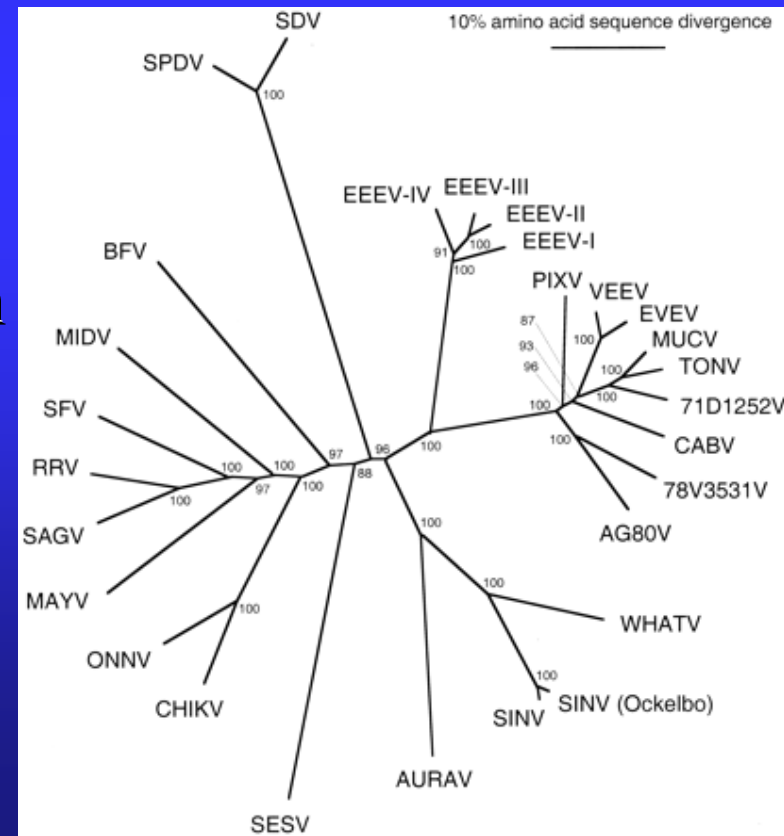
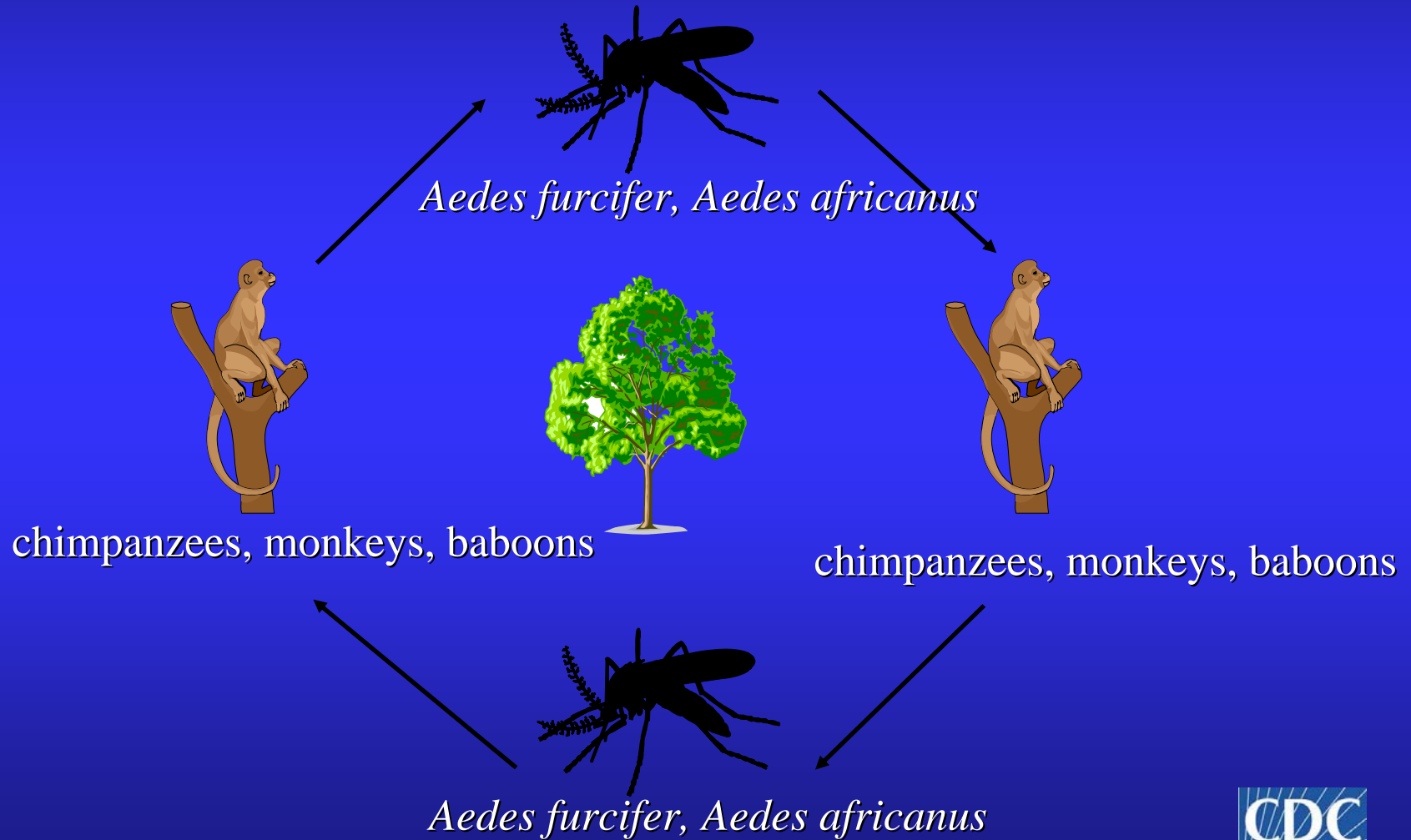


Chikungunya Virus

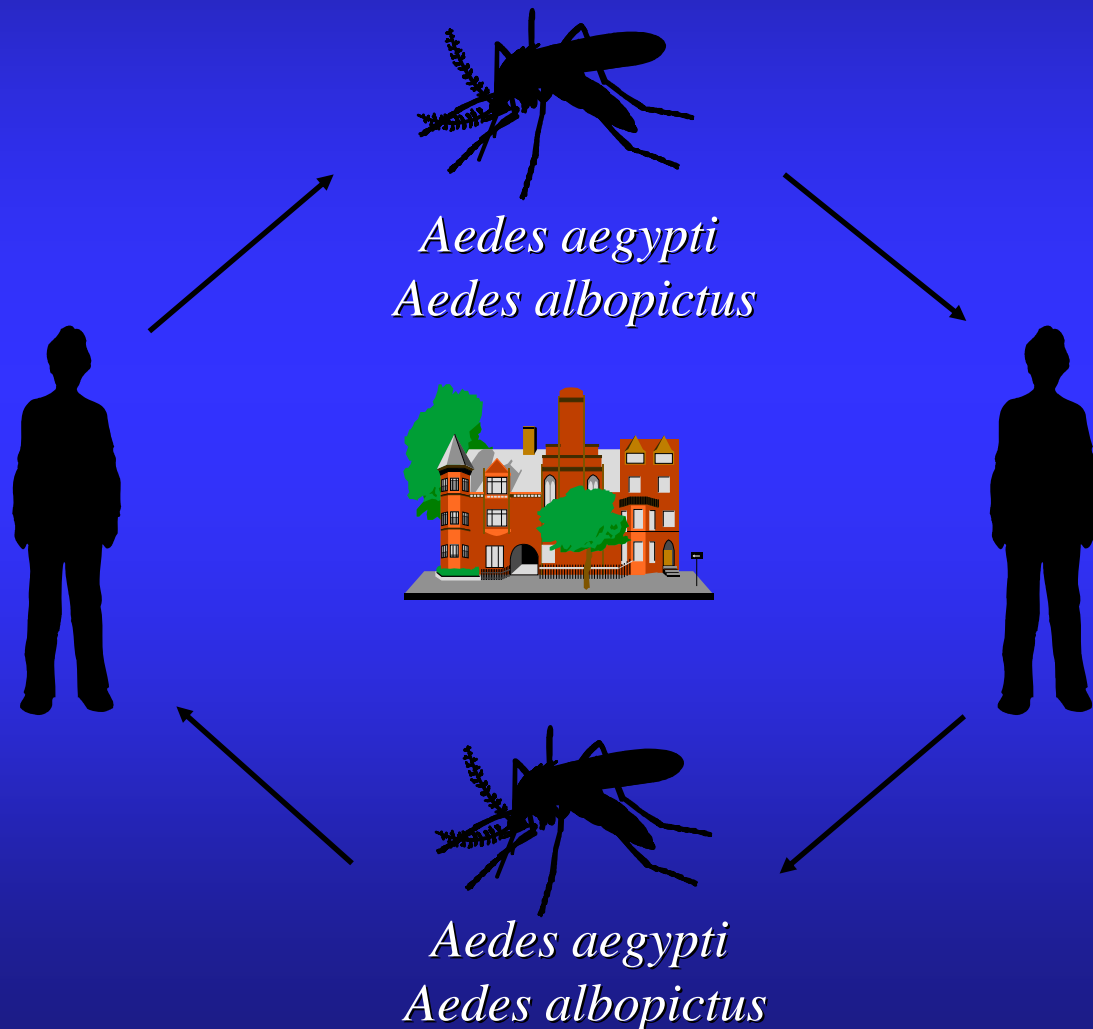
- ◆ Family *Togaviridae*, genus *Alphavirus*
 - ◆ Enveloped, single stranded RNA virus
 - ◆ Plus-sense, unsegmented genome of 11.5-11.8 kilobases
- ◆ First isolated from human serum during outbreak in Tanganyika - 1953
- ◆ Distinct biological and transmission patterns between African and Asian strains
- ◆ Classical clinical presentation
 - ◆ Fever
 - ◆ Severe joint pain
 - ◆ Rash (maculopapular)



