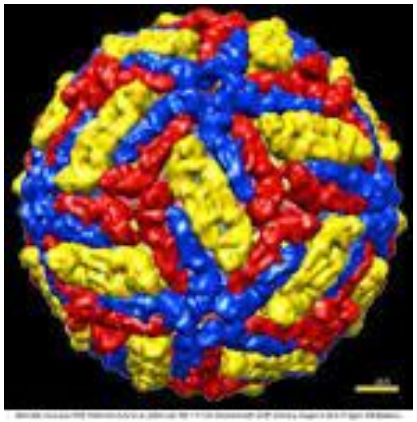
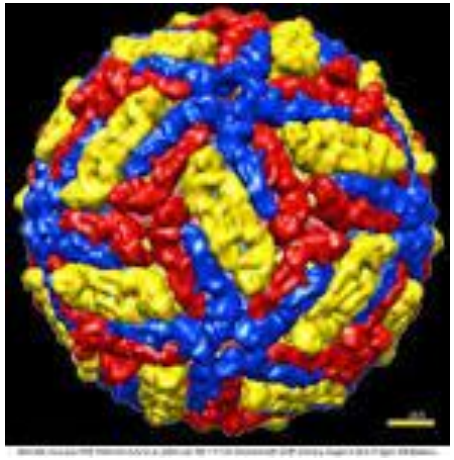
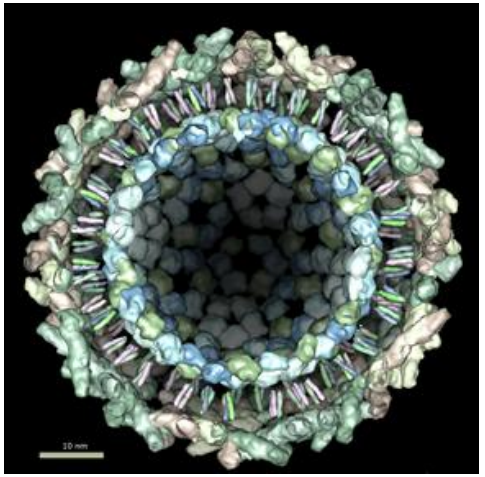


Sorveglianza estiva delle malattie trasmesse da vettori: dati del 2017 e linee operative per il 2018

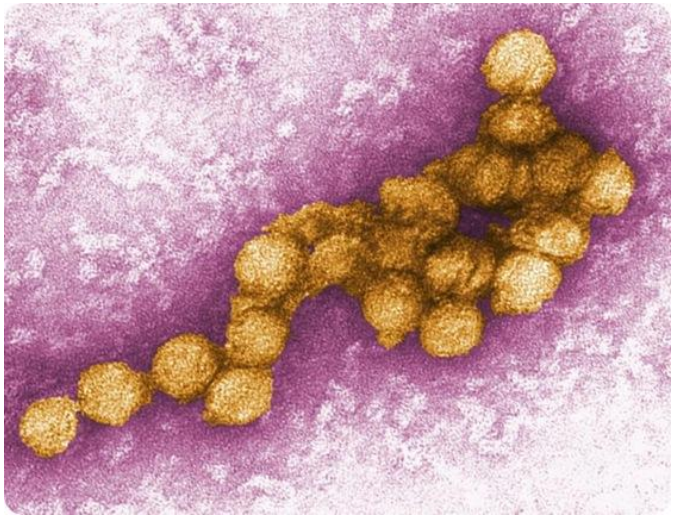
Zeno Bisoffi

Centro Malattie Tropicali
NEGRAR - VERONA - ITALY
Centre for Tropical Diseases
Ospedale Sacro Cuore Don Calabria
FONDAZIONE DON GIOVANNI CALABRIA
PER LE MALATTIE TROPICALI





