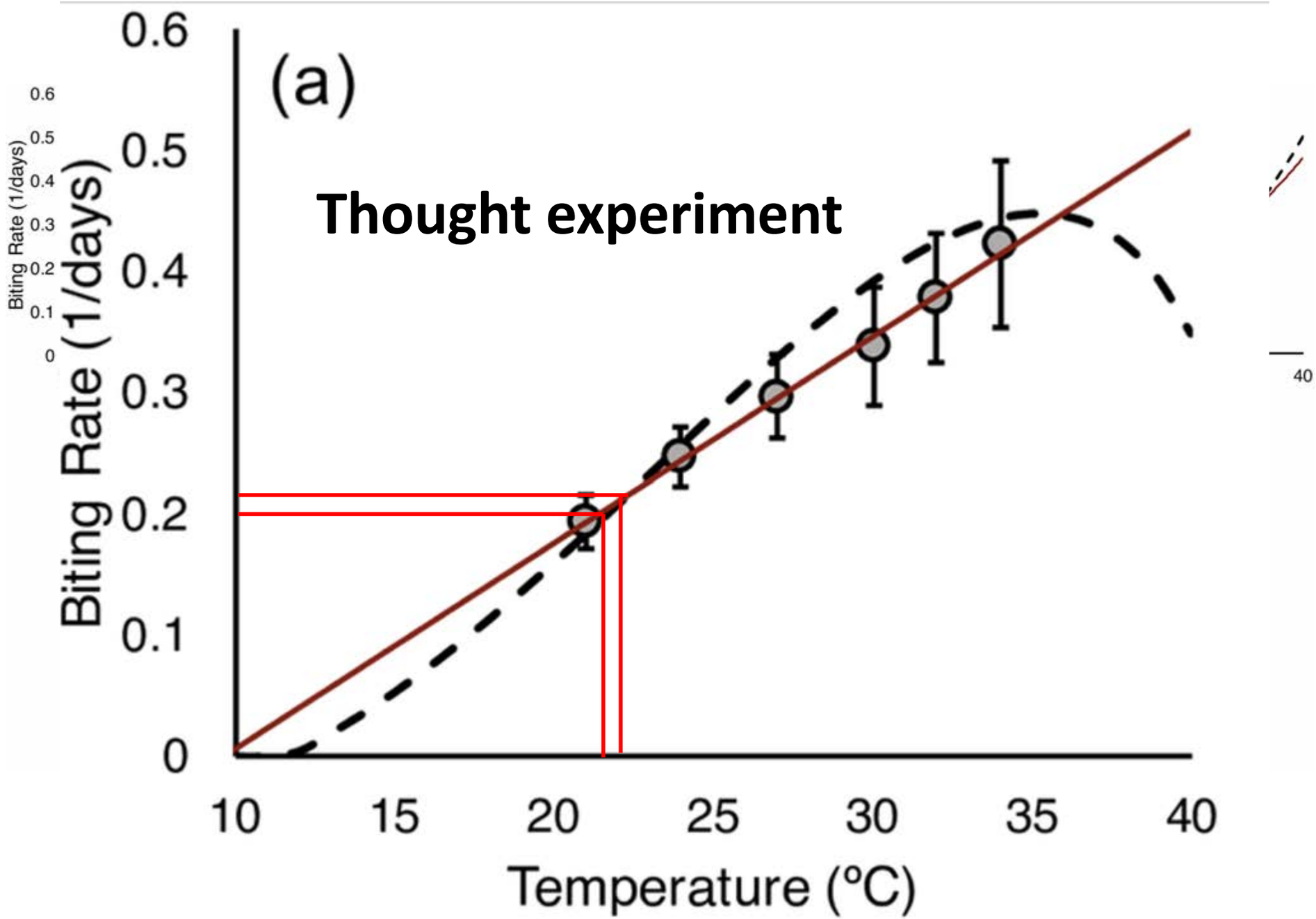
