Emerging Arboviruses, detection and alert:

Exemple with Chikungunya virus in the Americas

Dr Christine PRAT

French National Reference Center on Arboviruses
IRBA Marseille

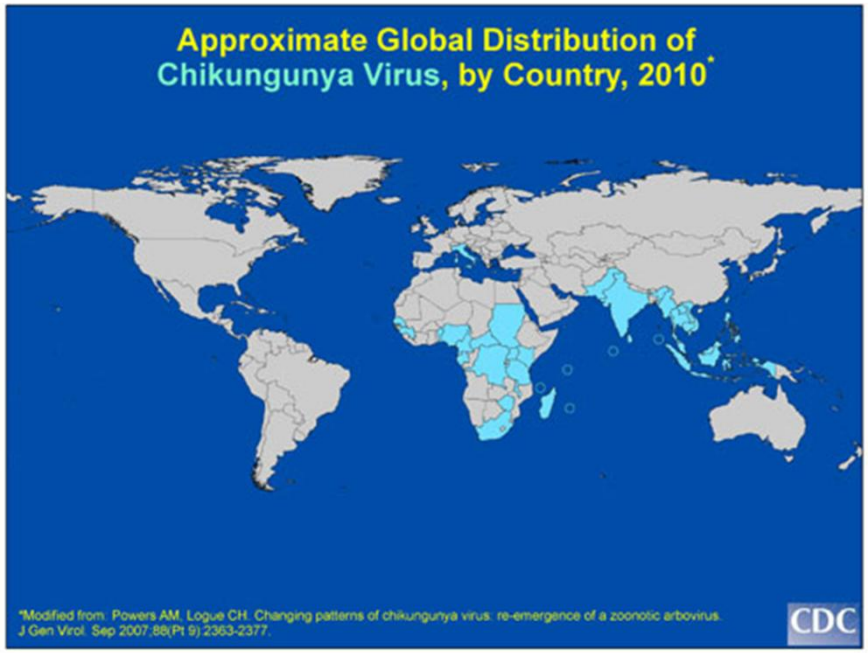
Emerging arboviruses

I. Chikungunya virus
II. Alert
III. Epidemiological surveillance
IV. Risks for Europe
V. French National anti-dissemination plan
VI. Diagnostic: strategy and evaluation of kits

I. Chikungunya virus

- ✓ Arbovirus (*arthropod-borne viruses)* : Virus transmitted by blood sucking arthropods
- ✓ Vector: mosquitos from genus *Aedes*
- ✓ *Togaviridae*, genus *Alphavirus*

Aedes albopictus (2-10mm)



- ✓ Since 2005, 1.9 million cases in South East Asia (WHO data)
- ✓ In 2007, 197 cases in Italy

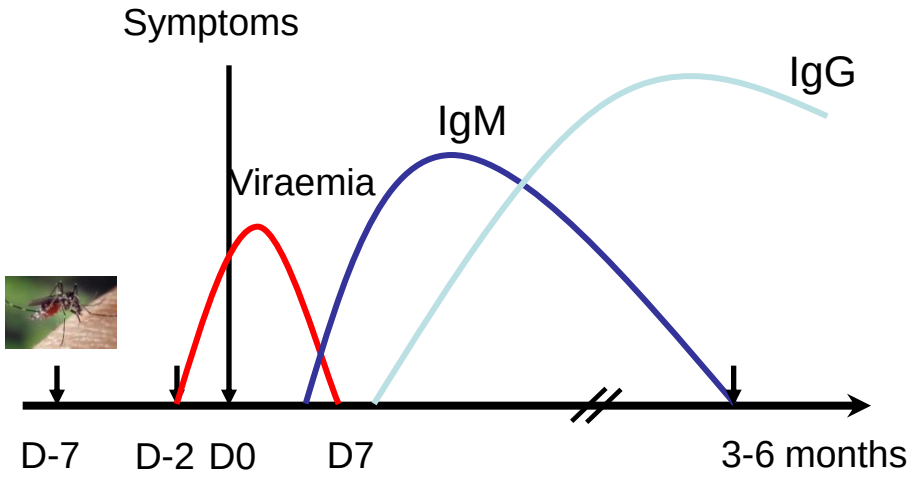
I. Chikungunya virus

✓ Clinical manifestations:

- Sudden onset with high grade fever (> 38,5°C)
- severe arthralgias
- myalgias
- headache
- skin rash
- chronic arthritis for several months in some patients

I. Chikungunya virus

✓ Diagnostic:



≤ 7 days : viral genome detection by RT PCR (+ viral isolation)
≥ 5 days: Serology techniques, IgM and IgG detection

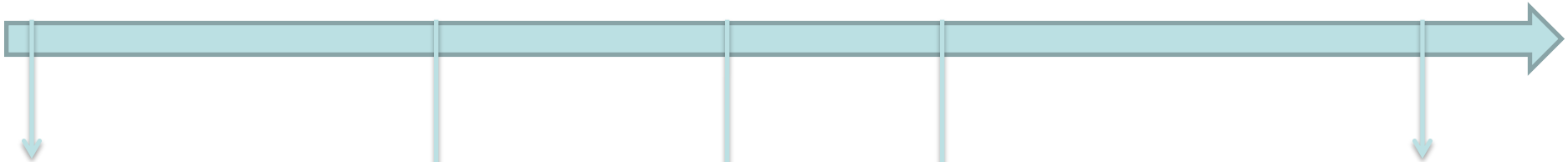
Emerging arboviruses

I. Chikungunya virus
II. Alert
III. Epidemiological surveillance
IV. Risks for Europe
V. French National anti-dissemination plan
VI. Diagnostic: strategy and evaluation of kits


Saint Martin
Miami
Everglades National Park
The Bahamas
La Habana
Pinar del Río
Matanzas
Santa Clara
Nueva Gerona
Cienfuegos
Morón
Cuba
Florida
Turks and Caicos Islands
Holguín
Las Tunas
Bayamo
Mayarí
Guantánamo
Manzanillo
Santiago de Cuba
Cayman Islands
Gonaïves
Haïti
República Dominicana
Haiti
Dominican Republic
Jérémie
Higüey
San Juan
British Virgin Islands
Anguilla
Puerto Rico
Gustavia
Basseterre
Montego Bay
Jamaica
Hayes
Les Cayes
Jacmel
Montserrat
Guadeloupe
Dominica
Martinique
St Lucia
Barbados
St. Vincent and the Grenadines
Grenada
Caribbean Sea
Bilwi
San Andres
Aruba
Curaçao
Curacao
Punto Fijo
Coro
Santa Marta
Maicao
Porlamar
Cumaná
Trinidad and Tobago
Cartagena
Valledupar
Maracaibo
Caracas