Sorveglianza 2017



Sorveglianza DENV/CHIK/ZIKA/WNF, Veneto

Anno	dengue pos/ tot	chikungunya pos/ tot	Zika virus pos/ tot	WNF pos/ tot
2010*	14/79 (17.7%)	1/79 (1.2%)		4/38 (10.5%)
2011	3/29 (10.3%)	0/29 (0%)		3/51 (5.8%)
2012	7/126 (5.5%)	2/126 (1.5%)		17/319 (5.3%)
2013	14/203 (6.9%)	0/209 (0%)		16/330 (4.8%)
2014	11/113 (9.7%)	13/133 (9.7%)		1/185 (1.1%)
2015	17/131 (12.9%)	7/128 (5.4%)		1/300 (0.3%)
2016	17/115 (14.8%)	4/129 (3.1%)	15/129 (11.6%)	13/195 (6.7%)
2017	18/198 (9,0%)	1/267 (0,3%)	4/214 (1,8%)	17/347*

ECDC-Dengue	2010	2011	2012	2013	2014
	Cases	Cases	Cases	Cases	Cases
Italy	51	44	74	142	79

DENGUE

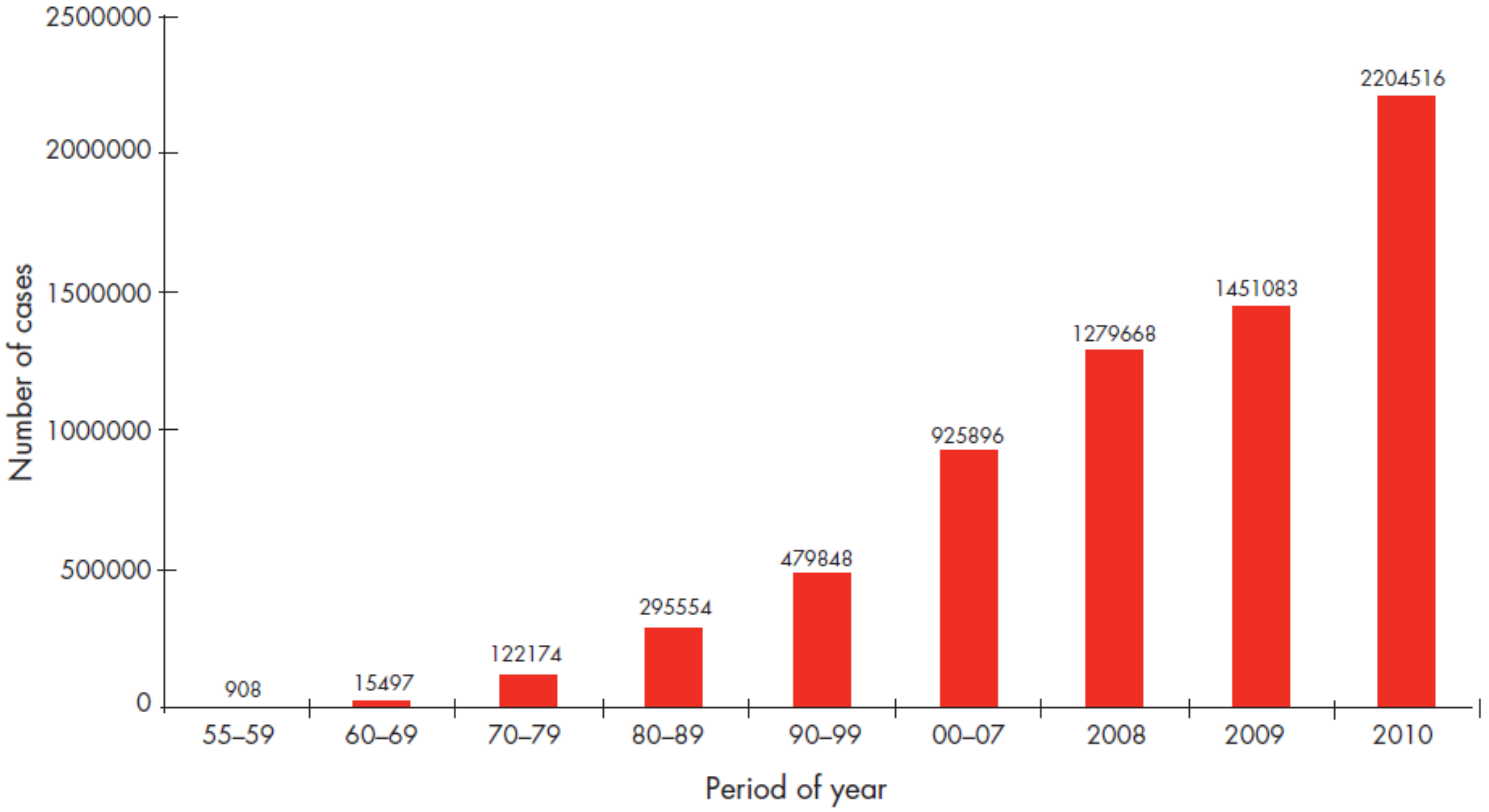
SOGGIORNO	N. CASI
SRI LANKA	6
THAILANDIA	3
INDONESIA	1
PERU'	1
MALDIVE	2
GHANA	1
INDIA	2
GUINEA	1
MYANMAR	1
Totale complessivo	18