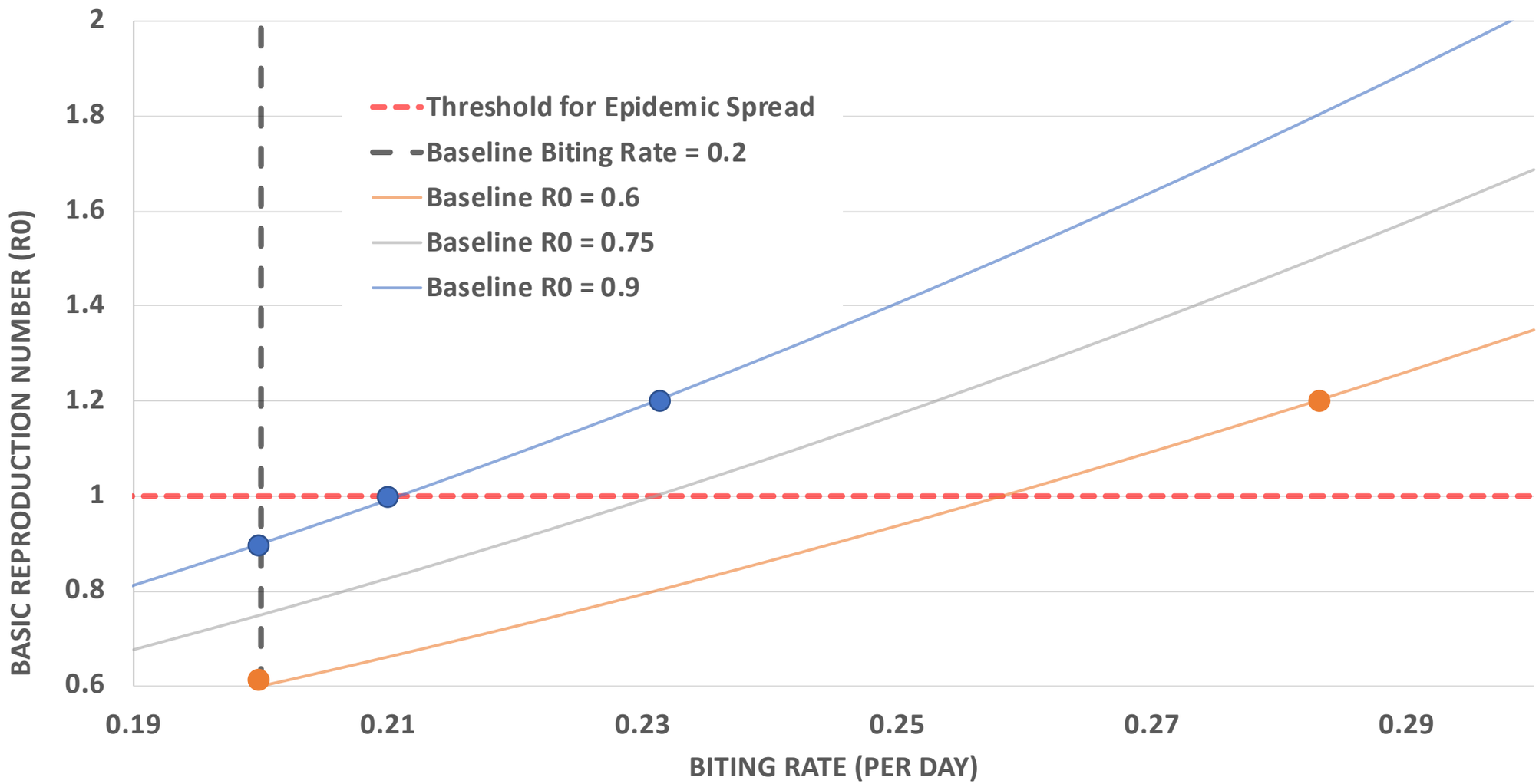