18th November 2013:
5 patients without any travel history presenting severe arthralgia after a « dengue-like » fever episode
Petites Cayes
Anse Marcel
Grandes Cayes
Baie du Cul-de-Sac
Îlet de Pinel
Baie de Grand Case
Salines
Happy Bay
Étang Gulchard
Étang Chevrise
Anse des Pères
Orient Bay
Salines d'Orient
Baie de Potence
Rambaud
Colombier
A
Étang aux Poissons
Baie de L'Embouchure
Rue de Coralita
Baie Rouge
Baie aux Prunes
Anse des Sables
Marigot
Baie de Marigot
Rue des Terres Basses
Rue de Sandy Ground
Baie Nettlé
Anse aux Cajoux
Grand Étang
Baie Longue
Saint-Martin
Sint Maarten
Baie Lucas
Oyster Pond
Simpson Bay Lagoon
Rue de Hollande
L.B. Scott Rd
Rhine Rd
Mullet Bay Pond
Airport Rd
Maho Beach
Burgeaux Bay
Simpson Bay
Cole Bay
Welfare Rd
Arch Rd
Bush Rd
Sucker Garden Rd
Guana Bay
Philipsburg
Lay Bay
Cole Bay
Little Bay Pond
Cay Bay
Little Bay
Great Bay
Back Bay
Point Blanche Bay
Imagerie ©2014 CNES / Astrium, DigitalGlobe, Landsat, U.S. Geological Survey, Données cartographiques ©2014 Google

II. Alert



26/11/2013:
French National Reference Center (NRC) alert. Sending of samples

02/12/2013:
Analysis at the French NRC: serology and RT-PCR

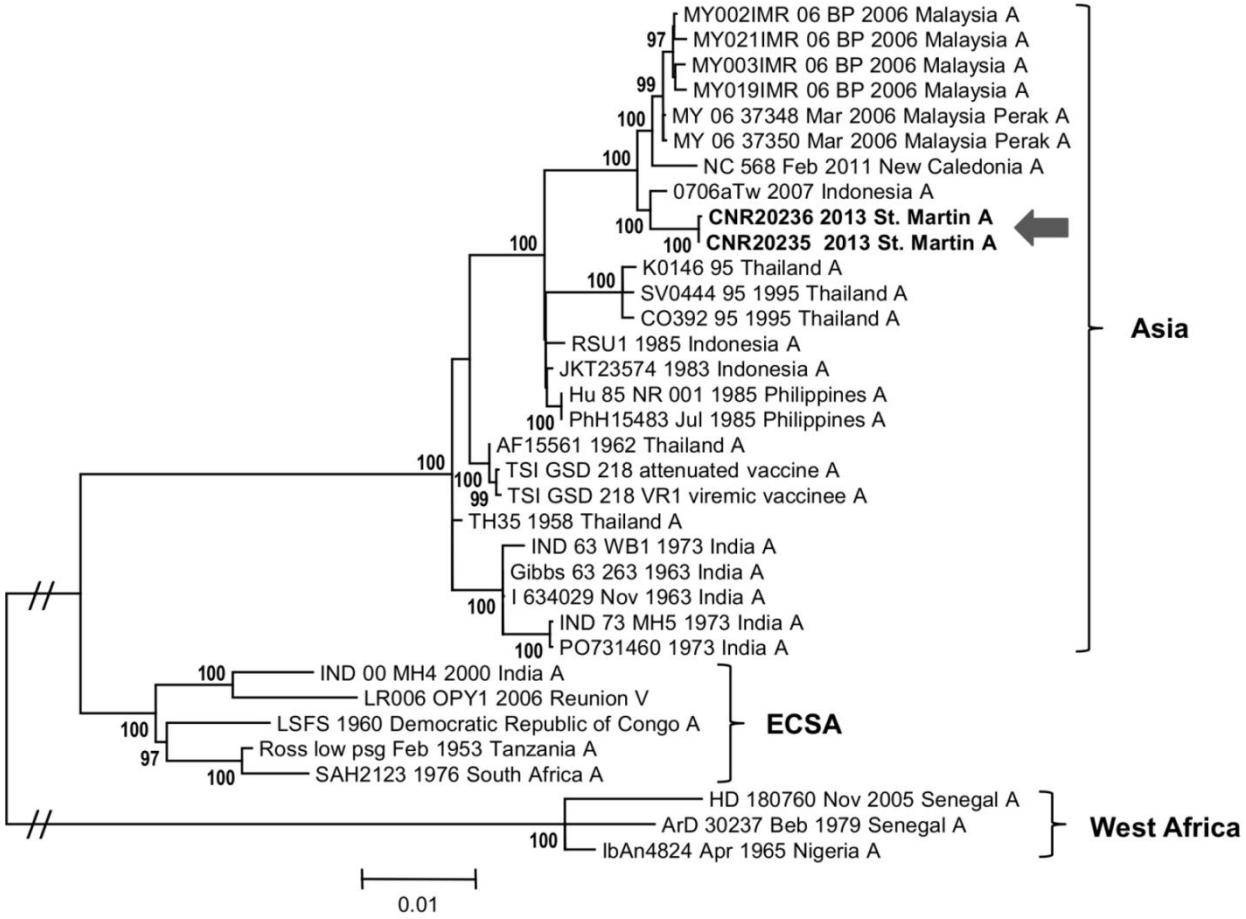
03/12/2013:
Discovery of a recent alphavirus infection
(IgM cross-reactivity with Tonate, Mayaro and Chikungunya…)

05/12/2013:
1st positive CHIKV RT-PCR.
CHIKV emergence in the Americas is confirmed

10/12/2013:
NGS sequencing: the virus belongs to the Asian genotype, and not African.

II. Alert

✓ Phylogeny of CHIKV from Saint Martin



From Leparc-Goffart et al, 2014 The Lancet

Emerging arboviruses

I. Chikungunya virus
II. Alert
III. Epidemiological surveillance
IV. Risks for Europe
V. French National anti-dissemination plan
VI. Diagnostic: strategy and evaluation of kits

III. Epidemiological Surveillance

- ✓ <u>Objectives for public health authorities:</u>
  - Rapidly detect every new suspect case
  - Collect epidemiological data
  - Confirm cases by laboratory tests
  - Document the spread of the epidemy

III. Epidemiological Surveillance

✓ Public health surveillance plan in the Caribbean:

PSAGE chikungunya

Phase 1. Absence de transmission autochtone → éviter infestation vecteur

- 1a. Pas d'épidémie dans une des zones d'échange avec les DFA
- 1b. Épidémie dans une zone d'échange avec les DFA ou la COM
- 1c. Épidémie dans un des DFA ou une des COM

Phase 2. Transmission autochtone modérée (>= 1 cas +) → prévenir dissémination

Phase 3. Épidémie → limiter l'impact de l'épidémie

- 3a. Chaînes locales de transmission
- 3b. Épidémie généralisée

Phase 4. Fin d 'épidémie → bilan

III. Epidemiological Surveillance

✓ <u>Biological diagnostic of patients:</u>

- No Chikungunya diagnostic capabilities in french caribbean: all samples from suspect cases are sent to the French National Reference Center
- Nearly 1500 samples received in 2 months
- Reinforcement of two technicians at the NRC for 2 months

Problematic:

- Concomittant dengue epidemic with similar clinical symptoms
- How can we document the emergence of a new virus clinically similar to dengue ?

