

Anticipating (re)emerging infections to ensure blood safety

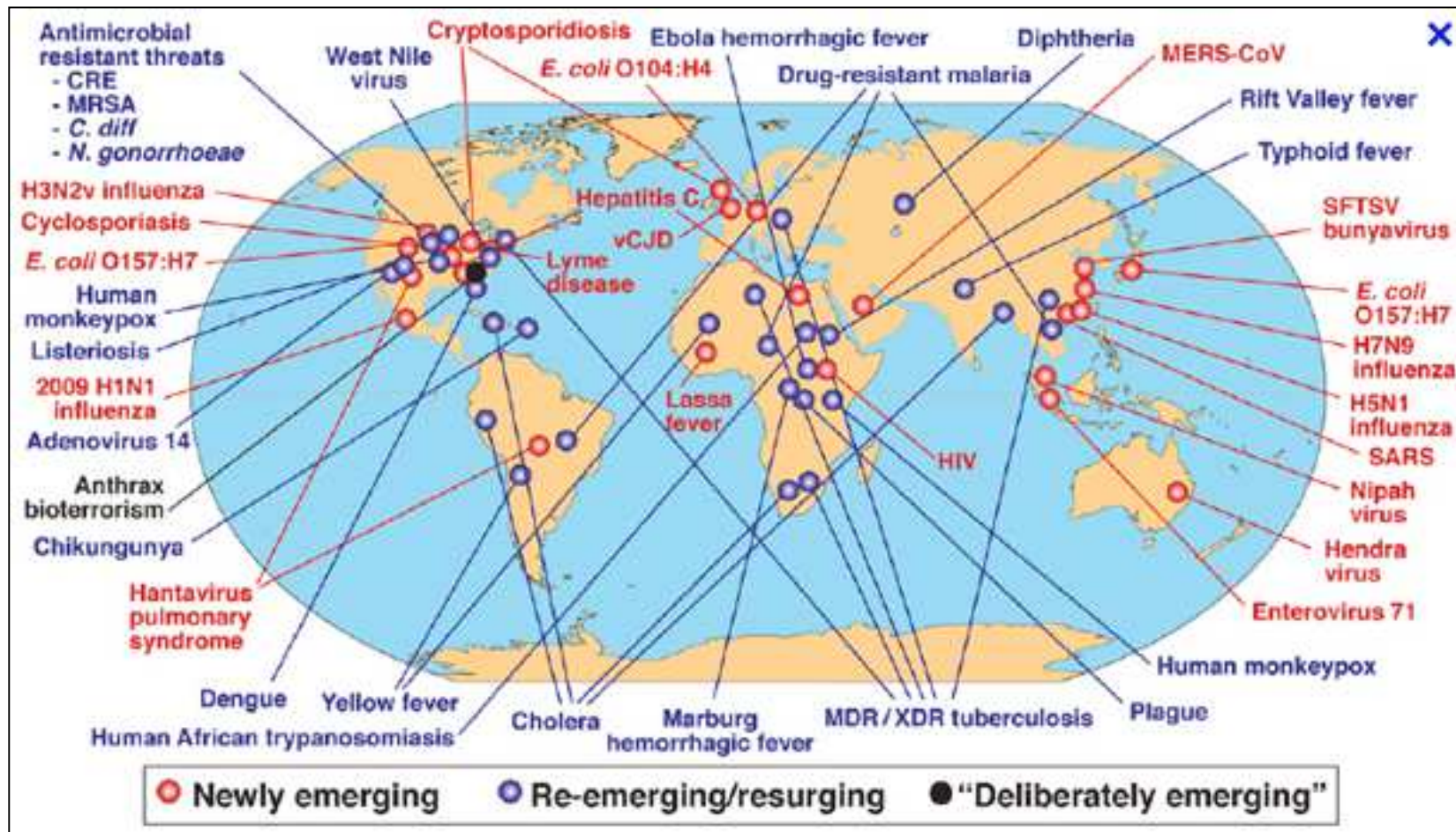
Pierre Tiberghien

*Etablissement Français du Sang, St-Denis and
Université de Franche-Comté, Besançon, France*

*IPFA/PEI 23rd International Workshop on Surveillance and
Screening of Blood Borne Pathogens, Lisbon, Portugal
May 25th, 2016*

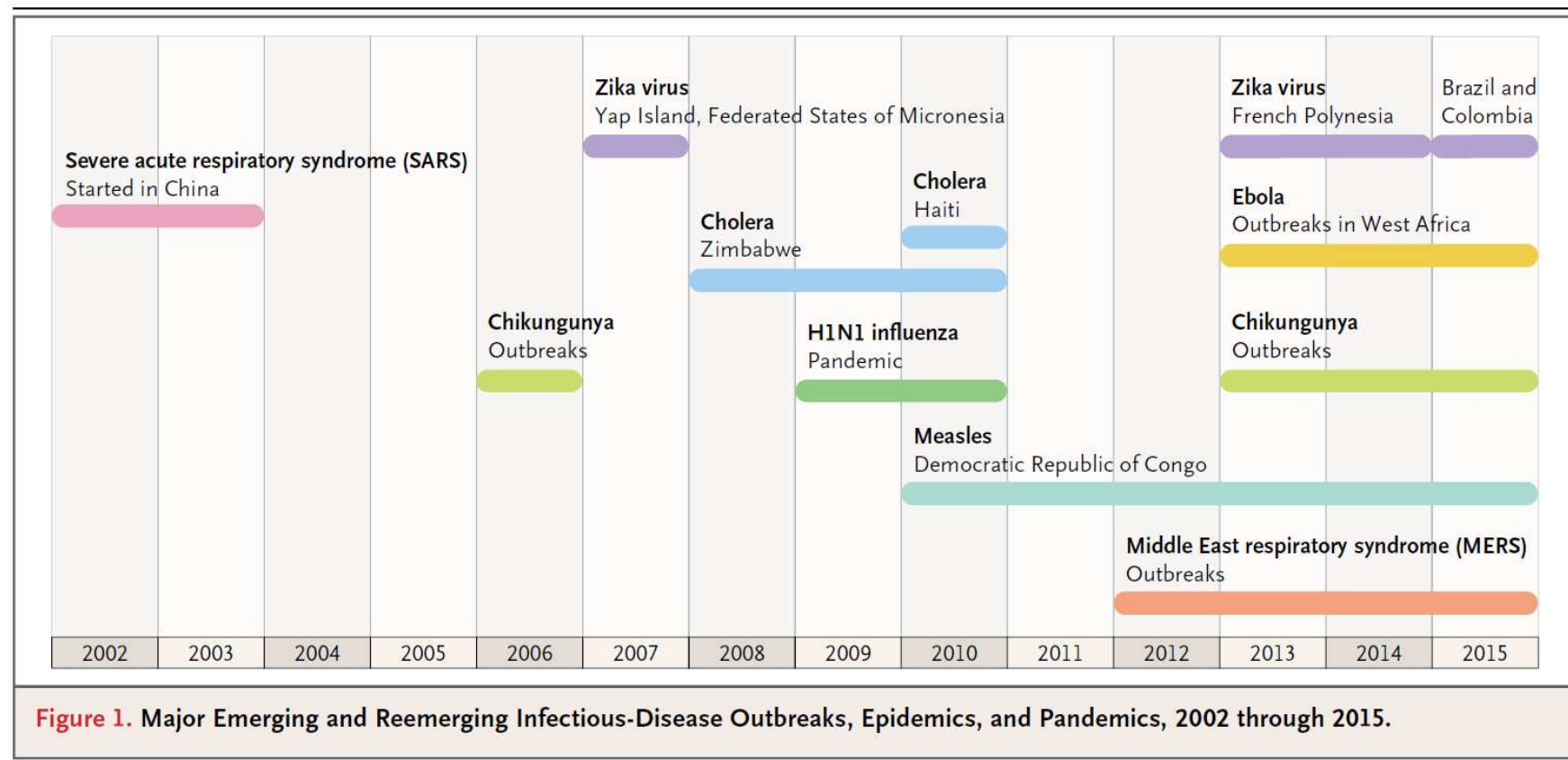
Conflict of interest disclosure: none, other than being employed by the French transfusion public service (Etablissement Français du Sang)

(Re)emerging infectious diseases



Morens DM, Folkers GK, Fauci AS.
Lancet Infectious Diseases, 8:710-719,
 2008

(Re)emerging infectious diseases

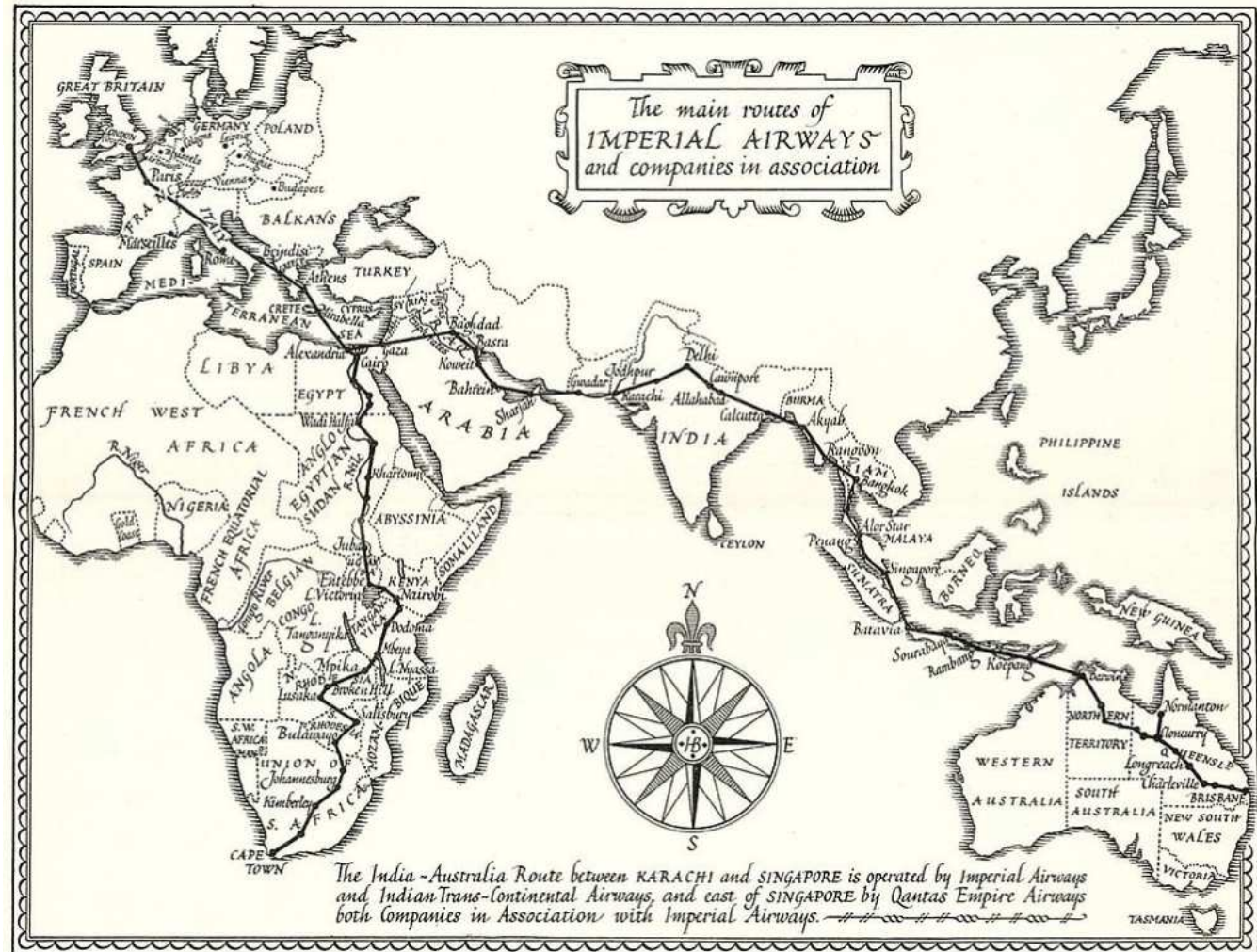


The Neglected Dimension of Global Security — A Framework for Countering Infectious-Disease Crises

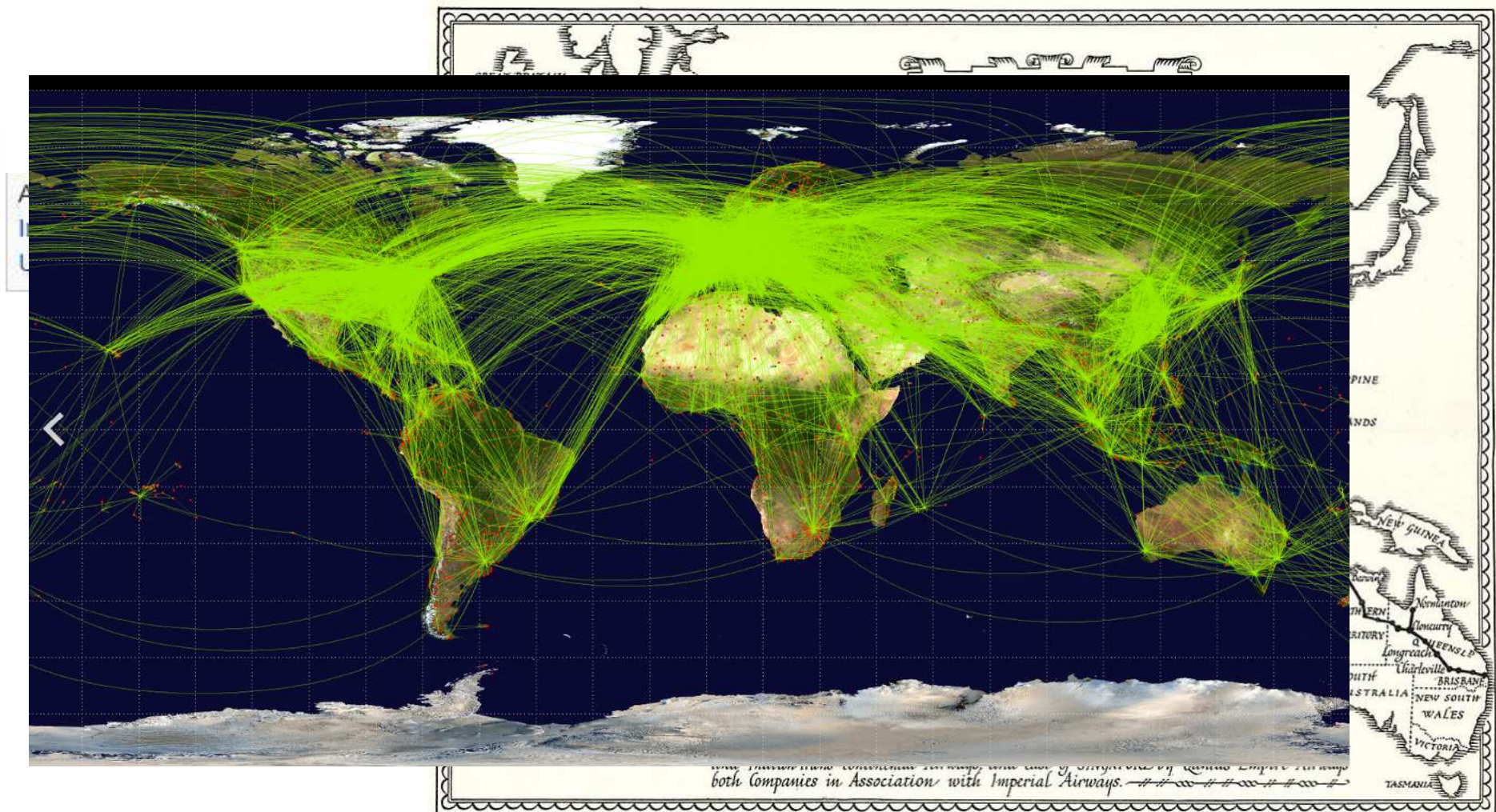
Peter Sands, M.P.A., Carmen Mundaca-Shah, M.D., Dr.P.H., and Victor J. Dzau, M.D.