ULSS	N. CASI
3	1
4	1
6	2
8	6
9	8
Totale compl.	18

F	9
M	9

Dengue – Recent Global Epidemiology

Figure 1. Average number of dengue and severe dengue cases reported to WHO annually in 1955–2007 and number of cases reported in recent years, 2008–2010



•One recent estimate indicates 390 million dengue infections per year (95% credible interval 284–528 million), of which 96 million (67–136 million) manifest clinically (WHO, updated 24 April 2017)

RAPID COMMUNICATIONS

Miscarriage following dengue virus 3 infection in the first six weeks of pregnancy of a dengue virus-naive traveller returning from Bali to Italy, April 2016

M Zavattoni [1,2], F Rovida [1,2], G Campanini [1], E Percivalle [1], A Sarasini [1], G Cristini [3], LR Tomasoni [4], F Castelli [4], F Baldanti [1,5]

1. Molecular Virology Unit, Microbiology and Virology Department, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy
2. These authors contributed equally to this work
3. Department of Infectious Diseases, Spedali Civili General Hospital, Brescia, Italy
4. University Department of Infectious and Tropical Diseases, University of Brescia and Spedali Civili General Hospital, Brescia, Italy
5. Department of Clinical, Surgical, Diagnostic and Pediatric Sciences, University of Pavia, Pavia, Italy

We report miscarriage following dengue virus (DENV)-3 infection in a pregnant woman returning from Bali to Italy in April 2016. On her arrival, the woman had fever, rash, asthenia and headache. DENV RNA was detected in plasma and urine samples collected the following day. Six days after symptom onset, she had a miscarriage. DENV RNA was detected in fetal material, but in utero fetal infection cannot be demonstrated due to possible contamination by maternal blood.

Previous dengue enhancing subsequent infection

Science

REPORTS

Cite as: L. C. Katzelnick *et al.*, *Science*
10.1126/science.aan6836 (2017).

Antibody-dependent enhancement of severe dengue disease in humans

Leah C. Katzelnick,[1] Lionel Gresh,[2] M. Elizabeth Halloran,[3,4] Juan Carlos Mercado,[5] Guillermina Kuan,[6] Aubree Gordon,[7] Angel Balmaseda,[5] Eva Harris[1]*

[1]Division of Infectious Diseases and Vaccinology, School of Public Health, University of California, Berkeley, USA. [2]Sustainable Sciences Institute, Managua, Nicaragua. [3]Department of Biostatistics, University of Washington, USA. [4]Vaccine and Infectious Disease Institute, Hutchinson Research Center, Seattle, Washington, USA. [5]Laboratorio Nacional de Virología, Centro Nacional de Diagnóstico y Referencia, Ministry of Health, Managua, Nicaragua. [6]Centro de Salud Sócrates Flores Vivas, Ministry of Health, Managua, Nicaragua. [7]Department of Epidemiology, School of Public Health, University of Michigan, USA.

*Corresponding author. Email: eharris@berkeley.edu

For dengue viruses (DENV1-4), a specific range of antibody titer has been shown to enhance viral replication in vitro and severe disease in animal models. Although suspected, such antibody-dependent enhancement (ADE) of severe disease has not been shown to occur in humans. Using multiple statistical approaches to study a long-term pediatric cohort in Nicaragua, we show that risk of severe dengue disease is highest within a narrow range of pre-existing anti-DENV antibody titers. By contrast, we observe protection from all symptomatic dengue disease at high antibody titers. Thus, immune correlates of severe dengue must be evaluated separately from correlates of protection against symptomatic disease. These results have implications for studies of dengue pathogenesis and for vaccine development, because enhancement, not just lack of protection, is of concern.