Sylvatic CHIK Transmission Cycle



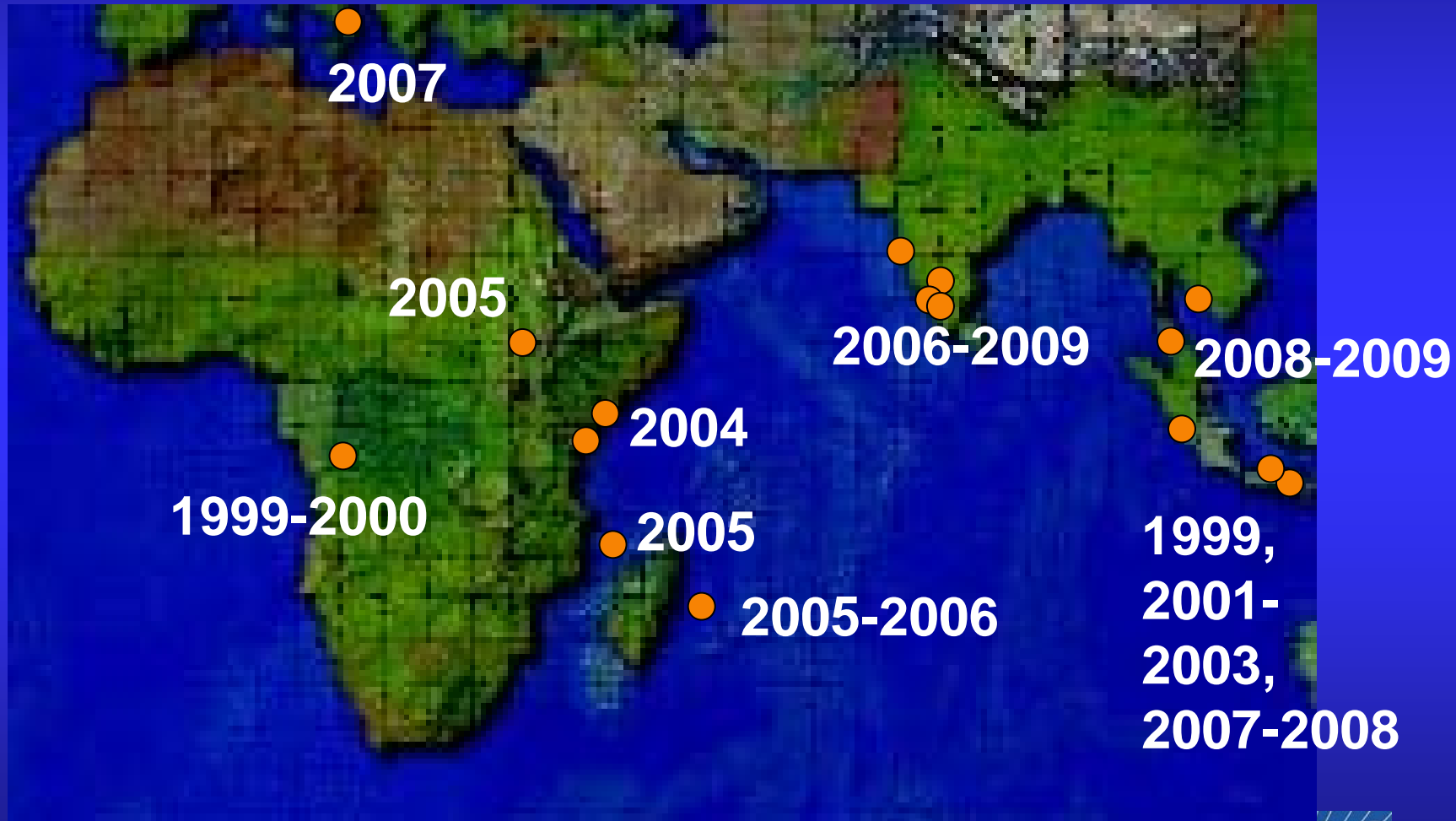
Urban CHIK Transmission Cycle



Distribution of CHIKV – prior to 1999



Recent Outbreaks of CHIKV

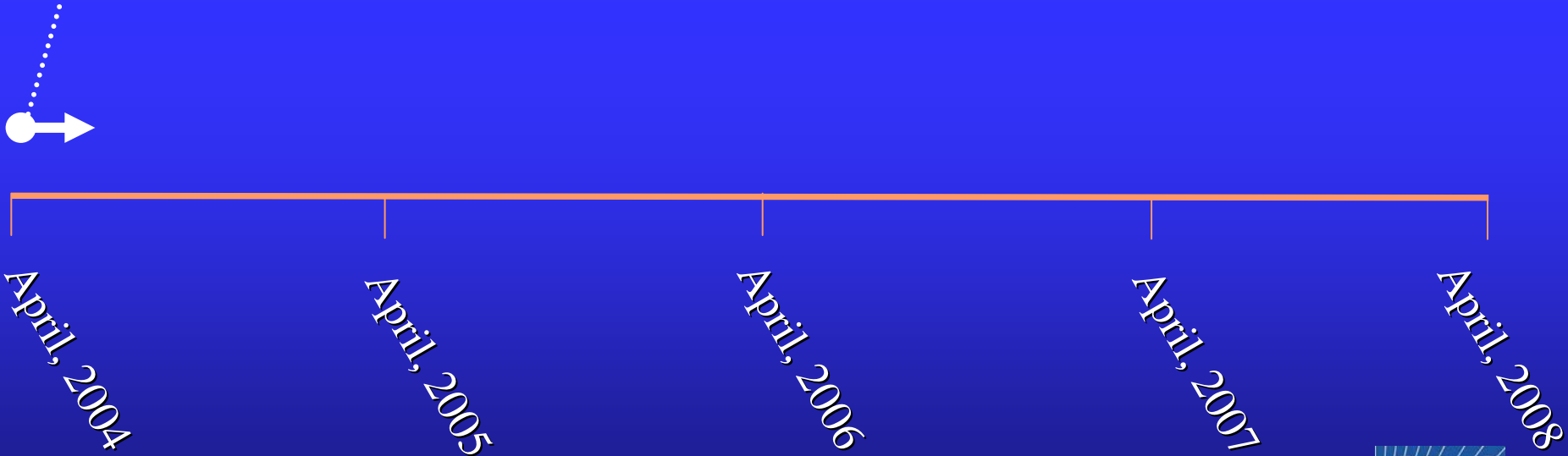


Re-emergence of CHIKV: 2004-2006

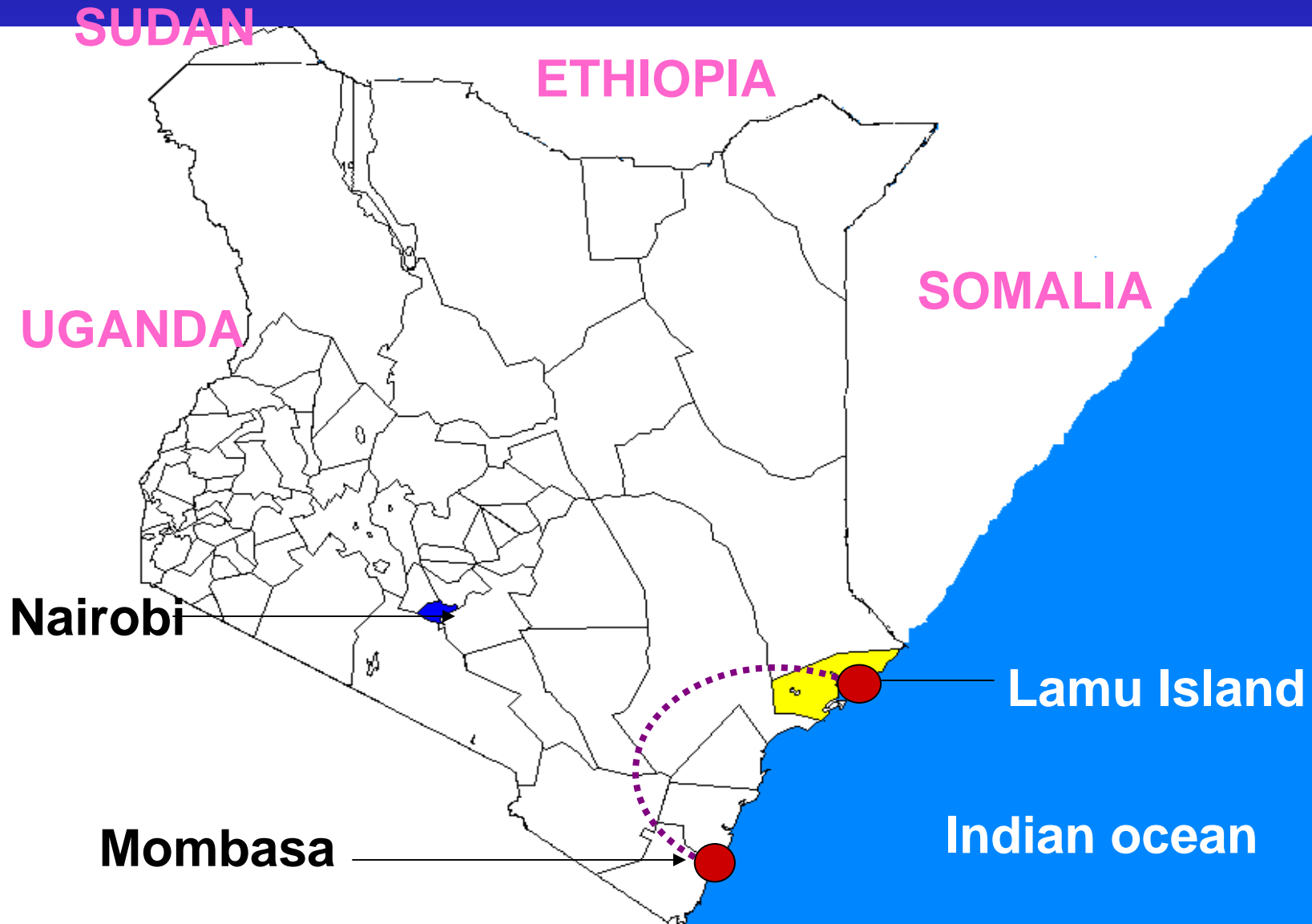


Timeline

First cases identified in East Africa



Kenya



Lamu Island Outbreak

- ✦ July 2004, unusual increase of “malaria” cases
- ✦ Severity of joint pains unusual
- ✦ 91% blood smears negative for Malaria
- ✦ Out of 10 sera, IgM Ab to CHIK detected in 3 sera



