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CHIKUNGUNYA
Emergence – Réémergence & Globalisation

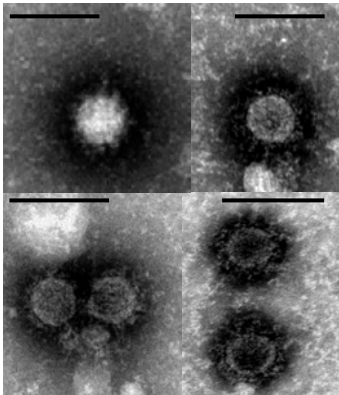
Dr Philippe PAROLA
 Faculté de Médecine de Marseille

DESC Pathologies Infectieuses et Tropicales
 Paris 7 janvier 2008





WHAT IS CHIKUNGUNYA VIRUS ?

genus *Alphavirus*
 family *Togaviridae*





1950s: Africa
 sylvatic cycle involving wild primates + forest dwelling *Aedes* spp. mosquitoes (similar to yellow fever virus).



1950's: Asia
 associated with the urban *Aedes aegypti* possibly supplemented by *A. albopictus*:

- absence of an animal reservoir
- direct H to H transmission by urban mosquito
- similar to dengue cycle


 Robinson MC. Trans R Soc Trop Med Hyg. 1955;49:28-32
 

« CHIKUNGUNYA »

a Makonde word meaning “**that which bends up**”:

a reference to the inability of some patients to walk upright

due to the **severe crippling pains in the acute stages**

Many patients remain in severe pain for months.

- Knowledge of its clinical features based on the descriptions of South African teams in the late 1970's:
+ brief fever +/- headache +/- myalgias +/- evanescent rash
- Long been considered as benign

Fourie & Morrison. S A Med J 1979;56:130-132

Brighton et al. S A Med J. 1983

Kennedy et al. J Rheumatol 1980;7:231-236



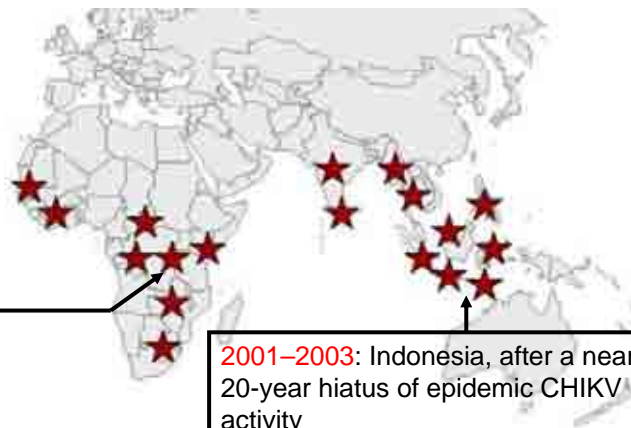
CHIKV SINCE 1950'S

potential for major epidemics
that re-emerge after an unpredictable period of silence

1999–2000:

Democratic Republic of the Congo, an estimated 50,000 persons infected

after 39 years without any isolation of the virus



2001–2003: Indonesia, after a near 20-year hiatus of epidemic CHIKV activity

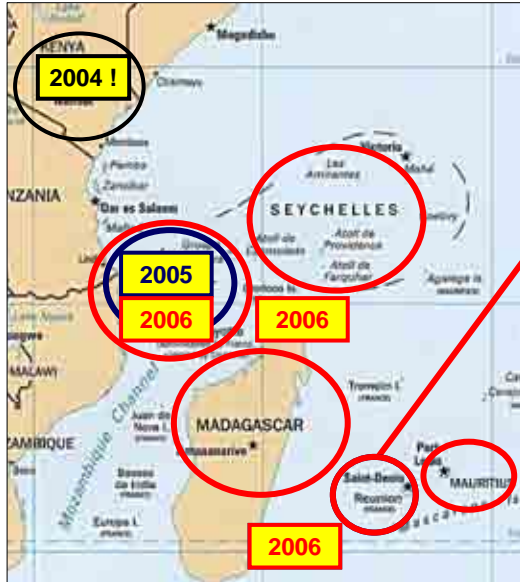


Pastorino et al. J Med Virol 2004;74:277-82

Laras K et al. Trans R Soc Trop Med Hyg 2005;99:128-141



2004-2006 : THE GIANT OUTBREAK !



September 18th, 2006:

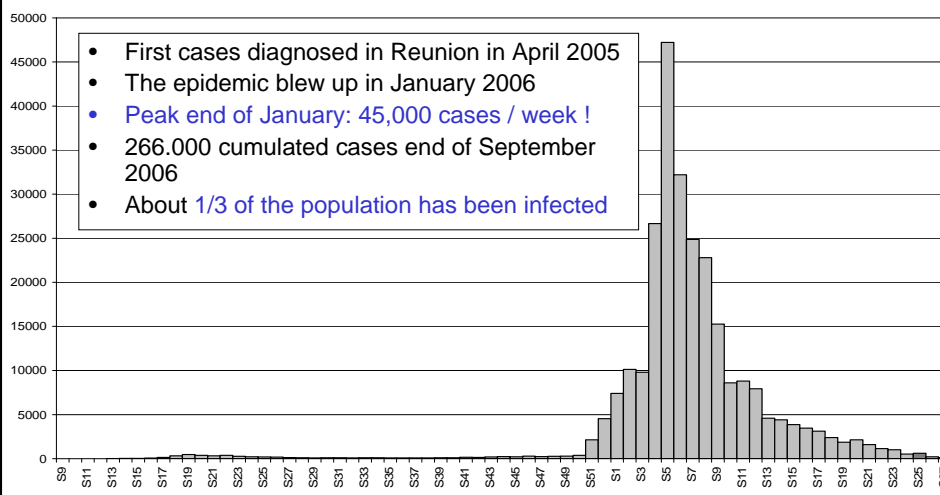
an estimate of 266,000 residents infected (population 770,000)

248 death certificates mentioning "CHIKV" as the possible cause of death !!!

Charrel et al. N Engl J Med 2007; 356:769-771



CHIKV IN REUNION ISLAND: Two epidemic waves but a single epidemic force



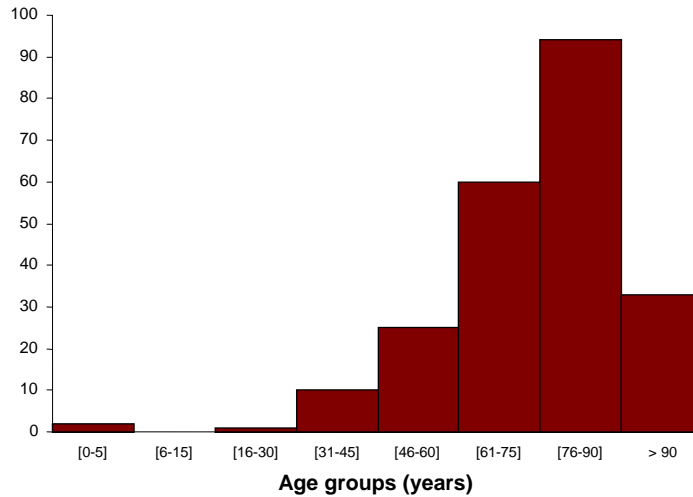
www.invs.sante.fr

Boelle & Flahault. Vect Born Zoon Dis 2007

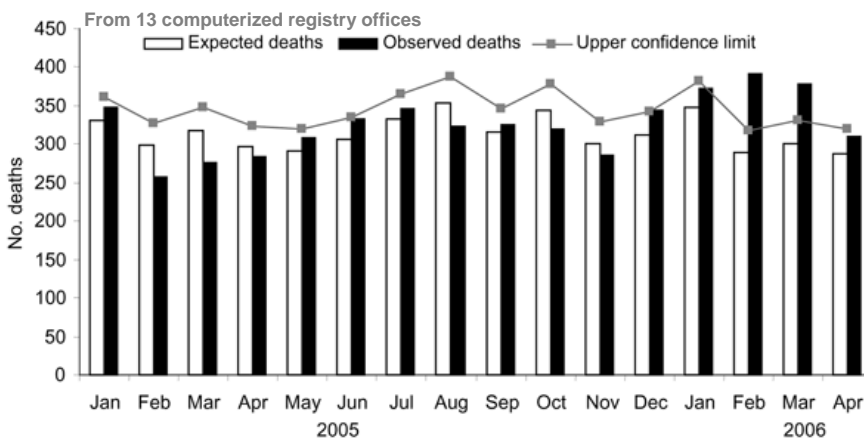


CHIKV IN REUNION ISLAND: 248 Death certificates mentioning « chikungunya »

Number of deaths



CHIKV IN REUNION ISLAND: crude death rate



likely responsible for most of the excess deaths observed during the first 4 months of 2006



Josseran et al. Emerg Infect Dis 2007 12:1994-1995



CHIKV IN REUNION ISLAND: Why a so devastating outbreak ?

Most likely : Invasion of a region

where the population is immunologically naive for CHIKV

+

Where a vector, *Aedes albopictus* is proliferating profusely.



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 Yazelle¹, Sara Moutailler², Daniel Coudrier³, Claudine Rousseaux⁴, Huot Khun⁵, Michel Huevre⁴, Julien Thiria⁴, Jean-Sébastien Dehecq⁴, Didier Fontenille⁶, Isabelle Schuffenecker⁷, Philippe Despres⁸, Anna-Bella Failoux^{2,1}

CHIK isolate	Date	Localisation	E1-226	E1-284
05.115	June 2005	La Réunion	Ala	Asp
06.21	Nov. 2005	La Réunion	Val	Asp
06.111	Feb. 2006	Mayotte	Val	Asp
06.117	1999-2000	RDC	Ala	Glu

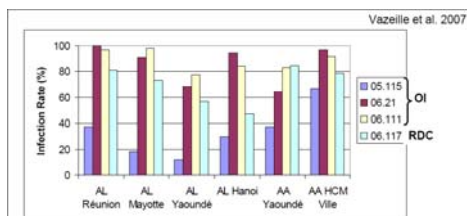
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A highly competent vector *Ae. albopictus* which allowed an efficient replication and dissemination of CHIKV 06.21 (collected in November 2005 with a substitution A226V).

Has this mutation been selected as more adapted to an alternative, abundant mosquito, *Ae. albopictus*?

Vertical transmission?
Ovaries are infected at day 6 after experimental infection consequences ?



THE VECTOR(S) IN INDIAN OCEAN



The Asian tiger mosquito *Aedes albopictus*: the implicated vector in Reunion

Comoros, Mauritius, Seychelles: *Aedes aegypti* ?