Philippines halts programme for 'dangerous' dengue fever vaccine given to 730,000 children

Vaccine used in £51.5m immunisation drive can cause severe cases of potentially fatal infection, admits manufacturer

Chris Baynes | Friday 1 December 2017 12:18 GMT | 1 comment

DENGUE VACCINE

New data conclusively indicate that persons receiving the Tetravalent Dengue Vaccine by Sanofi Pasteur who had not been infected with dengue virus prior to vaccination have a higher risk of more severe illness and hospitalization due to dengue compared to unvaccinated persons, regardless of age

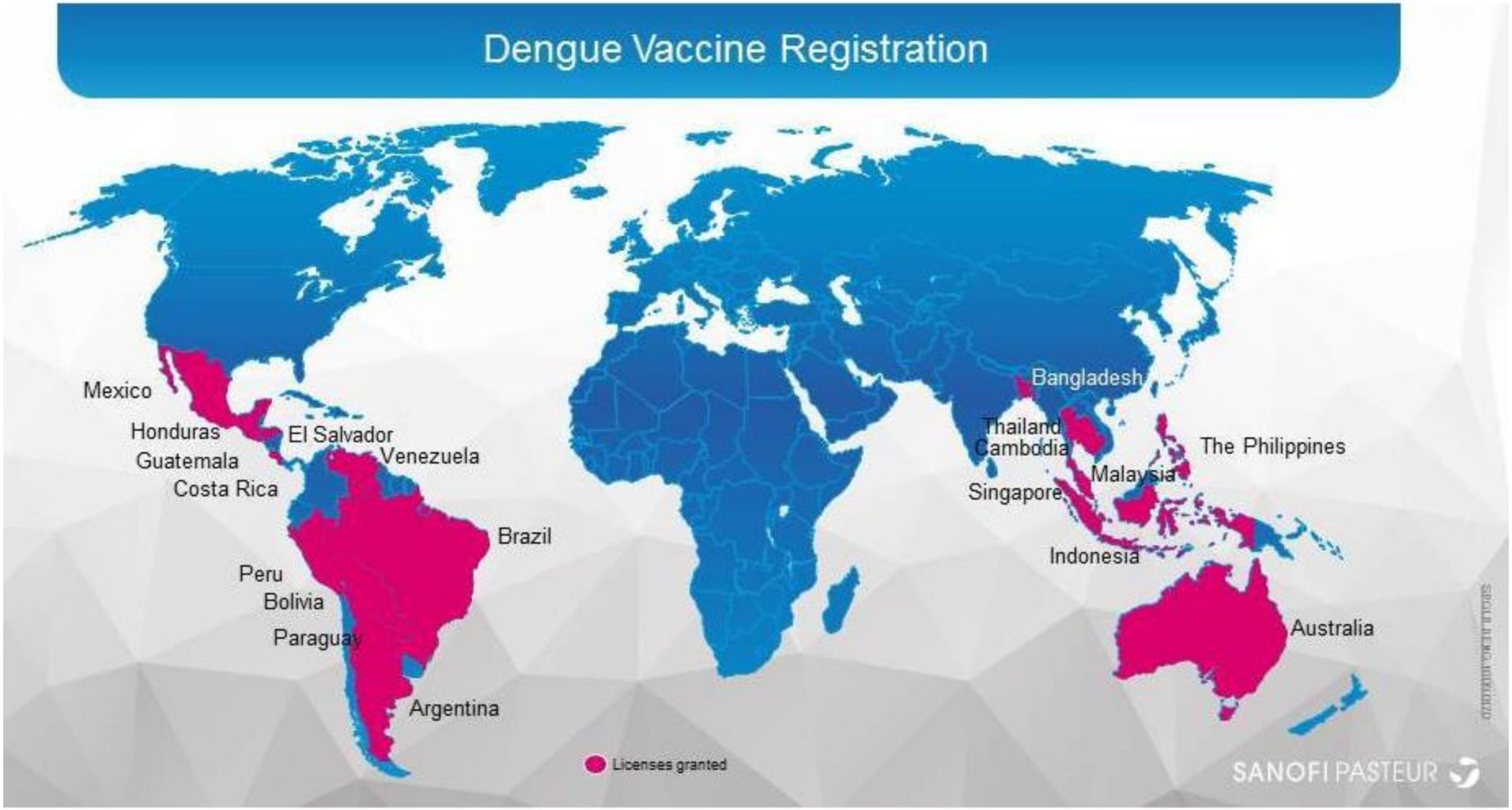
WHO now recommends that this specific vaccine only be administered to persons with proven dengue infection prior to vaccination, which effectively precludes most travelers