Early Findings

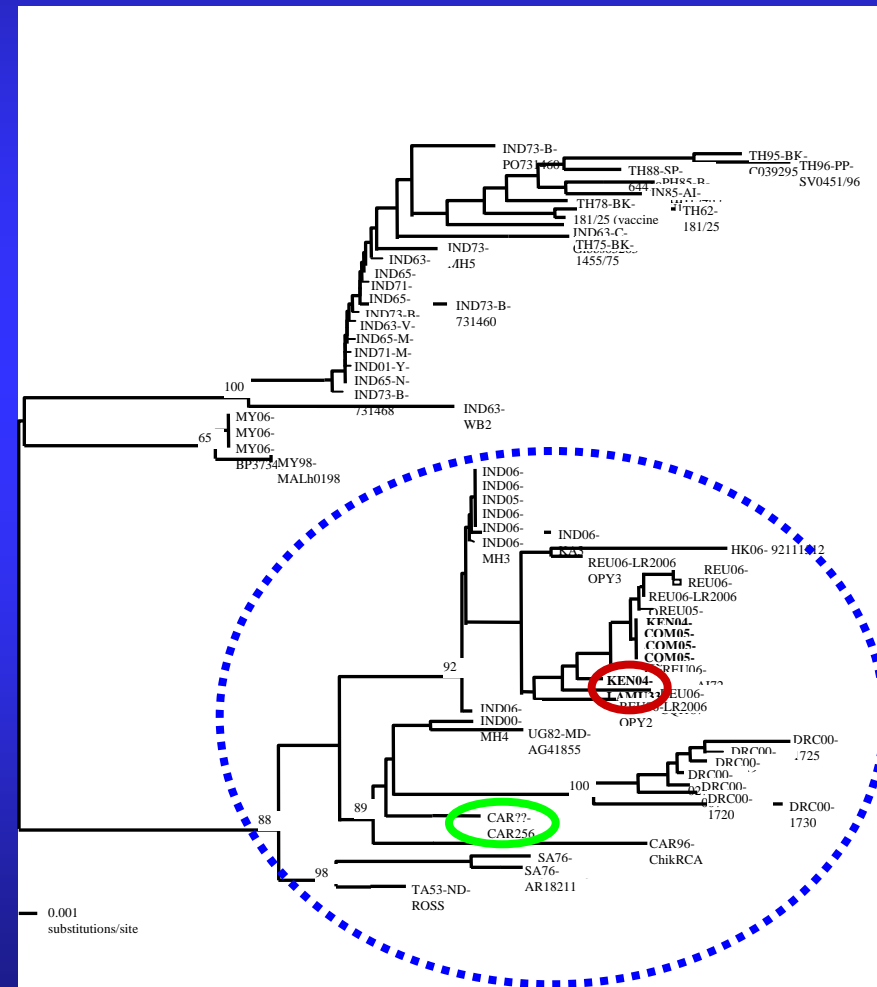
- ◆ At least 1300 suspected cases counted
- ◆ IgM ELISAs negative for Dengue, Yellow Fever, West Nile, RVF, and Sindbis
- ◆ CHIK infection diagnosis by
 - ◆ IgM ELISA (60 cases)
 - ◆ Virus isolation (22 cases)
- ◆ CHIK confirmed by genomic sequencing
- ◆ No deaths reported

Magnitude of Outbreak

- ◆ The attack rate was 75%.
- ◆ 13,500 persons (95% CI 12,458-14328) infected.
(Lamu population=18,000)
- ◆ 86% of cases hospitalized/ stayed home in bed for a mean of 7 days (range 1-90).