AEDES ALBOPICTUS

Breeding sites

Artificial



Natural

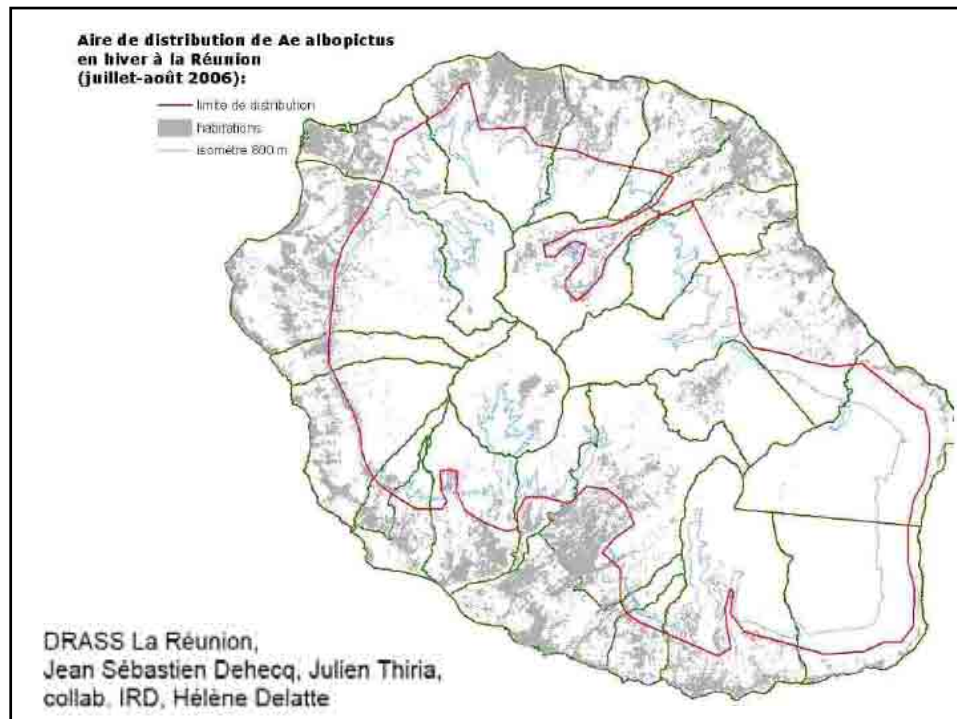


AEDES ALBOPICTUS

Breeding sites

Domestic





***Aedes albopictus* breeding sites on 9 localities of La Réunion (urban sites) in summer**

Containers	No positive/ No inspected	No positive/total No of positive breeding sites
Flower plates	226/1154 (20%)	226/513 (44%)
Small wastes (cans, plates, bags...)	99/296 (33%)	99/513 (19%)
Small containers (10-50L)	80/183 (44%)	80/513 (16%)
Used tires	49/106 (46%)	49/513 (10%)
Flower pots	17/99 (17%)	17/513 (3%)
Large wastes (buckets, small plastic tanks...)	24/50 (48%)	24/513 (5%)
Large containers (50-100L)	11/32 (34%)	11/513 (2%)
Gutters	0/2 (0%)	0/513 (0)
Car shelves	2/2 (100%)	2/513 (0,4%)
Others	5/15 (33%)	5/513 (1%)
Total	513/1939 (27%)	

Delatte *et al.* 2007 VBZD

***Aedes albopictus* breeding sites typology on 2 peri-urban localities of La Réunion (Saint Pierre and Sainte Anne) in winter**

Containers	No positive/ No inspected (immature stages)	No positive/ No inspected (pupae)
Leaf axilla	4/15 (27%)	3/15 (20%)
Bamboo stumps	55/58 (95%)	24/58 (41%)
Palm leaves	1/5 (20%)	0/5 (0%)
Rock holes	33/39 (85%)	17/39 (44%)
Tree holes	1/2 (50%)	0/2 (0%)
Basins	5/5 (100%)	4/5 (80%)
Cans	9/15 (60%)	8/15 (53%)
Tin cans	5/6 (83%)	3/6 (38%)
Bottles	8/77 (10%)	6/77 (8%)
Lids	3/6 (50%)	2/6 (33%)
Small plastic wastes	8/20 (40%)	5/20 (25%)
Barrels	7/10 (70%)	7/10 (70%)
Saucepans	1/7 (14%)	1/7 (14%)
Used tires	7/10 (70%)	6/10 (60%)
Pots	15/36 (42%)	13/36 (36%)
Buckets	4/6 (67%)	1/6 (17%)
Flower plates	24/37 (65%)	15/37 (41%)
Total	190/356 (53%)	115/356 (32%)

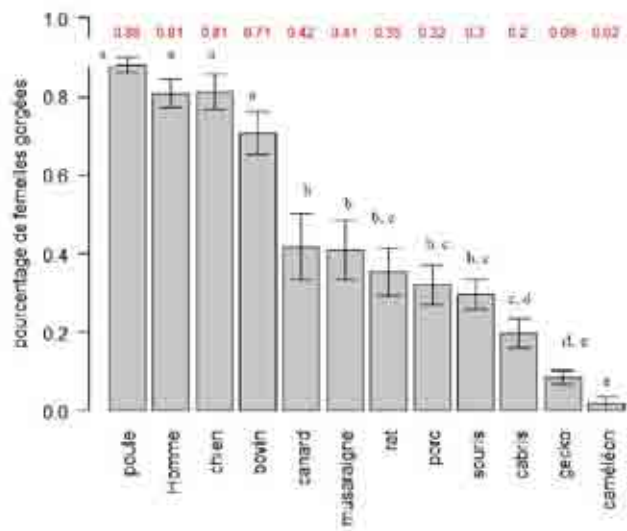
Natural

Artificial

Delatte *et al.* 2007 VBZD



Trophic preferences of *Ae. albopictus* from la Réunion Island



Delatte *et al.*, unpublished results

TRAVELERS



In 2005, the total number of passengers transported by air in the European Union (EU) rose by 8.5% compared to 2004, to more than 700 million. Passenger numbers rose by 8.8% in 2004 and by 4.9% in 2003. Of these passengers, 35% were carried on external-EU flights (Fuente Layos 2006).

TRAVELERS & INDIAN OCEAN ISLANDS

Indian Ocean islands : popular tourist destinations.

WTO, 2004:

719,000 tourists arrived in Mauritius,

430,000 in Reunion Island

229,000 in Madagascar

121,000 in the Seychelles in 2004.

European tourists +++

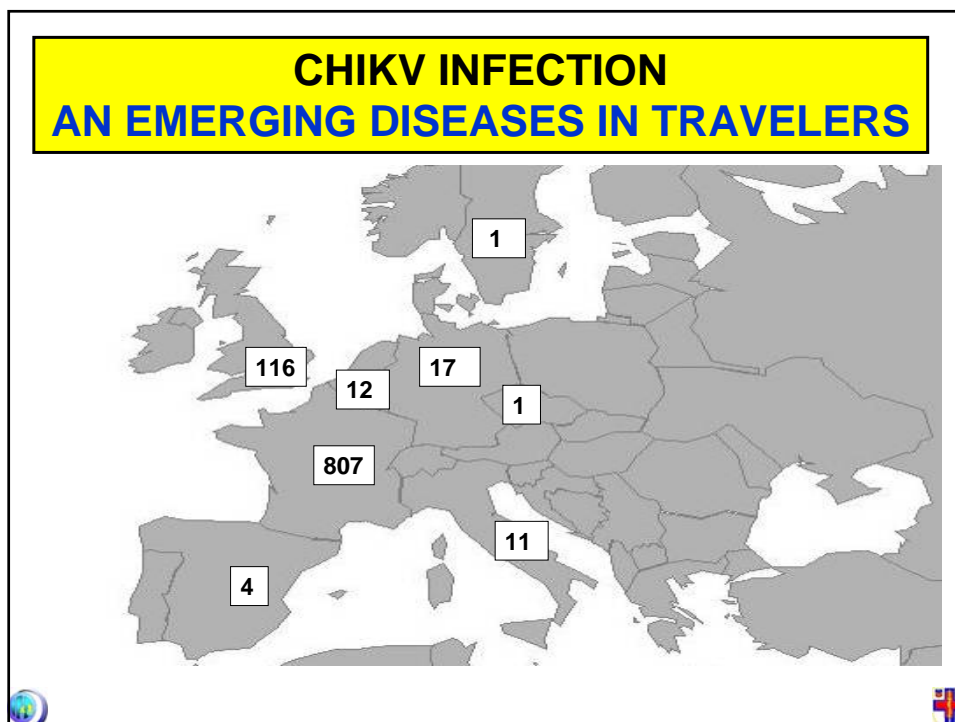
During the past months several CHIKV-infected visitors returned home to countries



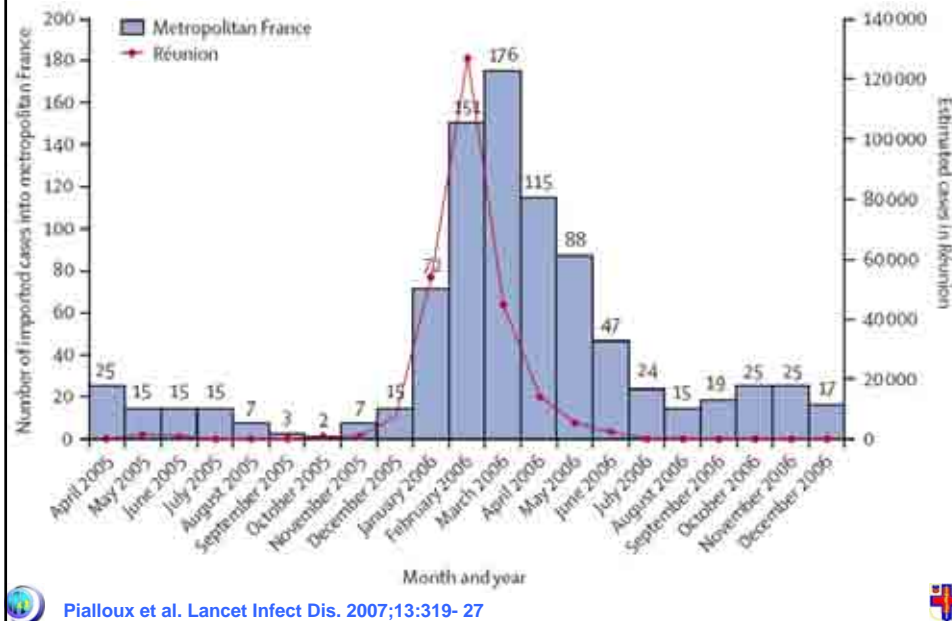
Table 1. Example of passenger traffic in metropolitan France in 2005 (from Chikungunya or Dengue-endemic regions). From Ministère Français de l'Équipement des Transports, de l'Aménagement du territoire du Tourisme et de la Mer (2006).

