

**IPFA/PEI 22ND INTERNATIONAL WORKSHOP ON
“SURVEILLANCE AND SCREENING OF BLOOD BORNE PATHOGENS”**



PRAGUE

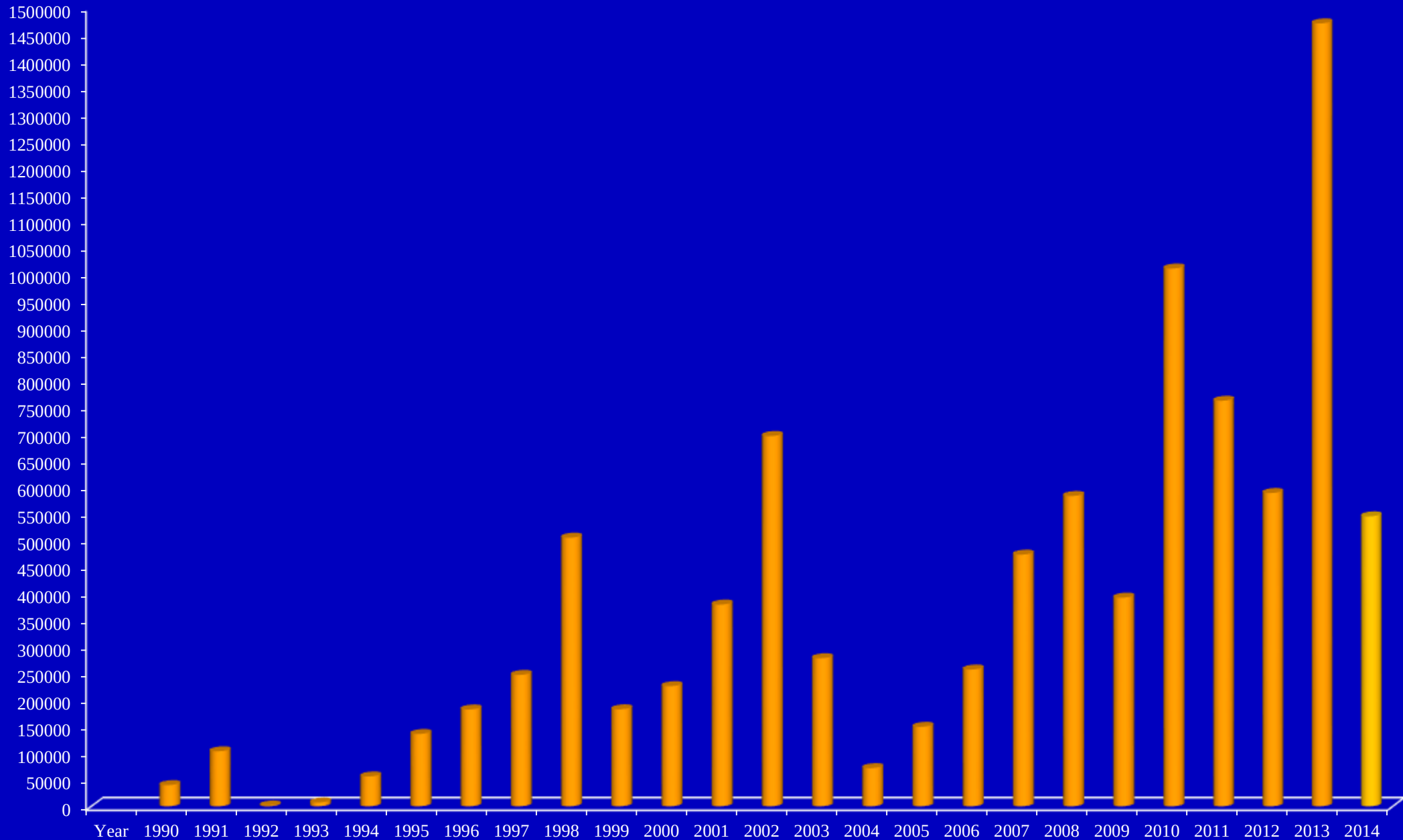
Arboviruses and Blood Safety

José Eduardo Levi

DENGUE

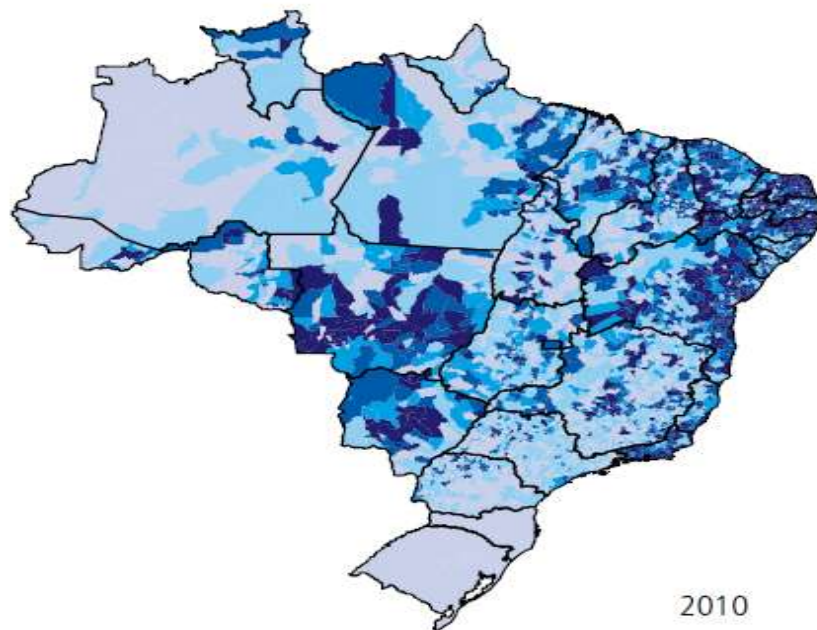


Dengue Cases Brazil 1990 - 2014

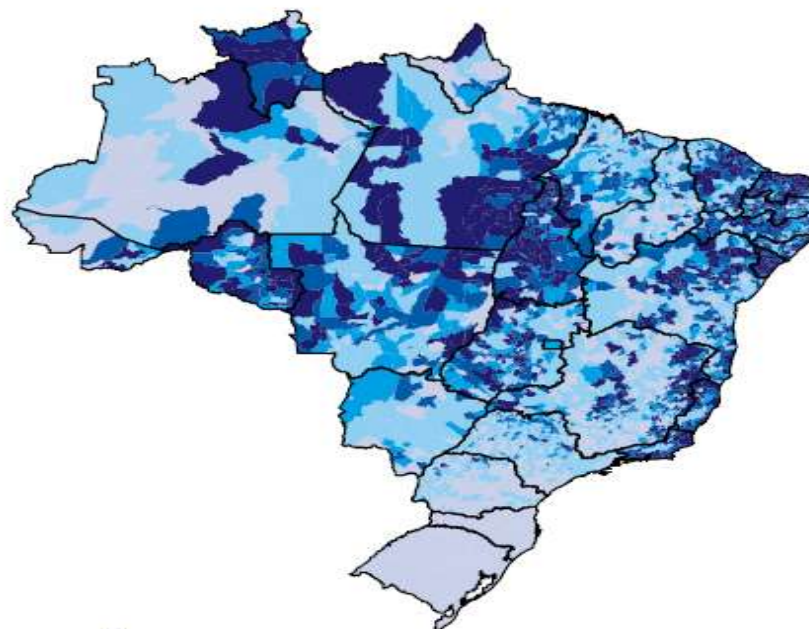


AFFECTED MUNICIPALITIES AND INCIDENCE

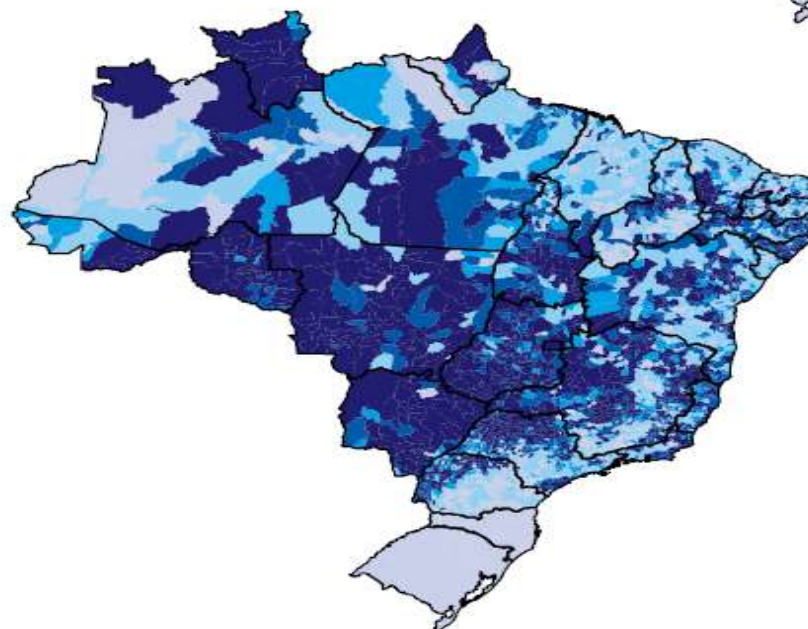
2002



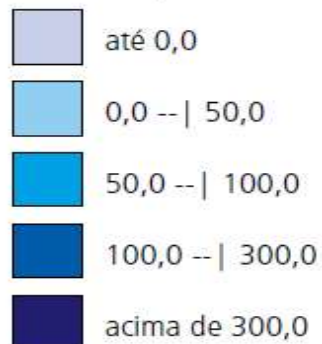
2008



2010



Incidência por 100.000 hab.



The global distribution and burden of dengue

504 | NATURE | VOL 496 | 25 APRIL 2013

Table 1 | Estimated burden of dengue in 2010, by continent

	Apparent	Inapparent
	Millions (credible interval)	Millions (credible interval)
Africa	15.7 (10.5–22.5)	48.4 (34.3–65.2)
Asia	66.8 (47.0–94.4)	204.4 (151.8–273.0)
Americas	13.3 (9.5–18.5)	40.5 (30.5–53.3)
Oceania	0.18 (0.11–0.28)	0.55 (0.35–0.82)
Global	96 (67.1–135.6)	293.9 (217.0–392.3)

RATE SYMPTOMATIC/ ASYMPTOMATIC = 1:3

EVIDENCE OF TRANSFUSION-TRANSMITTED DENGUE

VIREMIC DONOR (RNA+)



RECIPIENT PRE-TX NEGATIVE AND POST-TX POSITIVE



**SIGNS, SYMPTOMS AND LABORATORY MARKERS COMPATIBLE
WITH DENGUE OCCURRING 1-14 DAYS POST-TRANSFUSION**

DENGUE LABORATORY MARKERS AMONG BLOOD DONORS FROM SANTOS, BRAZIL. LEVI, UNPUBLISHED

		IgG	IgM	IgG + IgM	TMA
MONTH/YEAR	N=				
JAN/2010	500	74,0%	7,2%	5,8%	0,0%
FEB/2010	493	64,5%	8,5%	6,9%	1,4%
MARCH/2010	495	68,7%	15,2%	13,7%	1,2%
APRIL/2010	500	70,2%	24,4%	23,8%	0,8%
JULY/2010	500	71,6%	17,8%	17,8%	0,0%
JULY/2011	500	74,4%	8,6%	7,8%	0,0%
MEAN		70,6%	13,6%	12,6%	0,6%

Grifols (formerly Novartis) – Sponsor, Santos Dengue Blood Donors Study

HYPOTHESIS FOR THE LOW NUMBER OF TT CASES REPORTED:

- 1) Hemovigilance may be deficient**
- 2) Presence of protective immunity in recipients in endemic areas**