Nature of Virus

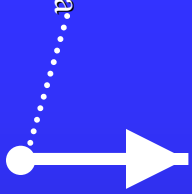
- ◆ Central / East African genotype
- ◆ Less than 3% divergent at nucleotide level from closest historical relative



Timeline

Virus moves to Comoros

First cases identified in East Africa



April, 2004

April, 2005

April, 2006

April, 2007

April, 2008

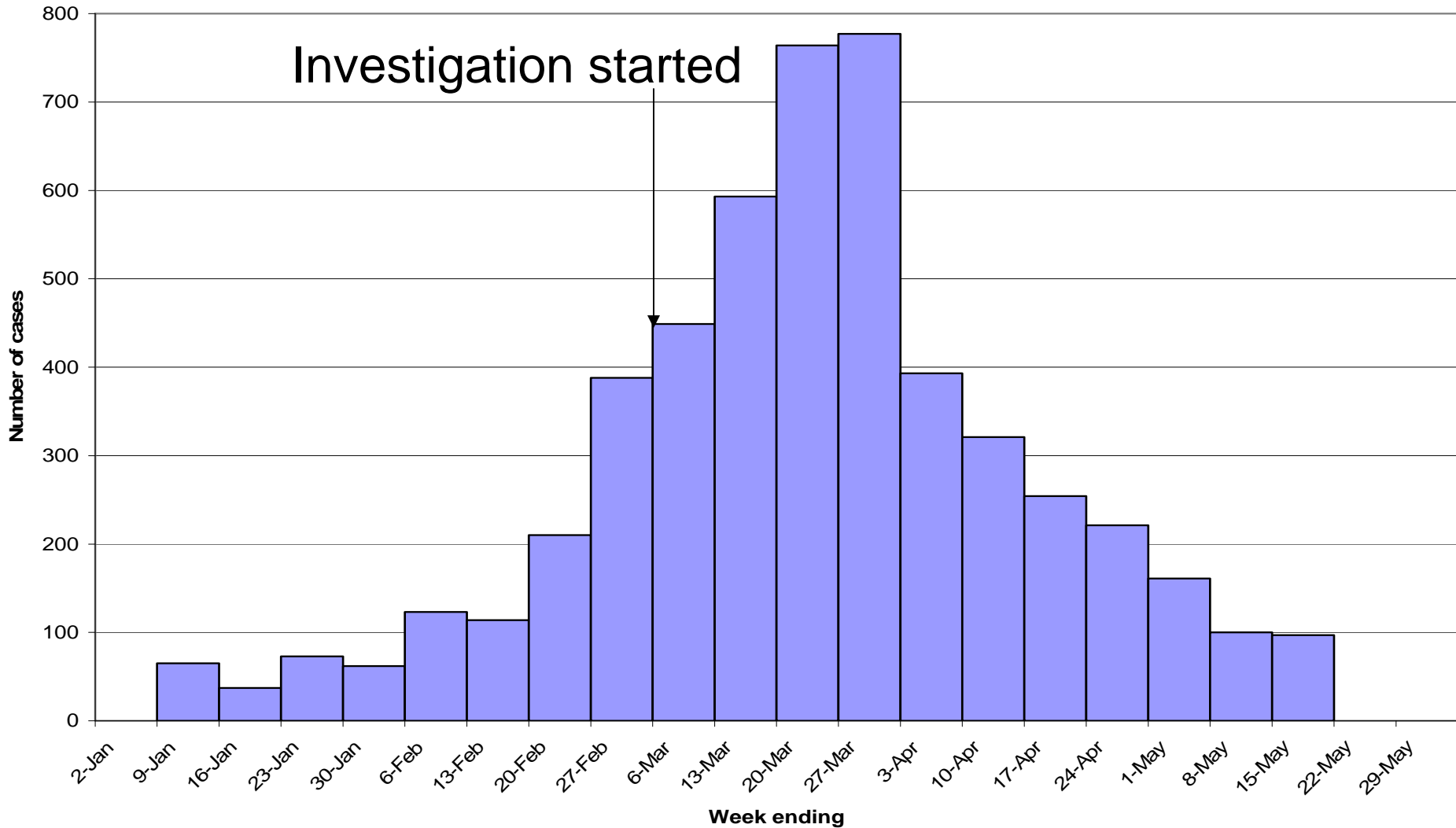
Comoros Island Outbreak



Comoros Island Outbreak

- ◆ Suspected Dengue outbreak reported in February 2005.
- ◆ 25 Sera analyzed
 - ◆ All negative for Dengue
 - ◆ 9 positive for IgM CHIK Antibodies
 - ◆ 6 positive for CHIK by PCR

Epidemic curve



Antibody Testing Results

(N=331)

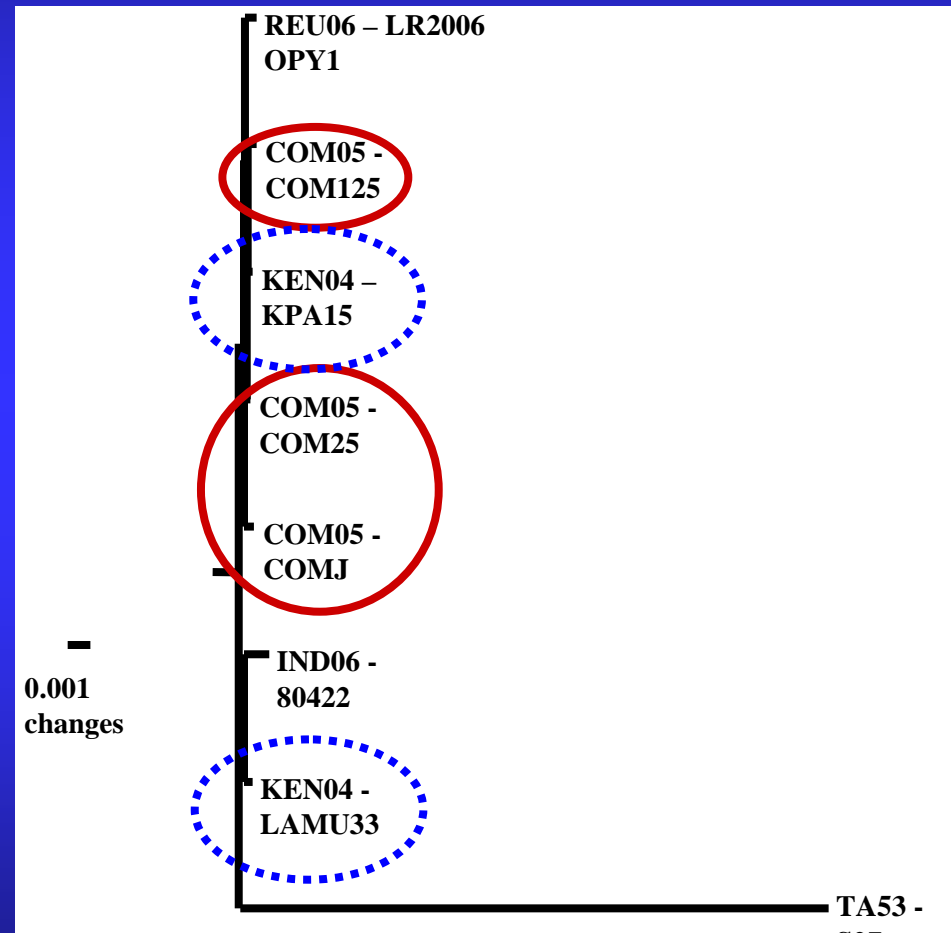
| | IgG | IgM | IgG or IgM |
|----------|-----------|-----------|------------|
| Positive | 89 (27%) | 198 (60%) | 209 (63%) |
| Negative | 242 (73%) | 133 (40%) | 122 (37%) |

Magnitude of Outbreak

- ✦ Attack rate of infection was 63%
- ✦ 214,830 persons (95% CI 196,757-233,244 persons) infected on Island.
- ✦ 79% of cases hospitalized/ stayed at home in bed, mean = 6 days (range 1-30 days)