Region, country	Number of passengers arriving in France in 2005
Africa, Cameroon	98,364
Africa, Gabon	56,310
Africa, Mauritius	222,215
Africa, Kenya	29,335
Asia, India	278,453
Asia, Malaysia	72,408
Asia, Thailand	189,861
Asia, Vietnam	133,678
South America, Brazil	419,944
South America, French Guyana	95,342
All French overseas departments	1,538,294

Didier Fontenille, Anna Bella Failloux and Roberto Romi



CHIKV INFECTION IN FRANCE



CHIKV INFECTION IN FRANCE



Paris

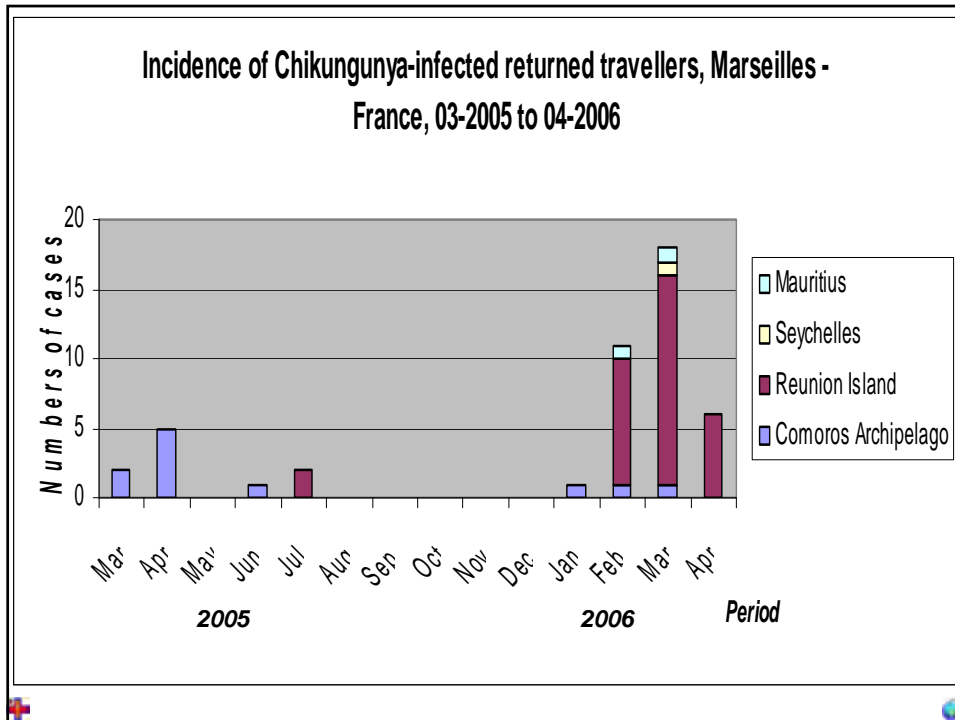


First cases hospitalized as early as 2005

Marseilles: +++

70,000 inhabitants originating from the « capital » or the « 5th Island » of the Comoros

Parola P, et al. Emerg Infect Dis 2006; 12:1493-9
Hochedez et al. Emerg Infect Dis. 2006;12:1565-7



Emerging Infectious Diseases • www.cdc.gov/eid

**Chikungunya Fever,
Hong Kong**

To the Editor: Vol. 12, No. 11, November 2006

Nelson Lee,^{*} Chun K. Wong,^{*}
Wai Y. Lam,^{*} Ann Wong,[†]
Wilina Lim,[‡] Christopher W.K. Lam,^{*}
Clive S. Cockram,^{*}
Joseph J. Y. Sung,^{*}
Paul K.S. Chan,^{*}
and Julian W. Tang^{*}

**Chikungunya Virus
Infection in
Traveler to
Australia**

To the Editor: Vol. 13, No. 3, March 2007

Julian D. Druce,^{*}
Douglas F. Johnson,[‡]
Thomas Tran,^{*}
Michael J. Richards,[‡]
and Christopher J. Birch^{*}

LESSONS FROM THE (ON GOING ?) OUTBREAK

The Virus

Clinical Aspects

Travelers – Vectors & Risk of Globalisation

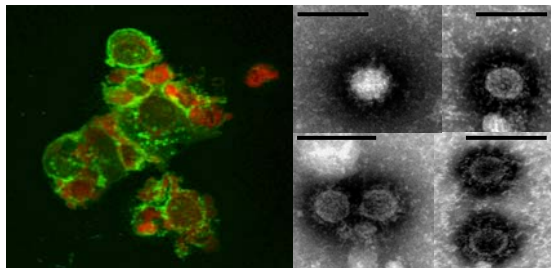


THE VIRUS

Novel Chikungunya Virus Variant in Travelers Returning from Indian Ocean Islands

Philippe Parola,*†, Xavier de Lamballerie,‡§, Jacques Jourdan,¶, Clarisse Rovey,*
Véronique Vaillant,#, Philippe Minodier,* Philippe Brouqui,*†, Antoine Fiahaul,**, Didier Raoult,†‡
and Rémi N. Charrel‡§

Emerging Infectious Diseases Vol. 12, No. 10, October 2006



A 73-year-old man returned from Reunion Island

Medical history: cancer

Severe arthralgia

Extremely painful arthritis and tenosynovitis with a specific pain under applied pressure at the wrists

Severe thrombocytopenia and neutropenia, complicated by septicæmia.



Parola P, et al. Emerg Infect Dis 2006; 12:1493-9

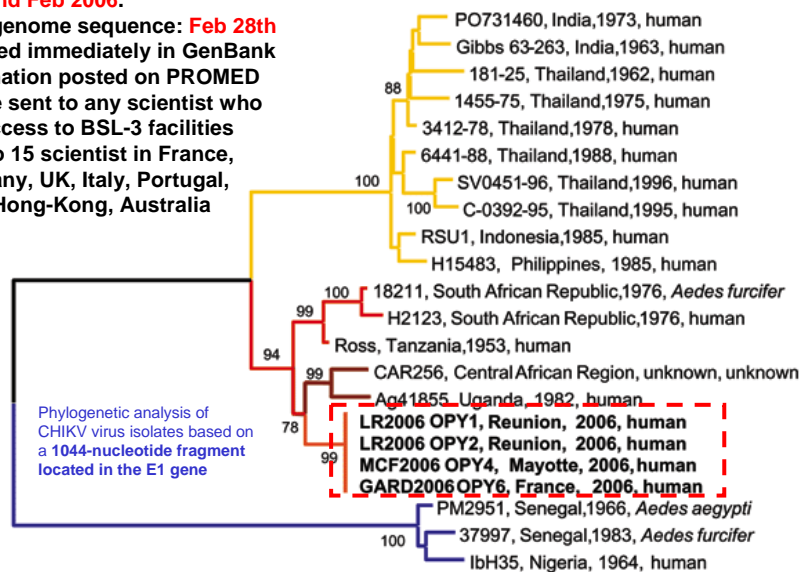


A CHIKV VARIANT OF AFRICAN ORIGIN

Patient: **22nd Feb 2006.**

Complete genome sequence: **Feb 28th**

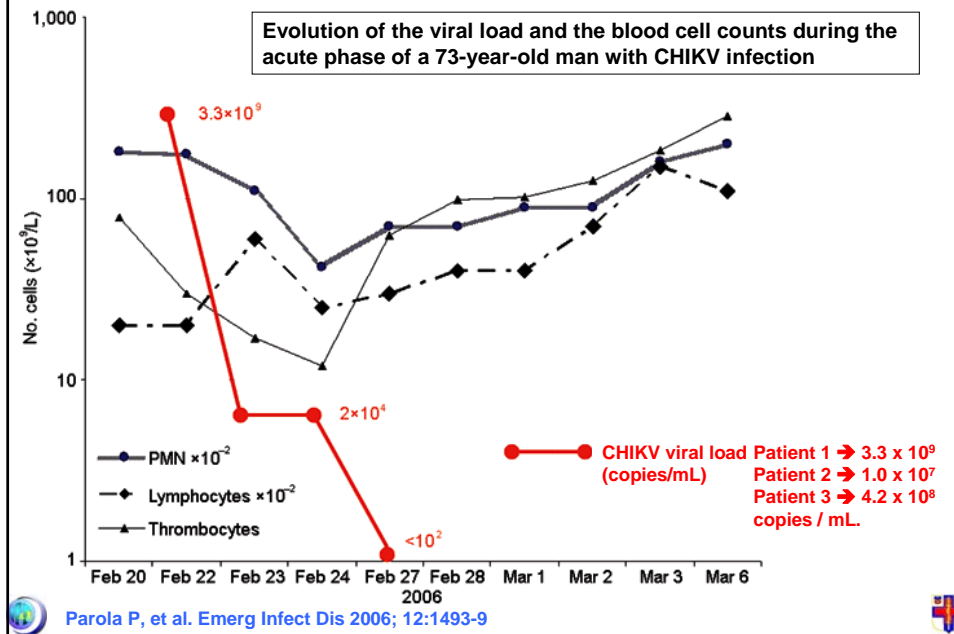
- released immediately in GenBank
- information posted on PROMED
- can be sent to any scientist who has access to BSL-3 facilities
- sent to 15 scientist in France, Germany, UK, Italy, Portugal, USA, Hong-Kong, Australia



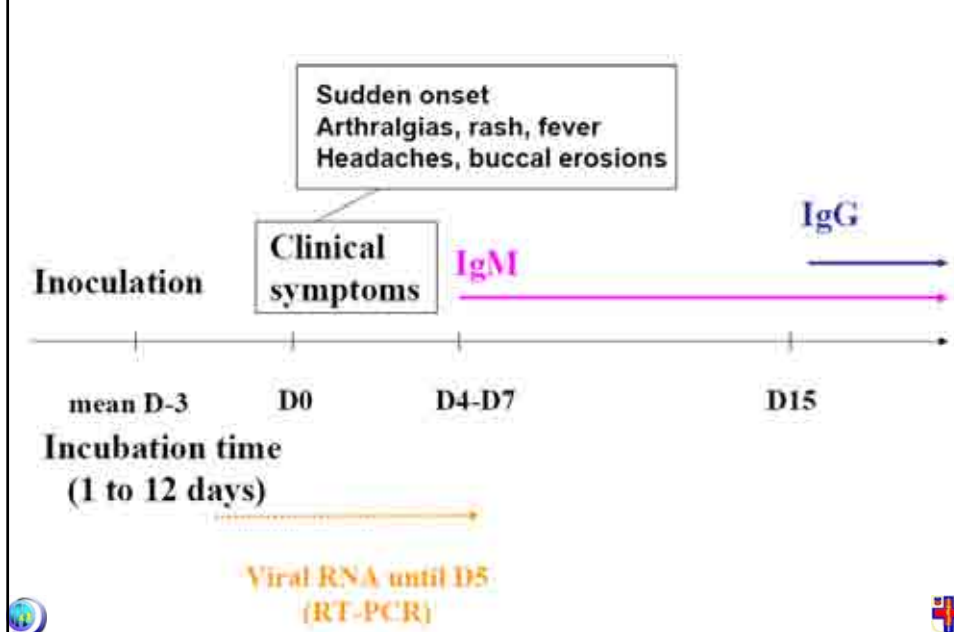
Parola P, et al. Emerg Infect Dis 2006; 12:1493-9