- 3) Frequent cotransfusion of antibody-positive units which neutralize infectivity of viremic donations**
- 4) Clinical outcomes may not be as severe in immunosuppressed patients infected with dengue**
- 5) Need for mosquito saliva to enhance dengue replication and virulence;**

Dengue Hemorrhagic Fever Transmitted by Blood Transfusion

N ENGL J MED 359;14 WWW.NEJM.ORG OCTOBER 2, 2008

Table 1. Characteristics of the Donor and Recipients.

Patient	Age yr	Sex	Coexisting Conditions	Symptoms of Dengue Fever	Signs of Capillary Leak	Results of Serologic Testing	Findings on PCR Assay*	Outcome
Donor	52	M	None	Fever and myalgia after donation (not hospital- ized)	None	Not done	Dengue virus type 2	Full recovery
Recipient of fresh- frozen plasma	64	M	Diabetes mellitus, hypertension, ischemic heart disease, recent coronary-artery bypass graft, chronic renal impairment	Day 2 after trans- fusion (hospi- tal day 12): fe- ver, jaundice, malaise, and worsening thrombocy- topenia	Worsening of bilateral pleu- ral effusions	Seroconversion (on July 19, negative for IgG and IgM; on July 31, positive for both)	Dengue virus type 2	Discharged in good health
Recipient of packed red cells	72	M	Diabetes mellitus, hypertension, ischemic heart disease, peptic ulcer disease	Day 2 after trans- fusion (hospi- tal day 6): fever, myalgia, malaise	Small right pleu- ral effusion	IgG-positive on follow-up	Dengue virus type 2	Discharged in good health
Recipient of platelets	74	M	Hepatocellular carcinoma	None	None	Positive for both IgG and IgM on follow-up	Not done	Discharged in good health

Real-time symptomatic case of transfusion-transmitted dengue

*José Eduardo Levi,^{1,2} Anna Nishiya,¹ Alvina Clara Félix,² Nanci Alves Salles,¹
Luciana Ribeiro Sampaio,¹ Fátima Hangai,¹ Ester Cerdeira Sabino,³ and Alfredo Mendrone Jr¹*