Nature of Virus

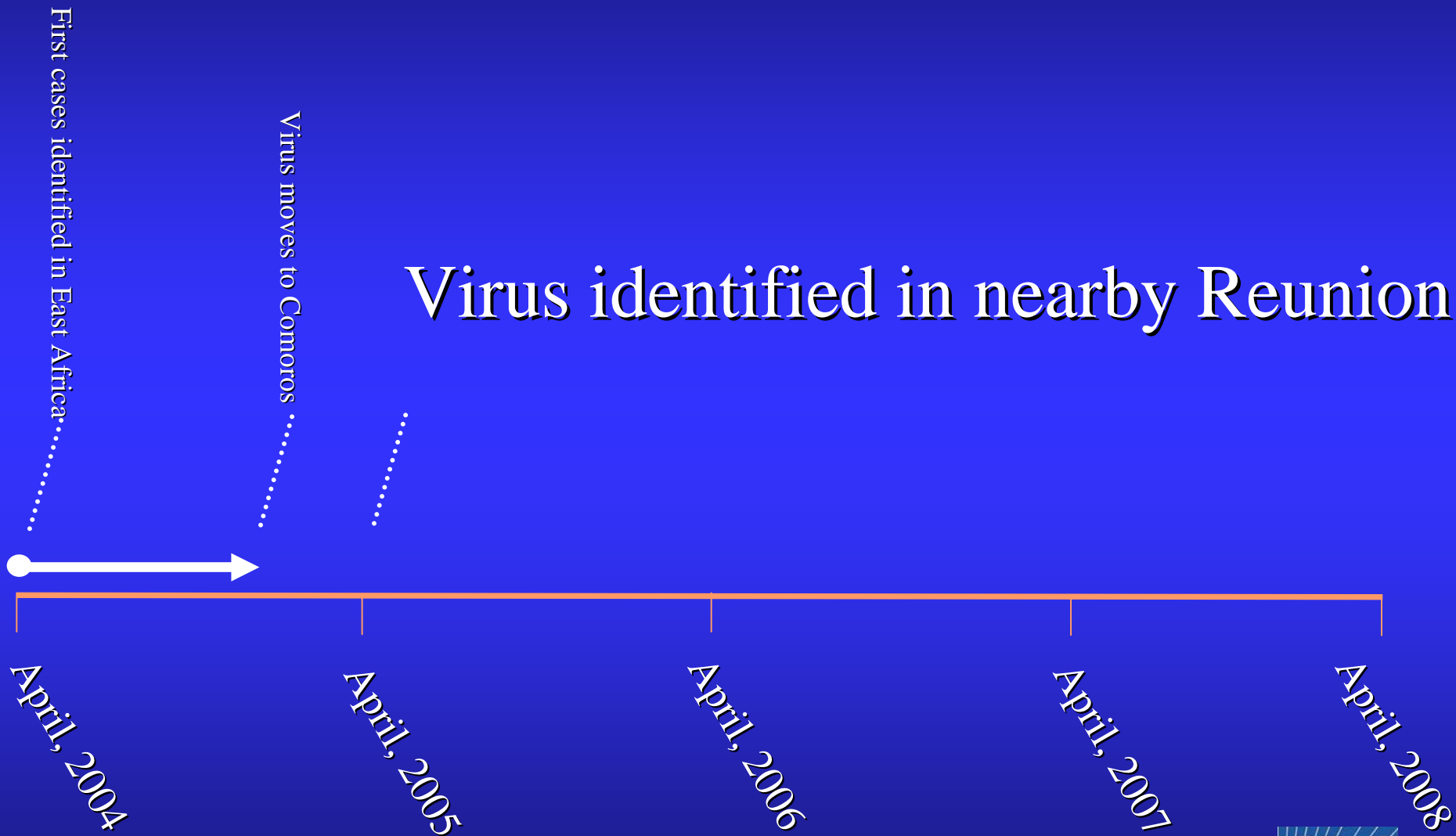
- ◆ Central / East African genotype
- ◆ Virtually identical to isolates from Mombasa and Lamu



| Species | Method | Sex | Number | pools | + Pools | MIR |
|--------------------|--------------------|--------|------------|-----------|---------------|-------------|
| <i>A.aegypti</i> | Asp | Male | 60 | 8 | 0 | - |
| <i>A. aegypti</i> | Asp | Female | 65 | 11 | 2 | 30.8 |
| <i>A. aegypti</i> | HLC | Male | 392 | 34 | 0 | - |
| <i>A. aegypti</i> | HLC | Female | 944 | 81 | 2 (1*) | 2.1 |
| <i>A. simpsoni</i> | HLC | Female | 65 | 6 | 0 | - |
| <i>A. bromeli</i> | HLC | Female | 10 | 1 | 0 | - |
| <i>A. vittatus</i> | Asp | Female | 1 | 1 | 0 | - |
| <i>A. simpsoni</i> | HLC | Female | 41 | 3 | 0 | - |
| <i>Aedes. sp</i> | Asp | Female | 42 | 4 | 2 | 47.6 |
| | | | | | | |
| <i>Culex</i> | HLC | Female | 74 | 5 | 0 | - |
| <i>Culex</i> | Asp | Female | 354 | 16 | 1 | 2.8 |
| <i>Culex</i> | Asp/ HLC | Males | 189 | 9 | 0 | - |
| | | | | | | |
| | | | | | | |

Timeline

Virus identified in nearby Reunion

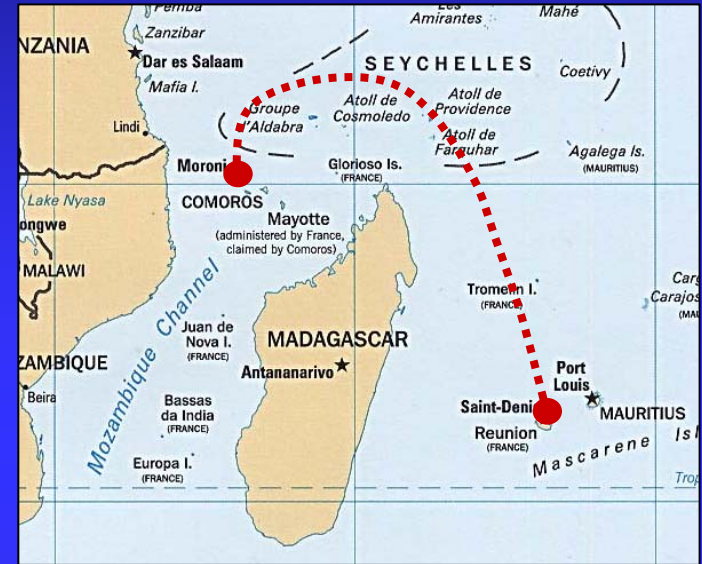


La Reunion Outbreak

✦ First cases: March 2005

✦ Major increase in cases during summer rainy season (mid-December – April, 2006)

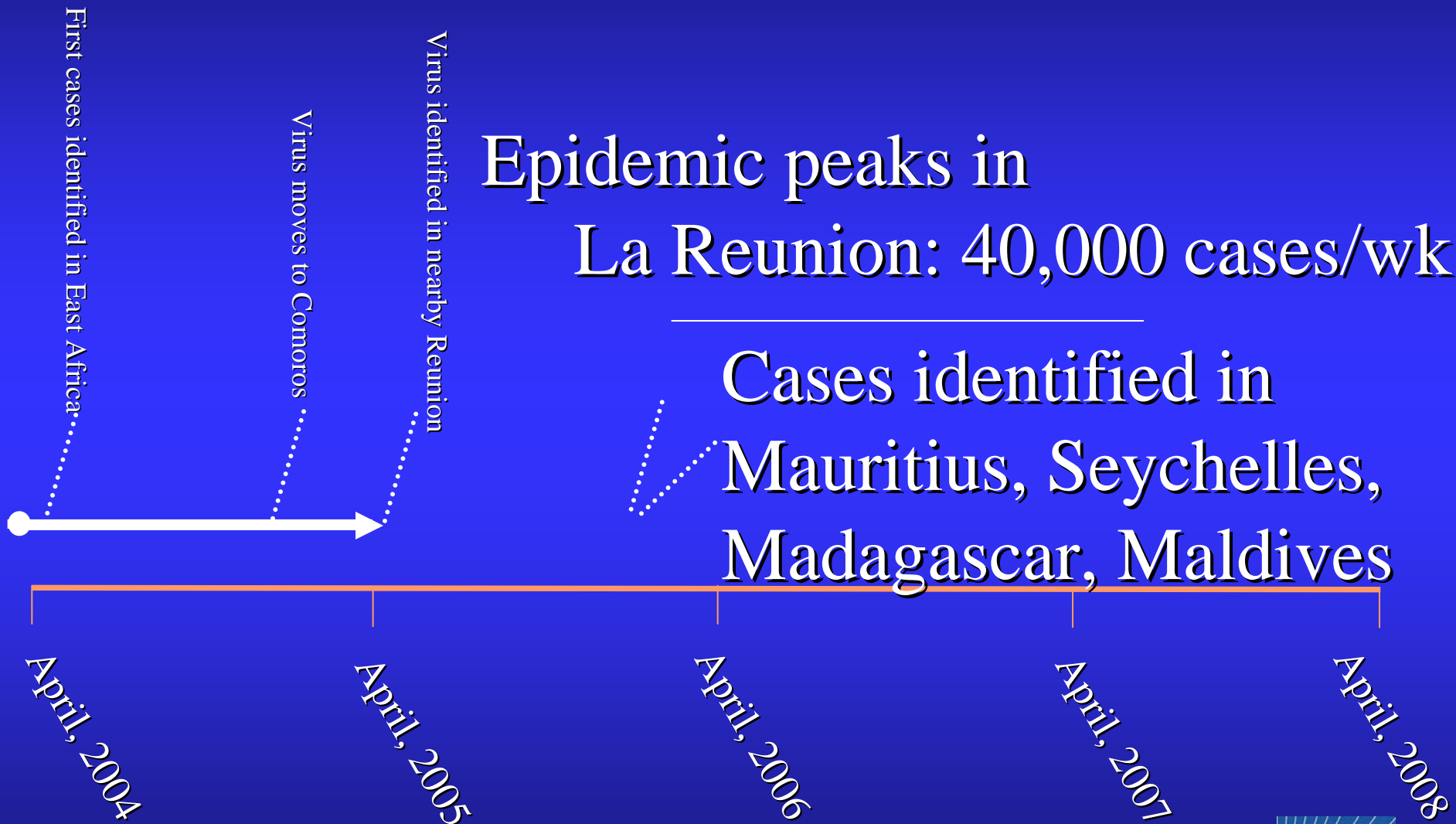
✦ Total number of cases estimated at 244,000



Timeline

Epidemic peaks in
La Reunion: 40,000 cases/wk

Cases identified in
Mauritius, Seychelles,
Madagascar, Maldives



La Reunion – changing patterns?