A traveled world

April 1935 map showing
Imperial Airways' routes from the
UK to Australia and South Africa

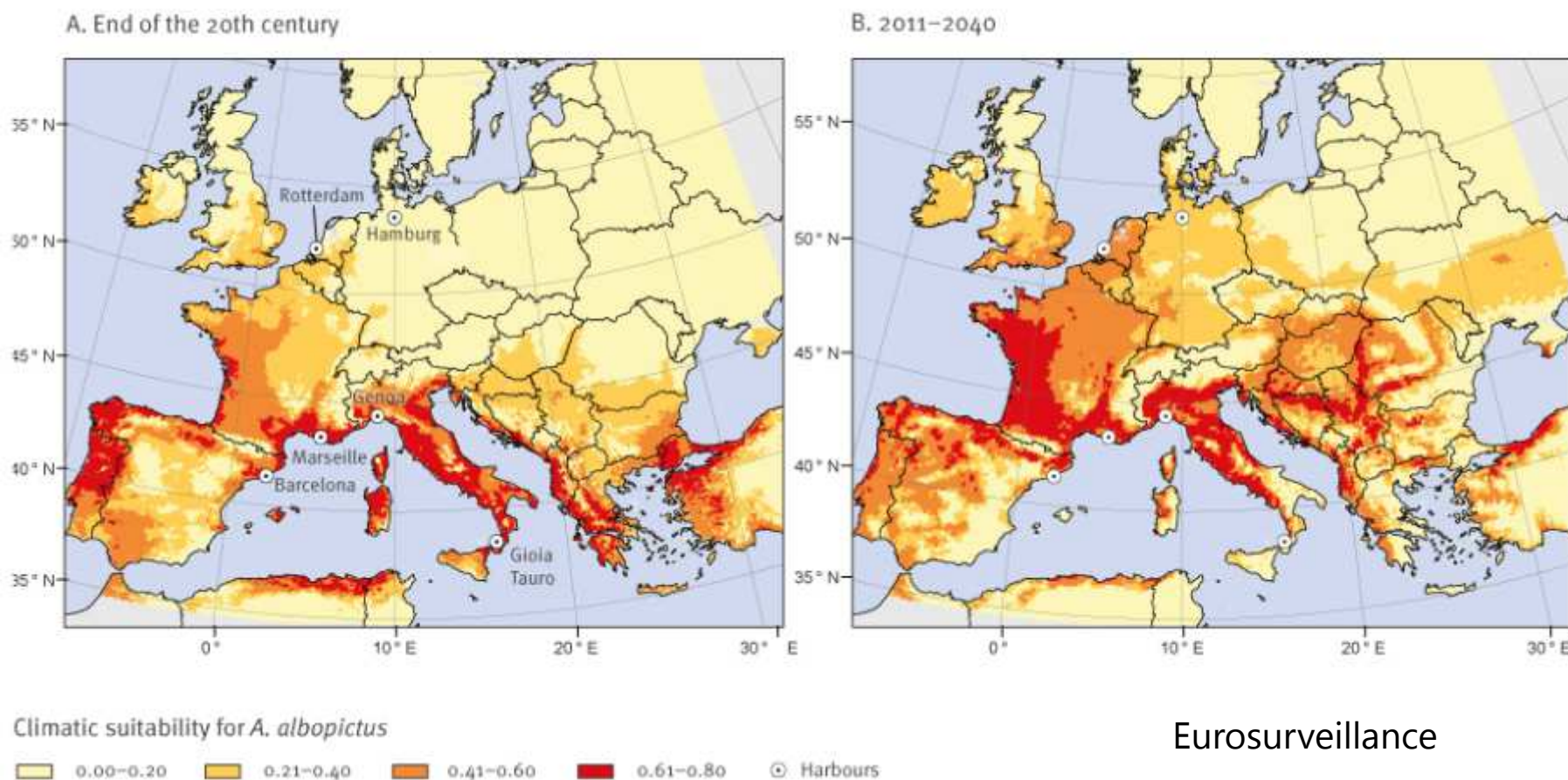


A traveled world



A warmer world

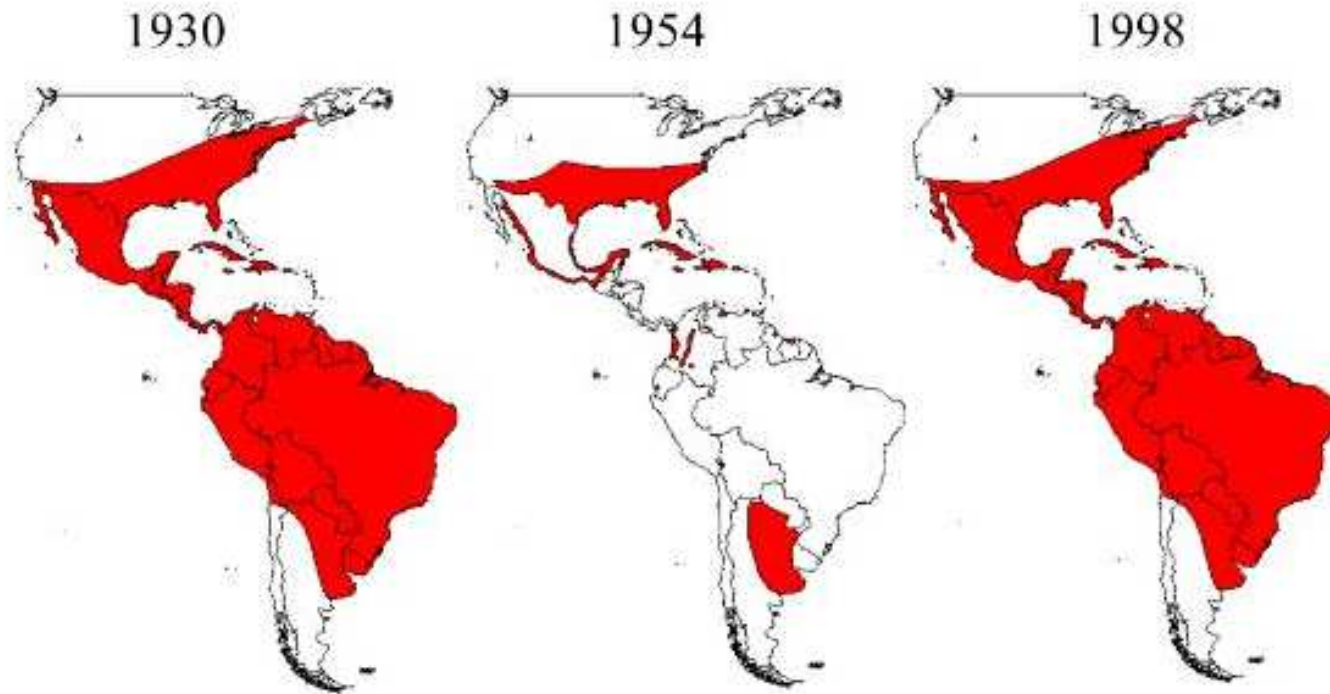
End of the 20th century (A) and projected (2011–2040) (B) climatic suitability of *Aedes albopictus* in Europe, with locations of important harbours

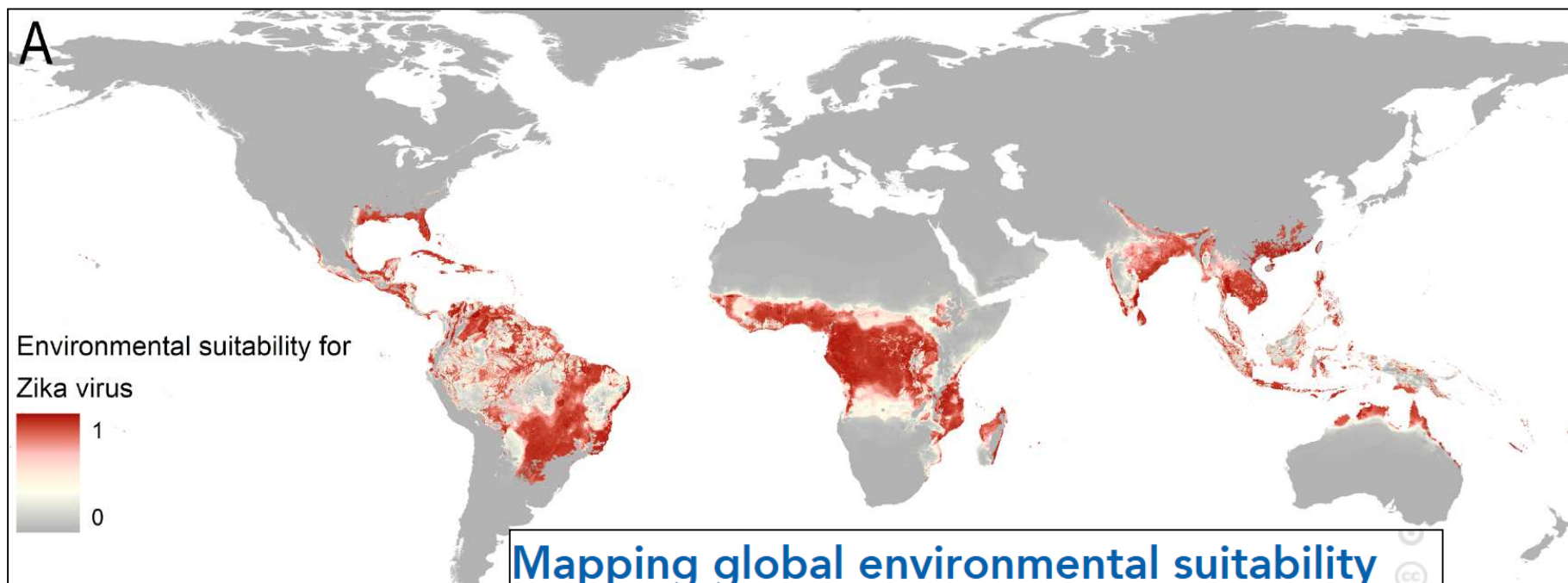


Eurosurveillance

A world with changing human interventions

Maps showing the geographical distribution of *Aedes aegypti* (presence shown in red) at different times in the Americas.





Mapping global environmental suitability for Zika virus



April, 2016

Jane P Messina , Moritz UG Kraemer, Oliver J Brady, David M Pigott, Freya M Shearer, Daniel J Weiss, Nick Golding, Corrine W Ruktanonchai, Peter W Gething, Emily Cohn, John S Brownstein, Kamran Khan, Andrew J Tatem, Thomas Jaenisch, Christopher JL Murray, Fatima Marinho, Thomas W Scott, Simon I Hay

University of Oxford, United Kingdom; University of Melbourne, United Kingdom; University of Southampton, United Kingdom; Harvard Medical School, United Kingdom; Harvard Medical School, United States; University of Toronto, Canada; Heidelberg University Hospital, Germany; University of Washington, Seattle, United States; Ministry of Health Brazil, Brazil; University of California Davis, United States

A

Environmental suitability for

WHO boss: Zika result of 'massive' mosquito control failures



By Euan McKirdy, CNN

Updated 0652 GMT (1452 HKT) May 24, 2016



Hospital, Germany; University of Washington, Seattle, United States; Ministry of Health Brazil, Brazil; University of California Davis, United States

Global environmental suitability

Horitz UG Kraemer, Oliver J Brady, David M
er, Daniel J Weiss, Nick Golding, Corrine W
W Gething, Emily Cohn, John S Brownstein,
w J Tatem, Thomas Jaenisch, Christopher JL
ho, Thomas W Scott, Simon I Hay

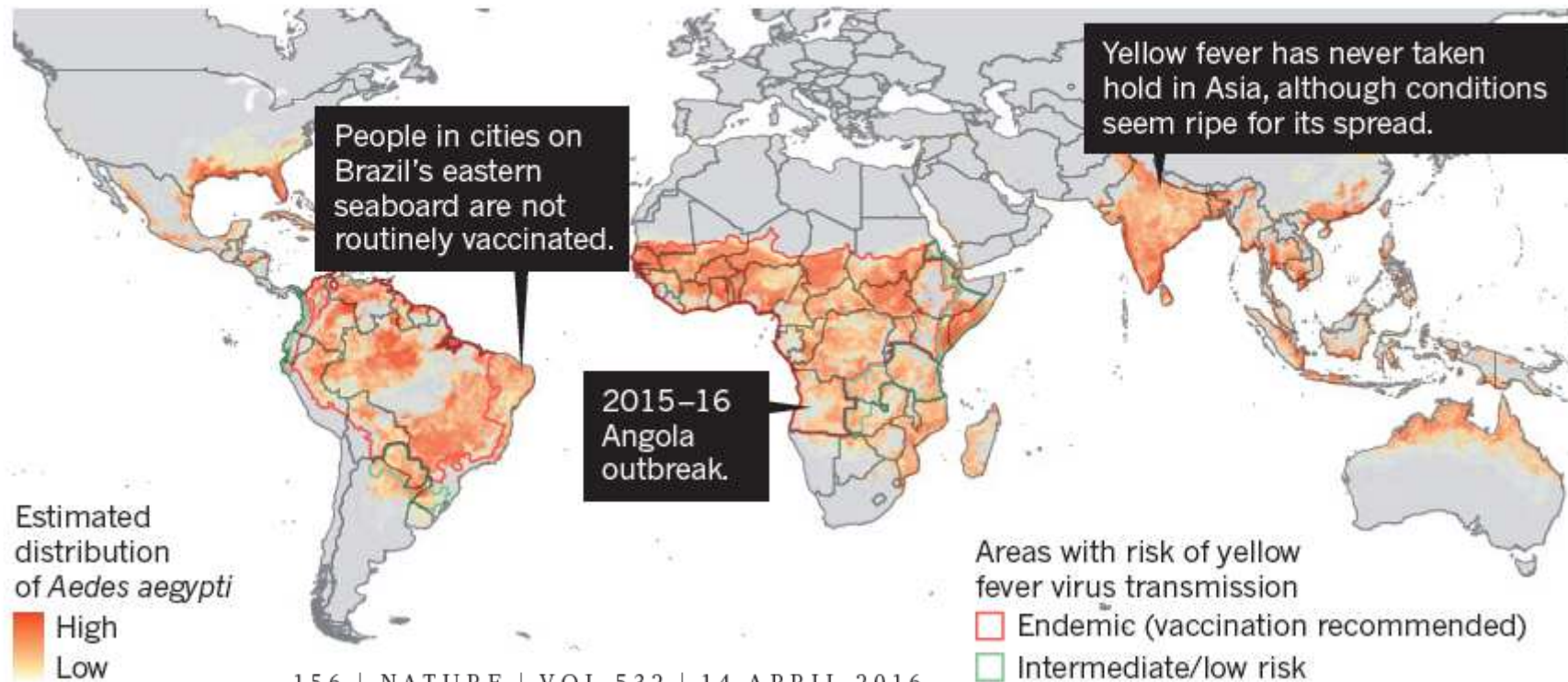
Kingdom; University of Melbourne, United Kingdom; University
gdom; Harvard Medical School, United Kingdom; Harvard
es; University of Toronto, Canada; Heidelberg University

Fears rise over yellow fever's next move

Scientists warn vaccine stocks would be overwhelmed in the event of large urban outbreaks.