Chikungunya	Dengue
Sudden onset of fever >38,5°C	Sudden onset of fever >38,5°C
Arthralgia of the extremities of the limb	At least one algia sign: headache, arthralgia, myalgia, retro-orbital pain
Absence of any other etiological orientation	Absence of any other etiological orientation

III. Epidemiological Surveillance

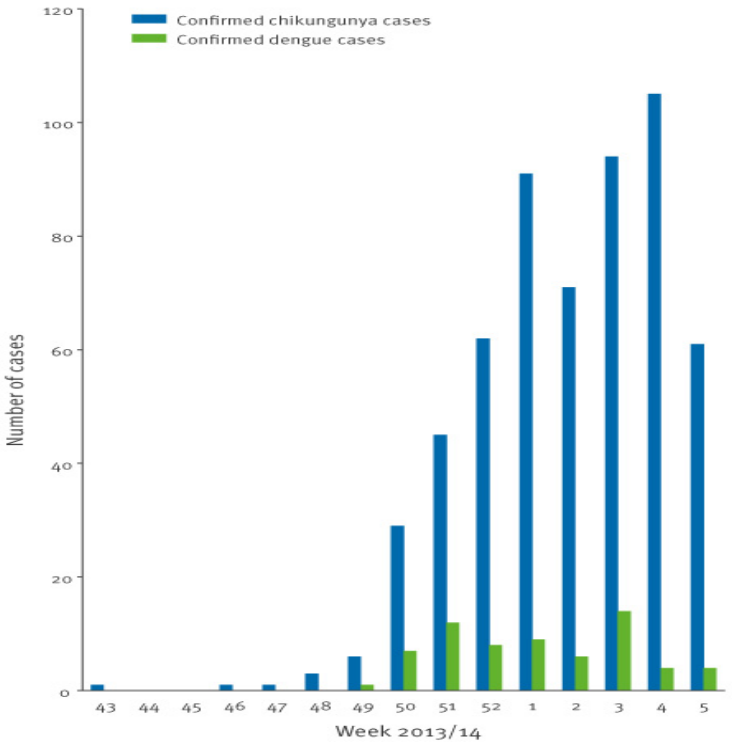
✓ <u>Biological diagnostic of patients:</u>

The French NRC received all samples for suspect cases corresponding to the Chikungunya case definition

Since dengue and chikungunya fever are clinically similar, there was a surprising low number of samples diagnosed with dengue (4% only of received samples)

FIGURE 1

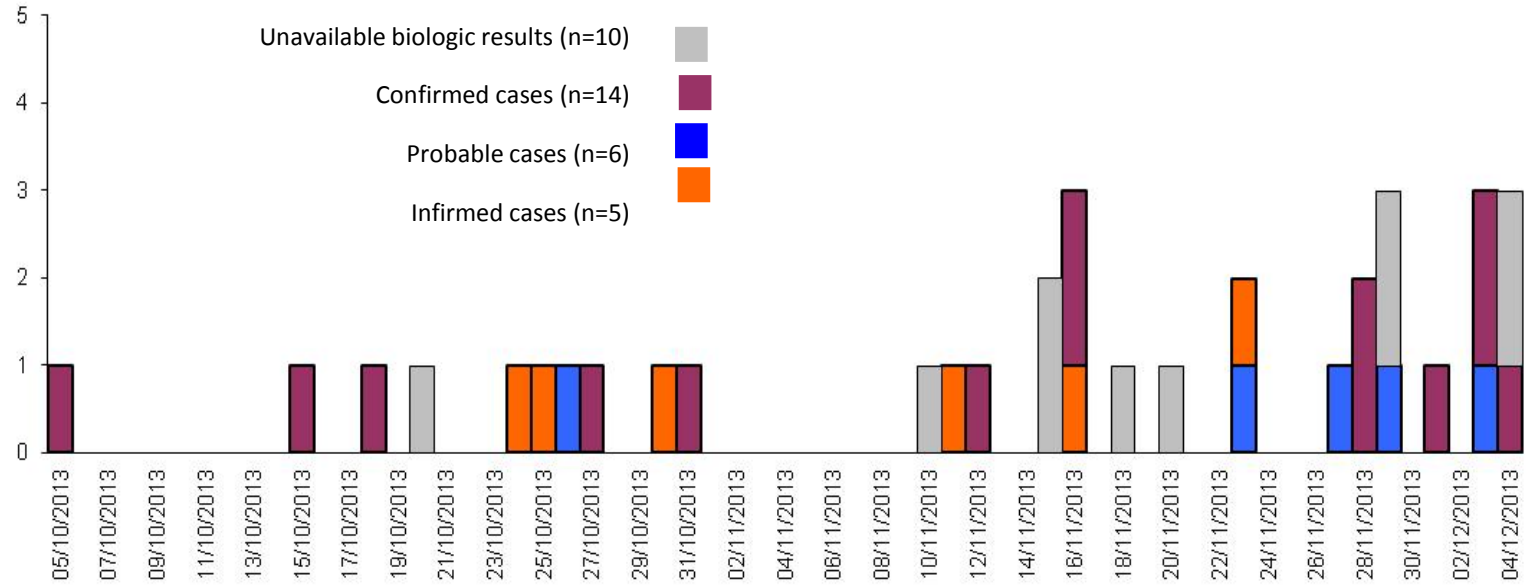
Confirmed chikungunya (n=570) and dengue (n=65) cases, Saint Martin, 4 December 2013–31 January 2014



From Omarjee et al. 2014, Eurosurveillance

II. Alert

✓ Epidemic curve of chikungunya cases in St martin:



✓ First confirmed autochtonous CHIKV cases in French territories:

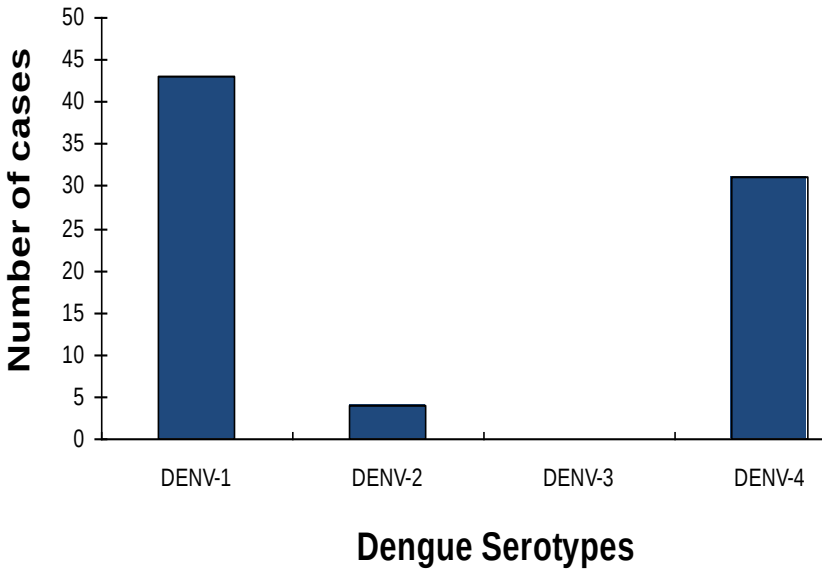
Martinique: 18 december 2013
Guadeloupe: 24 december 2013