- ✦ New, “virulent” genotype?
- ✦ Neurological involvement
- ✦ Intrauterine transmission (?) /neonatal disease
- ✦ CHIKV-associated deaths (underlying conditions)
- ✦ Transmission by alternate vector (?)

Possible increase in virulence?

| | | | | | | |
|----|---------|------------|-------------------------------|-------|-----------|-----------------------------------|
| 13 | Réunion | ? | ? | S | 25-May-05 | Classical |
| 14 | Réunion | North | Ste Clotilde | S | 25-May-05 | Classical |
| 15 | Réunion | North | Ste Clotilde | S | 27-May-05 | Classical |
| 16 | Réunion | North | Ste Clotilde | S | 28-May-05 | Classical |
| 17 | Réunion | South-West | Les Aviron | S | 4-June-05 | Classical |
| 18 | Réunion | South | La Rivière St Louis | S | 7-June-05 | Classical |
| 19 | Réunion | South | La Rivière St Louis | S | 7-June-05 | Classical |
| 20 | Réunion | South | St Louis | serum | 7-Sept-05 | Neonatal encephalopathy |
| 21 | Réunion | South | La Rivière St Louis | S | 11-Oct-05 | Classical |
| 22 | Réunion | South | St Louis | S | 21-Oct-05 | Classical |
| 23 | Réunion | South | La Rivière St Louis | S | 21-Oct-05 | Classical |
| 24 | Réunion | South | La Rivière St Louis | P | 26-Oct-05 | Classical |
| 25 | Réunion | South | St Joseph | P | 9-Nov-05 | Classical |
| 26 | Réunion | South | La Rivière St Louis | P | 10-Nov-05 | Classical |
| 27 | Réunion | South | St Louis | P | 20-Nov-05 | Classical |
| 28 | Réunion | South | La Rivière St Louis | P | 21-Nov-05 | Classical |
| 29 | Réunion | South | La Rivière St Louis | S | 23-Nov-05 | Classical |
| 30 | Réunion | South | La Rivière St Louis (parents) | S | 28-Nov-05 | Neonatal encephalopathy |
| 31 | Réunion | South | St Joseph | S | 23-Nov-05 | Classical |
| 32 | Réunion | South | La Rivière St Louis | P | 24-Nov-05 | Classical |
| 33 | Réunion | South | Le Tampon | P | 26-Nov-05 | Classical |
| 34 | Réunion | South | Ravine des Cabris | P | 25-Nov-05 | Classical |
| 35 | Réunion | South | St Joseph (parents) | S | 29-Nov-05 | Neonatal encephalopathy |
| 35 | Réunion | South | St Joseph (parents) | CSF | 29-Nov-05 | Neonatal encephalopathy |
| 36 | Réunion | South | St Louis | S | 2-Dec-05 | Classical |
| 37 | Réunion | South | St Louis | P | 8-Dec-05 | Classical |
| 38 | Réunion | South | Ravine des Cabris | S | 9-Dec-05 | Meningo-encephalitis |
| 39 | Réunion | South | St Louis | P | 13-Dec-05 | Classical |
| 40 | Réunion | South | La Rivière St Louis | P | 27-Dec-05 | Classical |
| 41 | Réunion | South | St Pierre | P | 27-Dec-05 | Severe vesicular rash lower limbs |

Aedes albopictus as a vector of CHIKV

OPEN ACCESS Freely available online

PLoS one

Two Chikungunya Isolates from the Outbreak of La Reunion (Indian Ocean) Exhibit Different Patterns of Infection in the Mosquito, *Aedes albopictus*

Marie Vazeille¹, Sara Moutailler², Daniel Coudrier², Claudine Rousseaux³, Huot Khun⁴, Michel Huerre⁴, Julien Thiria⁵, Jean-Sébastien Dehecq⁵, Didier Fontenille⁶, Isabelle Schuffenecker⁷, Philippe Despres⁸, Anna-Bella Failloux^{2*}

OPEN ACCESS Freely available online

PLoS PATHOGENS

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

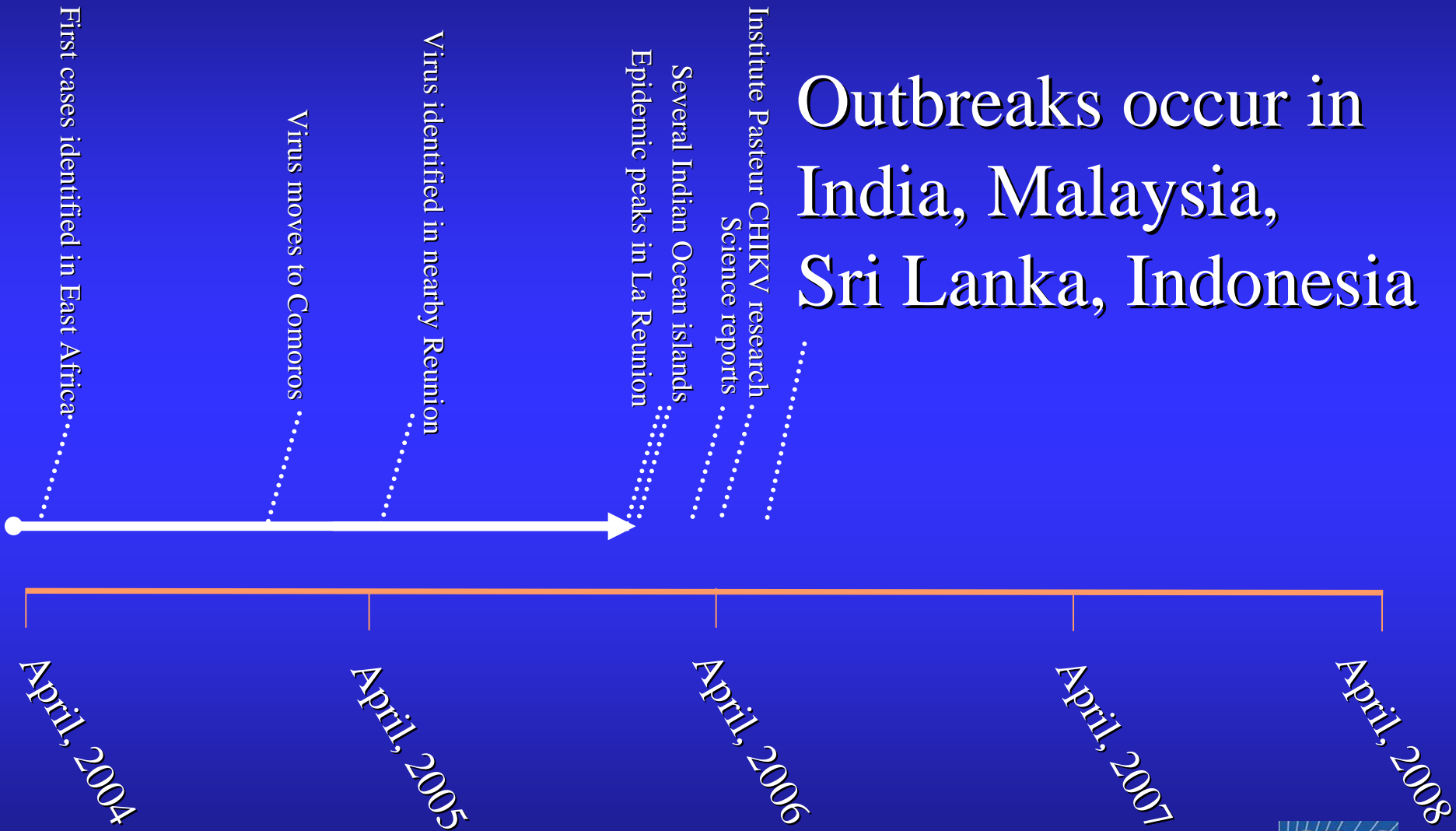
Konstantin A. Tsetsarkin, Dana L. Vanlandingham, Charles E. McGee, Stephen Higgs*