Biological and virological parameters (1)



Biological and virological parameters (2)



A CHIKV VARIANT OF AFRICAN ORIGIN

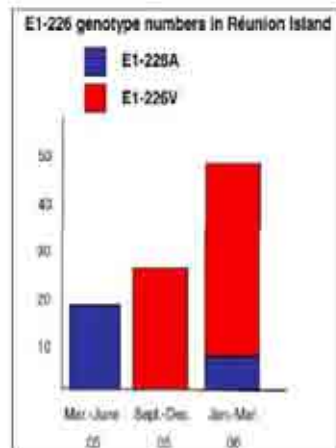
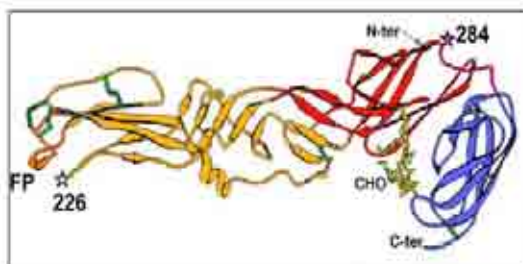
Indian Ocean : 92 sequences from 89 patients

Date	Sequences	A226	V226
March to June 2005	19	19	0
September to December	27	0	27
January to March 2006	46	6	40

Switch from A226 to V226 between the 2 epidemic waves



Schuffenecker et al. PLoS Medicine 2006; 3:e-263



Schuffenecker et al. PLoS Medicine 2006; 3:e-263



First autochthonous nosocomial case of CHIKV infection

A nurse with direct contact with the blood of a viremic patient during hemostasis

➤ Very high viral loads in CHIKV infection: viral loads are 100,000 times higher than in Hepatitis C

➤ 1 μ L of CHIKV viremic serum contains a number of virions equivalent to 100 mL of HCV infected serum !



Parola P, et al. Emerg Infect Dis 2006; 12:1493-9



CLINICAL ASPECTS IN REUNION ISLAND A previously unknown case mix

- Many “classic” forms with polyarthralgia or arthritides BUT:
- 48 neonatal transmissions
 - Meningo-encephalitis, skin rash,...
 - 1 death
- 2 – 4 % hospitalized
- Few asymptomatic cases
- 237 severe diseases including
 - Meningo-encephalitis (RT-PCR): death 1/8
 - Polyradiculitis, Guillain-Barré syndrome (4)
 - Cardiac / liver (paracetamol!)/ kidney failures
 - 63 deaths



CLINICAL ASPECTS IN REUNION ISLAND

Dermatologic aspects



Typical rash « dengue-like »



The French Task Force on Research on Chikungunya



CLINICAL ASPECTS IN REUNION ISLAND

Dermatologic aspects



Keratolysis
palms and plants



The French Task Force on Research on Chikungunya



CLINICAL ASPECTS IN REUNION ISLAND
Dermatologic aspects



Dyshidrotic eczema like lesions



The French Task Force on Research on Chikungunya



CLINICAL ASPECTS IN REUNION ISLAND
Dermatologic aspects



Petechial



The French Task Force on Research on Chikungunya



CLINICAL ASPECTS IN REUNION ISLAND
Dermatologic aspects



Vesicular and Bullous



The French Task Force on Research on Chikungunya



CLINICAL ASPECTS IN REUNION ISLAND
Dermatologic aspects



Aphthous



The French Task Force on Research on Chikungunya



CLINICAL ASPECTS IN REUNION ISLAND
Dermatologic aspects



**Psoriasis like
/ purpuric**



The French Task Force on Research on Chikungunya



CLINICAL ASPECTS IN REUNION ISLAND
Dermatologic aspects



Erythema nodosum like



The French Task Force on Research on Chikungunya



CLINICAL ASPECTS IN REUNION ISLAND

Dermatologic aspects / Vascular disorders



The French Task Force on Research on Chikungunya



CLINICAL ASPECTS IN REUNION ISLAND

Dermatologic aspects in children



Bullous



The French Task Force on Research on Chikungunya

Pialoux et al. Lancet Infect Dis. 2007;13:319- 27



CLINICAL ASPECTS IN REUNION ISLAND Dermatologic aspects in children



Bullous epidermolysis

Pialoux et al. Lancet Infect Dis. 2007;13:319- 27



The French Task Force on Research on Chikungunya



CLINICAL ASPECTS IN REUNION ISLAND Enanthematous / Petechial



The French Task Force on Research on Chikungunya



CLINICAL ASPECTS IN REUNION ISLAND Fœtal and New Borne transmissions

- Most of CHIKV infections in pregnant women: no problem
- High risk if delivery during viremic period
- 18 neonatal confirmed infections within 151 infected pregnant women,
- New-bornes got a severe disease :
 - 7 encephalopathies
 - 4 with collapsus
 - 4 IVDC



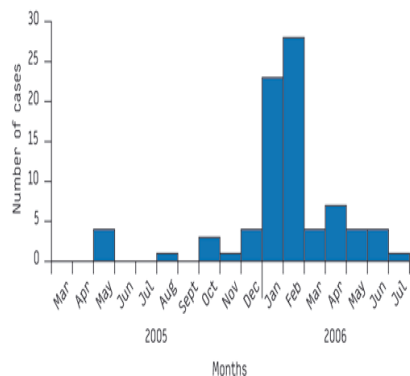
www.invs.sante.fr



CLINICAL ASPECTS IN IMPORTED CASES (1)

FIGURE

Imported cases of chikungunya by month of onset,
Pitié-Salpêtrière Hospital, France 2005-2006



80 patients
**Median delay between onset
 of symptoms / consultation
 = 35 days**



Hochedez et al. Emerg Infect Dis. 2006;12:1565-7
 Hochedez et al. Eurosurveillance 2007, 12: 1



CLINICAL ASPECTS IN IMPORTED CASES (1)

All patients

- **Fever = 3 days**
- **Joint pains = mainly peripheral**
wrist, ankles, phalanges > 70% of the patients.

Erythematous exanthema = 75%

Bleeding from the nose or gums = 11%

After the first week of symptoms:

Main complaints =
persistent arthralgia, peripheral oedema,
lethargy and sadness



Hochedez et al. *Eurosurveillance* 2007, 12: 1



CLINICAL ASPECTS IN IMPORTED CASES (2)

Chikungunya Infection

An Emerging Rheumatism Among Travelers Returned From Indian Ocean Islands. Report of 47 Cases

Fabrice Simon, MD, Philippe Parola, MD, PhD, Marc Grandadam, PhD, Sabrina Fourcade, MD, Manuela Oliver, MD, Philippe Brouqui, MD, PhD, Pierre Hance, MD, Philippe Kraemer, MD, Ali Mohamed, MD, Xavier de Lamballerie, MD, PhD, Rémi Charrel, MD, PhD, and Hugues Tolou, MD, PhD

Medicine

Volume 86, Number 3, May 2007



PATIENTS / TRAVEL

- 29 individuals permanently residing in metropolitan France and who travelled for tourism
- 10 VFRs of Comorian origin living in Marseille (2 pregnant women)
- 7 residents in an Indian Ocean island who travelled to metropolitan France,
- a 5-month Canadian child whose family stopped for a few days in France after visiting Reunion Island before returning to Canada.

Length of stay = 9 - 180 days

Disease onset = during travel in 26 of the patients *versus* 21 after return.



Simon et al. *Medicine*, 86 (3), May 2007



PATIENTS

13 patients presented less than 10 days after the disease onset

6 of them were hospitalized:

- febrile illness accompanied by painful and handicapping polyarthritits
- 1 severe pancytopenia + gram-negative septicaemia
- 1 transient myocarditis

33 more other patients presented more than 10 days after the disease onset

3 hospitalized for severe persistent joints pain



Simon et al. *Medicine*, 86 (3), May 2007



ACUTE STAGE: THE RASH (1)



Simon et al. *Medicine*, 86 (3), May 2007



THE RASH (2)



mean duration of the rash: 2.3 days range: 1-4 d



Simon et al. *Medicine*, 86 (3), May 2007



THE RASH (3)



 Simon et al. *Medicine*, 86 (3), May 2007



THE RASH (4)

common oedema of the
face accompanying the
rash

 Simon et al. *Medicine*, 86 (3), May 2007



ACUTE STAGE: ARTHRITIS (1)

Arthritis: 100% during the acute stage
sometimes asynchronous with fever and rash.

Adult patients:
mostly bilateral and symmetric (40/45)
> 8 peripheral joint groups (37/45).

Most frequently affected joints:
fingers, wrists, toes and ankles

**An exquisite pain at the pressure of the right wrist
was noted.**

Often in association with periarticular inflammatory
oedema (20/45)

 Simon et al. *Medicine*, 86 (3), May 2007



ACUTE STAGE: ARTHRITIS (2)



 Simon et al. *Medicine*, 86 (3), May 2007



ACUTE STAGE: ARTHRITIS (3)



After a 4-day anti-inflammatory treatment

 Simon et al. *Medicine*, 86 (3), May 2007



ACUTE STAGE: ARTHRITIS (4)

Large joint effusion
7/45

mostly on
a knee

presence
of IgM anti-
CHIK in 1
synovial
fluid



 Simon et al. *Medicine*, 86 (3), May 2007



ACUTE STAGE: BURSITIS AND HYGROMA



 Simon et al. *Medicine*, 86 (3), May 2007



OTHER: Conjunctivitis



 Parola P, et al. *Emerg Infect Dis* 2006; 12:1493-9



LABORATORY FINDINGS

Common early laboratory findings in both mild and severe cases :

elevated enzymes

LDHlactate dehydrogenase, ASAT, ALAT, CPK, and gamma glutamyl transaminaseGGT = 50 %

mild thrombocytopenia 50%

leucopenia 75 %



Simon et al. Medicine, 86 (3), May 2007



SECOND PHASE

After Day 10:

38 / 45 patients (82%) remained symptomatic

- Persistence or recrudescence of joints pain
- Tenosynovitis + + + commonly > two tendons
- Carpal or cubital tunnel syndromes (7)
- Six women described *de novo* Raynaud's phenomenon or erythralgia on fingers
- None had recurrent fever or rash



Simon et al. Medicine, 86 (3), May 2007



RHEUMATISM & INCAPACITATING PAIN (1)



Simon et al. *Medicine*, 86 (3), May 2007



RHEUMATISM & INCAPACITATING PAIN (2)



Simon et al. *Medicine*, 86 (3), May 2007



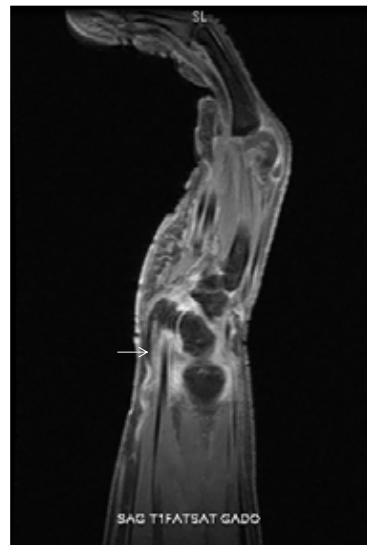
RHEUMATISM & INCAPACITATING PAIN (3)



 Simon et al. *Medicine*, 86 (3), May 2007



TENOSYNOVITIS MRI ASPECTS



 Simon et al. *Medicine*, 86 (3), May 2007



BONE SCINTIGRAPHY



intense focus of tracer uptake particularly on the left side in the left metacarpo-phalangeal, wrist and the first distal interphalangeal joints



Parola P, et al. Emerg Infect Dis 2006; 12:1493-9



TREATMENTS

- Analgesics
- Local and/or systemic NSAIDs
- Physiotherapy
- Short-term systemic corticotherapy
- Chloroquine phosphate ?