WHERE MIGHT YELLOW FEVER GO NEXT?

An ongoing outbreak of yellow fever in Angola has scientists worried that the virus might spread to cities that harbour its urban carrier, the *Aedes aegypti* mosquito.



A poorly known world

Hepatitis E: The 'New Kid on the Block' or an Old Friend?

Harry R. Dalton

Transfusion Medicine
and Hemotherapy

Editorial

Transfus Med Hemother 2014;41:6-9
DOI: 10.1159/000358103

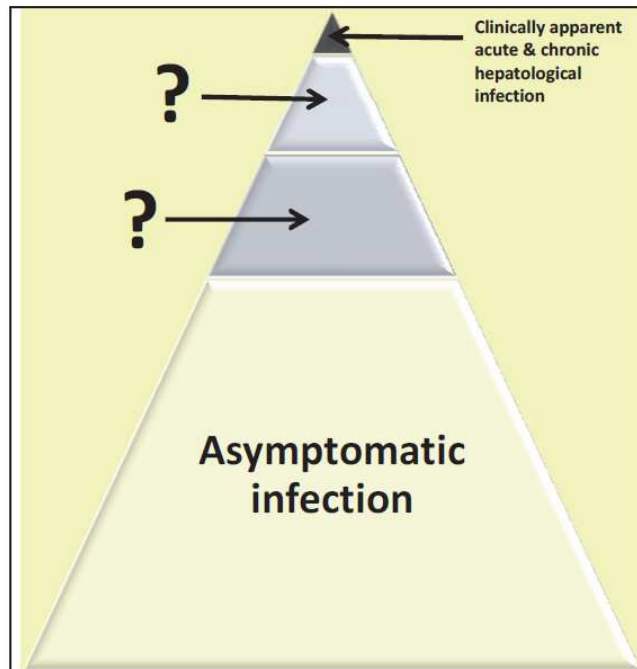
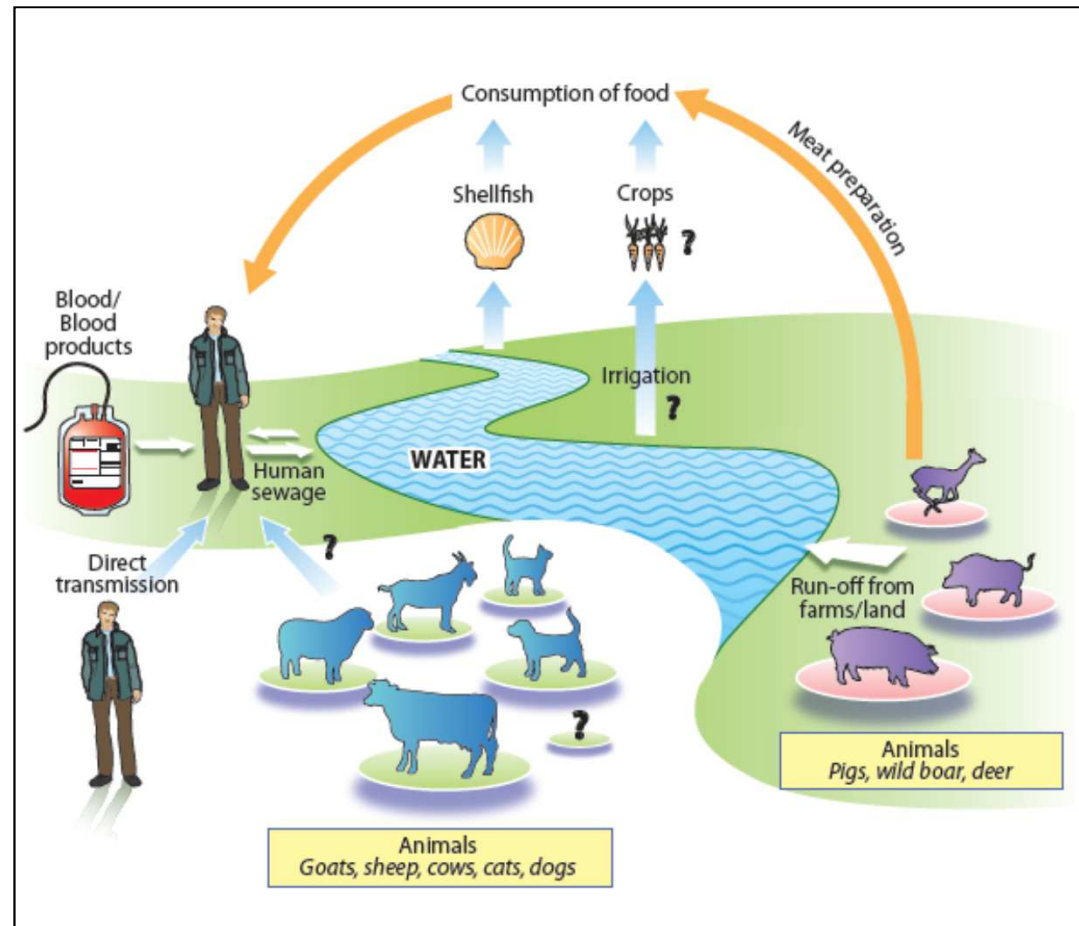


Fig. 1. Most cases of zoonotic, locally acquired, hepatitis E in developed countries are asymptomatic. Only a small minority has clinically evident hepatitis. The grey areas represent emerging clinical phenotypes of HEV infection, including a range of neurological syndromes.

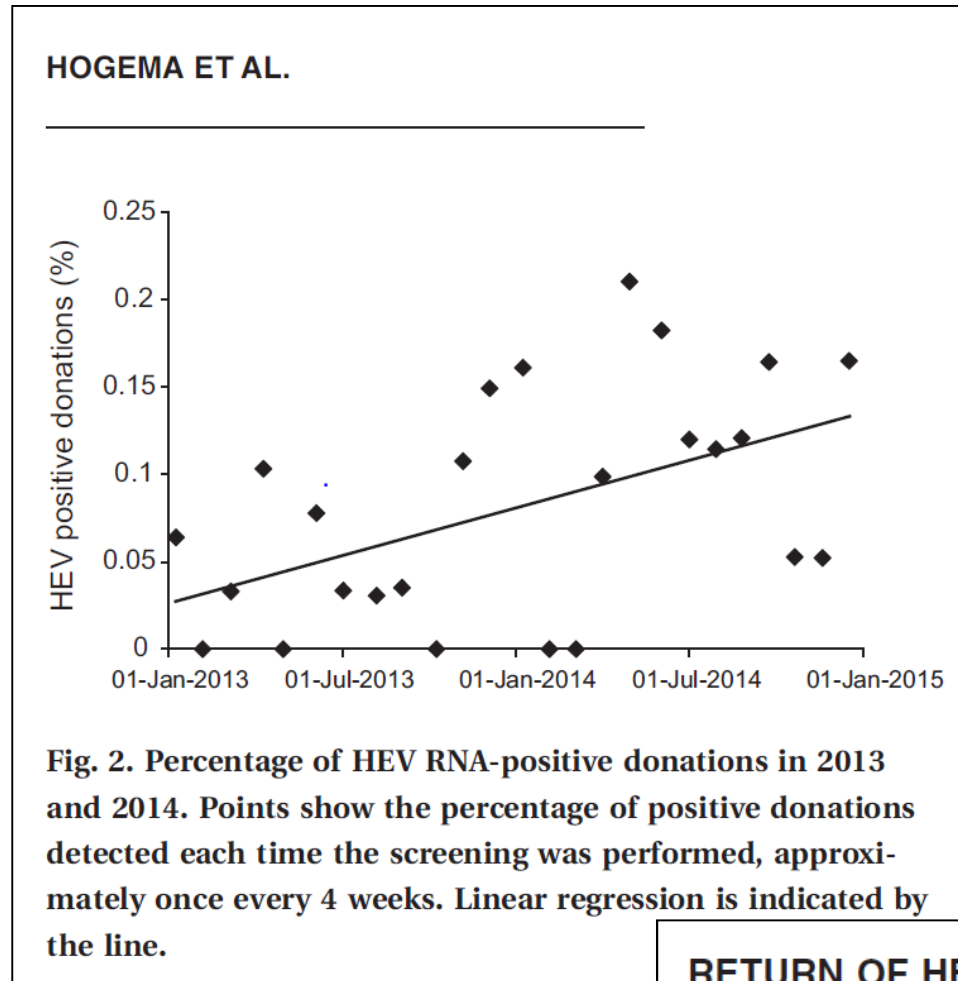


Source and route of HEV infection (Kamar et al, Lancet 2012)

An ever changing world

No Artifact, Hepatitis E Is Emerging

Zaaijer HL, Hepatology, 2015



Hogema et al
Transfusion, 2014
and 2016

An ever changing world

No Artifact, Hepatitis E Is Emerging

Zaaijer HL, Hepatology, 2015

HOGEMA ET AL.

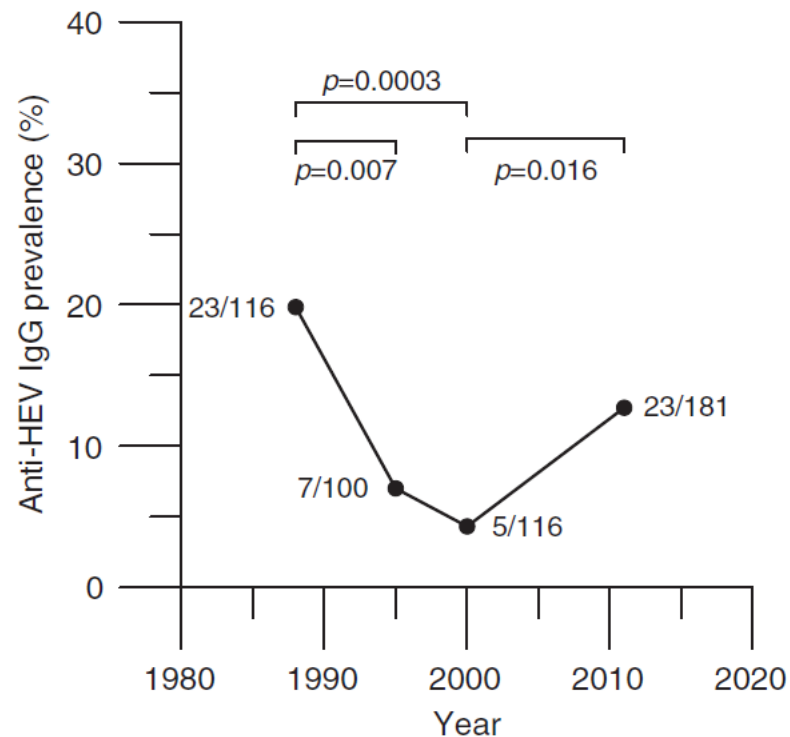


Fig. 2. Anti-HEV IgG seroprevalence among donors aged 18 to 21 in 1988, 1995, 2000, and 2011. The total number of samples and the number of anti-HEV-positive samples are indicated for each time point. The numbers above the bars denote the two-sided p values calculated using the chi-square method.

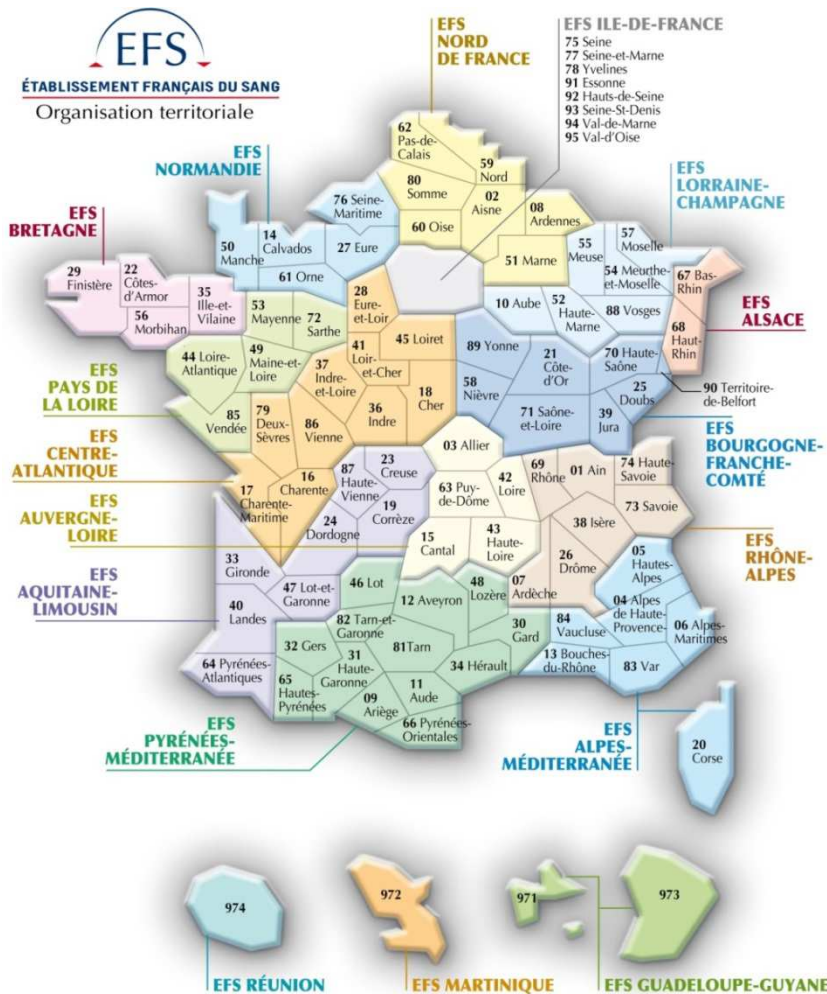
Hogema et al
Transfusion, 2014
and 2016

01-Jul-2014 01-Jan-2015

Donations in 2013
of positive donations
performed, approxi-
ssion is indicated by