TABLE 1. Laboratory results of donor and recipients

	Date	IgG	IgM	RNA*
Donor				
Index donation	April 4, 2014	Negative	Negative	Undetectable
	May 5, 2014	Positive	Positive	Undetectable
Recipient 1				
Pretransfusion	April 18, 2014	Negative	Negative	Undetectable
	April 23, 2014	Negative	Negative	Positive (VL, 872,100 copies/mL)
	April 30, 2014	Negative	Positive	Positive (VL, 6,192 copies/mL)
Recipient 2				
Posttransfusion	April 24, 2014	Negative	Negative	Undetectable
	May 8, 2014	Negative	Negative	Undetectable

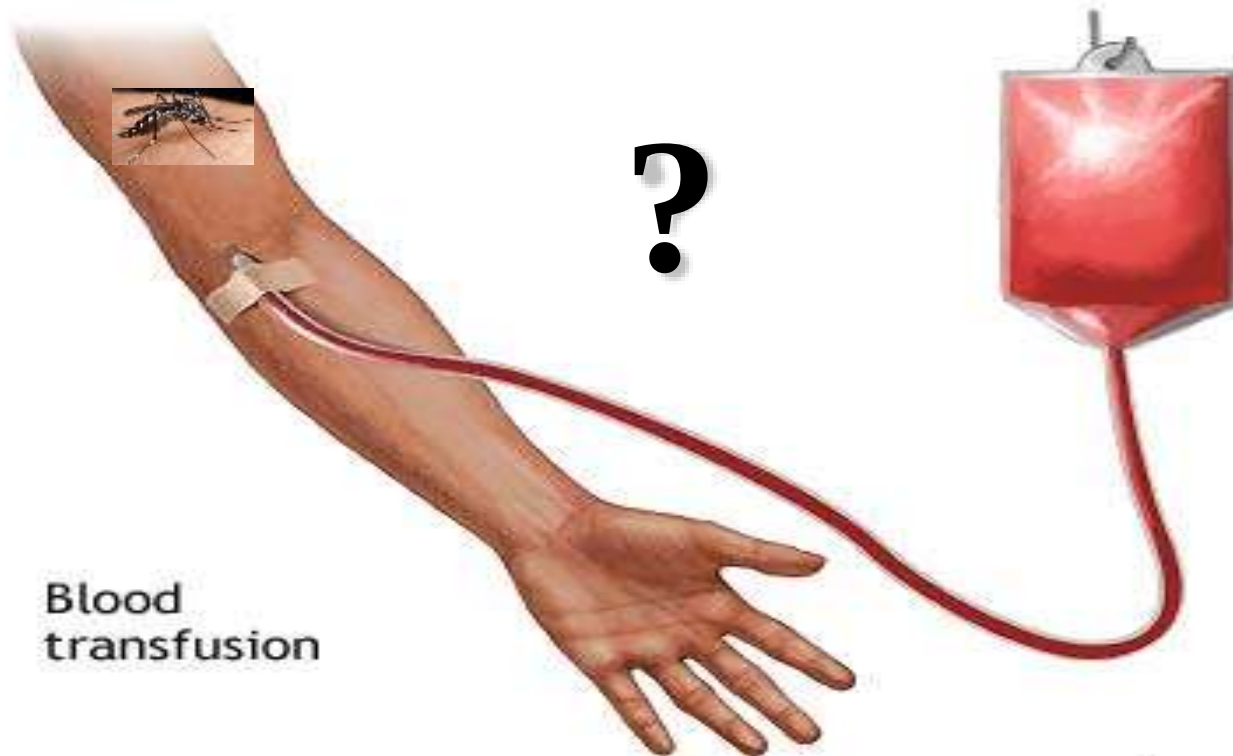
* In-house quantitative PCR; limit of detection, 350 copies/mL.

VL = viral load.

Bitten by a bug or a bag? Transfusion-transmitted dengue: a rare complication in the bleeding surgical patient

TRANSFUSION 2015;00;00–00

*Han Boon Oh,¹ Vaishnavi Muthu,¹ Zubin J. Daruwalla,² Shir Ying Lee,³ Evelyn S. Koay,⁴
and Paul A. Tambyah⁵*



HYPOTHESIS FOR THE LOW NUMBER OF TT CASES REPORTED:

- 1) Hemovigilance may be deficient
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- 3) Frequent co-transfusion of antibody-positive units which neutralize infectivity of viremic donations
- 4) Clinical outcomes may not be as severe in immunosuppressed patients infected with dengue
- 5) Need for mosquito saliva to enhance dengue replication and virulence;

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30% x 30% = 9% CHANCE OF BOTH DONOR AND RECIPIENT SERONEGATIVE



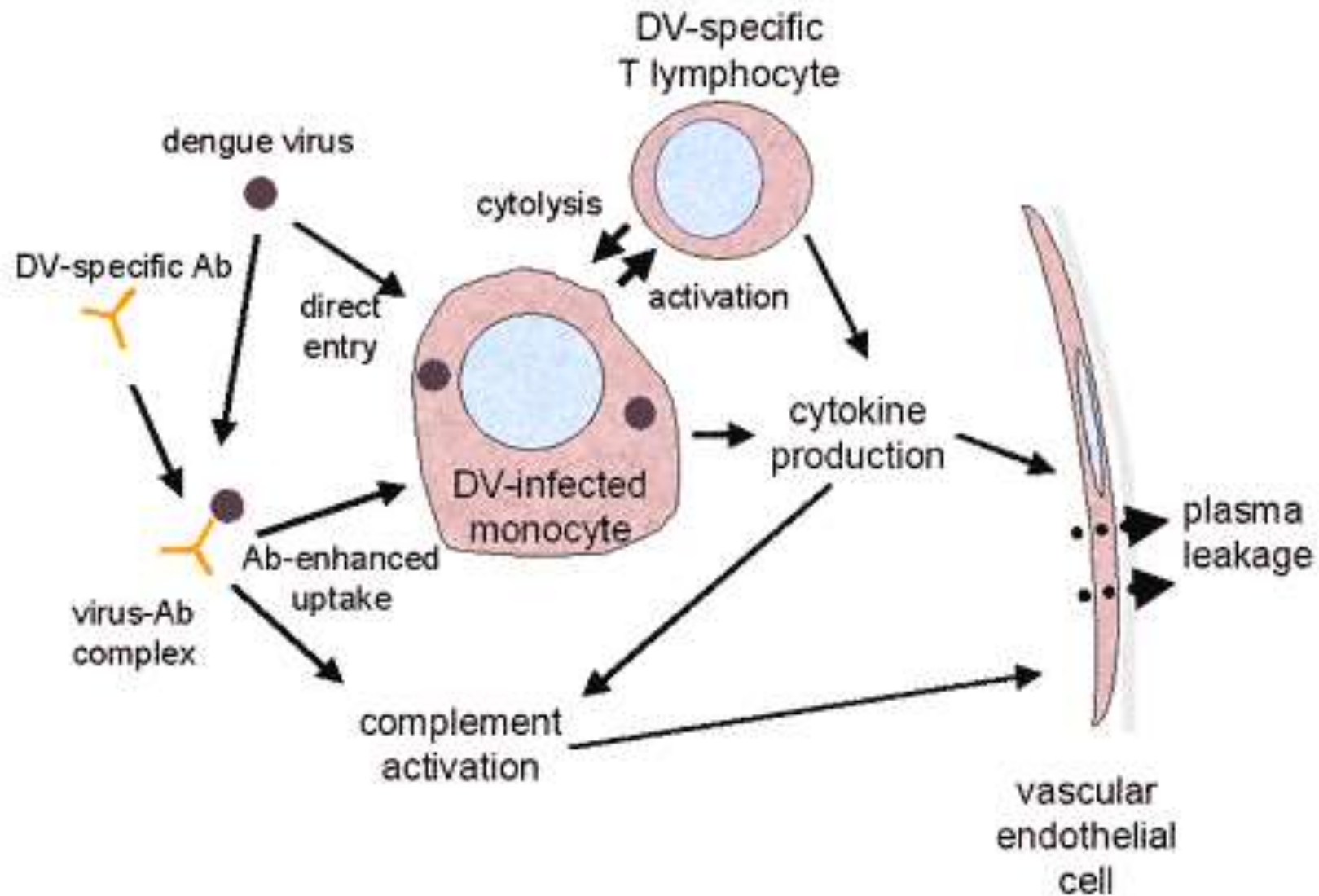
Sao Paulo
15,000,000 inhabitants
< 1,000 dengue cases in 2010