FOLLOW-UP (1)

Last analysis of the cohort in October 2006:

overall mean follow-up = 8 months

28 patients still under follow-up.

For most patients who complained of persistent incapacitating pain :

- severe discomfort in daily life lasting weeks to months
- particularly while walking and using the hands
- 3 reported depression

Among patients who have been followed up

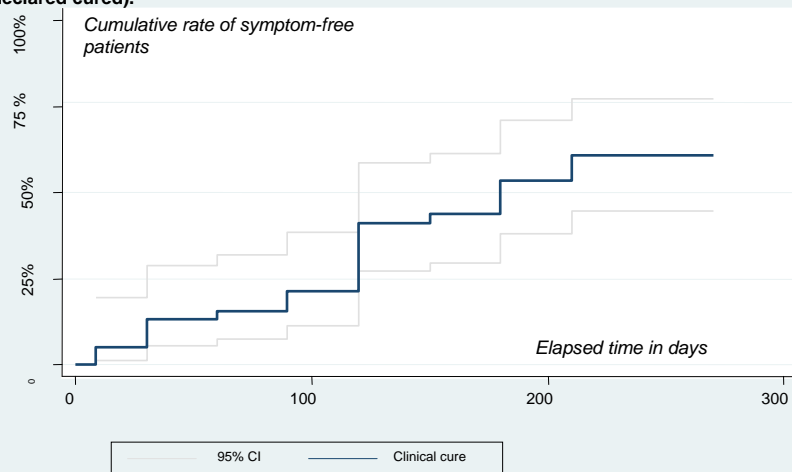
to **1**, **3**, and **6** months after disease onset,

88%, **86%**, and **48 %** were symptomatic respectively.



FOLLOW-UP (2)

Kaplan-Meier estimate of clinical outcome among 38 Chikungunya-infected travellers followed-up in Marseilles, France, March 2005 – October 2006. (truncated data after 9 months : 38 followed-up patients, 55% self-declared cured).



FOLLOW-UP IN REUNION ISLAND

Colloque international
« Chikungunya et autres arboviroses émergentes en milieu tropical »

3 et 4 décembre 2007
Saint-Pierre - La Réunion

147 patients checked after 12-18 months
57% still symptomatic (63% with permanent manifestations)

Sissoko et al, 2007

120 symptomatic patients after 6 months
80%: unspecific joint pains
20% (9 women + 6 men): rheumatoid arthritis

Ribera et al, 2007

By the way, IS IT DIFFICULT TO DIFFERENTIATE WITH DENGUE ?

Robinson in 1955, about CHIKV infection :

“absence of adenopathy, the frequent dissociation of the rash and the secondary rise of the temperature, the lack of post-orbital pain, or pain on moving the eyes, and the long continuance of chronic joint pains” .

Here, more keys to differentiate:

- “two-phased” disease evolution
- multiple peripheral tenosynovitis
- typical pain on pressure to the wrists
- delayed onset of Raynaud syndrome

Robinson MC. Trans R Soc Trop Med Hyg. 1955;49:28-32
Parola P, et al. Emerg Infect Dis 2006; 12:1493-9
Simon et al. Medicine, 86 (3), May 2007



AFTER INDIAN OCEAN ISLANDS: INDIA !

Circulation of the virus has been documented in India where CHIKV has spread rapidly

> 1,100,000 cases reported by the health authorities since December 2005

101,500 laboratory confirmed cases



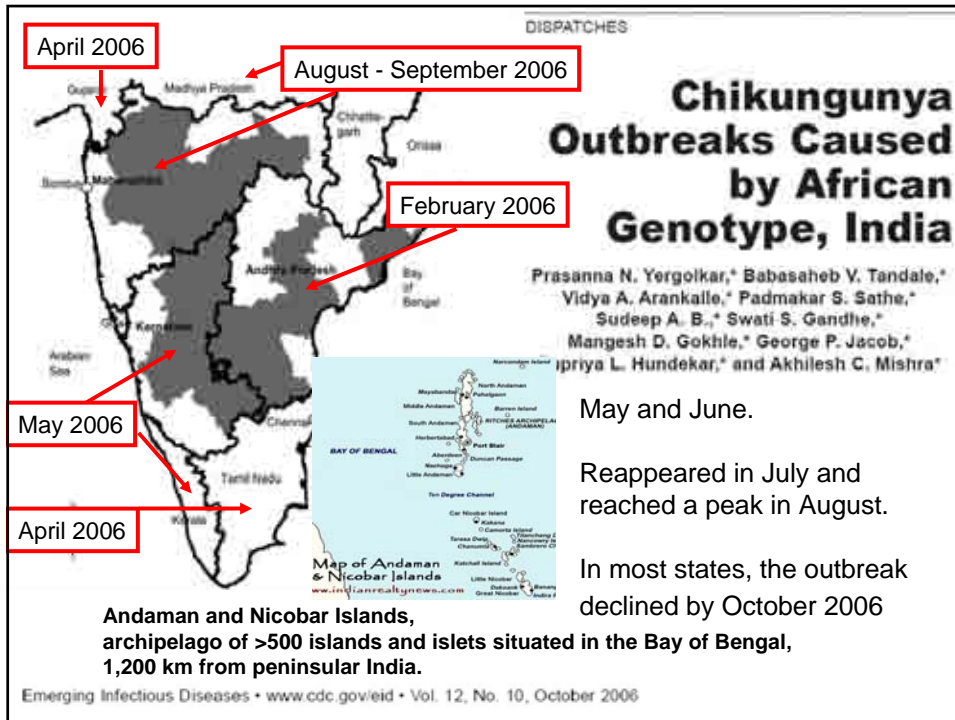
Chikungunya epidemic in India: a major public-health disaster

Country	Cases	Deaths reported/ (estimated)	Mortality rate per 100 000 cases
Réunion (France)	258 000	237	91.8
India reported by government	1391165	0	0
India conservative estimate	1391165	(1194)	91.8
India moderate estimate	6.5 million*	(6389)	91.8
India full estimate	6.5 million	(19168)	275.6†

*Assuming under reporting—actual numbers estimated as five times the reported number. †Assuming mortality in India is three times that in Réunion.

Table: Reported cases, deaths, and estimated deaths in Réunion and India

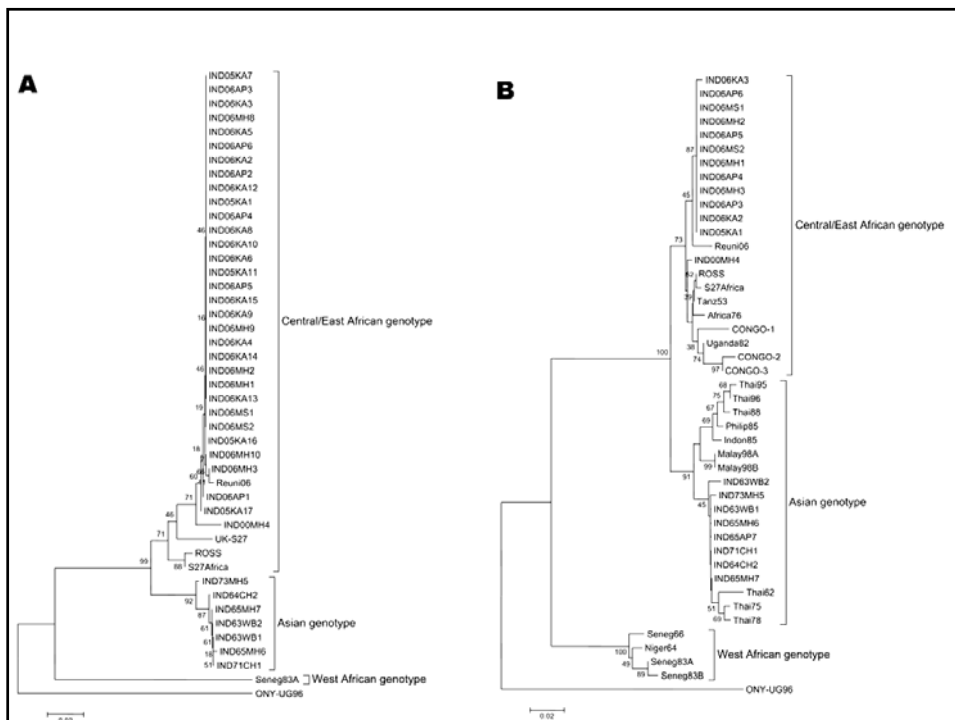
<http://infection.thelancet.com> Vol 7 May 2007



May and June.

Reappeared in July and reached a peak in August.

In most states, the outbreak declined by October 2006



1: [Vector Borne Zoonotic Dis.](#) 2007 Nov 2 [Epub ahead of print]

East Central South African Genotype as the Causative Agent in Reemergence of Chikungunya Outbreak in India.

[Dash PK](#), [Parida MM](#), [Santhosh SR](#), [Verma SK](#), [Tripathi NK](#), [Ambuj](#), [Saxena P](#), [Gupta N](#), [Chaudhary M](#), [Babu JP](#), [Lakshmi V](#), [Mamidi N](#), [Subhalaxmi MV](#), [Rao PV](#), [Sekhar K](#).

Division of Virology, Defence R & D Establishment (DRDE), Gwalior, Madhya Pradesh, India.