Saint Barthélémy: 30 december 2013
French Guyanna: 19 february 2014

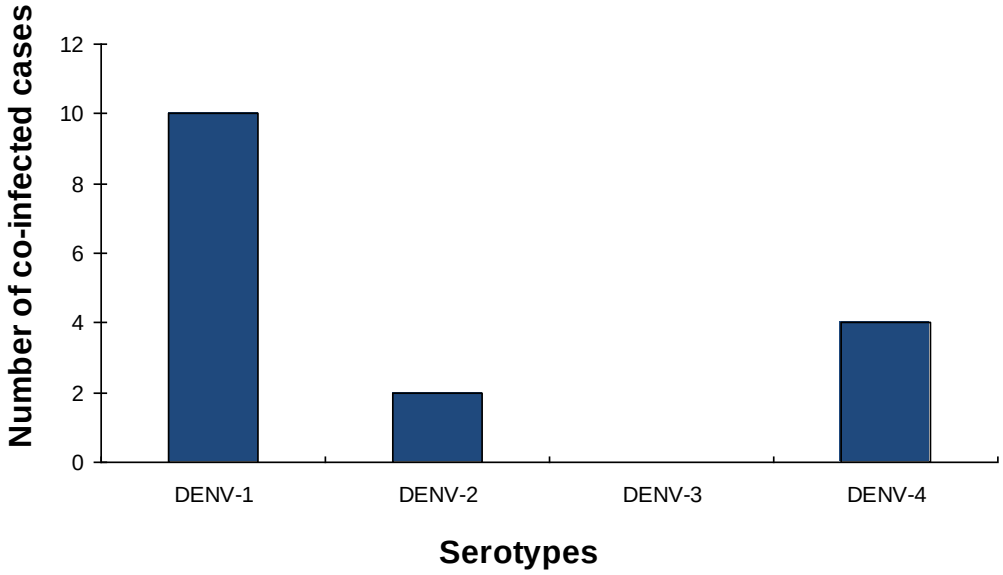
III. Epidemiological Surveillance

2.8% of CHIKV-DENV co-infections, similar to co-infection rates previously described during CHIKV emergence in Gabon

DENV confirmed cases
Dengue virus serotype repartition



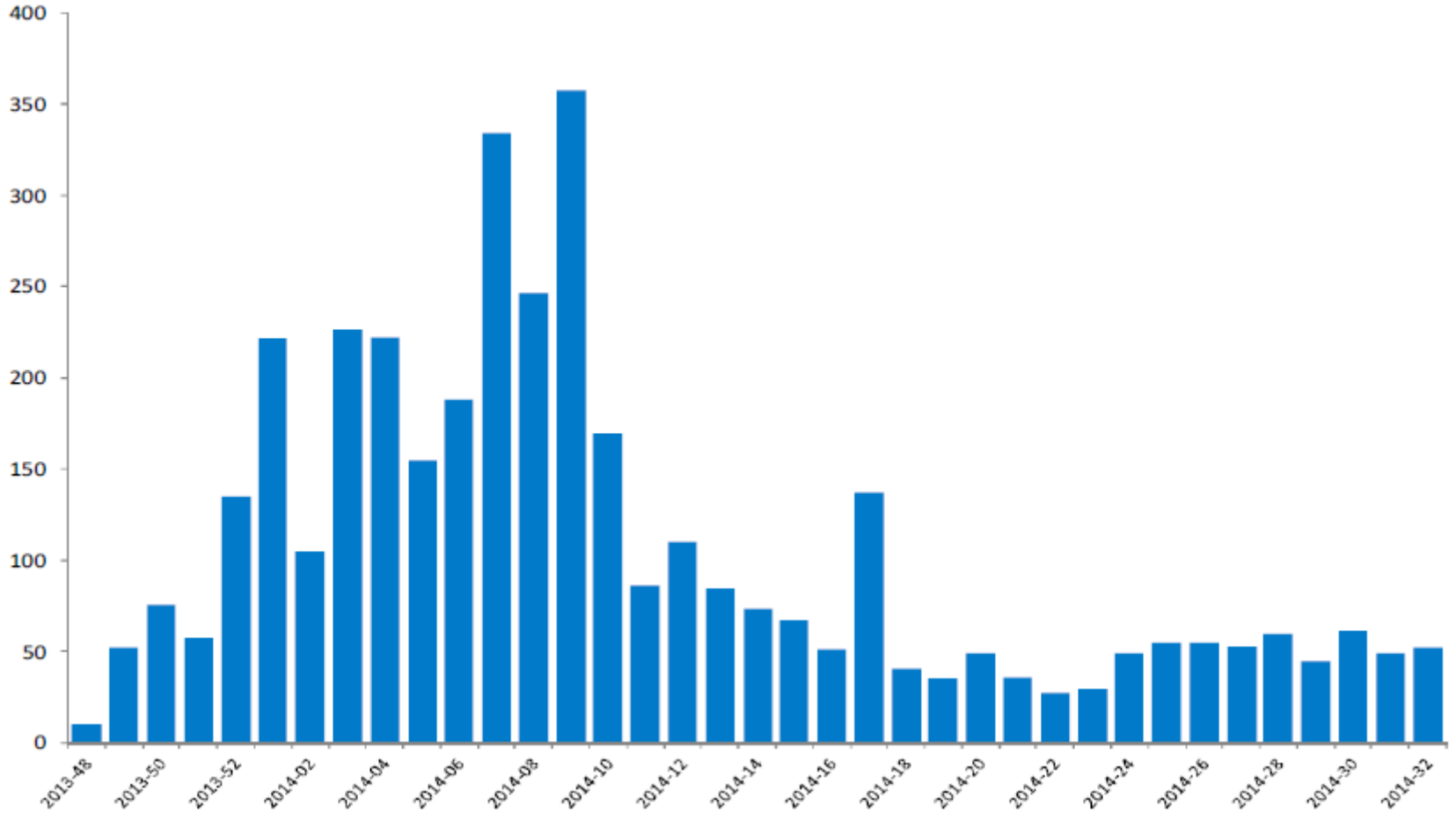
co-infection CHIKV and DENV Dengue virus serotype repartition