Santos
800,000 inhabitants
> 20,000 dengue cases in 2010



Cross-Reacting Antibodies Enhance Dengue Virus Infection in Humans



DENGUE SEROTYPES CIRCULATING IN BRAZIL, 2012



HYPOTHESIS FOR THE LOW NUMBER OF TT CASES REPORTED:

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- 4) **Clinical outcomes may not be as severe in immunosuppressed patients infected with dengue**
- 5) Need for mosquito saliva to enhance dengue replication and virulence;

Endemic and opportunistic infections in Brazilian solid organ transplant recipients

M. V. Batista^{1,2}, L. C. Pierrotti¹, E. Abdala^{1,3}, W. T. Clemente⁴, E. S. Girão⁵, D. R. T. Rosa⁶, L. E. Ianhez⁷, P. R. Bonazzi^{1,3}, A. S. Lima⁴, P. F. C. B. C. Fernandes⁵, M. V. Pádua-Neto⁶, T. Bacchella³, A. P. P. Oliveira⁴, C. F. G. Viana⁵, M. S. Ferreira⁶ and M. A. Shikanai-Yasuda^{1,2}

Tropical Medicine and International Health

VOLUME 16 NO 9 PP 1134–1142 SEPTEMBER 2011

Dengue virus infection in renal allograft recipients: a case series during 2010 outbreak

N. Prasad, D. Bhadauria, R.K. Sharma, A. Gupta, A. Kaul, A. Srivastava. Dengue virus infection in renal allograft recipients: a case series during 2010 outbreak.

Transpl Infect Dis 2012; **14**: 163–168. All rights reserved

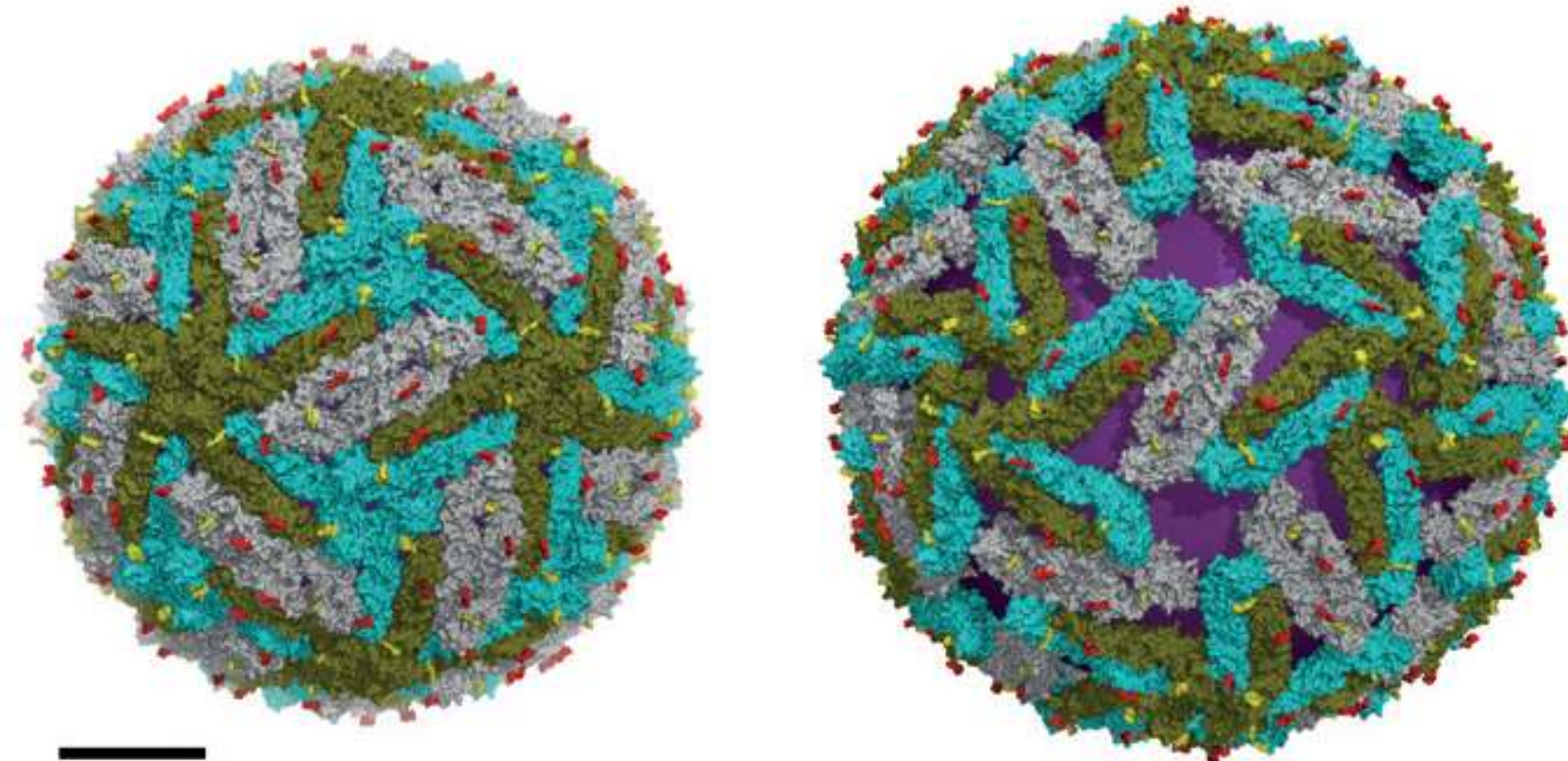
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- 5) **Need for mosquito saliva to enhance dengue replication and virulence;**

Two hosts, two structures

23 MAY 2013 | VOL 497 | NATURE | 443

Dengue virus has a highly ordered structure when grown in mosquito cells at 28 °C. The finding that the virus expands into a less ordered form at 37 °C indicates that the human immune system does not see it as we previously thought.