Chikungunya fever is an important arboviral infection prevalent through out Africa and Southeast Asia. Recently, in 2006, it has reemerged in many parts of India, affecting more than a million persons. A detail serological, virological, and molecular investigation of this unprecedented outbreak was carried out by collecting and studying 540 samples from all the affected regions of India during this epidemic. An in-depth investigation revealed the presence of anti-Chikungunya antibodies in 68% of the samples and genomic RNA in 49% of them. In addition 32 Chikungunya viruses were isolated from 45 representative polymerase chain reaction-positive samples. The nucleotide sequences of partial E1 gene of 25 representative Chikungunya viruses were deciphered. The sequence analysis indicated that all the isolates of this epidemic belonged to the new Indian Ocean island clade of East Central South (ECS) African genotype. Phylogenetic analysis also revealed that earlier Indian isolates were clustered into the Asian genotype. This study conclusively proved the genotype shift from Asian to ECS African as the major factor in the reemergence of Chikungunya in an unprecedented outbreak in India after a gap of 32 years.

DISPATCHES

Chikungunya Virus in US Travelers Returning from India, 2006

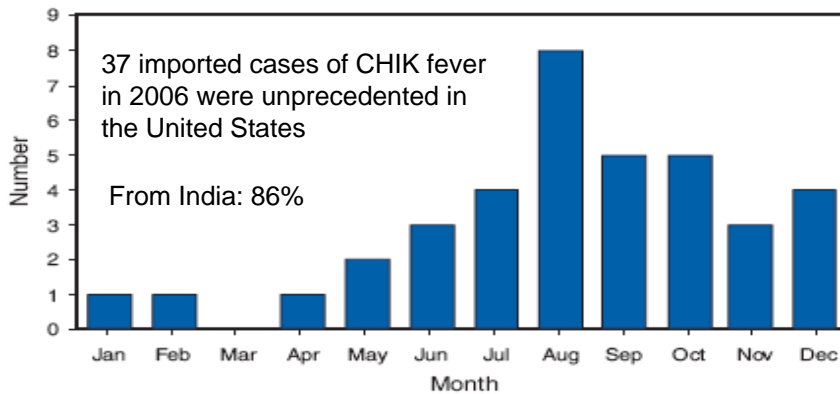
Robert S. Lanciotti,* Olga L. Kosoy,* Janeen J. Laven,* Amanda J. Panella,* Jason O. Velez,* Amy J. Lambert,* and Grant L. Campbell*

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 13, No. 5, May 2007

returning travelers with high viremia !!

Update: Chikungunya Fever Diagnosed Among International Travelers United States

FIGURE. Number (37) of confirmed cases of chikungunya fever, by month of illness onset — United States, 2006



Morb Mortal Wkly Rep

March 30, 2007 / 56(12);276-277



OTHER REEMERGENCES

Reemergence of Endemic Chikungunya, Malaysia

Sazaly AbuBakar,* I-Ching Sam,*
Pooi-Fong Wong,* NorAziyah MatRahim,*
Poh-Sim Hooi,* and Nuruliza Roslan*

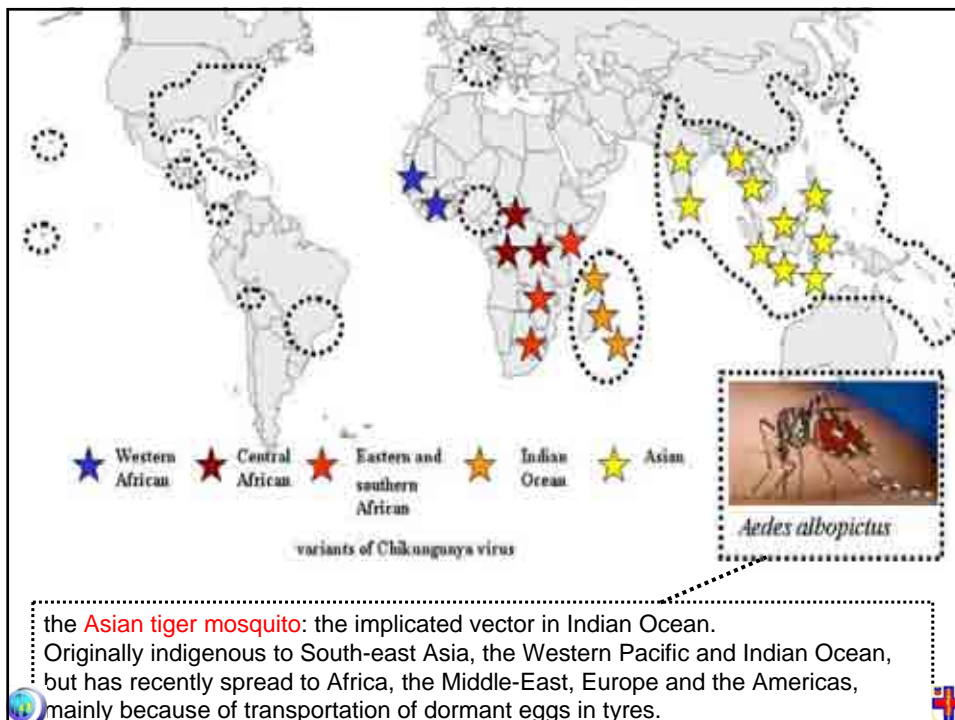
Chikungunya virus infection recently reemerged in Malaysia after 7 years of nondetection. Genomic sequences of recovered isolates were highly similar to those of Malaysian isolates from the 1998 outbreak. The reemergence of the infection is not part of the epidemics in other Indian Ocean countries but raises the possibility that chikungunya virus is endemic in Malaysia.

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 13, No. 1, January 2007



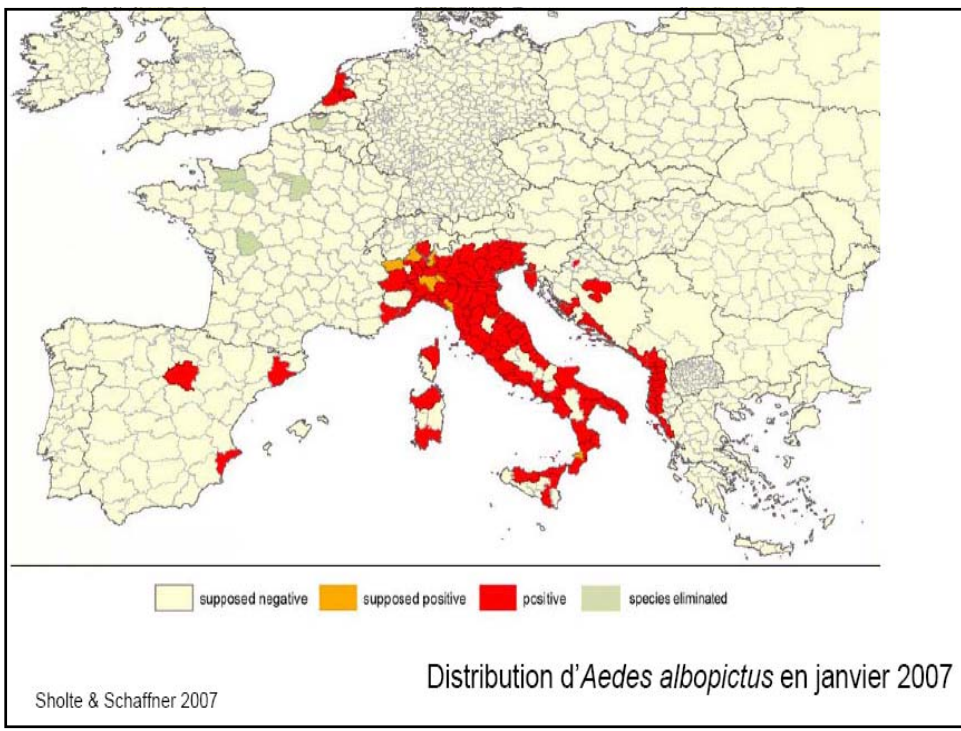
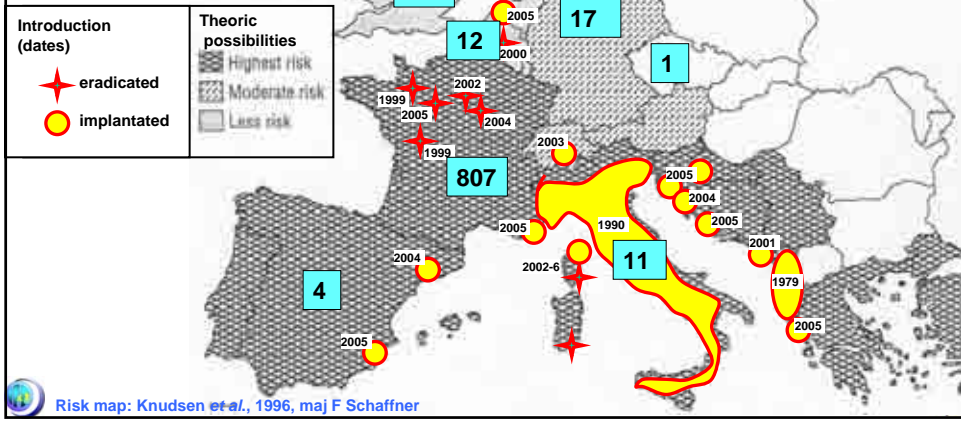