RETURN OF HEV IN THE NETHERLANDS

Etablissement Français du Sang: The french transfusion public service



15 Regional Blood Banks.

- 12 in metropolitan France.
- 3 in overseas territories (Guadeloupe-French Guiana, Martinique, Island of la Reunion-Mayotte)

Headquarters in Paris (St Denis, Paris)

Blood products delivered in 2015:

- Red blood cell concentrates: 2 415 230
- Platelets concentrates: 304 381
 - Apheresis platelets concentrates: 130 509
 - Whole blood derived platelets: 173 872
- Plasma : 353 977

Preventing transfusion- transmitted infections

- Donor screening
- Deferral of individuals with identified risk factors (infectious symptoms, lifestyle, eating habits, traveling, both personal and partner-related)
- Skin preparation
- Use of sterile bags (and outer bags)
- Diversion of the initial blood draw
- Pathogen detection
- Pathogen reduction
- Post-donation information

Preventing transfusion- transmitted infections

Pathogen detection - 2016

- HIV, HBC, HBV serology and NAT
- HTLV1 and 2 serology
- Syphilis serology
- Chagas and Malaria serology for at risk donors
- CMV serology for a fraction of blood donations
- HEV NAT for a fraction of blood donations (plasma)
- ZIKA NAT for Martinique and Guadeloupe blood donations

actors
ts,
d)

Preventing transfusion- transmitted infections

Pathogen detection - 2016

- HIV, HBC, HBV serology and NAT
- HTLV1 and 2 serology
- Syphilis serology
- Chagas and Malaria serology for at risk donors
- CMV serology for a fraction of blood donations
- HEV NAT for a fraction of blood donations (plasma)
- ZIKA NAT for Martinique and Guadeloupe blood donors

actors
ts,
d)

Production of pathogen-reduced blood products - 2016

- Intercept® platelets (8% of transfused platelets): Alsace, Reunion Island, Martinique, Guadeloupe
- Intercept® plasma (20% of transfused plasma: pooled whole blood-derived plasma, apheresis plasma)

Recent EFS responses to (re) emerging diseases occurring in France

- Hepatitis E virus
- Chikungunya:
 - Martinique, Guadeloupe and French Guiana, 2014
- Zika virus
 - Martinique, Guadeloupe and French Guiana since January 2016

EFS responses to (re) emerging diseases occurring outside France:

- Differing travelers from affected regions
- Participating to the EbolaTx study: plasma from Ebola convalescent donors to Ebola patients in Conakry, Guinea (Van Griesven et al, NEJM, 2016)

Occurrence of transfusion-transmitted hepatitis E in France

Background

- Hepatitis E virus (HEV) infection in France is mainly a **zoonotic disease** and is **usually an acute self-limiting disease**
- However, HEV may cause **chronic hepatitis** with rapidly progressive cirrhosis in **organ transplant** recipients and patients with hematological malignancy, as well a **fulminant hepatitis** in patients with **chronic liver disease**.
- Hepatitis E virus has been recognized since 2004 as a **transfusion transmissible infectious agent**
- Frequency of RNA HEV positive blood donations in France : **1 out of 2000** in 2013 (*Gallian et al, EID, 2014*). More recent data suggests a higher frequency (close to **1/1000 donations**)

Transfusion-transmitted hepatitis E in France

- **21 cases of HEV-TT reported between 2006 and 2015, most since 2012.**
- Viral phylogenetic analysis established **transfusion imputability**.
- All cases are **genotype 3** (mainly 3f) except for 1 (genotype 4)
- **All type of blood products are involved:**
 - red blood concentrates (n=5)
 - platelet concentrates (n=9), including pooled whole blood-derived (n=5 + 1 Intercept®) platelets and apheresis (n=3) platelets)
 - plasma (n=7), including solvent-detergent (SD)-plasma (n=4), Intercept® plasma (n=2) and quarantine plasma (n=1)
- Patients, aged **5 to 88 years old**, kidney (n=5) or liver **transplants** (n=3) and **hemopathies** mainly
- All cases suspected by **biological liver abnormalities** (cholestasis or cytolysis), for 2 a result of investigation from another case
- **Spontaneous resolution in 12 patients**
- **Chronic hepatitis requiring ribavirine treatment in 9 patients**, all immunosuppressed, and among which 2 patients developing significant liver fibrosis.

Transfusion-transmitted hepatitis E in France

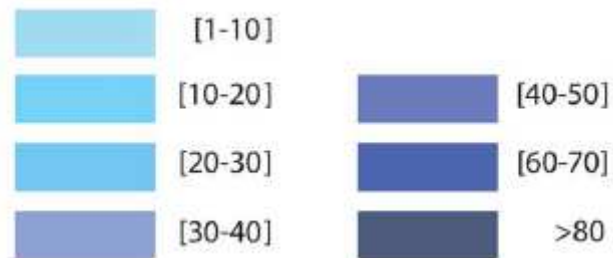
- **21 cases of HEV-TT reported between 2006 and 2015, most since 2012.**

- How frequently is HEV transmitted by an HEV-containing blood product?
- How protective is prior immunization? Are there genetically determined protective factors?
- Do we know all about HEV infection?; how sure are we about « low-risk » patients?
- How severe can be chronic HEV infection? Are all HEV chronic infection accessible to treatment?

- Patients, aged **5 to 88 years old**, kidney (n=5) or liver **transplants** (n=3) and **hemopathies** mainly
- All cases suspected by **biological liver abnormalities** (cholestasis or cytolysis), for 2 a result of investigation from another case
- **Spontaneous resolution in 12 patients**
- **Chronic hepatitis requiring ribavirine treatment in 9 patients**, all immunosuppressed, and among which 2 patients developing significant liver fibrosis.

Anti-HEV IgG and IgM prevalence in France

Risk factors for seropositivity



Mansuy et al Hepatology, 2016

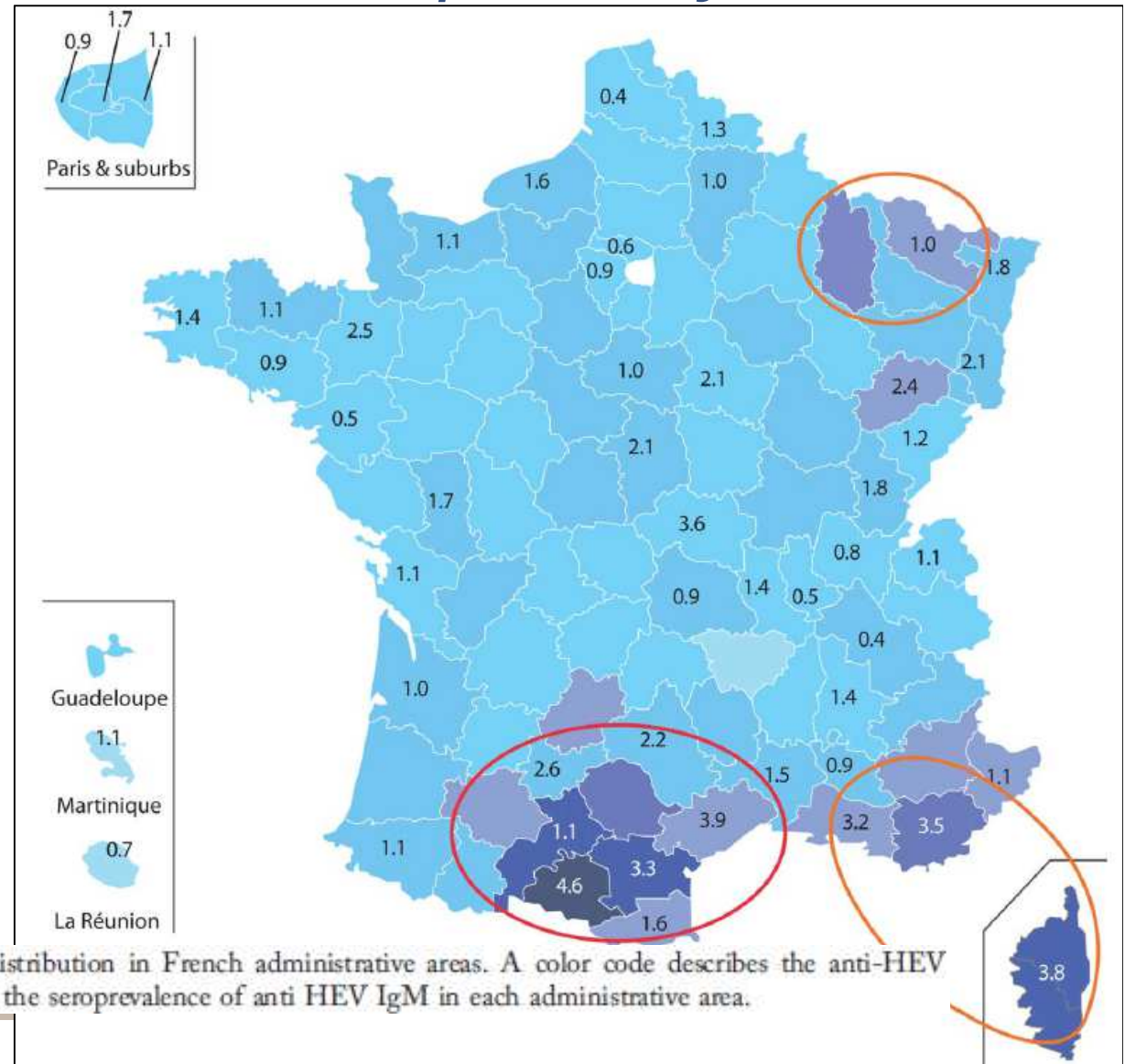


FIG. 1. Prevalence of anti-HEV IgG and IgM: distribution in French administrative areas. A color code describes the anti-HEV IgG seroprevalence classes. Black numbers represent the seroprevalence of anti HEV IgM in each administrative area.

Anti-HEV IgG and IgM prevalence in France

Risk factors for seropositivity

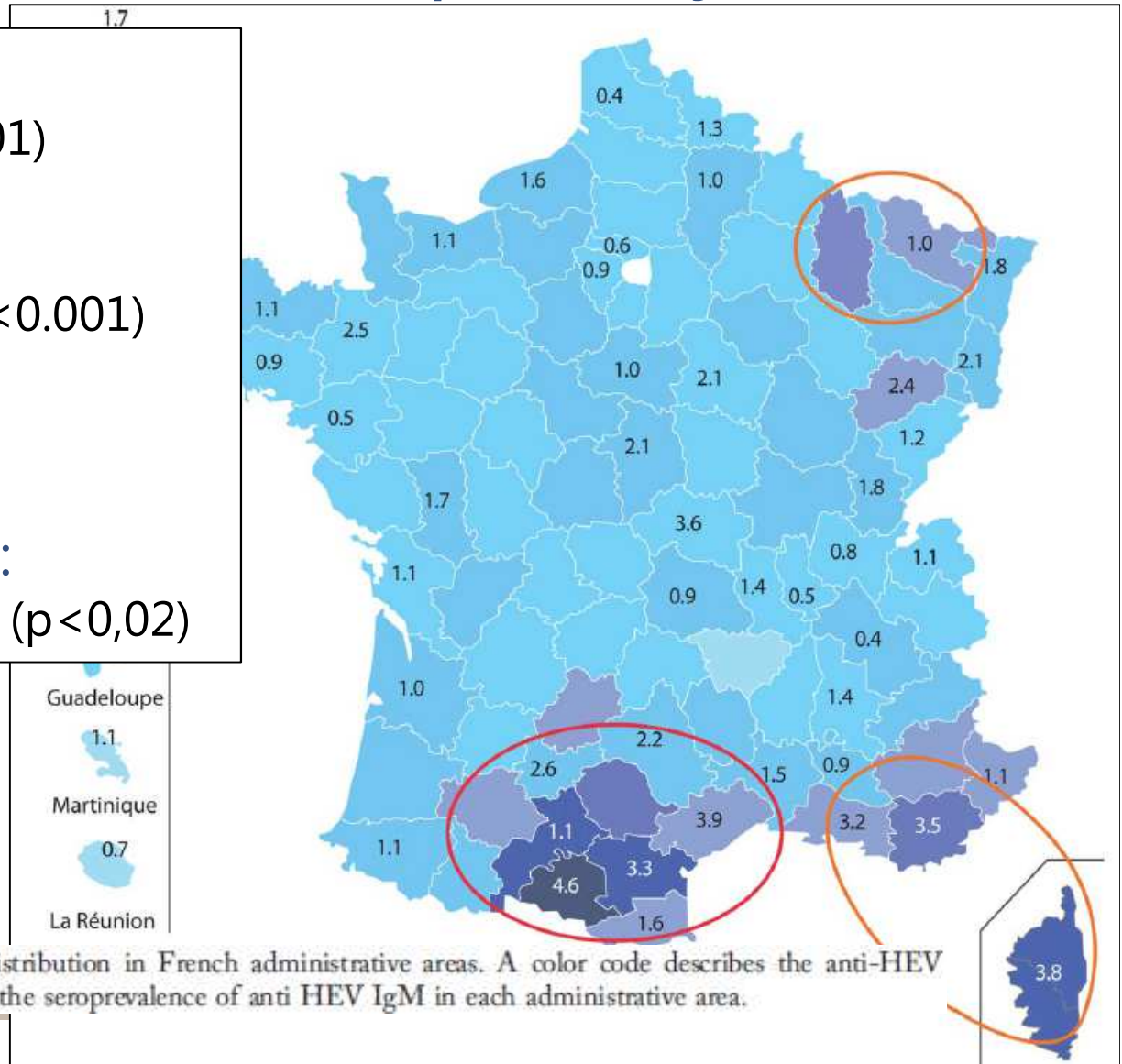
HEV risk factors:

- ✓ increasing age ($p < 0.001$)
- ✓ eating:
 - pork meat ($p = 0.03$)
 - pork liver sausages ($p < 0.001$)
 - game meat ($p < 0.01$)
 - offal ($p < 0.001$)
 - oysters ($p = 0.02$).

HEV protective factor:

- ✓ drinking bottled water ($p < 0.02$)

Mansuy et al Hepatology, 2016



Transfusion-transmitted hepatitis E in France

- **21 cases of HEV-TT reported between 2006 and 2015, most since 2012.**

HEV RNA testing

Real Star HEV RT PCR Altona (EUROBIO) : SD 95% = 23 UI/ml (WHO standard)

January 2013 to December 2014:

- SD-Plasma produced by the EFS (Bordeaux), 70 liter pool, 100 apheresis plasma donations

Since January 2015:

- A fraction (30%) of plasma (quarantine or Intercept) intended for high-risk patients:
 - ✓ Organ and allogeneic HSC transplantation recipients
 - ✓ Other severely immunosuppressed patients
 - ✓ Patients with chronic liver disease

2016: Expanding HEV testing for at least a fraction of all blood products is being considered

REVIEW ARTICLE

Edward W. Campion, M.D., Editor

Chikungunya Virus and the Global Spread of a Mosquito-Borne Disease

Scott C. Weaver, Ph.D., and Marc Lecuit, M.D., Ph.D.