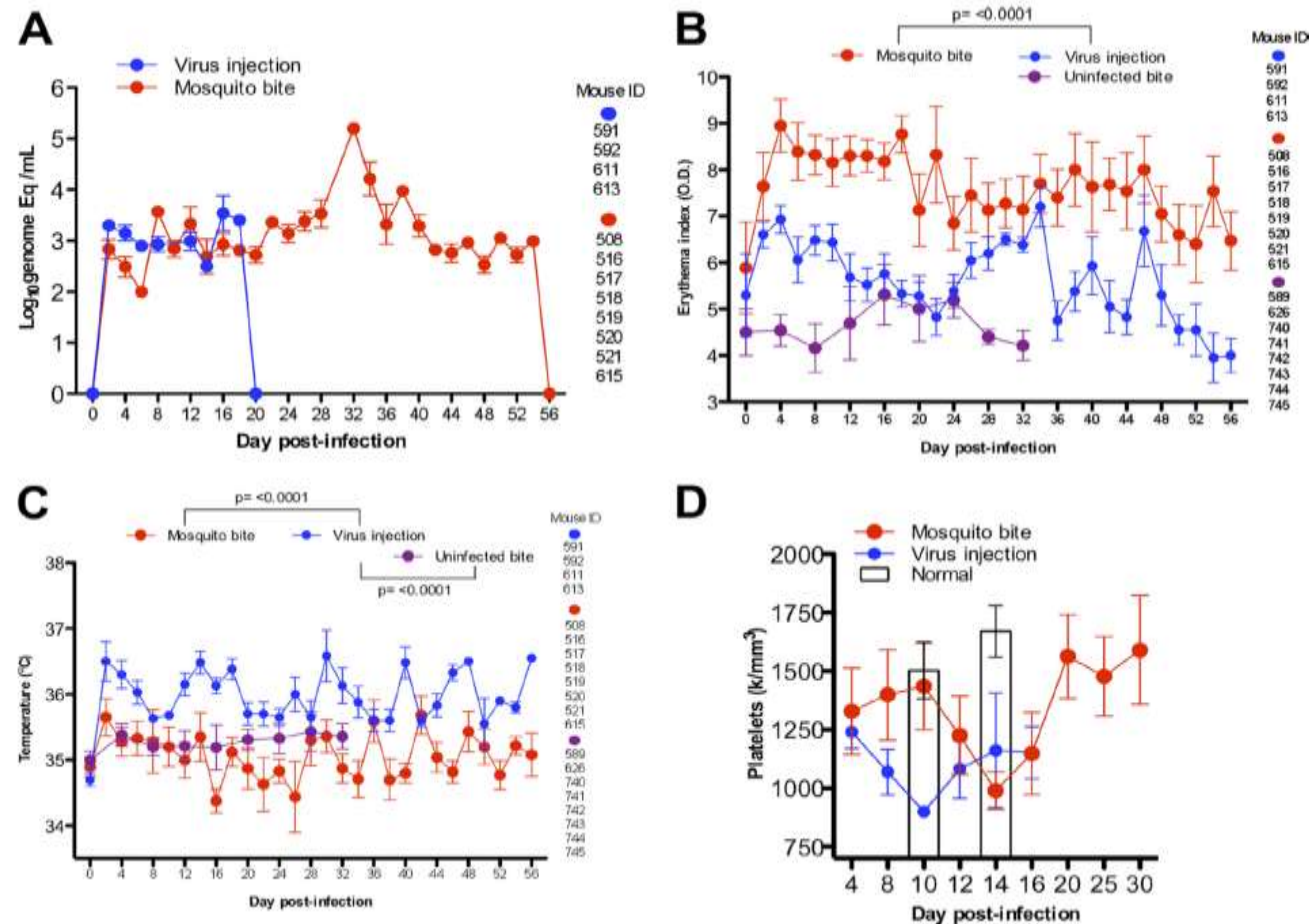
Mosquito Bite Delivery of Dengue Virus Enhances Immunogenicity and Pathogenesis in Humanized Mice

July 2012 Volume 86 Number 14

Journal of Virology p. 7637–7649

Rebeca Rico-Hesse^a

Department of Virology and Immunology, Texas Biomedical Research Institute, San Antonio, Texas, USA,^a and Departments of Medicine, Molecular Microbiology, Pathology, and Immunology, Washington University School of Medicine, St. Louis, Missouri, USA^b