Precludes all endemic individuals who have no access to testing for dengue antibodies

The Tetravalent Dengue Vaccine is approved in approximately 20 dengue-endemic countries; travelers and expatriates should be advised to avoid it unless they have reliable laboratory evidence of past dengue infection

Courtesy of Sanofi Pasteur

DENGUE VACCINE REGISTERED IN 19 COUNTRIES



To date, dengue vaccine has been registered in nineteen countries: Argentina, Australia, Bangladesh, Bolivia, Brazil, Cambodia, Costa Rica, El Salvador, Guatemala, Honduras, Indonesia, Malaysia, Mexico, Paraguay, Peru, The Philippines, Singapore, Thailand and Venezuela.

NEXT CANDIDATE - DENGUE

Live virus, native DENV-2 + chimeric -1,-3,-4

2 doses 1 yr apart optimal in dengue-naïve (travelers)

DENV serotype-specific antibodies at 18 months for all 4 serotypes

4.5% dengue attack rate in placebo; 1.5% in vaccines

Safety issues hard to know at this point

Immunogenicity and safety of one versus two doses of tetravalent dengue vaccine in healthy children aged 2–17 years in Asia and Latin America: 18-month interim data from a phase 2, randomised, placebo-controlled study

Xavier Sáez-Llorens, Vianney Tricou, Delia Yu, Luis Rivera, José Jimeno, Ana Cecilia Villarreal, Epiphany Data, Sonia Mazara, Maria Vargas, Manja Brose, Martina Rauscher, Suely Tuboi, Astrid Borkowski, Derek Wallace

Summary

Background Development of vaccines that are effective against all four dengue virus serotypes (DENV-1–4) in all age groups is important. Here, we present 18-month interim data from an ongoing study undertaken to assess the immunogenicity and safety of Takeda's tetravalent dengue vaccine (TDV) candidate over 48 months in children living in dengue-endemic countries.

Methods We undertook a phase 2, multicentre, randomised, double-blind, placebo-controlled study at three sites in

Lancet Infect Dis 2017

Published Online November 6, 2017 http://dx.doi.org/10.1016/S1473-3099(17)30632-1

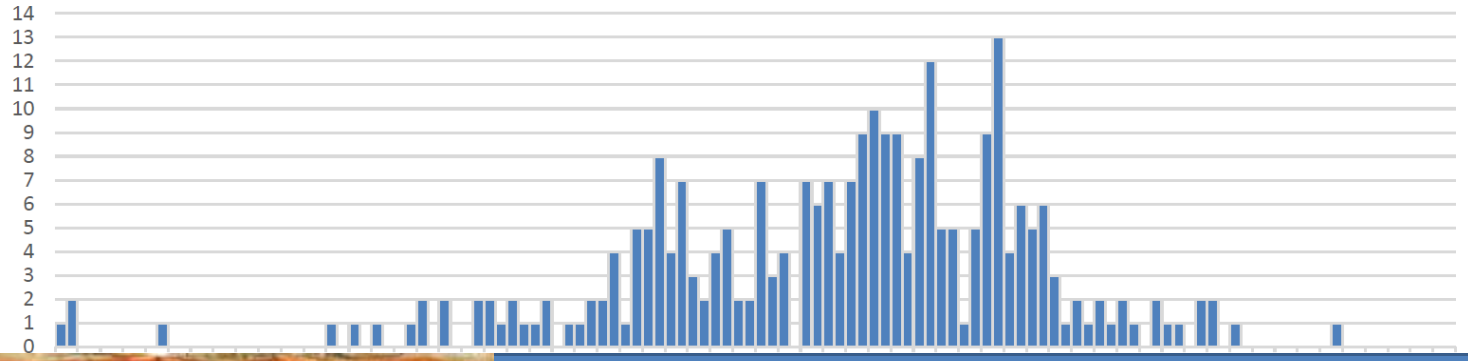
See Online/Comment http://dx.doi.org/10.1016/