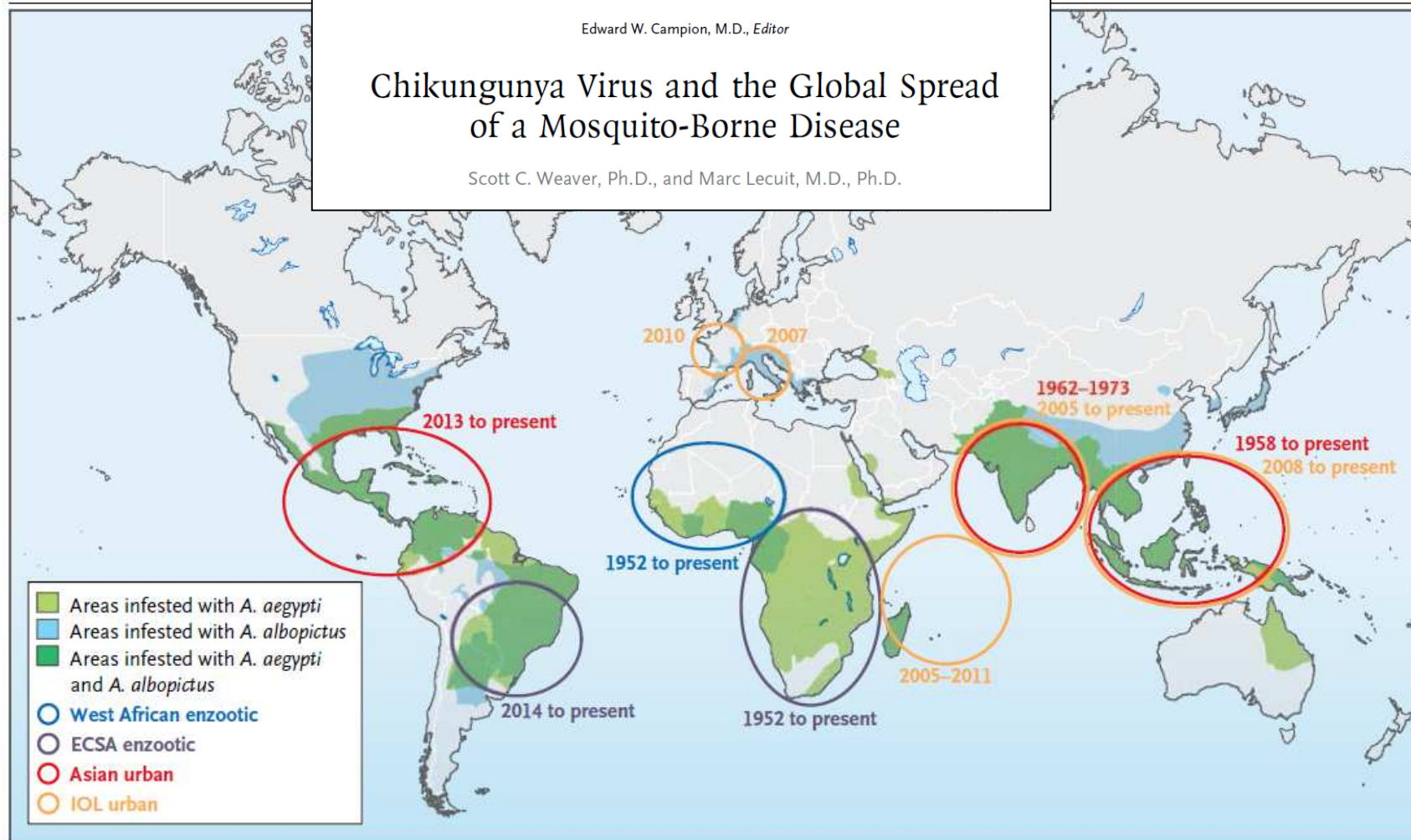
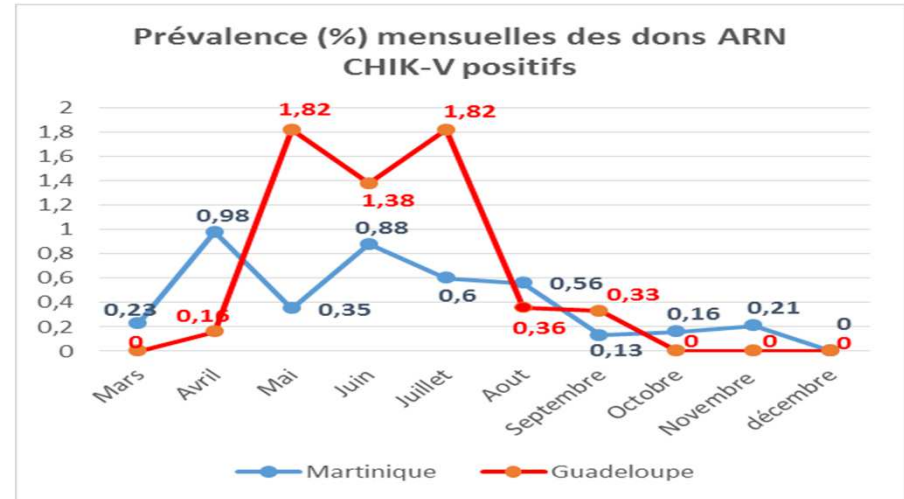


Figure 2. Origin, Spread, and Distribution of Chikungunya Virus and Its Vectors.

The map shows the African origins of enzootic chikungunya virus strains and the patterns of emergence and spread of the Asian lineage and Indian Ocean lineage (IOL) of the virus during epidemics since the 1950s, based on phylogenetic studies.^{4,5} The distributions of the peridomestic vectors, *Aedes aegypti* and *A. albopictus*, are also shown. ECSA denotes eastern, central, and southern African.

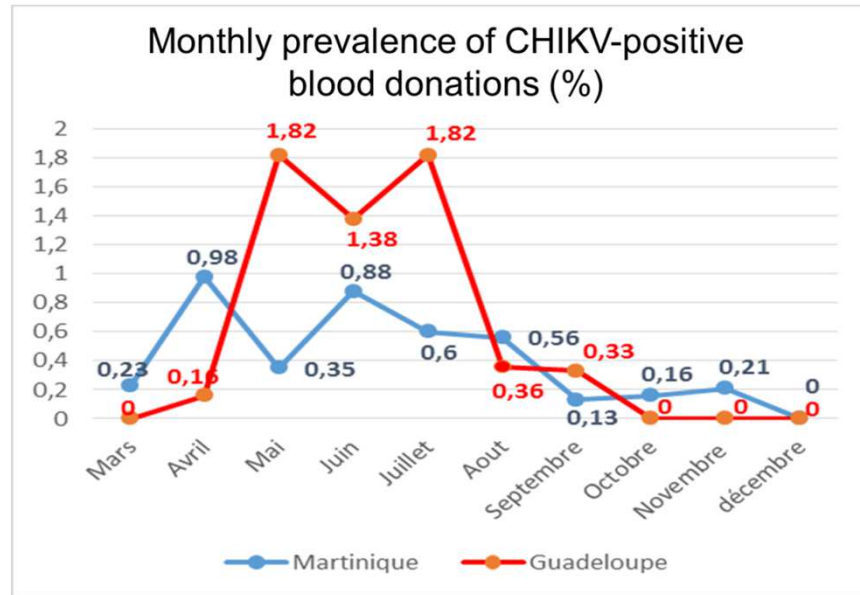
Chikungunya epidemic in the Caribbean in 2014

- Risk prevention measures included:
 - detection of CHIKV RNA (individual NAT in dedicated arboviral laboratory in Marseille)
 - 3-day quarantine combined with reinforced post-donation information
 - use of Intercept platelets



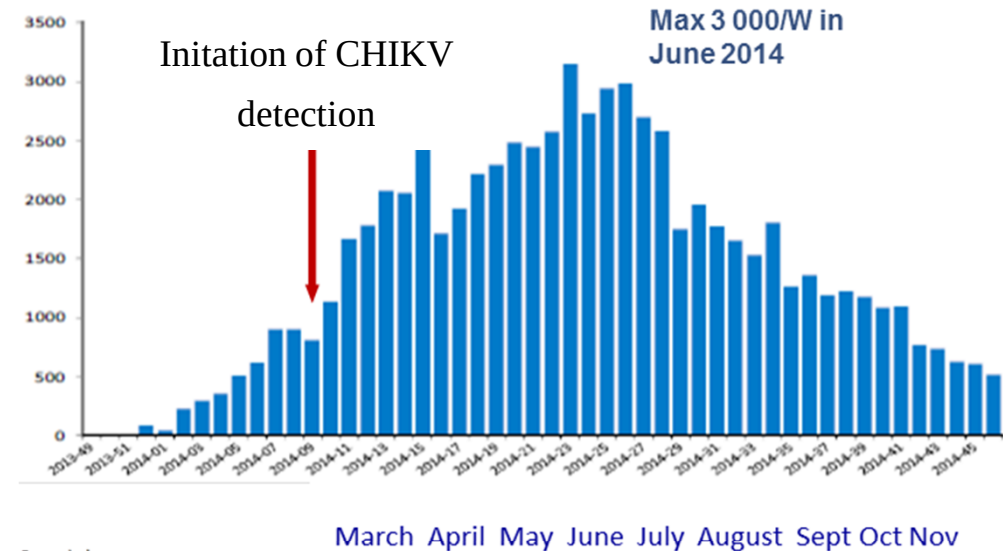
- Individual NAT screening of 16269 donations identified 63 CHIKV positive donations (0.4%, with 1 to 2% at the epidemic peak) for which related blood products were discarded except for platelets transfused before NAT results.
- A large majority of donors reported symptoms within 3 days after donation
- Intercept platelets from CHIKV positive donations were transfused to 10 recipients with no clinical evidence for transmission.

CHIKV clinical cases / CHIKV-NAT ratio

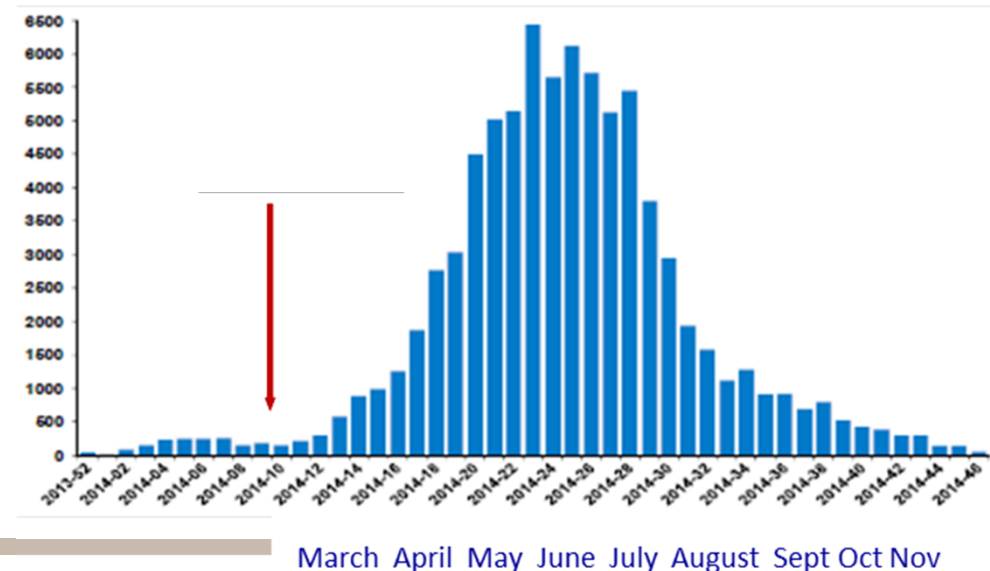


At peak of the epidemic (June 2014), the estimated ratio between CHIKV positive blood donors and reported CHIKV clinical cases was of 1/1000.

Martinique :



Guadeloupe :



REVIEW ARTICLE

Edward W. Campion, M.D., Editor

Chikungunya Virus and the Global Spread of a Mosquito-Borne Disease

D., Ph.D.

A critical issue: vector competence

- No autochthonous CHIKV cases in mainland France resulting from travelers returning from the Caribbean during the epidemic
- However, autochthonous CHIKV cases from a traveler returning from Cameroun