CONTROL AND PREVENTION

Timeline

Outbreaks occur in
India, Malaysia,
Sri Lanka, Indonesia



Movement to Asia



India outbreaks

- ✦ 13 states affected in 2005-2006 after 32 year interepidemic period
- ✦ Estimated 1.3 million cases
- ✦ Introduction of the Central/East African genotype into Asia



Imported Cases of CHIKV

- ◆ *Canada*
- ◆ *Hong Kong*
- ◆ *UK*
- ◆ *Belgium*
- ◆ *Czech Republic*
- ◆ *Germany*
- ◆ *Norway*
- ◆ *Switzerland*
- ◆ *Australia*
- ◆ *France*
- ◆ ***Italy***
- ◆ *Corsica*
- ◆ *Sri Lanka*
- ◆ *Singapore*
- ◆ *USA*
- ◆ *Spain*
- ◆ *Japan*
- ◆ *Taiwan*

Timeline

CHIKV in Italy

Outbreak resurges in India
A → V: albopictus

Outbreak explodes in India

Imported cases documented
Outbreaks occur in India,
Malaysia, Sri Lanka, Indonesia

Institute Pasteur CHIKV research
Science reports

Several Indian Ocean islands
Epidemic peaks in La Reunion

Virus identified in nearby Reunion

Virus moves to Comoros

First cases identified in East Africa

April, 2008