CHIKUNGUNYA

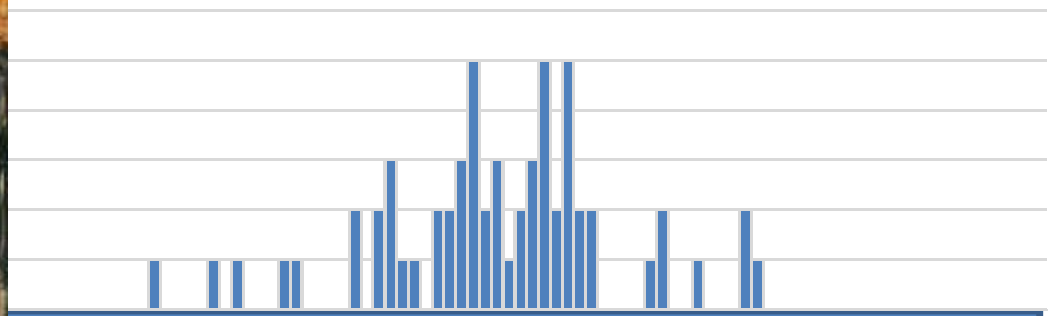
SOGGIORNO	N. CASI
BRASILE	1
Totale complessivo	1

ULSS	N. CASI
9	1
Totale compl.	1

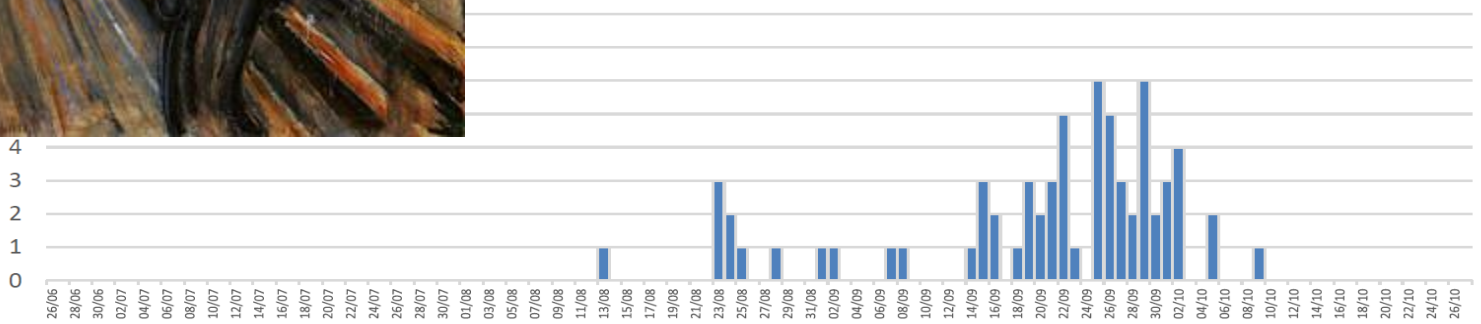
ANZIO: Curva Epidemica (abitanti ad Anzio o casi epidemiologicamente correlati), per data insorgenza
ANZIO: Epidemic curve (Anzio residents or cases or epidemiologically linked), date of onset



mica (nessuna storia di viaggio) per data insorgenza sintomi
idemic Curve (no history of travel), date of onset



davalle marina): Curva Epidemica, per data insorgenza sintomi
bria Region: Epidemic Curve, date of onset

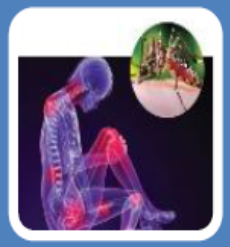


Ministero della Salute

ISTITVTO SVPERIORE DI SANITA

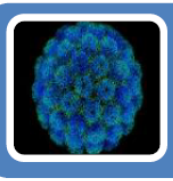
ITALIA: FOCOLAI AUTOCTONI DI INFEZIONE DA VIRUS CHIKUNGUNYA
(aggiornato al 27 ottobre 2017)