Unpublished data

III. Epidemiological Surveillance

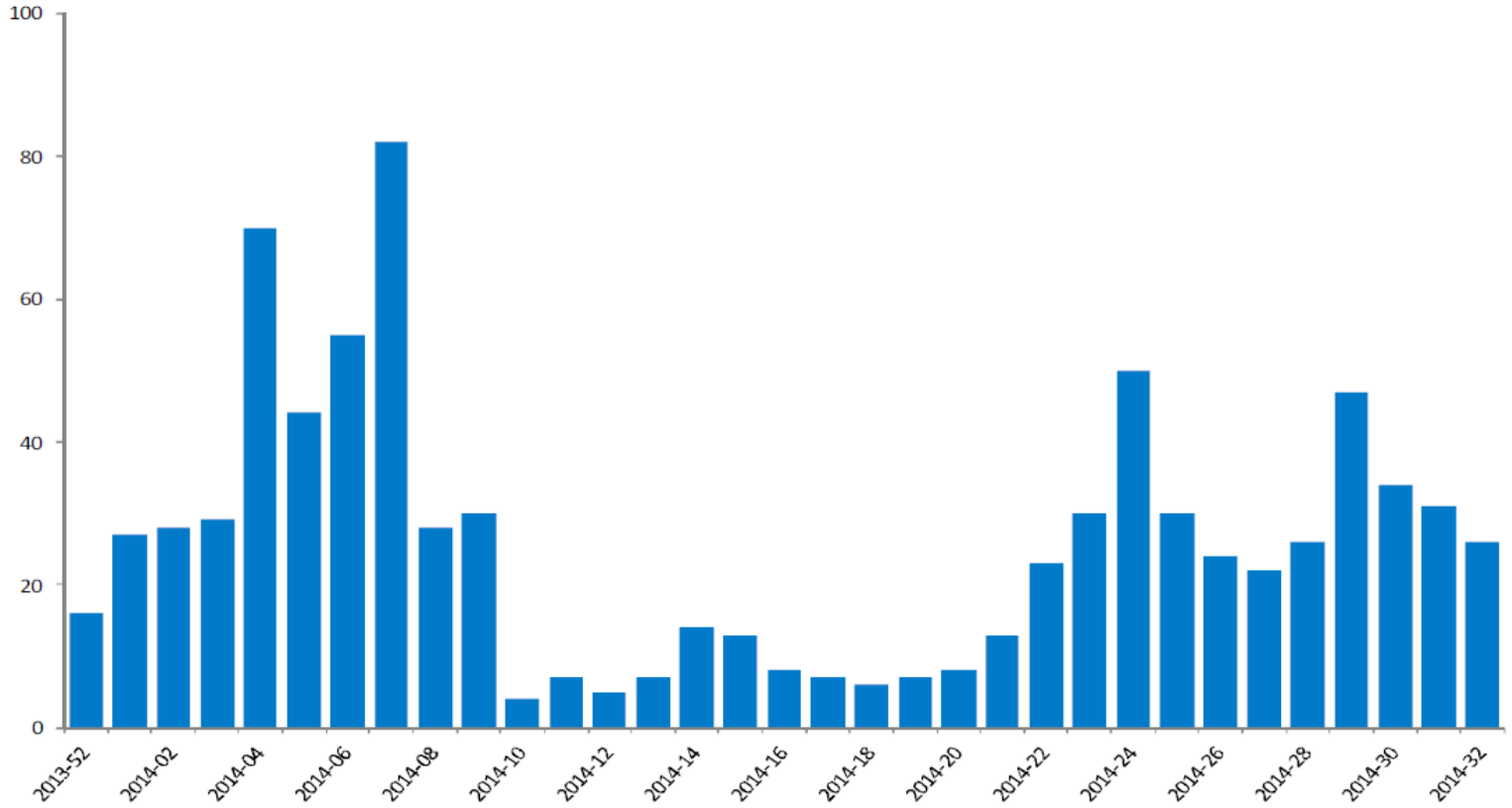
✓ Saint Martin island 2013-48 to 2014-32:



Data from French Institute for Public Health surveillance, French Caribbean and French Guyana antenna 2014, week 2014-32

III. Epidemiological Surveillance

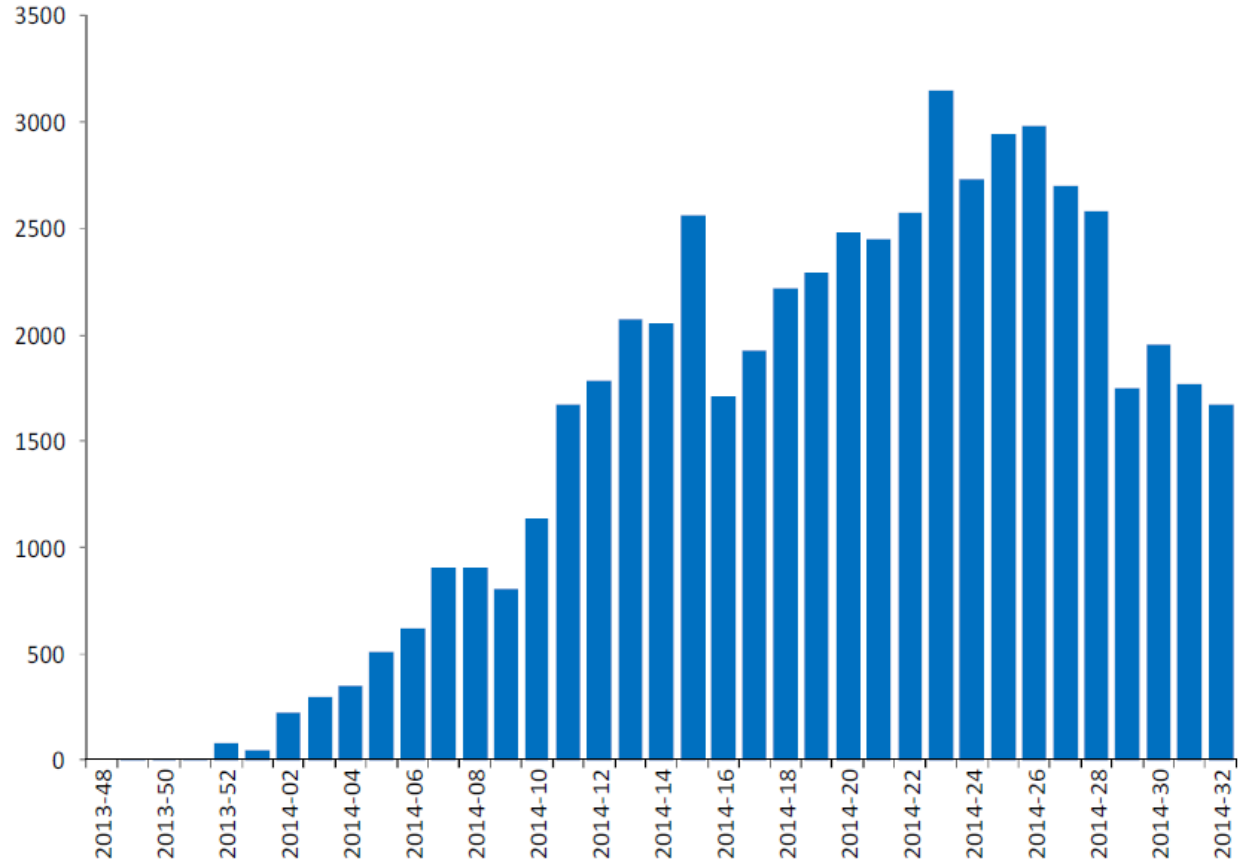
✓ Saint Barthelemy island 2013-48 to 2014-32