DONOR`S SCREENING: IF AND HOW

-EPIDEMIOLOGY

Important negative impact on donor availability

-CLINICAL SIGNS

Low efficiency

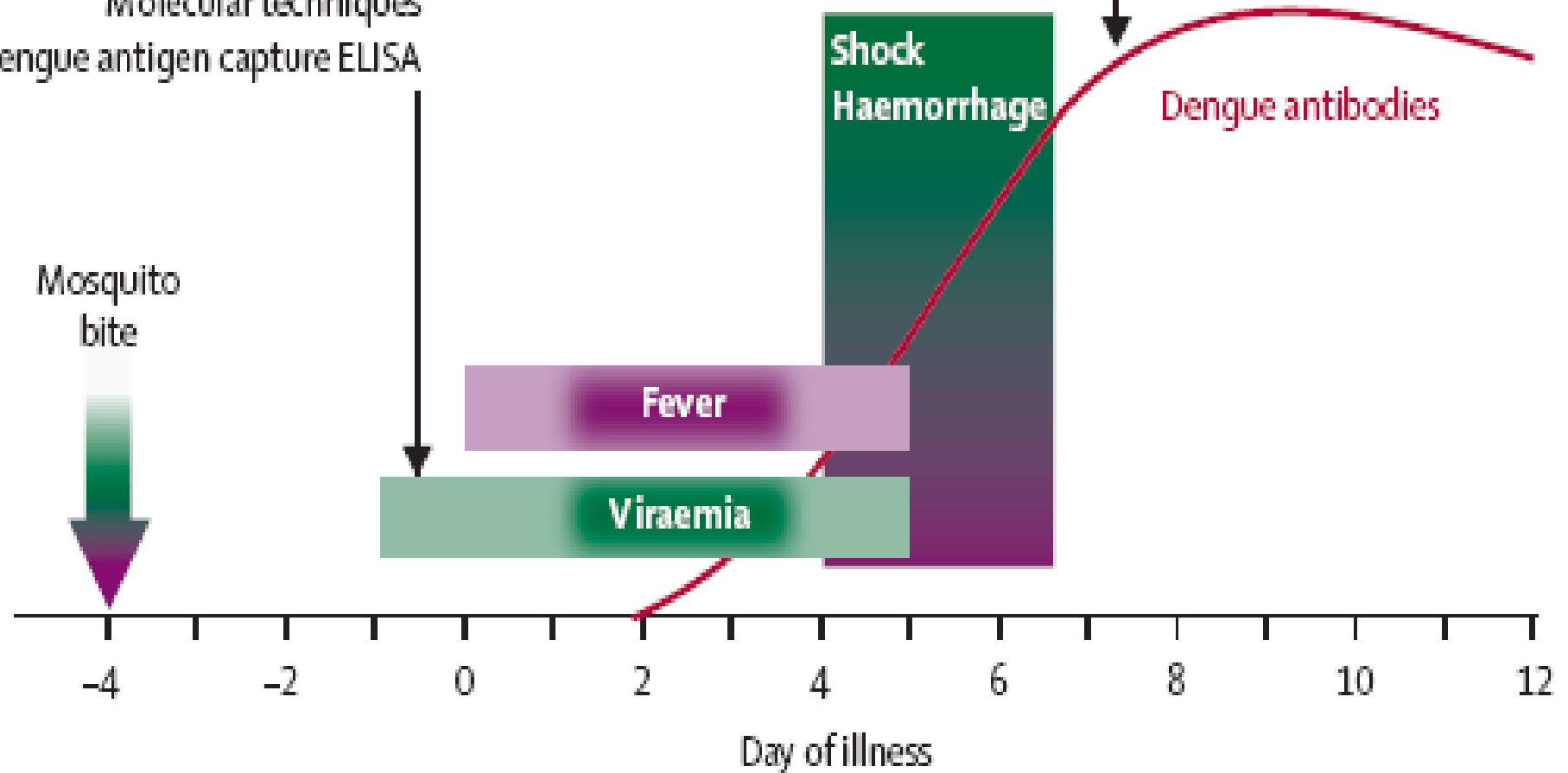
-LABORATORIAL ?

Lancet 2007; 370: 1644–52

Plaque reduction neutralisation test
Haemagglutination inhibition
IgM and IgG ELISA
Rapid tests

Virus isolation
Molecular techniques
Dengue antigen capture ELISA

Mosquito
bite



Low Sensitivity of NS1 Protein Tests Evidenced during a Dengue Type 2 Virus Outbreak in Santos, Brazil, in 2010

Alvina Clara Felix,^a Camila Malta Romano,^a Cristiane de Campos Centrone,^a Célia Lima Rodrigues,^a Lucy Villas-Boas,^a Evaldo Stanislau Araújo,^{a,b} Andréia Manso de Matos,^c Karina Inácio Carvalho,^c Celina Maria Turchi Martelli,^d Ésuper Georges Kallas,^c Cláudio Sérgio Pannuti,^a and José Eduardo Levi^a

Clinical and Vaccine Immunology D. 1972–1976

December 2012 Volume 19 Number 12

TABLE 2 NS1 results in primary and secondary acute dengue cases^a

Days since the onset of symptoms	No. of NS1-positive samples/total no. of samples (%)		
	Santos 2002	Goiânia 2005	Santos 2010
Primary infection			
1–3	2/2 (100)	15/16 (93.7)	2/4 (50)
4–5	6/7 (85)	18/19 (94.7)	19/25 (76)
6–7	6/7 (85)	19/19 (100)	8/14 (57)
8	1/1 (100)	5/7 (71.4)	3/5 (60)
Total	15/17 (88)	57/61 (93.4)	32/48 (67)
Secondary infection			
1–3	6/9 (66)	12/19 (63.1)	39/108 (36)
4–5	10/16 (62.5)	24/33 (72.7)	8/76 (11)
6–7	19/331 (61)	31/37 (83.7)	7/48 (15)
8	5/10 (50)	12/14 (85.7)	0/28 (0)
Total	40/66 (60)	79/103 (76.6)	54/260 (38)



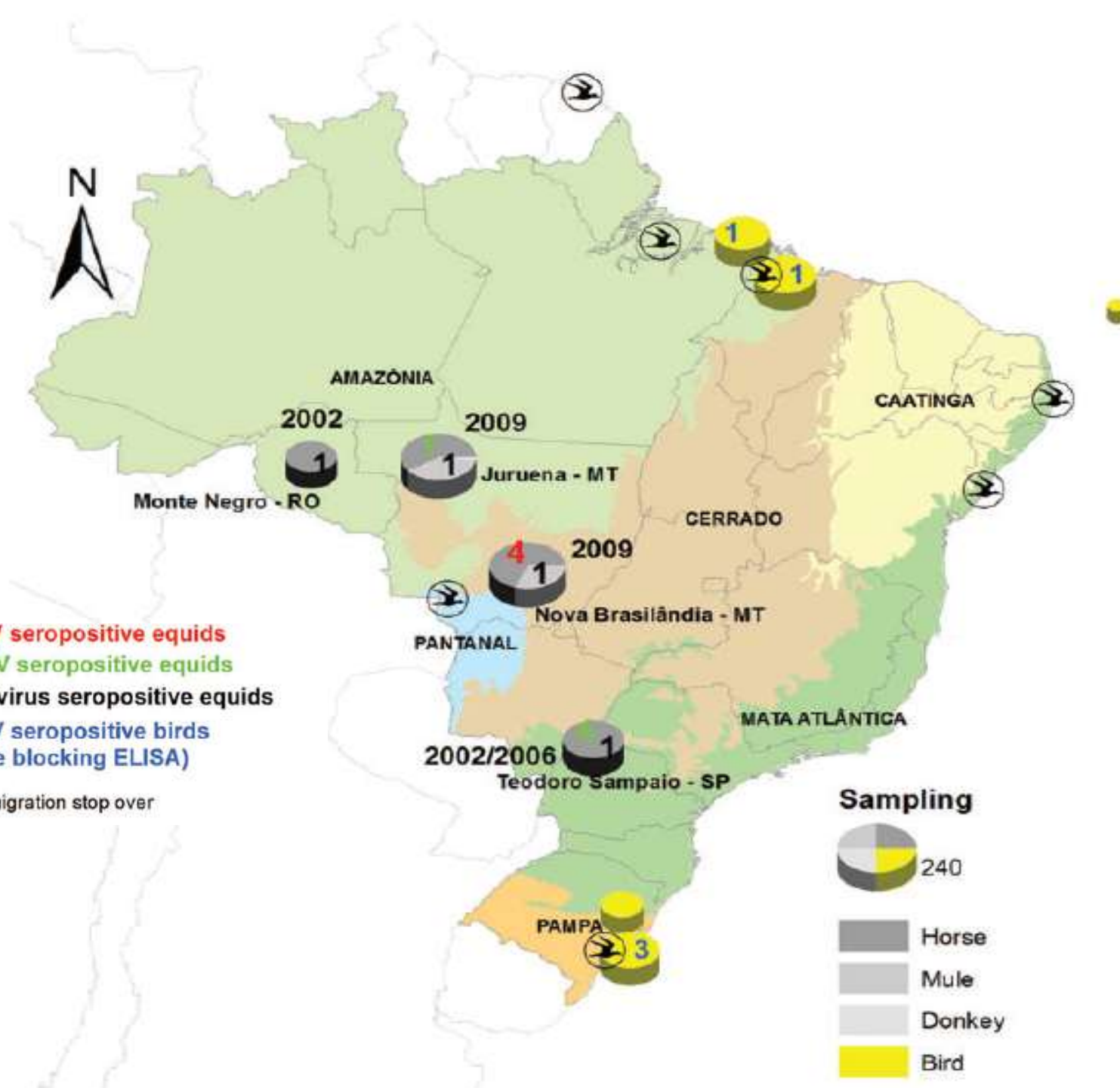
West Nile virus surveillance, Brazil, 2008–2010