April, 2007

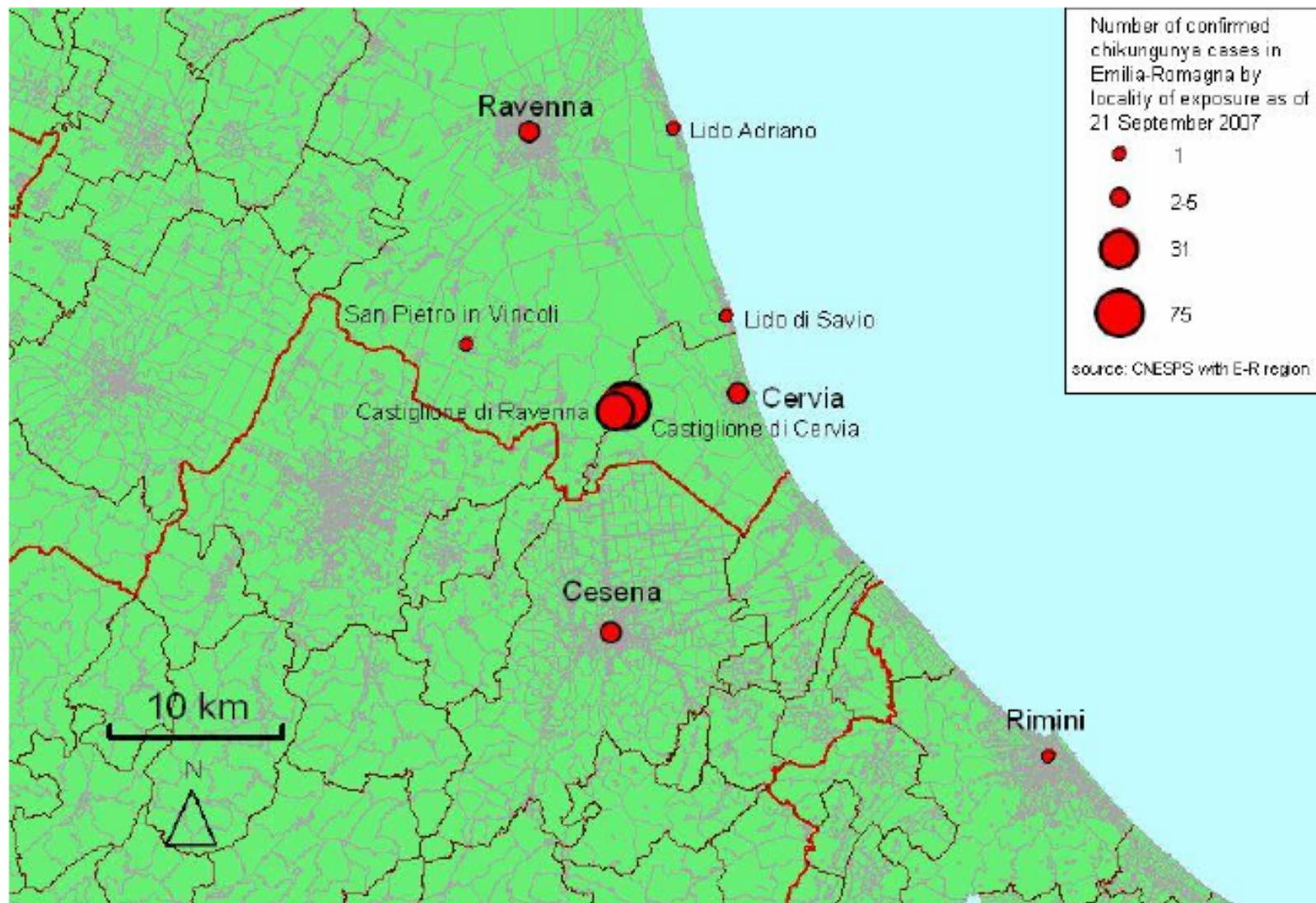
April, 2006

April, 2005

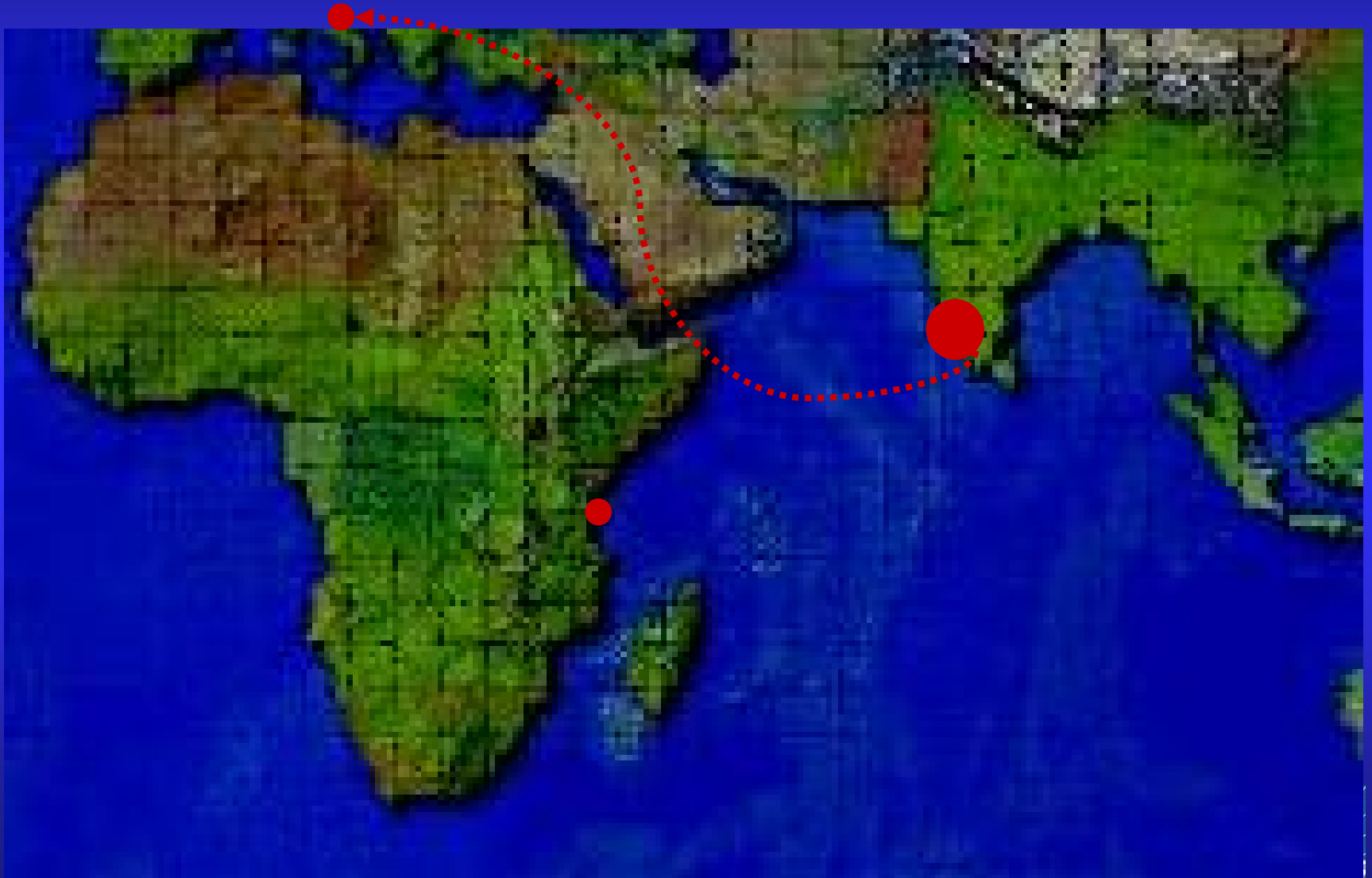
April, 2004



Confirmed cases of CHIKV in Italy



Movement to Italy



Italian Outbreaks

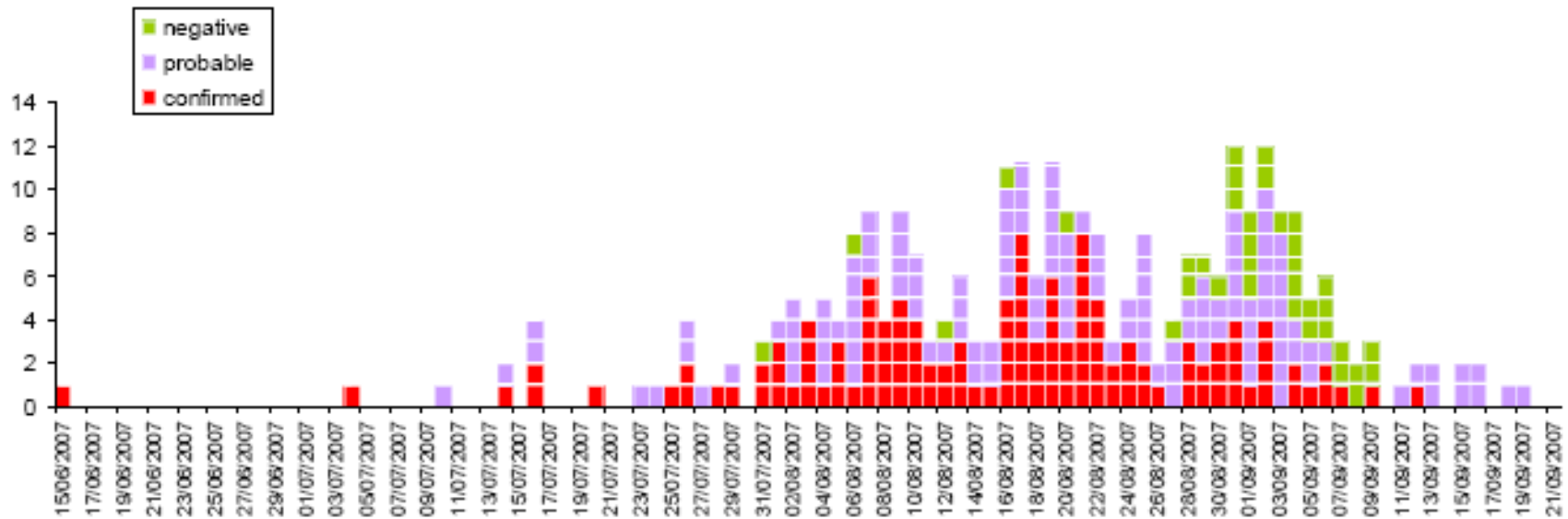
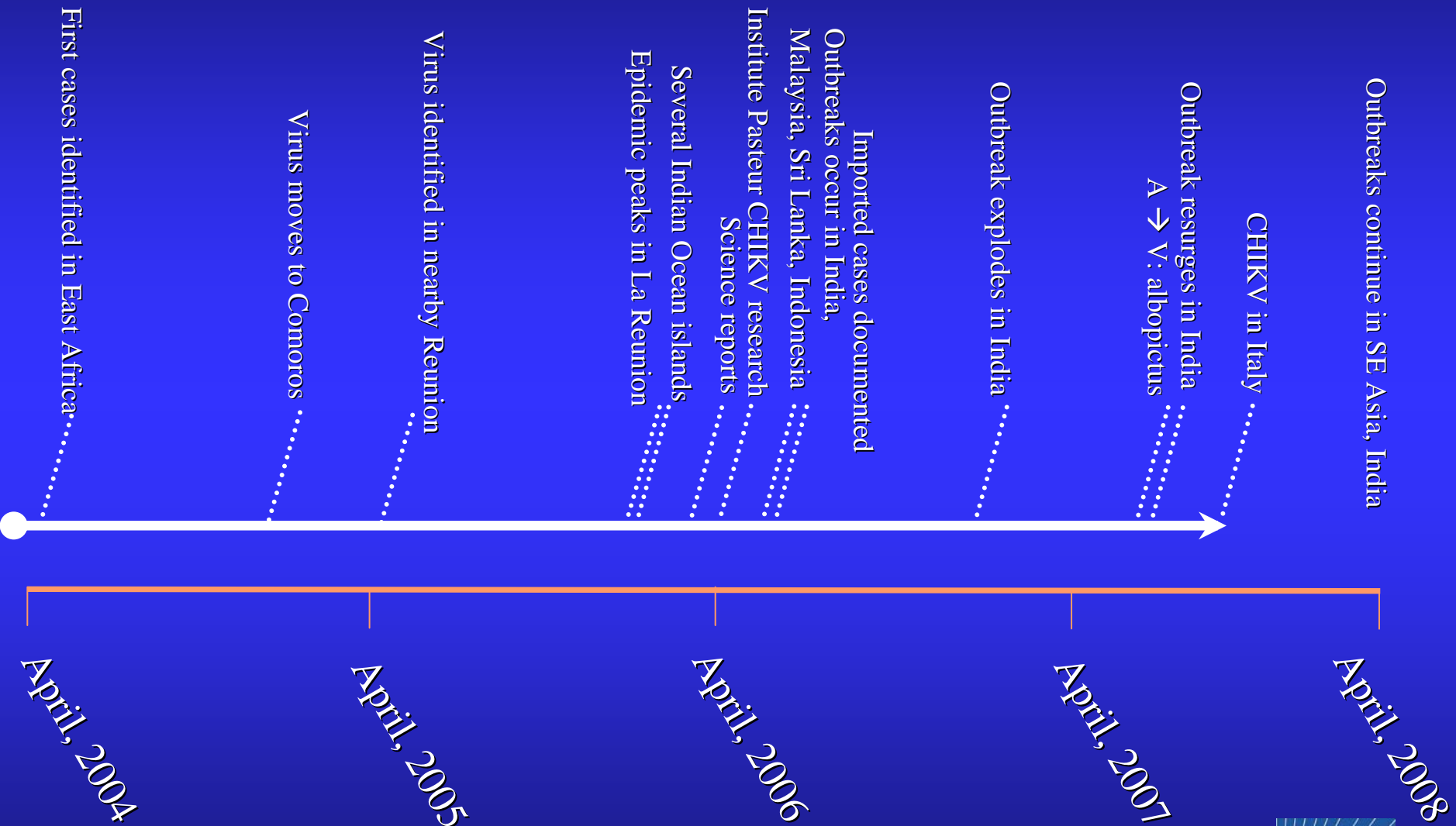


Figure 1. Distribution of suspected chikungunya fever cases by date of onset of symptoms, region of Emilia-Romagna, 15 June - 21 September 2007 (n = 292)

Timeline



Timeline

Outbreaks continue in SE Asia, India

Outbreaks continue in SE Asia, India

Continued & renewed activity in Thailand, India, Malaysia, La Reunion....

?????

April, 2008

April, 2009

April, 2010

April, 2011

Factors Affecting Emergence/Outbreaks

???

Factors Affecting Emergence/Outbreaks

- ◆ Environmental/ecological conditions
- ◆ Abundance of mosquito egg laying habitats
- ◆ Completely naïve pop
- ◆ Alternate vector(s), new ecological niches involved
- ◆ Viral genetics / mutations



Gracias!