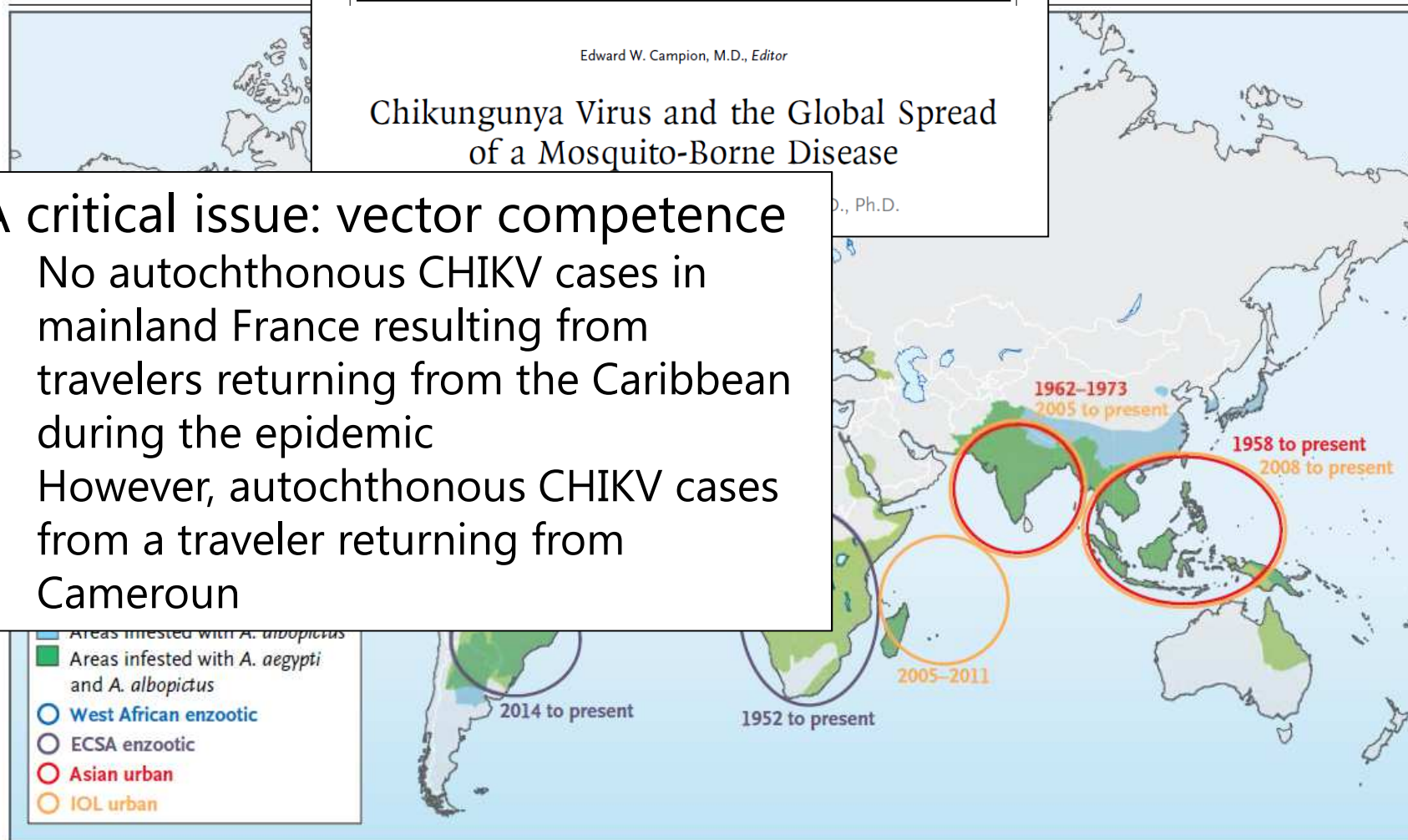
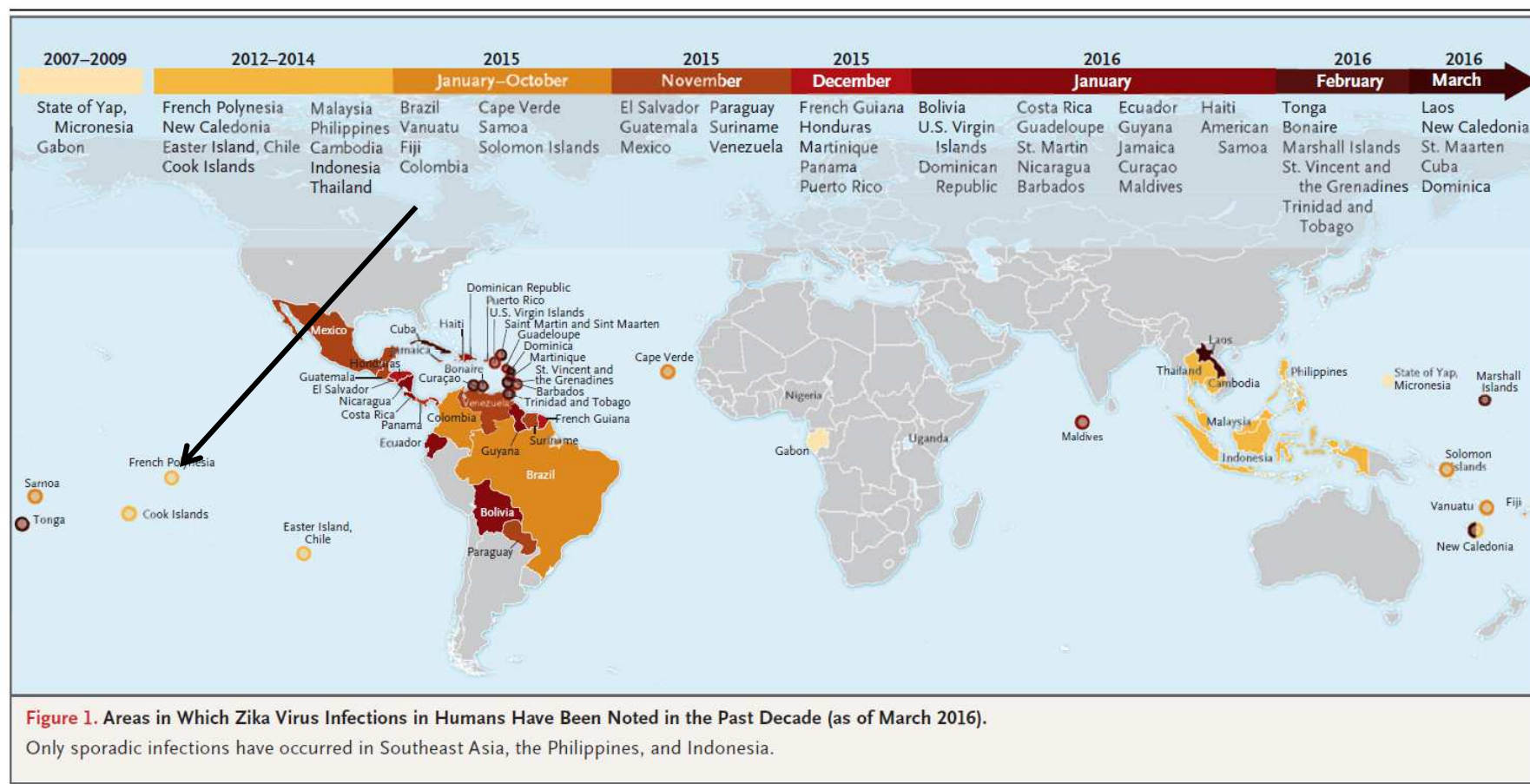


Figure 2. Origin, Spread, and Distribution of Chikungunya Virus and Its Vectors.

The map shows the African origins of enzootic chikungunya virus strains and the patterns of emergence and spread of the Asian lineage and Indian Ocean lineage (IOL) of the virus during epidemics since the 1950s, based on phylogenetic studies.^{4,5} The distributions of the peridomestic vectors, *Aedes aegypti* and *A. albopictus*, are also shown. ECSA denotes eastern, central, and southern African.

Zika Virus

Lyle R. Petersen, M.D., M.P.H., Denise J. Jamieson, M.D., M.P.H.,
Ann M. Powers, Ph.D., and Margaret A. Honein, Ph.D., M.P.H.



Zika Virus

Lyle R
Ann

RAPID COMMUNICATIONS

Potential for Zika virus transmission through blood transfusion demonstrated during an outbreak in French Polynesia, November 2013 to February 2014

D Musso (dmusso@ilm.pf)¹, T Nhan¹, E Robin¹, C Roche¹, D Bierlaire², K Zisou¹, A Shan Yan¹, V M Cao-Lormeau¹, J Broult²

1. Unit of Emerging Infectious Diseases, Institut Louis Malardé, Tahiti, French Polynesia

2. Centre hospitalier du Taaoe, Tahiti, French Polynesia

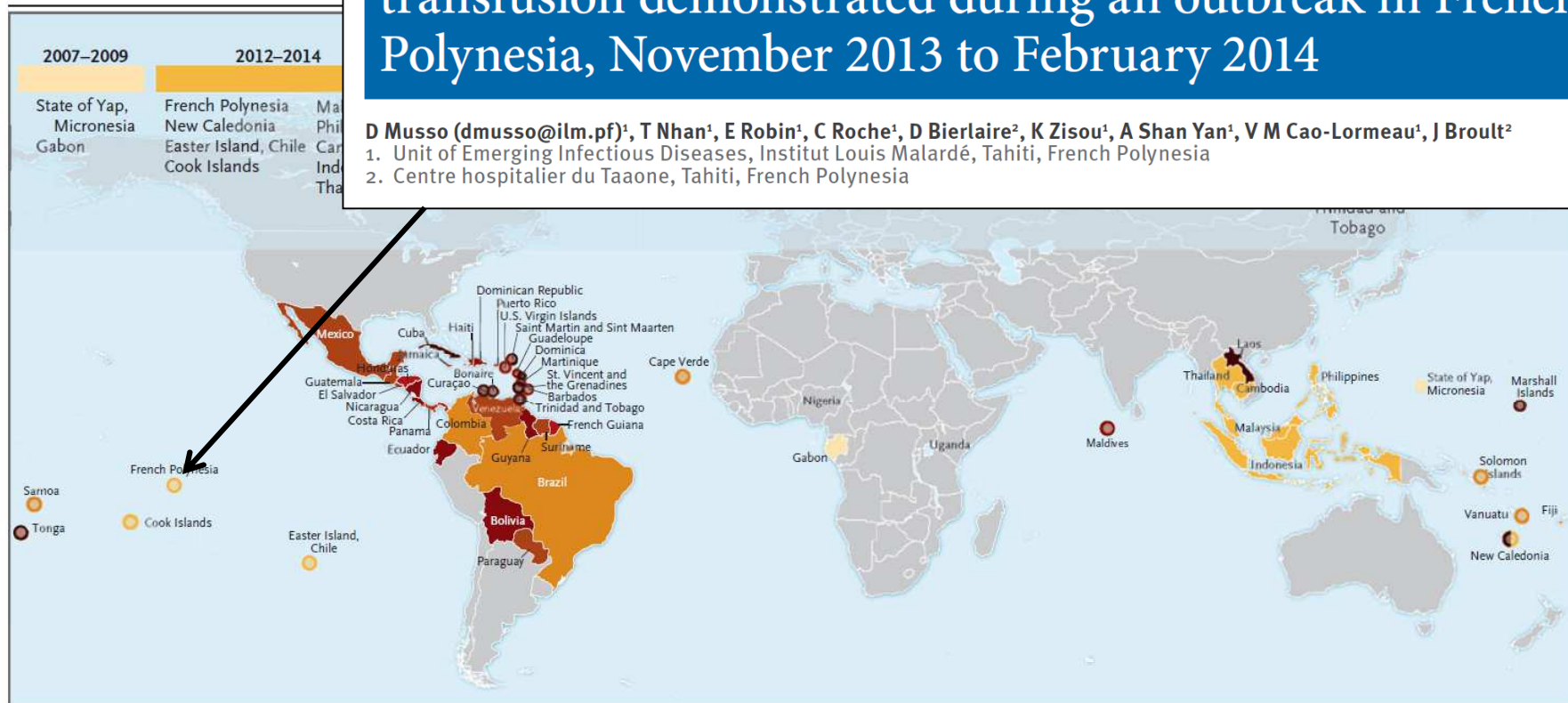


Figure 1. Areas in Which Zika Virus Infections in Humans Have Been Noted in the Past Decade (as of March 2016).

Only sporadic infections have occurred in Southeast Asia, the Philippines, and Indonesia.

THE NEW ENGLAND JOURNAL OF MEDICINE

ZIKA virus outbreak in the America

TTI preventive measures in Martinique, Guadeloupe and French Guiana

Epidemic state since late January (Martinique, French Guiana) and April 2016 (Guadeloupe)

Pre-existing measures :

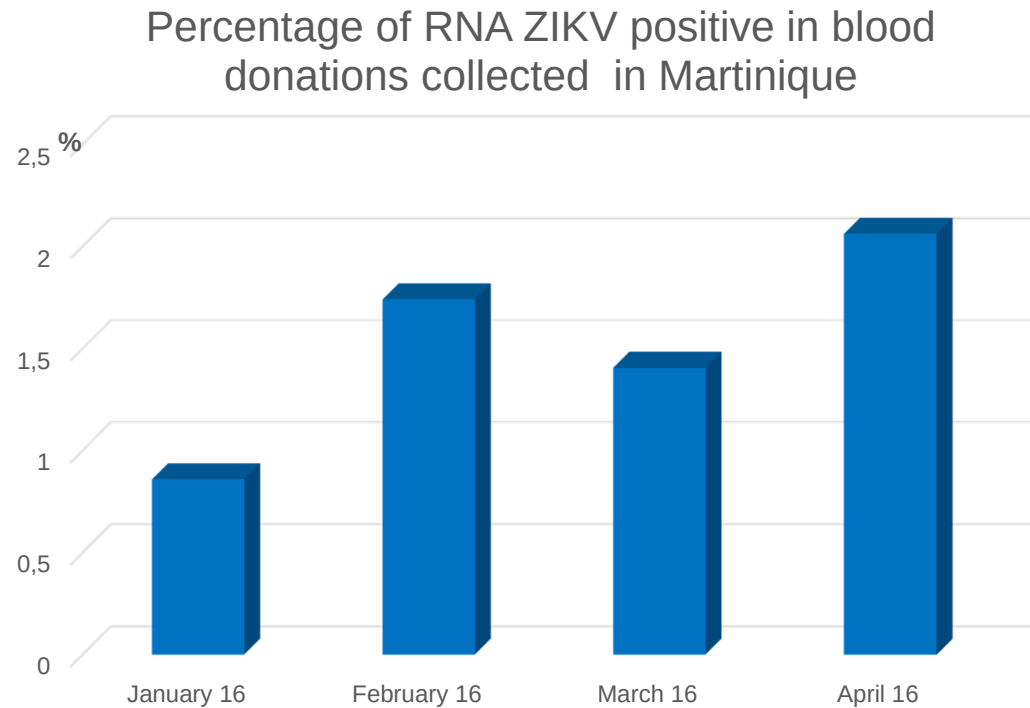
- 3-day quarantine & enhanced post-donation information request
- Intercept® treatment for platelets
- Plasma for transfusion provided from mainland France

Specific measures:

- Since Jan 4th 2016, RBC (and plasma) transfusion of pregnant women by blood products collected in mainland France
- Since Feb 15th 2016, implementation of an individual NAT ZIKV screening (dedicated arbovirus laboratory, Marseille)

ZIKA ID-NAT screening

Semi automated individual NAT Screening platform (RealStar® Zika Virus RT-PCR Kit) in a dedicated laboratory in Marseille. Estimated analytical sensitivity: LOD90% = 140 copies/mL (*with reference to the European Virus Archive Zika standard#1 (strain H/PF/2013))



ZIKA ID-NAT screening

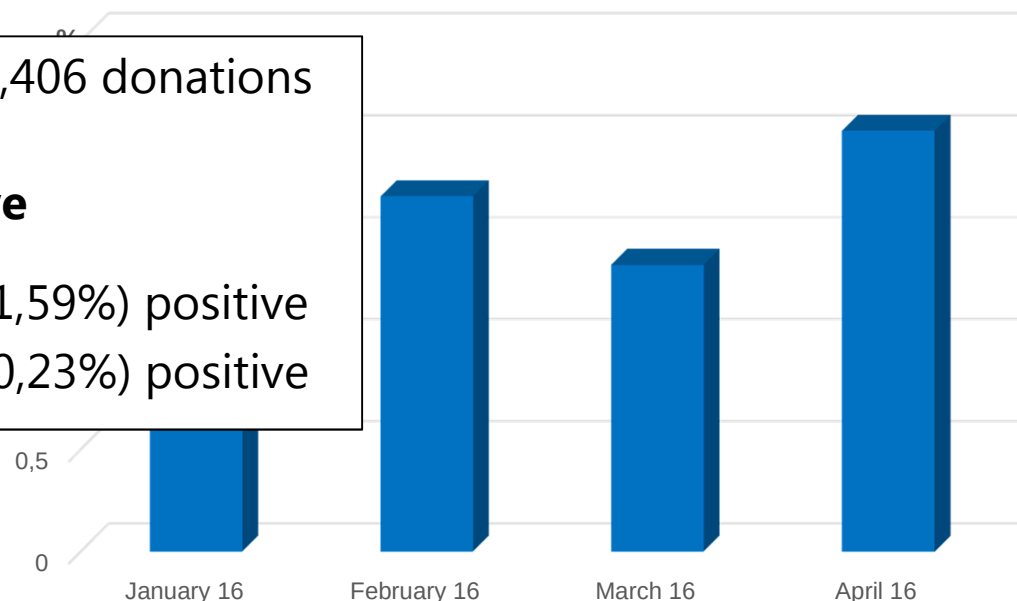
Semi automated individual NAT Screening platform (RealStar® Zika Virus RT-PCR Kit) in a dedicated laboratory in Marseille. Estimated analytical sensitivity: LOD90% = 140 copies/mL (*with reference to the European Virus Archive Zika standard#1 (strain H/PF/2013))

Percentage of RNA ZIKV positive in blood donations collected in Martinique

Between Jan 19 and Apr 18-2016: 4,406 donations tested

➔ **46 donations ZIKV RNA positive**

- Martinique: 42 / 2,642 donations (1,59%) positive
- Guadeloupe: 4 / 1,764 donations (0,23%) positive





RAPID RISK ASSESSMENT

Zika virus disease epidemic: potential association with microcephaly and Guillain–Barré syndrome

Fifth update, 11 April 2016

RAPID RISK ASSESSMENT

Zika virus disease epidemic:

Table 1. Time of detection and Zika virus RNA load in samples of infected individuals

Sample origin	Time of detection (days)		Viral RNA load	Isolation of replicative particles	References
	Before the onset of symptoms	After the onset of symptoms			
Blood	2-3	11	up to 8.1×10^6 copies/mL	+	[39]
Urine	-	10 to 20	$0.7-220 \times 10^6$ copies/mL	+	[22,40]
Saliva	-	2 to 8	NA	NA	[41,52]
Seminal fluid	-	21 to 62	$1.1 - 2.9 \times 10^7$ copies/mL	+	[42,53,54]
Breast milk	-	3 to 8 after delivery	up to 2.1×10^6 copies/mL	+	[43,55]

RAPID RISK ASSESSMENT

Zika virus disease epidemic: potential association with microcephaly and Guillain–Barré syndrome

EU (ECDC) recommendation: donors who have had a sexual contact with a man who travelled or lived in a Zika-affected during the 3 (to 6) months prior to the sexual contact may only give blood after at least 28 days after the last sexual contact.