Adriana Ometto^{a,*}, Edison Luiz Durigon^a, Jansen de Araujo^a, Rosalie Aprelon^b, Daniel Moura de Aguiar^c, Guadalupe Tenorio Cavalcante^d, Rosane Marini Melo^e, José Eduardo Levi^f, Severino Mendes de Azevedo Júnior^g, Maria Virginia Petry^h, Isaac Simão Netoⁱ, Patrícia Serafiniⁱ, Eliana Villalobos^j, Elenice Maria Sequetin Cunha^j, Marlene Carmo Custódio S. H. Lara^j, Alessandra Ferreira Dales Nava^k, Marcello Schiavo Nardi^l, Renata Hurtado^{a,m}, Roberta Rodrigues^g, Angelo Luís Sherer^h, Janete de Fátima Martins Sherer^h, Marcelo Plaisant Geraldini^f, Maria da Moraes de Seixas^a, Cassio Peterka^l, Debora de Souza Bandeira^l, Jennifer Pradel^b, Nathalie Vachieri^b, Mariana Bahia Labruna^m, Luiz Marcelo Aranha de Camargoⁿ, Robert Lanciotti^o and Thierry Lefrançois^b

^aLaboratório de Virologia Clínica e Molecular Instituto de Ciências Biomédicas (ICB), Universidade de São Paulo (USP), 05508-900 São Paulo, Brasil; ^bCIRAD UMR CMAEE CIRAD-INRA, 97170 Petit Bourg, Guadeloupe, France; ^cDepartamento de Clínica Médica Veterinária, Universidade Federal do Mato Grosso (UFMT), 78060-900 Cuiabá, Brasil; ^dInstituto de Física, Universidade de São Paulo, 05508-900 São Paulo, Brasil; ^eInstituto de Defesa Agropecuária do Estado do Mato Grosso (INDEA), 78050-970 Cuiabá, Brasil; ^fLaboratório de Virologia, Instituto de Medicina Tropical de São Paulo, Universidade de São Paulo, 05403-000 São Paulo, Brasil; ^gUniversidade Federal Rural de Pernambuco (UFRPE), 52171-900 Recife, Brasil; ^hUniversidade do Vale do Rio dos Sinos (UNISINOS), 93022-000 São Leopoldo, Brasil; ⁱCentro Nacional de Pesquisa e Conservação de Aves Silvestres (CEMAVE), 88053-700 Florianópolis, Brasil; ^jCentro de Pesquisa e Desenvolvimento de Sanidade Animal, Instituto Biológico, 04014-002 São Paulo, Brasil; ^kEcoHealth Alliance, 05508-270 São Paulo, Brasil; ^lInstituto de Pesquisas Ecológicas (IPÊ), 19280-000 Teodoro Sampaio, Brasil; ^mFaculdade de Medicina Veterinária e Zootecnia, Universidade de São Paulo, 05508-270 São Paulo, Brasil; ⁿInstituto de Ciências Biomédicas V, Universidade de São Paulo, 78965-300 São Paulo, Brasil; ^oCenters for Disease Control & Prevention (CDC), 80521 Fort Collins, United States

nb WNV seropositive equids
 nb SLEV seropositive equids
 nb flavivirus seropositive equids
 nb WNV seropositive birds
 (epitope blocking ELISA)