Figure 2. Decadal trends in seasonally averaged temperatures for Brazil and surrounding regions over the period 1960 to 2010. Monthly mean anomalies from CRUTEM3 (Brohan et al. 2006) are averaged over each 3 month season (December-January-February – DJF and June-July-August - JJA). Trends are fitted using the median of pairwise slopes method (Sen 1968, Lanzante 1996). There is higher confidence in the sign of trends if the 5th to 95th percentiles of the pairwise slopes do not encompass zero. This is shown by a black dot in the centre of the respective grid-box.

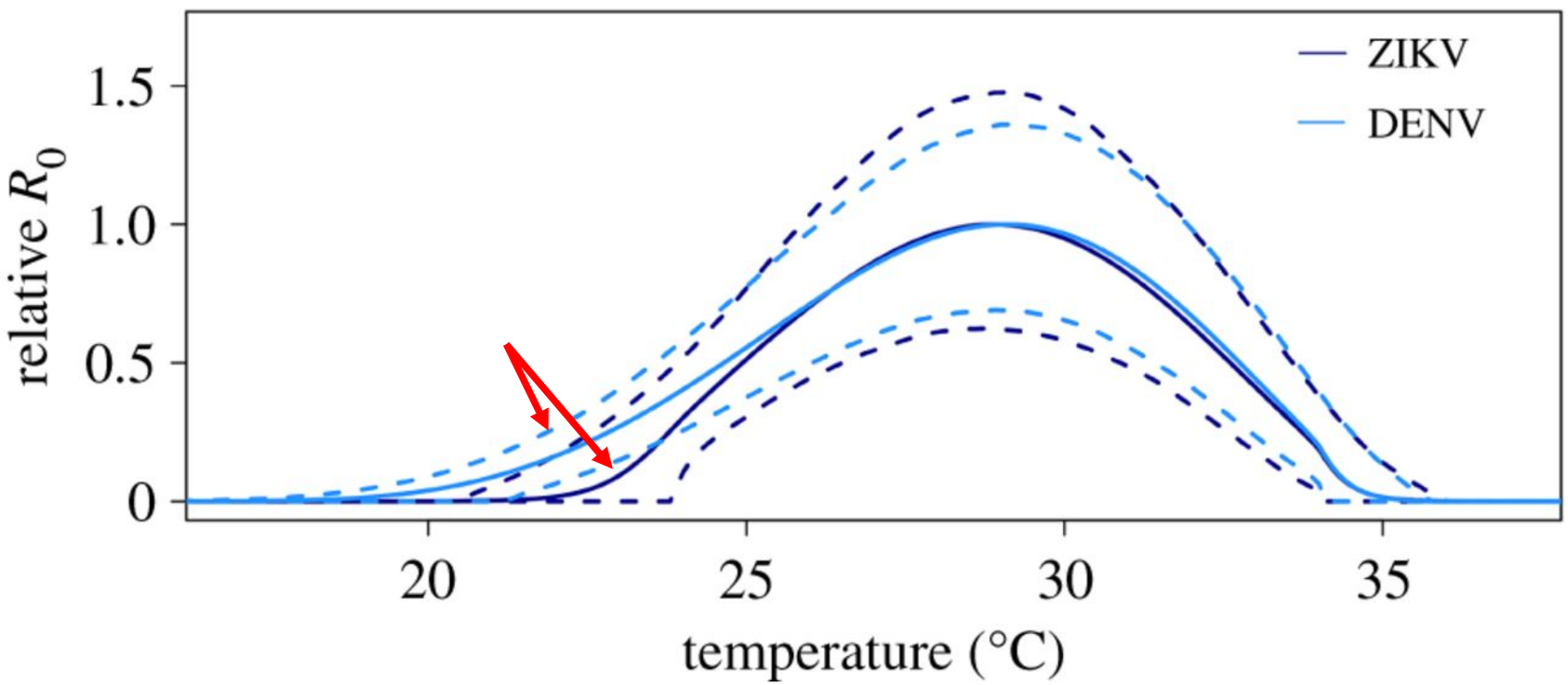
[Source: SN Gosling et al., University of Nottingham. Available via the Internet at http://eprints.nottingham.ac.uk/2040/7/Brazil.pdf

Temperature and R_0 for Vectorborne Disease


(a)
Thought experiment
Biting Rate (1/days)
0.6
0.5
0.4
0.3
0.2
0.1
0
10
15
20
25
30
35
40
Temperature (°C)


Threshold for Epidemic Spread
Baseline Biting Rate = 0.2
Baseline R0 = 0.6
Baseline R0 = 0.75
Baseline R0 = 0.9
BASIC REPRODUCTION NUMBER (R0)
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.19
0.21
0.23
0.25
0.27
0.29
BITING RATE (PER DAY)

Effect of temperature on R0.



PROCEEDINGS OF THE ROYAL SOCIETY B

Blanka Tesla et al. Proc. R. Soc. B 2018;285:20180795

Conclusions

- Global trade and travel at unprecedented levels, enhance risk (certainty?) of **introduction** of EID into new geographies.
- ”**Seed**” is necessary but not sufficient.
  - Often forget about **soil** **(R**, or **R_0)** when analyzing risk.
- R_0 not a fixed property of communicable diseases: varies with time, space, environment, and resources.
- **Don’t be Dr. Beck:** believe the data.