Recommendation implemented in mainland France (and Réunion island) since May 15th

Risk assessment (Santé Publique – France):

- Blood donation by a Zika positive donor resulting from a sexual transmission in mainland France: $1/0,49 \times 10^6$ to $1/11,6 \times 10^6$ (6/year to 1/4 years)
- Transfusing such a blood product to a pregnant women: 1/90 to 1/2100 years

Anticipating (re)emerging infections to ensure blood safety

- Assessing the risk of transfusion-mediated disease transmission

Anticipating (re)emerging infections to ensure blood safety

- Assessing the risk of transfusion-mediated disease transmission

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transmission of West Nile Virus from an Organ Donor to Four Transplant Recipients

Martha Iwamoto, M.D., M.P.H., Daniel B. Jernigan, M.D., M.P.H.,
Antonio Guasch, M.D., Mary Jo Trepka, M.D., M.S.P.H.,
Carina G. Blackmore, D.V.M., Ph.D., Walter C. Hellinger, M.D.,
Si M. Pham, M.D., Sherif Zaki, M.D., Ph.D., Robert S. Lanciotti, Ph.D.,
Susan E. Lance-Parker, D.V.M., Ph.D., Carlos A. DiazGranados, M.D.,
Andrea G. Winquist, M.D., Carl A. Perlino, M.D., Steven Wiersma, M.D., M.P.H.,
Krista L. Hillyer, M.D., Jesse L. Goodman, M.D., M.P.H.,
Anthony A. Marfin, M.D., M.P.H., Mary E. Chamberland, M.D., M.P.H.,
and Lyle R. Petersen, M.D., M.P.H.,
for the West Nile Virus in Transplant Recipients Investigation Team*

Anticipating (re)emerging infections to ensure blood safety

- As

Tr

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transmission of West Nile Virus through Blood Transfusion in the United States in 2002

Lisa N. Pealer, Ph.D., Anthony A. Marfin, M.D., M.P.H.,
Lyle R. Petersen, M.D., M.P.H., Robert S. Lanciotti, Ph.D., Peter L. Page, M.D.,
Susan L. Stramer, Ph.D., Mary Grace Stobierski, D.V.M., M.P.H.,
Kimberly Signs, D.V.M., Bruce Newman, M.D., Hema Kapoor, M.D.,
Jesse L. Goodman, M.D., M.P.H., and Mary E. Chamberland, M.D., M.P.H.,
for the West Nile Virus Transmission Investigation Team*

Susan L. Stramer, Ph.D., M.D., Carlos A. Diaz-Granados, M.D.,
Andrea G. Winquist, M.D., Carl A. Perlino, M.D., Steven Wiersma, M.D., M.P.H.,
Krista L. Hillyer, M.D., Jesse L. Goodman, M.D., M.P.H.,
Anthony A. Marfin, M.D., M.P.H., Mary E. Chamberland, M.D., M.P.H.,
and Lyle R. Petersen, M.D., M.P.H.,
for the West Nile Virus in Transplant Recipients Investigation Team*

Anticipating (re)emerging infections to ensure blood safety

- As

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transmission of West Nile Virus through Blood

Tr

West Nile Virus among Blood Donors in the United States, 2003 and 2004

Lyle R.

Susan L. Stramer, Ph.D., Chyang T. Fang, Ph.D., Gregory A. Foster, B.S.,
Annette G. Wagner, M.S., Jaye P. Brodsky, B.S., and Roger Y. Dodd, Ph.D.

Ki

Jesse

for the West Nile Virus Transmission Investigation Team*

Susan L. Stramer, Ph.D., Chyang T. Fang, Ph.D., Gregory A. Foster, B.S.,
Annette G. Wagner, M.S., Jaye P. Brodsky, B.S., and Roger Y. Dodd, Ph.D.,
Andrea G. Winquist, M.D., Carl A. Perlino, M.D., Steven Wiersma, M.D., M.P.H.,
Krista L. Hillyer, M.D., Jesse L. Goodman, M.D., M.P.H.,
Anthony A. Marfin, M.D., M.P.H., Mary E. Chamberland, M.D., M.P.H.,
and Lyle R. Petersen, M.D., M.P.H.,
for the West Nile Virus in Transplant Recipients Investigation Team*

Assessing the chikungunya transfusion risk

Despite presence of CHIKV virus in the blood of infected asymptomatic blood donors and animal models suggesting that intravenous inoculation is able to transmit infection, there has been no reported case of transfusion-transmitted CHIKV disease world-wide yet.

- Insufficient investigations?
- Difficulty to identify transfusion-transmitted CHIKV infections in a CHIKV epidemic setting ?
- A viral load in pre/asymptomatic donors inauspicious to blood CHIKV transmission?
- A rapid appearance of IgM Ab in infected (asymptomatic) donors and/ or a rapid increase in the % of CHIKV immunized transfusion recipients?
- Modulation of infectious virulence in relation with blood products manufacturing and storage?
- A less efficient direct blood transmission compared to an arthropod (saliva) - mediated transcutaneous transmission?

Anticipating (re)emerging infections to ensure blood safety

- Assessing the risk of transfusion-mediated disease transmission

The Journal of Infectious Diseases

MAJOR ARTICLE



Transfusion-Transmitted Dengue and Associated Clinical Symptoms During the 2012 Epidemic in Brazil

Ester C. Sabino,¹ Paula Loureiro,² Maria Esther Lopes,³ Ligia Capuani,¹ Christopher McClure,⁴ Dhuly Chowdhury,⁴ Claudia Di-Lorenzo-Oliveira,⁵ Lea C. Oliveira,¹ Jeffrey M. Linnen,⁶ Tzong-Hae Lee,⁷ Thelma Gonzalez,⁷ Donald Brambilla,⁴ Steve Kleinman,^{7,8} Michael P. Busch,^{7,9,a} and Brian Custer^{7,9,a}, for the International Component of the NHLBI Recipient Epidemiology and Donor Evaluation Study-III

¹Departamento de Moléstias Infecciosas e Parasitárias, Instituto de Medicina Tropical, Universidade de São Paulo, ²Faculdade de Ciências Médicas–UPE/Fundação Hemope, Recife, and ³Fundação Hemorio, Rio de Janeiro, Brazil; ⁴RTI International, Rockville, Maryland; ⁵Universidade Federal de São Joao del Rey, Divinópolis, Brazil; ⁶Hologic, San Diego, ⁷Blood Systems Research Institute, San Francisco, California; ⁸University of British Columbia, Vancouver, Canada; and ⁹Department of Laboratory Medicine, University of California–San Francisco

Anticipating (re)emerging infections to ensure blood safety

- Assessing the risk of transfusion-mediated disease transmission

The Journal of Infectious Diseases

MAJOR ARTICLE



Transfusion-Transmitted Dengue and Associated Clinical Symptoms During the 2012 Epidemic in Brazil

Ester C. Sabino,¹ Paula Loureiro,² Maria Esther Lopes,³ Ligia Capuani,¹ Christopher McClure,⁴ Dhuly Chowdhury,⁴ Claudia Di-Lorenzo-Oliveira,⁵ Lea C. Oliveira,¹ Jeffrey M. Linnen,⁶ Tzong-Hae Lee,⁷ Thelma Gonzalez,⁷ Donald Brambilla,⁴ Steve Kleinman,^{7,8} Michael P. Busch,^{7,9,a} and Brian Custer,^{7,9,a}

for the International

¹Departamento de M
Hemorio, Rio de Jane
San Francisco, Califor

During a large epidemic of DENV-4 infection in Brazil:

- > 0,5% of donations were RNA positive
- 37,5% (95%CI, 15,2%-64,6%) of RNA positive blood donations transmitted the DENV-4 to the recipients
- **No significant differences in symptoms and mortality between cases and controls**

Anticipating (re)emerging infections to ensure blood safety

- Assessing the risk of transfusion-mediated disease

Why has *Borrelia burgdorferi* not been transmitted by blood transfusion?

TRANSFUSION Volume 53, November 2013

Yelena Ginzburg

- Most spirochetemic patients are symptomatic
- Deferring individuals with recent tick bites, where implemented, may further eliminate a proportion of spirochetemic donors
- Spirochetemia is relatively short-lived
- Viable spirochetes present in whole blood may be as low as 1 spirochete/10 mL
- Host-adapted *B. burgdorferi* may not survive well under blood storage conditions

www.thelancet.com/infection Vol 16 May 2016

Anticipating (re)emerging infections to ensure blood safety

- Assessing the risk of transfusion-mediated disease

Why has *Borrelia burgdorferi* not been transmitted by blood transfusion?

TRANSFUSION Volume 53, November 2013

Yelena Ginzburg

- Most spirochetemic patients are symptomatic
- Deferring individuals with recent tick bites, where implemented, may further eliminate a proportion of



Identification of a novel pathogenic *Borrelia* species causing Lyme borreliosis with unusually high spirochaetaemia: a descriptive study

Bobbi S Pritt, Paul S Mead, Diep K Hoang Johnson, David F Neitzel, Laurel B Respicio-Kingry, Jeffrey P Davis, Elizabeth Schiffman, Lynne M Sloan, Martin E Schriefer, Adam J Replogle, Susan M Paskewitz, Julie A Ray, Jenna Bjork, Christopher R Steward, Alecia Deedon, Xia Lee, Luke C Kingry, Tracy K Miller, Michelle A Feist, Elitza S Theel, Robin Patel, Cole L Irish, Jeannine M Petersen

blood storage conditions

www.thelancet.com/infection Vol 16 May 2016

Anticipating (re)emerging infections to ensure blood safety

- Assessing the risk of transfusion-mediated disease transmission
- Deferring at risk donors

Anticipating (re)emerging infections to ensure blood safety

- Assessing the risk of transfusion-mediated disease transmission
- Deferring at risk donors
- Introducing a 2 to 3 day quarantine combined with enhanced post-donation information

Enhanced post donation information, combined with a 72 hours quarantine, can potentially reduce up to 75 % the risk of transfusing a CHIKV+ blood product.

Anticipating (re)emerging infections to ensure blood safety

- Assessing the risk of transfusion-mediated disease transmission
- Deferring at risk donors
- Introducing a 2 to 3 day quarantine combined with enhanced post-donation information
- Pathogen detection

Anticipating (re)emerging infections to ensure blood safety

- **Pathogen detection:**
 - Testing whole blood donation : 100% RBC, 90% plasma and 60% platelets (in France)
 - Requires individual technologies for each pathogen
 - Varying sensitivity depending on technology and pool size
 - A window period during which detection is impossible
 - Costly

Anticipating (re)emerging infections to ensure blood safety

- **Pathogen detection:**
 - Testing whole blood donation : 100% RBC, 90% plasma and 60% platelets (in France)
 - Requires individual technologies for each pathogen
 - Varying sensitivity depending on technology and pool size
 - A window period during which detection is

CDC Home



Centers for Disease Control and Prevention
CDC 24/7: Saving Lives. Protecting People.™

Morbidity and Mortality Weekly Report (MMWR)

Fatal West Nile Virus Infection After Probable Transfusion-Associated Transmission – Colorado, 2012

Weekly

August 9, 2013 / 62(31);622-624

Anticipating (re)emerging infections to ensure blood safety

- Assessing the risk of transfusion-mediated disease transmission
- Deferring at risk donors
- Introducing a 2 to 3 day quarantine combined with enhanced post-donation information
- Pathogen detection
- Pathogen reduction

Anticipating (re)emerging infections to ensure blood safety

- Assessing the risk of transfusion-mediated disease

Pathogen reduction :

- Efficiently neutralizes a large variety of pathogens: known, emerging, remerging or unknown
- No window period
- "One for all" at risk situations (almost)

Anticipating (re)emerging infections to ensure blood safety

Hepatitis E transmission by transfusion of Intercept blood system– treated plasma

Blood, 2014

Lisette Hauser, Anne-Marie Roque-Afonso, Alexandre Beylouné, Marion Simonet, Bénédicte Deau Fischer, Nicolas Burin des Roziers, Vincent Mallet, Pierre Tiberghien and Philippe Bierling

- - No window period
 - “One for all” at risk situations (almost)
-
-

Anticipating (re)emerging infections to ensure blood safety

Hepatitis E transmission by transfusion of Intercept blood system– treated plasma

Blood, 2014

Lisette Hauser, Anne-Marie Roque-Afonso, Alexandre Bevlouné, Marion Simonet, Bénédicte Deau
erling

Transmission of human immunodeficiency virus Type-1 by fresh-frozen plasma treated with methylene blue and light

Transfusion, 2016

*Manuel Álvarez,¹ Mar Luis-Hidalgo,¹ María Alma Bracho,² Amando Blanquer,¹ Luis Larrea,¹
José Villalba,¹ Nieves Puig,¹ Dolores Planelles,¹ José Montoro,¹ Fernando González-Candelas,² and
Roberto Roig¹*

Anticipating (re)emerging infections to ensure blood safety

Hepatitis E transmission by transfusion of Intercept blood system– treated plasma

Blood, 2014

Lisette Hauser, Anne-Marie Roque-Afonso, Alexandre Bevlouné, Marion Simonet, Bénédicte Deau
erling

Transmission of human immunodeficiency virus Type-1 by fresh-frozen plasma treated with methylene blue and light