 migration stop over

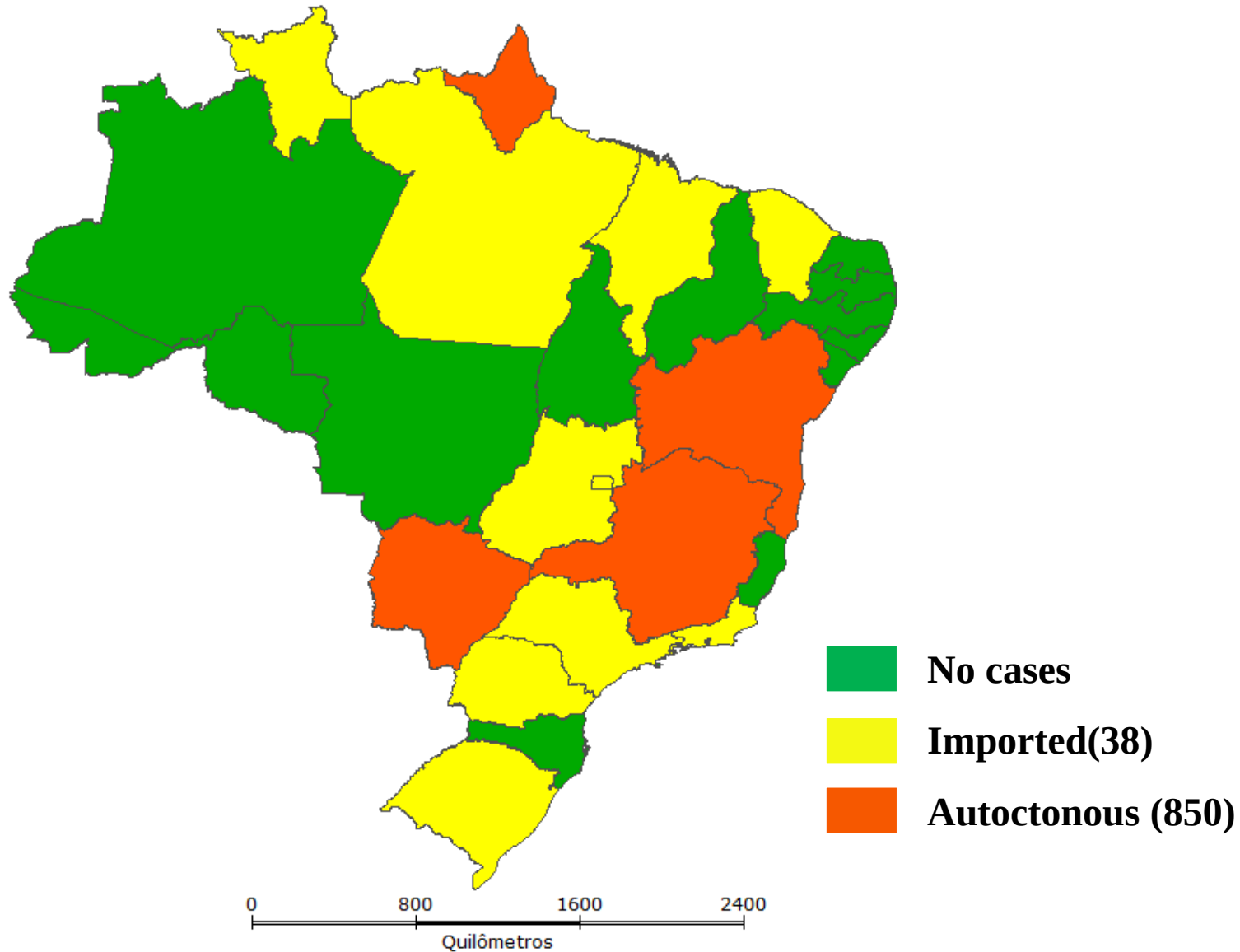


TROPICAL TRANSFER

Chikungunya virus has spread around the Caribbean since December 2013 (suspected plus confirmed cases shown)



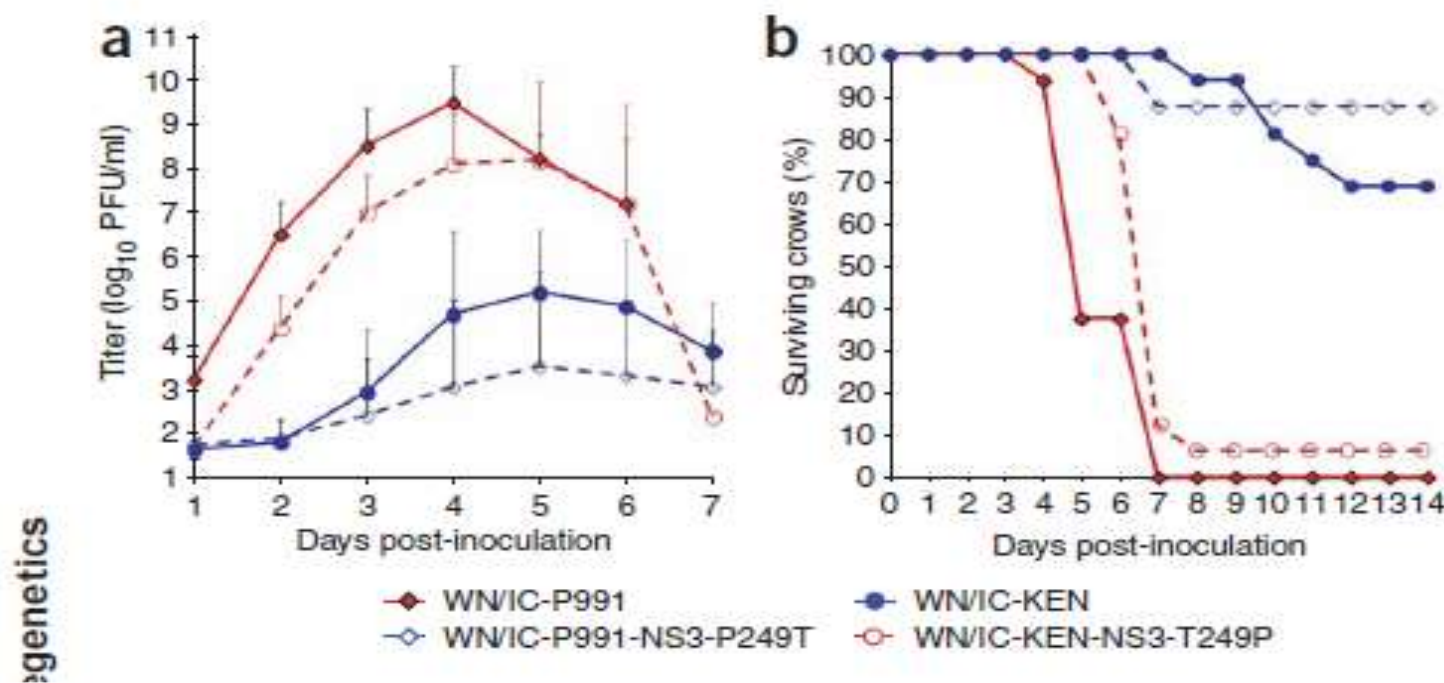
CHIKUNGUNYA CASES – BRAZIL NOVEMBER 2014



A single positively selected West Nile viral mutation confers increased virogenesis in American crows

Aaron C Brault^{1,2}, Claire Y-H Huang², Stanley A Langevin¹, Richard M Kinney², Richard A Bowen³, Wanichaya N Ramey¹, Nicholas A Panella², Edward C Holmes^{4,5}, Ann M Powers² & Barry R Miller²

VOLUME 39 | NUMBER 9 | SEPTEMBER 2007 NATURE GENETICS

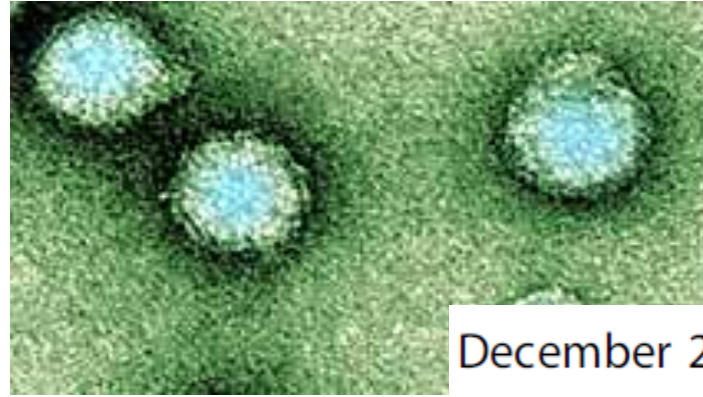


A Single Mutation in Chikungunya Virus Affects Vector Specificity and Epidemic Potential

Konstantin A. Tsetsarkin, Dana L. Vanlandingham, Charles E. McGee, Stephen Higgs*

Department of Pathology, University of Texas Medical Branch, Galveston, Texas, United States of America

E1-A226V



PLoS **PATHOGENS**

December 2007 | Volume 3 | Issue 12 | e201