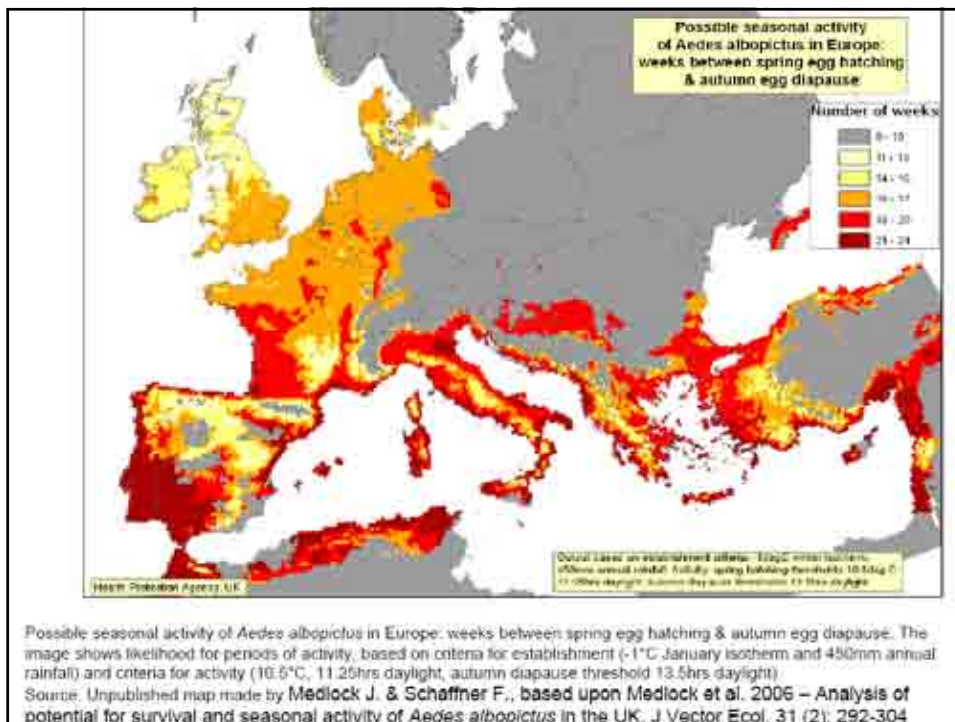
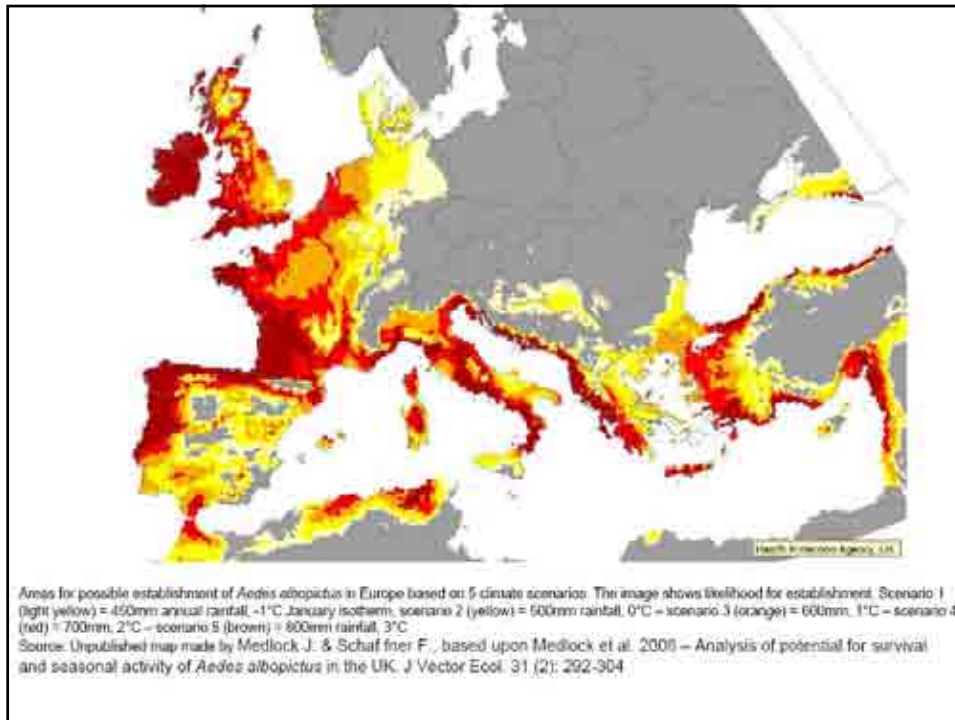
the potential spread of the disease



FOCUS IN EUROPE

Remember imported cases including viremic patients !





WHAT IS THE RISK OF GLOBALISATION ?

Would ecological conditions in southern Europe and north America support the development of a productive and persistent viral cycle in local vectors, during the period of activity of *Ae. Albopictus* ???

Capability of *Ae. albopictus* to transmit vertically and thus to transfer CHIKV to the next generation (and the next season) ??

→ if viremic patients arrive in places during the summer, when *Aedes albopictus* is prevalent and active, they might serve as a source of an outbreak

« If viremic patients arrive in Italy, France, or elsewhere in southern Europe during the summer, however, they could cause a European outbreak » Parola et al. *Emerg Infect Dis* October 2006

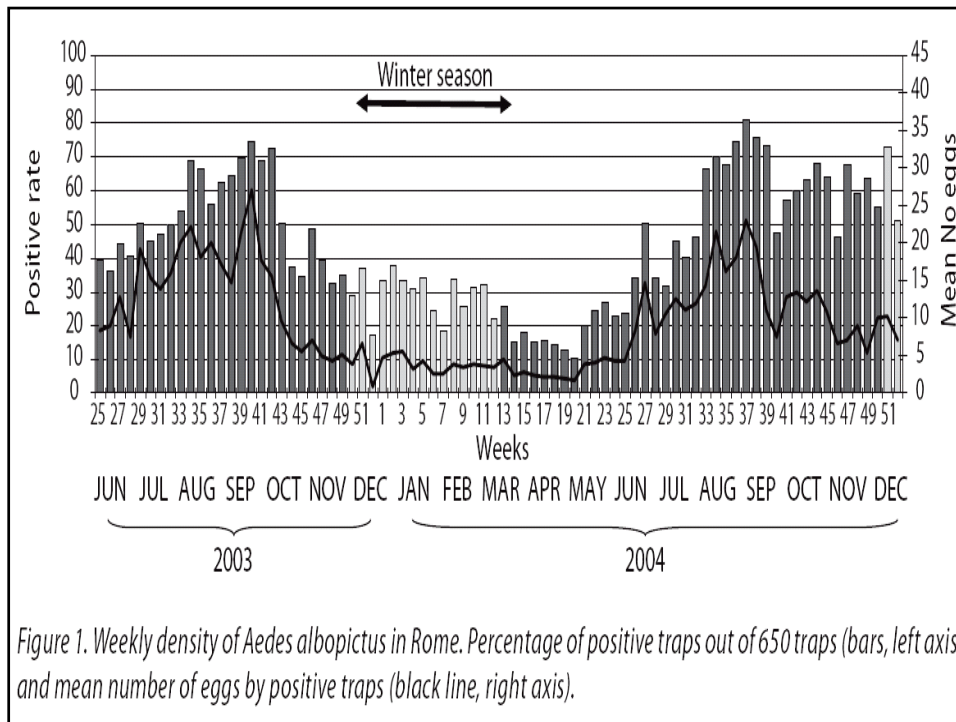


10. Should we expect Chikungunya and Dengue in Southern Europe?

Didier Fontenille, Anna Bella Failloux and Roberto Romi

It is difficult to estimate R_0 in Europe if viremic patients are bitten by mosquitoes. However, taking the following plausible values (based on published and non published data, see Hawley 1988) for R_0 parameters: $m = 20$, $a = 0.25$, $p = 0.85$, $n = 5$ (for CHIKV), $1/r = 4$, and considering that b and c are 0.7 each, one obtains $R_0 = 0.96$, close to 1 the threshold for having secondary cases. These values are rough estimations. Survival, duration of gonotrophic cycle, human biting rate and the extrinsic incubation period of the virus, may vary a lot depending on human and mosquito populations, virus strains and seasons. R_0 may therefore be much higher at certain times or in certain places. That means that secondary cases may occur if CHIK or DEN viruses are introduced in a given region where *Ae. albopictus* is abundant and anthropophilic during a warm period.

Emerging pests and vector-borne diseases in Europe



Imported Chikungunya Infection, Italy

Emerging Infectious Diseases
Vol. 13, No. 8, August 2007

Patient no.	Sex	Age, y	Reason for travel	Country of origin	Date of return (length of stay, d)	Date of first medical assessment after return (delay, d)	Last date of fever (length of fever, d)	Fever on date of return?
1*	M	32	Business	Réunion	Feb 23 (13)	Feb 25 (2)	Feb 26 (4)	Yes
2†	F	39	Tourism	Mauritius	Feb 28 (10)	Feb 28 (0)	Feb 28 (4)	Yes
3‡	M	48	Tourism	Mauritius	Mar 7 (10)	Mar 7 (0)	Mar 6 (5)	No
4‡	M	32	Tourism	Madagascar	Mar 7 (15)	Mar 8 (1)	Mar 4 (4)	No
5§	M	49	Tourism	Mauritius	Mar 08 (16)	Mar 15 (7)	Mar 4 (5)	No
6‡	M	66	Tourism	Madagascar	Mar 24 (15)	Mar 24 (0)	Mar 27 (5)	Yes
7§	M	36	Tourism	Mauritius	Apr 4 (15)	Apr 5 (1)	Apr 1 (6)	No
8*	F	43	Resident	Madagascar	Apr 10 (-)	Apr 11 (1)	Mar 2 (6)	No
9‡	F	46	Tourism	Réunion	Jan 30 (16)	Apr 13 (73)	NA (2)	-
10¶	F	44	Visit relatives	Mauritius	Apr 17 (33)	Apr 19 (2)	Apr 7 (12)	No
11‡	F	36	Tourism	Mauritius	Apr 30 (11)	May 3 (3)	May 3 (3)	Yes
12‡	M	31	Tourism	Réunion	Apr 21 (30)	May 4 (13)	Apr 5 (6)	No
13‡	M	44	Visit relatives	Cameroon	May 3 (24)	May 22 (19)	May 7 (6)	Yes
14*	M	35	Tourism	Seychelles	May 31 (9)	Jun 1 (1)	Jun 1 (2)	Yes
15*	M	38	Tourism	Mauritius	May 10 (11)	Jun 12 (2)	May 7 (4)	No
16‡	F	58	Missionary work	Central African Republic	Jun 24 (14 y)	Jun 10 (16)	Apr 26 (12)	No
17*	F	57	Business	India	Sep 8 (31)	Sep 9 (1)	Sep 10 (4)	Yes

*GISPI (Gruppo di Interesse e Studio delle Patologie di Importazione) center: Torino
 †GISPI center: Udine
 ‡GISPI center: Negros, NA, not available
 §GISPI center: Brescia
 ¶GISPI center: Triggiano

Infection with chikungunya virus in Italy: an outbreak in a temperate region *Lancet* 2007; 370: 1840-46

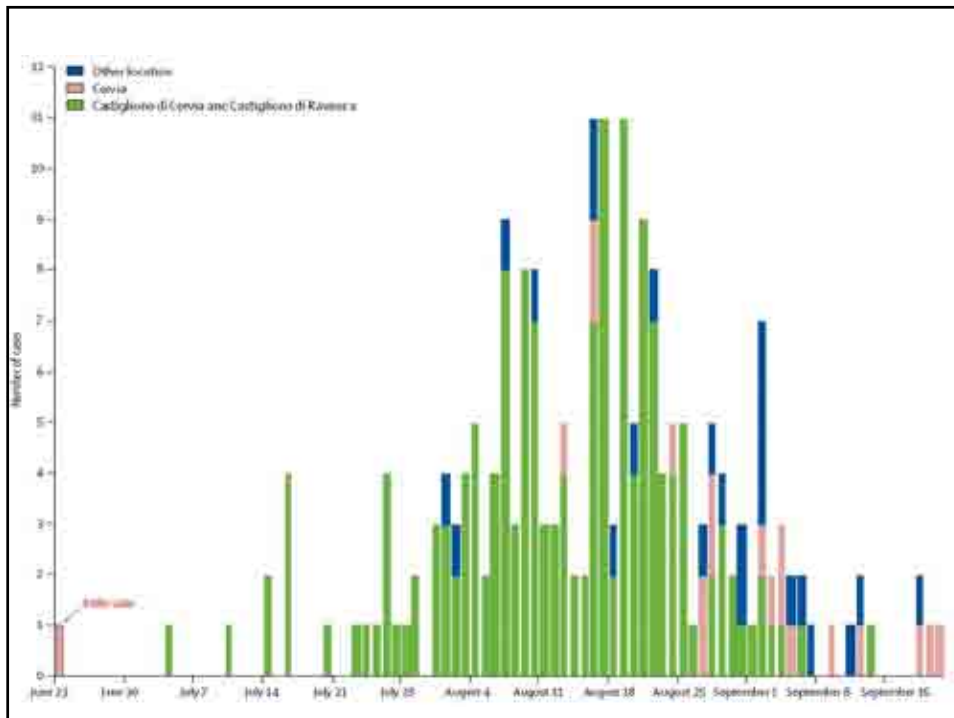
G. Rezza*, L. Nicoletti*, R. Angelini, R. Romi, A. C. Finarelli, M. Fanning, P. Cordioli, C. Fortuna, S. Boros, F. Magurano, G. Silvi, P. Angelini, M. Dottori, M. G. Ciufolini, G. C. Majari, A. Cassone, for the CHIKV study group†

August 2007:

local health authorities of the province of Ravenna, Italy: unusually high number of cases of febrile illness in Castiglione di Cervia and Castiglione di Ravenna, two small villages divided by a river.