ITALY: AUTOCHTONOUS CASES OF CHIKUNGUNYA VIRUS
(updated 27 October 2017)



402 Casi notificati totali:
331 Regione Lazio
63 Regione Calabria
5 Regione Emilia-Romagna
1 Regione Marche
2 Paesi Europei (Francia/Germania)

225 Casi confermati totali:
176 Regione Lazio (Anzio, Roma e Latina)
45 Regione Calabria (Guardavalle marina)
1 Regione Emilia-Romagna con legame epidemiologico Anzio
1 Regione Marche con legame epidemiologico Anzio
1 Francia con legame epidemiologico Anzio
1 Germania con legame epidemiologico Roma



Gravità dell'infezione
Ospedalizzati: **30** (**7** %)
Deceduti: **1** caso confermato

ZIKA virus

SOGGIORNO	N. CASI
CUBA	3
COSTA D'AVORIO	1
Totale complessivo	4

ULSS	N. CASI
3	1
7	1
8	1
9	1
Totale compl.	4

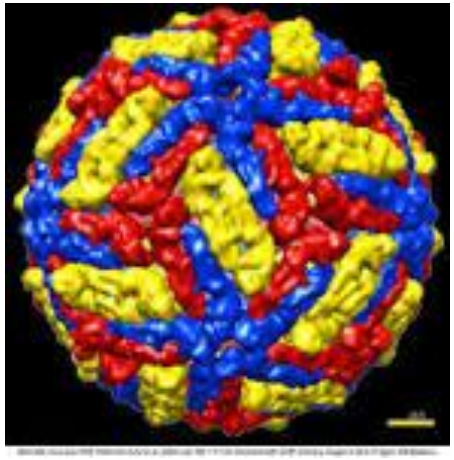
Non sono stati riportati casi in gravidanza

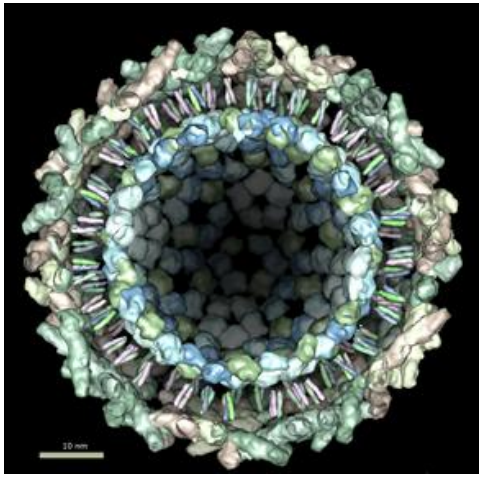
WEST-NILE

WNFever	Ulss	n.casi
	Ulss 3	1
	Ulss 5	2
	Ulss 6	4
	Ulss 8	2
	Ulss 9	1
	Tot.	10

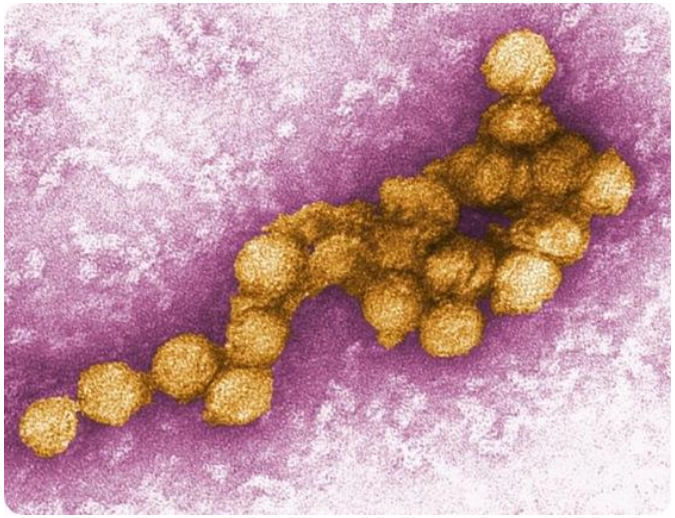
WNND	Ulss	n.casi
	Ulss 2	2
	Ulss 3	1
	Ulss 4	1
	Ulss 5	3
	Tot.	7