Data from French Institute for Public Health surveillance, French Caribbean and French Guyana antenna 2014, week 2014-32

III. Epidemiological Surveillance

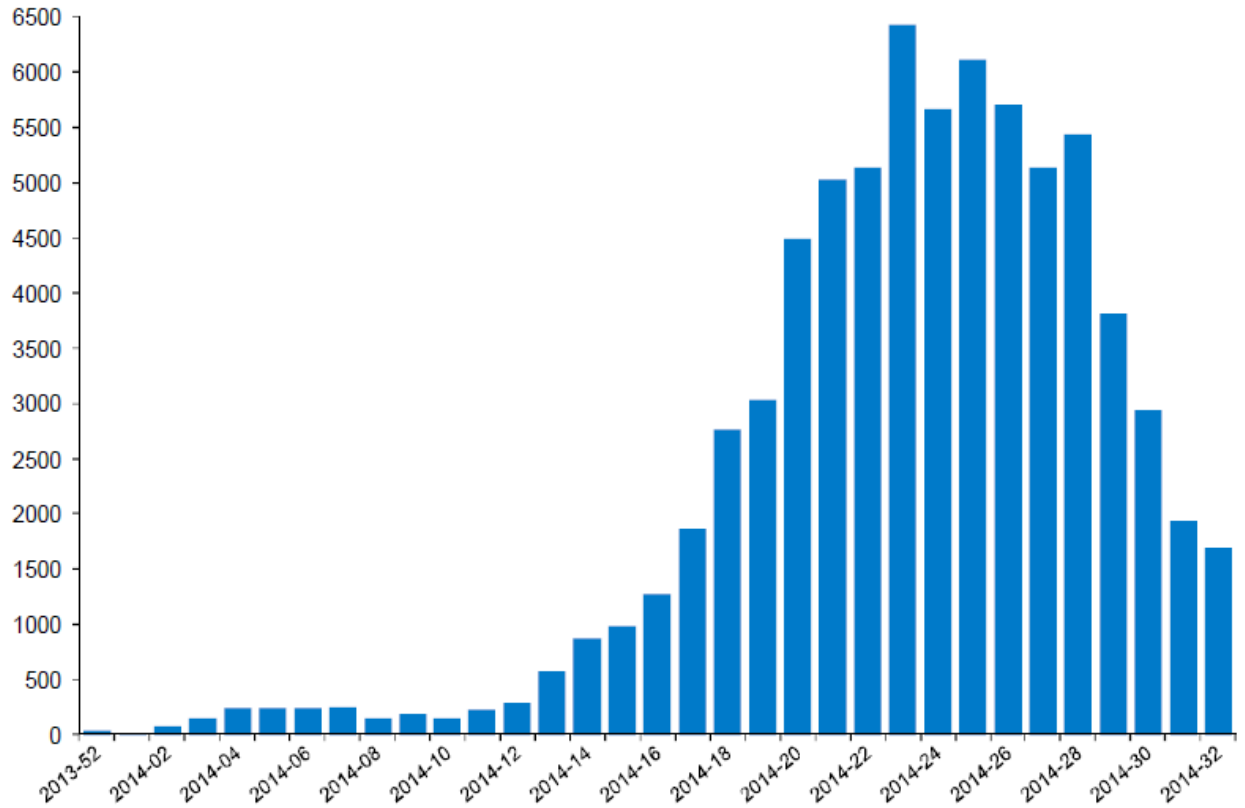
✓ Martinique island 2013-48 to 2014-32



Data from French Institute for Public Health surveillance, French Caribbean and French Guyana antenna 2014, week 2014-32

III. Epidemiological Surveillance

✓ Guadeloupe island 2013-48 to 2014-32



Data from French Institute for Public Health surveillance, French Caribbean and French Guyana antenna 2014, week 2014-32

III. Epidemiological Surveillance

7 autochthonous cases in Florida

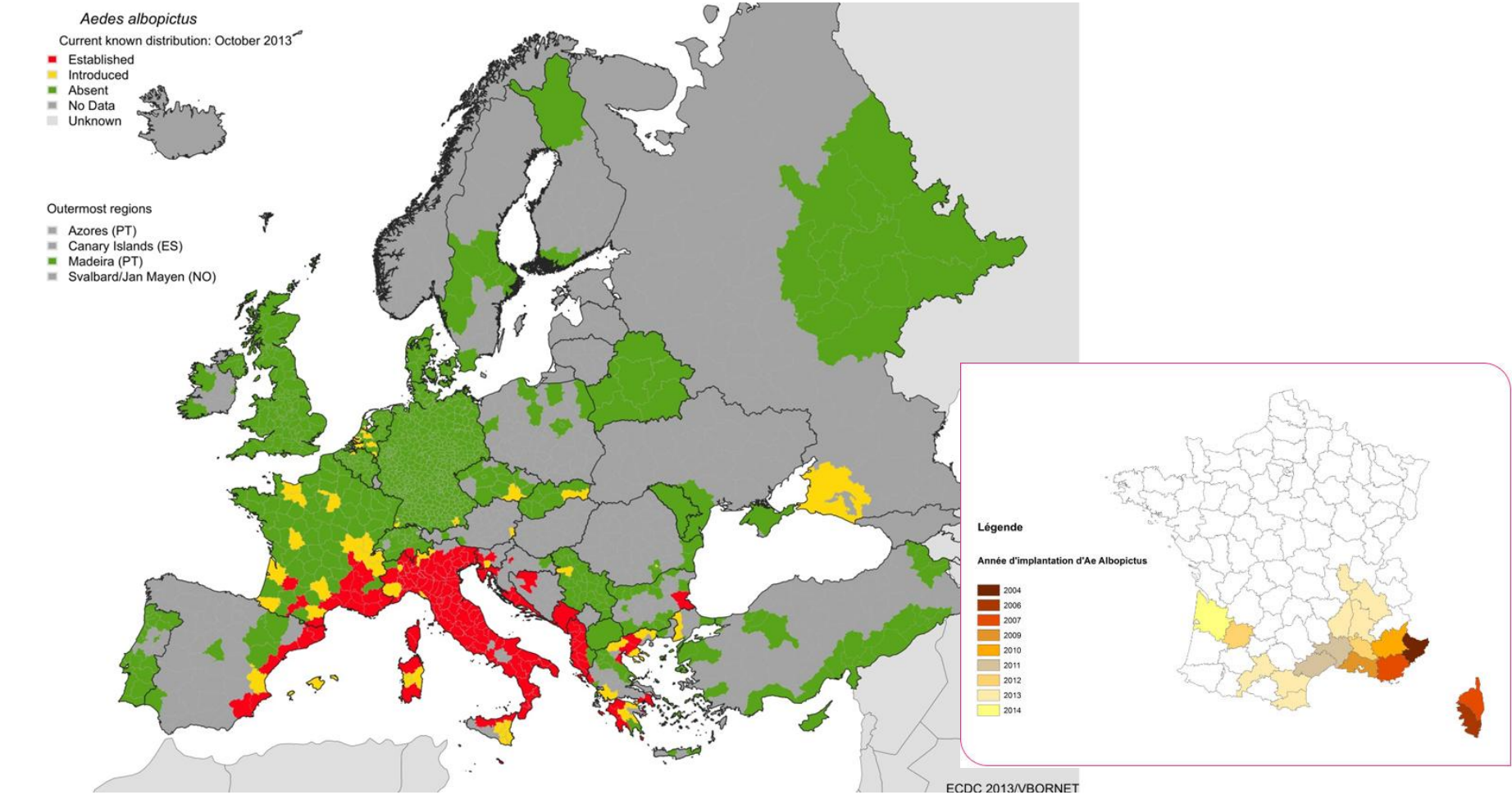
Data from Center for Disease Control 02 September 2014