Serological testing + PCR in patients: Chikungunya fever.

CHIKV detected by PCR in local *Aedes albopictus*



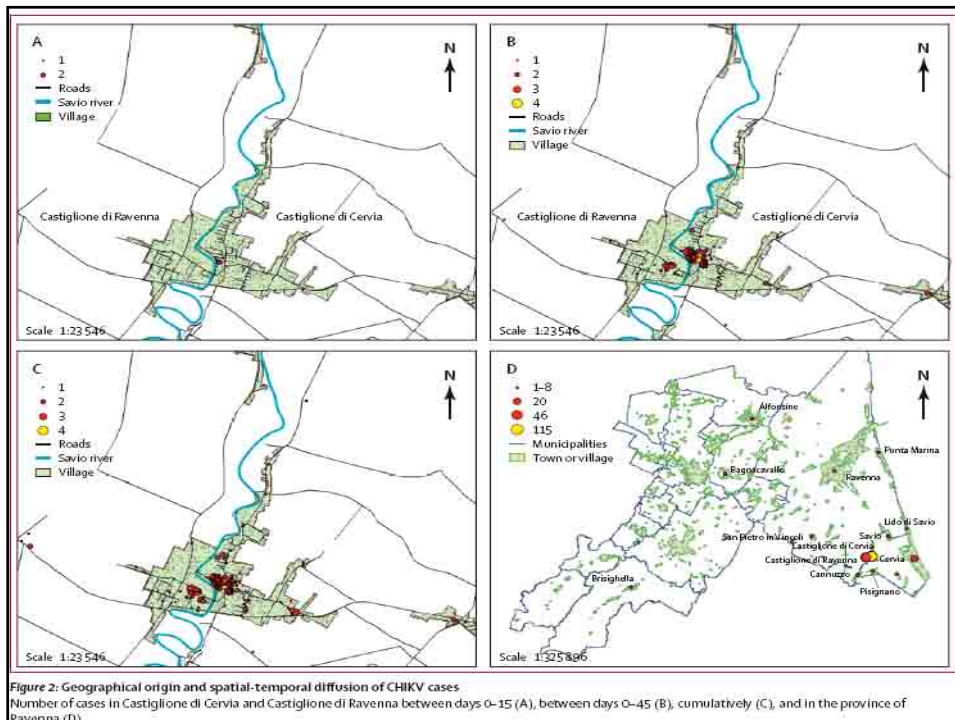


Figure 2: Geographical origin and spatial-temporal diffusion of CHIKV cases. Number of cases in Castiglione di Cervia and Castiglione di Ravenna between days 0-15 (A), between days 0-45 (B), cumulatively (C), and in the province of Ravenna (D).

	Number of cases (%)
Age (years)	
0-19	12 (6%)
20-39	26 (13%)
40-59	62 (30%)
60-70	78 (38%)
≥80	27 (13%)
Sex:	
Male	99 (48%)
Female	106 (52%)
Presumed place of infection	
Castiglione di Cervia or Castiglione di Ravenna	171 (83%)
Cervia	13 (6%)
Other/unknown	21 (10%)
Classification of cases	
Laboratory confirmed	175 (85%)
Clinically defined (untested)	30 (15%)

Table 1: Demographic characteristics of the 205 individuals infected with CHIKV

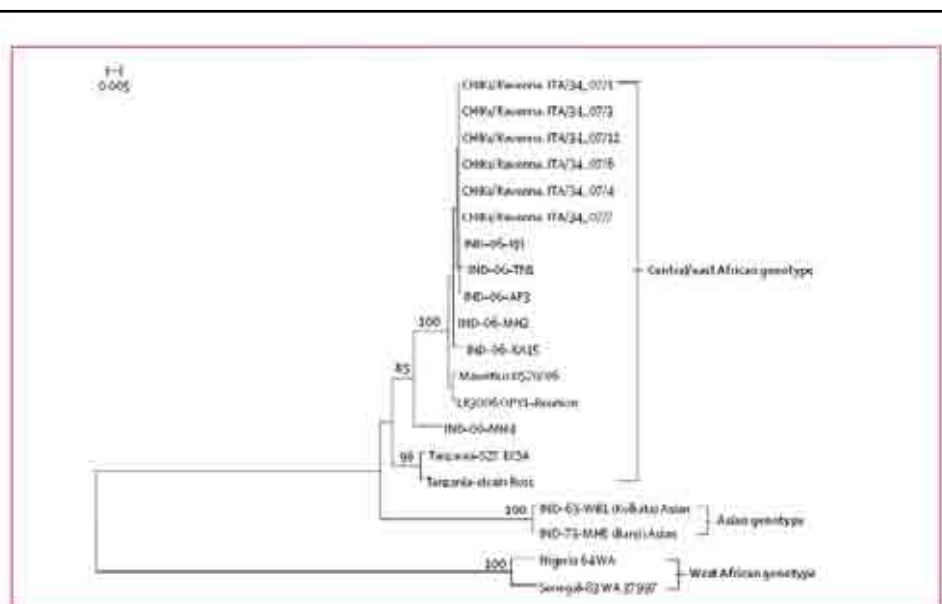


Figure 3: Phylogenetic analysis of the partial nucleotide sequences (1013 nucleotides) of the E1 gene of CHIKV strains identified in Italy and in different parts of the world



Available online at www.sciencedirect.com



Acta Tropica xxx (2007) xxx–xxx

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TROPICA

www.elsevier.com/locate/actatropica

Short note

Chikungunya: A risk for Mediterranean countries?

Marie Vazeille^a, Charles Jeannin^b, Estelle Martin^a,
Francis Schaffner^{b,1}, Anna-Bella Failloux^{a,*}

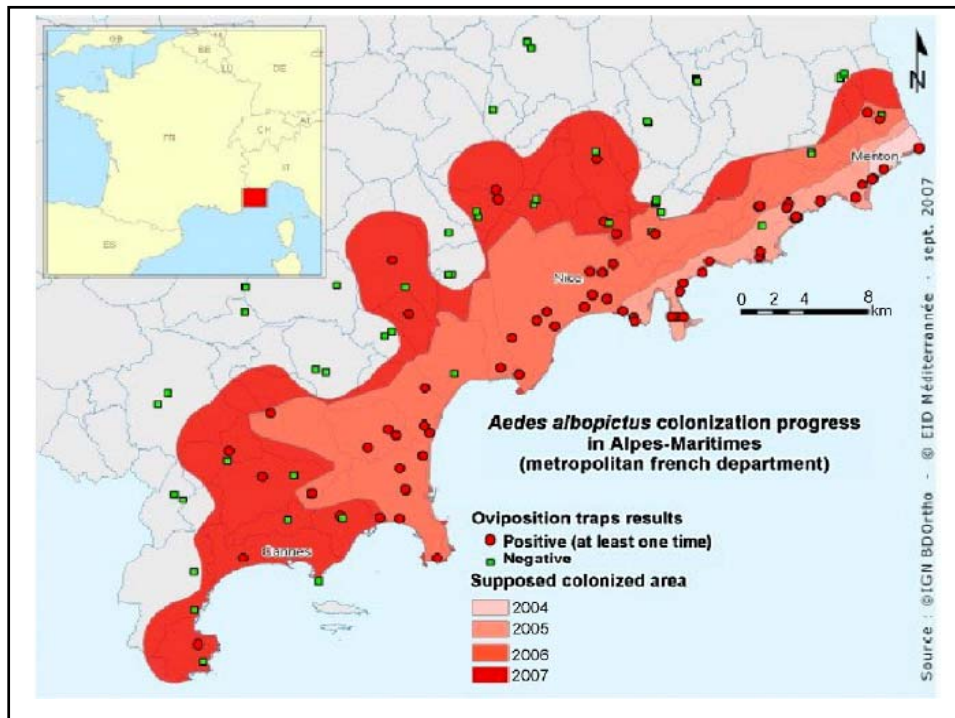


Table 1

Infection rates towards chikungunya virus of mosquito populations collected in southern France in October 2006

Species	Site of collection	%Infection (N)
<i>Aedes albopictus</i>	Alpes maritimes	77.1 (35)
<i>Aedes caspius</i>	Sainte-Marie de la Mer	25 (16)
<i>Aedes detritus</i>	Sainte-Marie de la Mer	67.3 (49)
<i>Aedes vexans</i>	Sainte-Marie de la Mer	0 (13)
<i>Culex pipiens</i>	Montpellier	0 (11)

N, number of females tested.

IS THERE A VACCINE ?

Initiated by investigators at Walter Reed in the 1960's

None of the efforts have yet resulted in a licensed vaccine

September 6th, 2006:

Material Transfer Agreement signed by the US Army Medical Research Institute for Infectious Diseases and the French National Institute of Health and Medical Research

→ transfer of records of previous clinical studies and supplies of the vaccine + seed stock from which it was made for further development of the vaccine, including additional clinical trials in affected areas



Press Release - Embassy of the United States of America, Paris, France. September 14, 2006



ACKNOWLEDGMENTS

French Task Force on Research on Chikungunya

A. Flahault, G. Aumont, V Boisson, X de Lamballerie, F. Favier, B.A. Gaüzère, D. Fontenille, S. Journeaux, V. Lotteau, C. Paupy, M.A. Sanquer, M. Setbon

Clinicians and Virologists In Marseille

F. Simon, P. Brouqui, P. Minodier, M. Grandadam, M. Oliver, P. Hance, R. Charrel, H. Tolou

Clinicians and Friends In Reunion and Comoros



 www.mit.ap-hm.fr 
<http://IFR48.timone.univ-mrs.fr>





THANK YOU !