NB. Per il secondo anno consecutivo il numero delle febbri (WNF) è superiore a quello delle forme neuroinvasive (WNND)





Sorveglianza 2018



Piano nazionale integrato di sorveglianza e risposta ai virus West Nile e Usutu - 2017

Criterio clinico	WNV Qualsiasi persona che presenti febbre o almeno una delle seguenti manifestazioni cliniche: - encefalite; - meningite a liquor limpido; - poliradicolo-neurite (simil Guillain-Barré); - paralisi flaccida acuta.	USUTU Qualsiasi persona che presenti febbre o almeno una delle seguenti manifestazioni cliniche: - encefalite; - meningite a liquor limpido; - poliradicolo-neurite (simil Guillain-Barré); - paralisi flaccida acuta.

NB è stato successivamente chiarito che per USUTU si procede solo in caso di malattia neuroinvasiva

Sorveglianza 2018

Visti i buoni risultati del 2017 nonostante si sia di fatto usciti dalla fase di progetto pilota per entrare in quella di sorveglianza ordinaria, non si prevedono sostanziali modifiche del piano per il 2018, a meno di diverse indicazioni ministeriali, ad ora non pervenute.

NB: è stato segnalato dal Laboratorio di riferimento di Padova che nel corso del 2017 sono pervenute parecchie richieste di test per chikungunya in soggetti che non avevano viaggiato, questo anche prima del recente outbreak in Lazio e in Calabria.
È opportuno ricordare ai colleghi interessati, e verrà ribadito con chiarezza ancora maggiore nel piano 2018, che tali richieste sono improprie, e che in caso di dubbio caso autoctono è necessario interpellare il collega reperibile del CMT – Negrar per discutere il caso

BRAZIL YF MAP

2016

Da dic 2016
>2000 casi/>500 decessi

Current

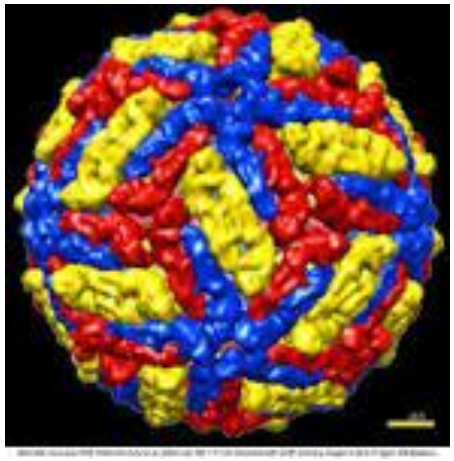
16 casi in viaggiatori, tutti non vaccinati!

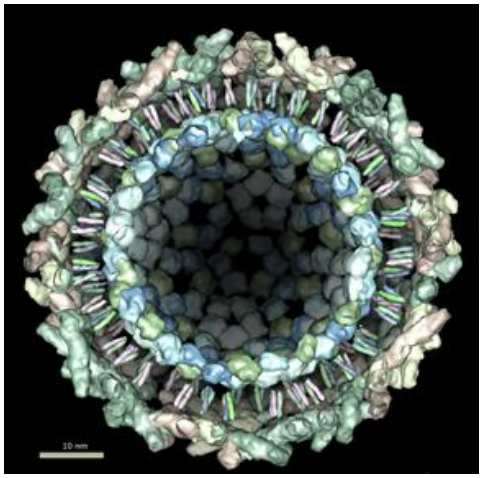
10 casi in viaggiatori da gennaio al 16/3/2018

UNCERTAINTY OF LIFE-LONG PROTECTION OF YFV FOR TRAVELLERS

- Little evidence for life-long protection after a single dose of YFV
  - esp for travellers from non endemic areas
- Studies included: majority of vaccinees lived or stayed for a prolonged period of time
  - role of natural immunity/natural "booster"
- Methods of measuring immune response after YFV differed by studies
- Rapid decline was seen in immunocompetent travellers (Niedrig et al., 1999)
- Vaccine failure might be underestimated (Camara et al., 2008)
- Role of T-cells?
  - repetitive stimulation for long-term immune response (Campi-Azevedo et al., 2016)

Grazie per l'attenzione…





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