Emerging arboviruses

I. Chikungunya virus
II. Alert
III. Epidemiological surveillance
IV. Risks for Europe
V. French National anti-dissemination plan
VI. Diagnostic: strategy and evaluation of kits

IV. Risks for Europe

Mosquito *Aedes Albopictus* in Europe



From European Center for Disease Control 2013

IV. Risks for Europe

- ✓ Italy 2007: 197 cases from only 1 index imported case from India
- ✓ France, Fréjus 2010: 2 cases from only 1 index imported case from India
- ✓ Intense human population exchange between french caribbeans and metropolitan France

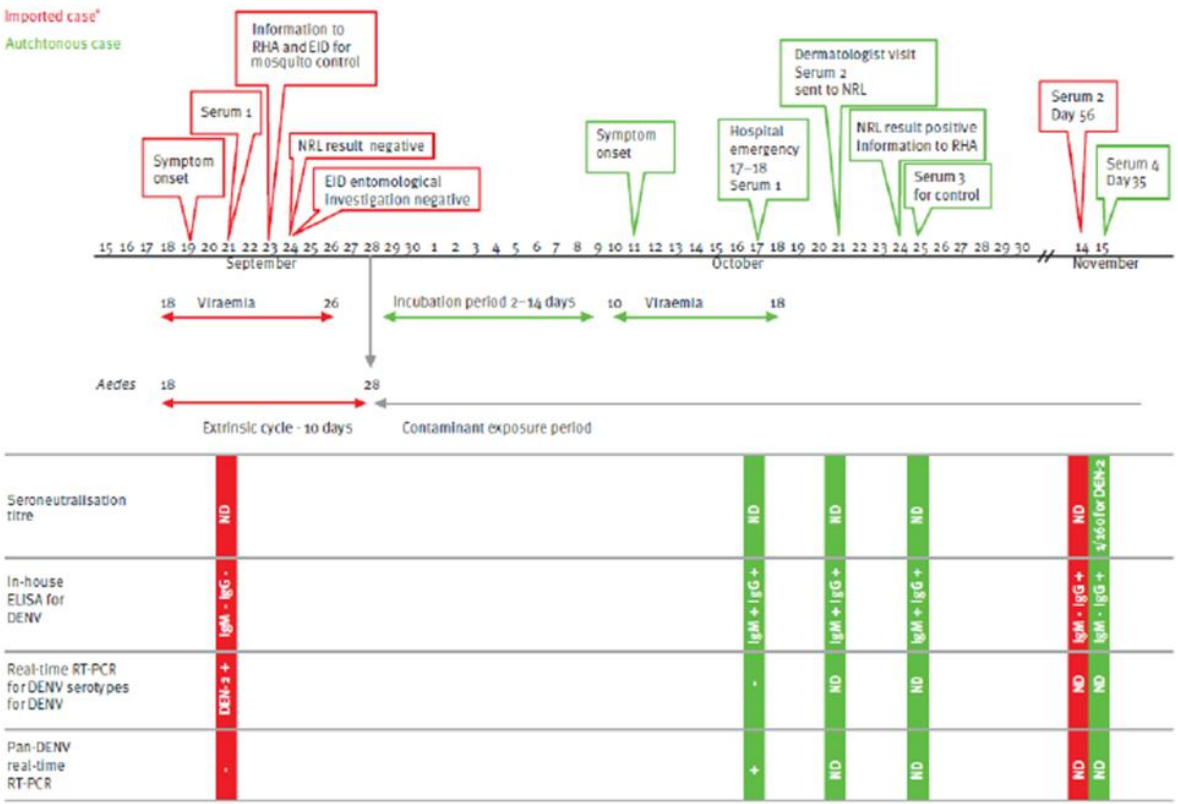
⇨ Very strong emerging risk in the EU for 2014 mosquito season
(329 imported Chikungunya cases so far in metropolitan France, in departments where *Aedes Albopictus* is present and active)

IV. Risks for Europe

✓ Authochtonous Dengue case 2013, Jouques, Bouches-du-Rhône

FIGURE 1

Timeline of epidemiological features and laboratory results of sera from autochthonous and imported case of dengue, Bouches-du-Rhône, France, September–November 2013



From Marchand et al. 2013, Eurosurveillance

IV. Risks for Europe

✓ Authochtonous Dengue case 2014, Toulon, Var:

- Onset of symptoms: 05/08/2014

- First blood sample 07/08/2014: RT-PCR positive for dengue 1

- Second blood sample 20/08/2014: IgM positive dengue

- Next Generation Sequencing: Dengue 1 genotype V, South America origin

Emerging arboviruses

I. Chikungunya virus
II. Alert
III. Epidemiological surveillance
IV. Risks for Europe
V. French National anti-dissemination plan
VI. Diagnostic: strategy and evaluation of kits

VI. French national anti-dissemination plan

Ministry of Health, Instruction N°DGS/RI1/2014/136 , 29th Avril 2014

In all French departments where *Aedes Albopictus* is active:

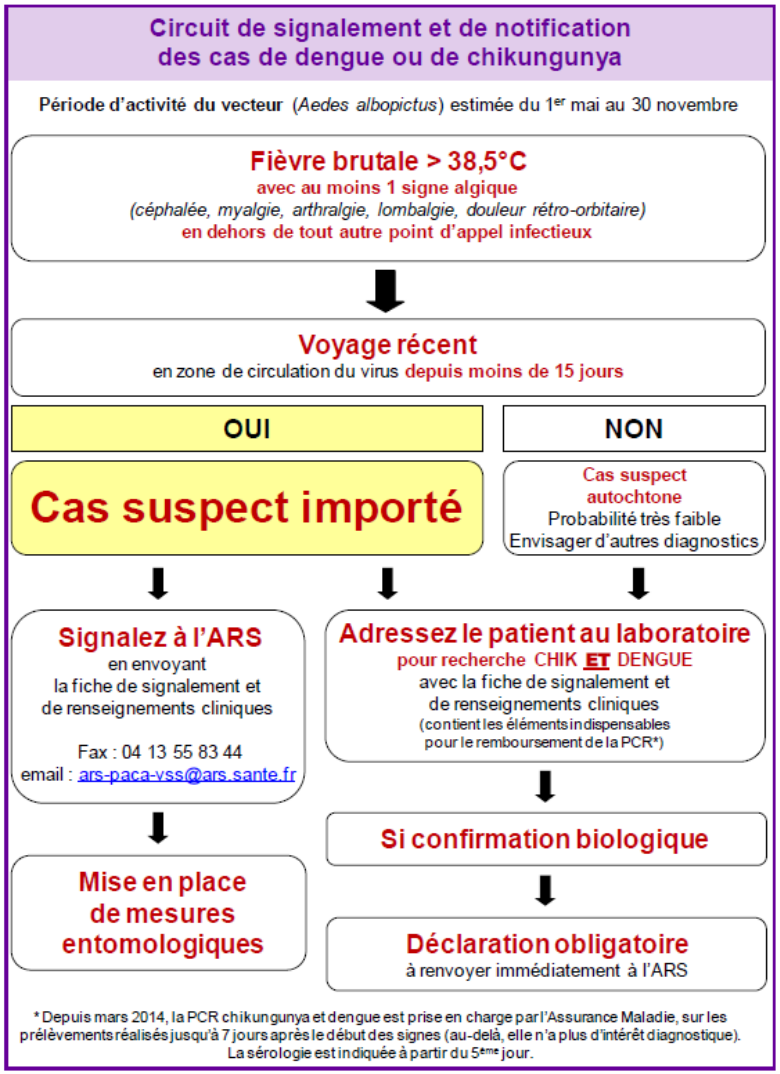
- Reporting of imported suspect cases to local public health authorities
- Diagnostic by front line laboratories

AND

- In parallel, epidemiological investigation (anti-vector control measures if necessary)
- In certain cases, confirmation or investigation by French National Reference Center

Important number of suspect cases

VI. French national anti-dissemination plan

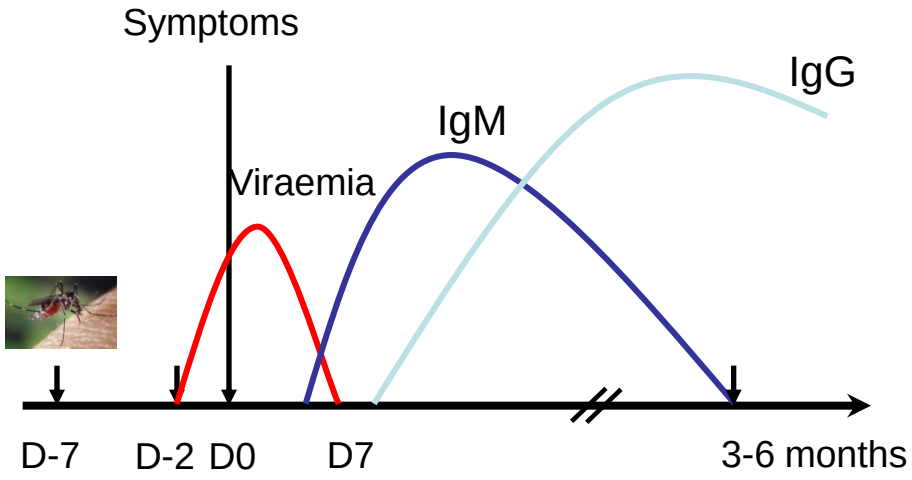


Emerging arboviruses

I. Chikungunya virus
II. Alert
III. Epidemiological surveillance
IV. Risks for Europe
V. French National anti-dissemination plan
VI. Diagnostic: strategy and evaluation of kits

V. Evaluation of diagnostic kits

✓ Diagnostic strategy:



≤ 7 days : viral genome detection by RT PCR (+ viral isolation)
≥ 5 days: Serology techniques, IgM and IgG detection

V. Evaluation of diagnostic kits

✓ Evaluation of RT-PCR kits for chikungunya

- RealStar® Chikungunya:

  Sensitivity: equivalent to our in house RT-PCR

  Specificity: detection of O'nyong-nyong

- Bioevolution® Chikungunya:

  Sensitivity: 1 log less than our in house RT-PCR

  Specificity: not done considering the bad sensitivity results

V. Evaluation of diagnostic kits

✓ Rapid Detection Tests for Chikungunya serology:

- Commercial test SD Bioline IgM Chikungunya:

Sensitivity	30% (3/10)	57% false positives (4/7)
Specificity	71% (10/14)	39% false négativess (7/18)
Overall agreement	52% (13/25)	

- Commercial test CTK Biotech IgM Chikungunya:

Sensitivity	20% (2/10)	33% false positives (1/3)
Specificity	93% (14/15)	36% false négativess (8/22)
Overall agreement	64% (16/25)	

⇒ Not usable

From Prat et al. 2014, Emerging Infectious Disease

V. Evaluation of diagnostic kits

✓ <u>ELISA IgM and IgG Chikungunya:</u>

- Commercial test IBL IgM and IgG ELISA:

IgM			IgG		
Sensitivity	79% (22/28)	12% false positive	Sensitivity	52% (14/27)	7% false positive
Specificity	88% (22/25)	21% false negative	Specificity	96% (25/26)	34% false negative

- Commercial test EuroImmun IgM and IgG ELISA:

	IgM		IgG	
Sensitivity	85%	18% false positives	88%	5% false positives
Specificity	82%	15% false négatives	95%	12% false négatives

From Prat et al. 2014, Emerging Infectious Disease

Conclusion

In metropolitan France, doctors and biologists need to be aware of emerging arboviruses (Dengue, Chikungunya, Zika…).

Clinical information, such as date of onset of symptoms and travel history is critical for a good diagnostic.

Network

French Public Health Institute (InVS, CIRE)

Regional Health Agency

Network of French medical biology laboratories (hospital and private)

Research Unit « Virus Emergents » X. De Lamballerie

EFS

<u>National Reference Center for Arboviruses (IRBA):</u>

Dr Isabelle Leparc-Goffart, Dr Olivier Flusin, Dr Christine Prat

Dr Riyadh Omarjee, Dr Raafat Fares

Patrick Gravier, Laetitia Boubis, Bernard Tenebray, Olivier Merle