Transfusion, 2016

Manuel Álvarez,¹ Mar Luis-Hidalgo,¹ María Alma Bracho,² Amando Blanquer,¹ Luis Larrea,¹
José Villalba,¹ Nieves Puig,¹ Dolores Planelles,¹ José Montoro,¹ Fernando González-Candelas,² and

Effect of Plasmodium inactivation in whole blood on the incidence of blood transfusion-transmitted malaria in endemic regions: the African Investigation of the Mirasol System (AIMS) randomised controlled trial

Lancet, 2016

Jean-Pierre Allain, Alex K Owusu-Ofori, Sonny Michael Assennato, Susanne Marschner, Raymond P Goodrich, Shirley Owusu-Ofori

Transmission of Plasmodium by whole blood treated with the Mirasol pathogen reduction technology system

Anticipating (re)emerging infections to ensure blood safety

Pathogen reduction :

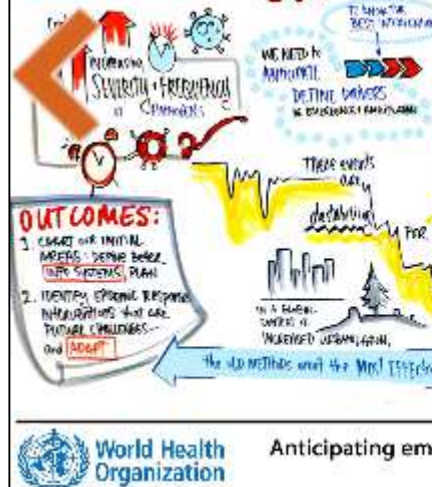
- Efficiently neutralizes a large variety of pathogens: known, emerging, reemerging or unknown
- No window period
- One for all at risk situations (almost)
- Not (yet) available for RBC
- Induces qualitative and quantitative alterations
 - Lesser hemostatic efficacy of pathogen-reduced platelets?
 - Less hemostatic proteins in pathogen-reduced plasma
- Very costly

Anticipating (re)emerging infections to ensure blood safety

- Assessing the risk of transfusion-mediated disease transmission
- Deferring at risk donors
- Introducing a 2 to 3 day quarantine combined with enhanced post-donation information
- Pathogen detection
- Pathogen reduction
- **Allocating available resources in due proportion of the health risk**



ANTICIPATING EMERGING INFECTIOUS DISEASE EPIDEMICS



CURING and not HARMING: THAT IS THE QUESTION

CLINICAL PRACTICES & EMERGING DISEASES



SYSTEMIC VIEW: INFECTIONS IN HEALTH CARE FACILITIES



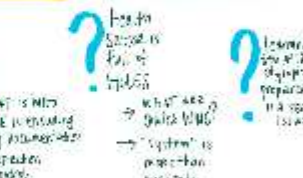
PATIENT-DOCTOR RELATIONSHIP IN AGE OF THE INTERNET



STRENGTHEN the OVERALL HEALTH SYSTEM



DISCUSSION



Anticipating emerging infectious disease epidemics: an informal consultation
1-2 December 2015, Geneva

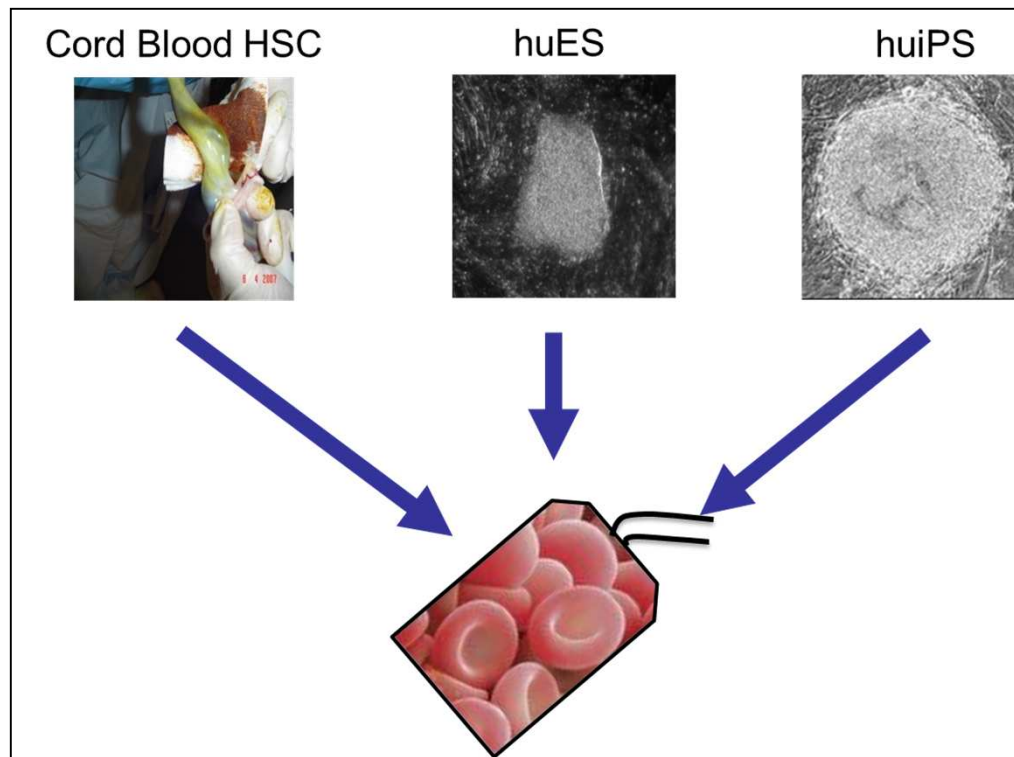
drawn live
graphic recording | Drawing Change

The ultimate anticipation for (re) emerging diseases ?

Proof of principle for transfusion of *in vitro* generated red blood cells

Marie-Catherine Giarratana, Hélène Rouard, Agnès Dumont, Laurent Kiger, Innocent Safeukui, Pierre-Yves Le Pennec, Sabine François, Germain Trugnan, Thierry Peyrard, Tiffany Marie, Séverine Jolly, Nicolas Hebert, Christelle Mazurier, Nathalie Mario, Laurence Harmand, Hélène Lapillonne, Jean-Yves Devaux and Luc Douay

BLOOD, 10 NOVEMBER 2011 • VOLUME 118, NUMBER 19

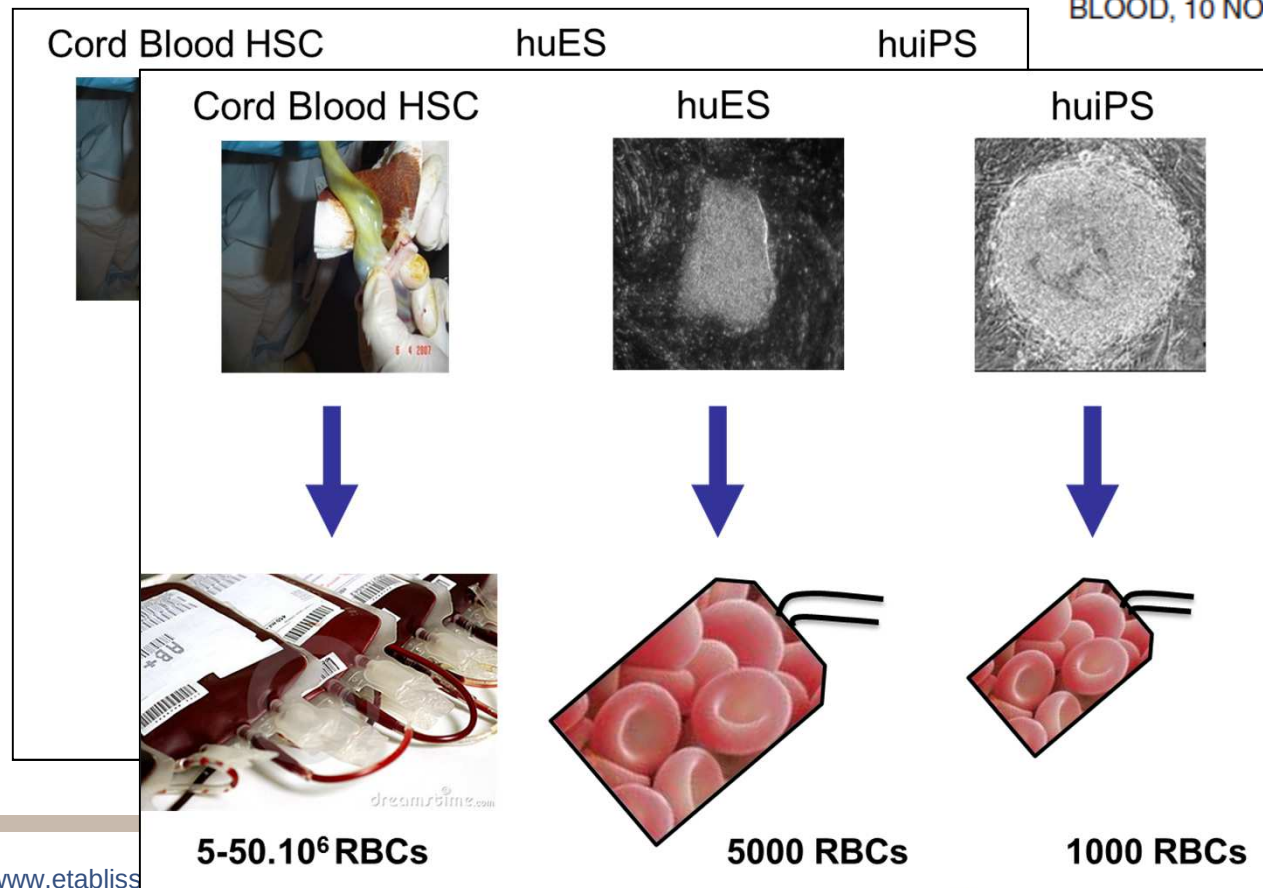


The ultimate anticipation for (re) emerging diseases ?

Proof of principle for transfusion of *in vitro* generated red blood cells

Marie-Catherine Giarratana, Hélène Rouard, Agnès Dumont, Laurent Kiger, Innocent Safeukui, Pierre-Yves Le Pennec, Sabine François, Germain Trugnan, Thierry Peyrard, Tiffany Marie, Séverine Jolly, Nicolas Hebert, Christelle Mazurier, Nathalie Mario, Laurence Harmand, Hélène Lapillonne, Jean-Yves Devaux and Luc Douay

BLOOD, 10 NOVEMBER 2011 • VOLUME 118, NUMBER 19

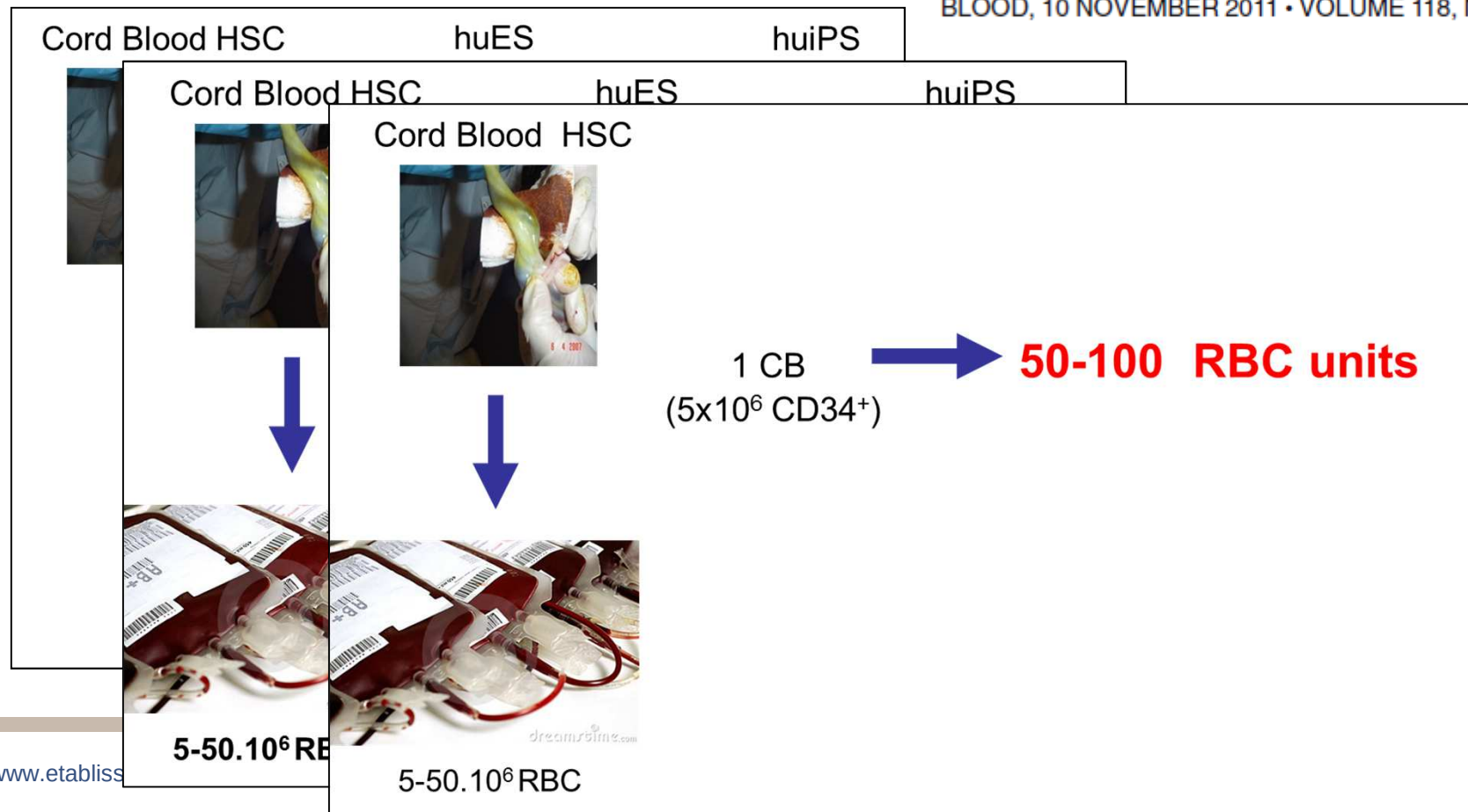


The ultimate anticipation for (re) emerging diseases ?

Proof of principle for transfusion of *in vitro* generated red blood cells

Marie-Catherine Giarratana, Hélène Rouard, Agnès Dumont, Laurent Kiger, Innocent Safeukui, Pierre-Yves Le Pennec, Sabine François, Germain Trugnan, Thierry Peyrard, Tiffany Marie, Séverine Jolly, Nicolas Hebert, Christelle Mazurier, Nathalie Mario, Laurence Harmand, Hélène Lapillonne, Jean-Yves Devaux and Luc Douay

BLOOD, 10 NOVEMBER 2011 • VOLUME 118, NUMBER 19



Anticipating (re)emerging infections to Ensure Blood Safety

Pierre Tiberghien

*Etablissement Français du Sang, St-Denis and
Université de Franche-Comté, Besançon, France*

*IPFA/PEI 23rd International Workshop on Surveillance and
Screening of Blood Borne Pathogens, Lisbon, Portugal
May 25th, 2016*