UNIVERSITÀ DEGLI STUDI
DI MODENA E REGGIO EMILIA

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Modena
Policlinico

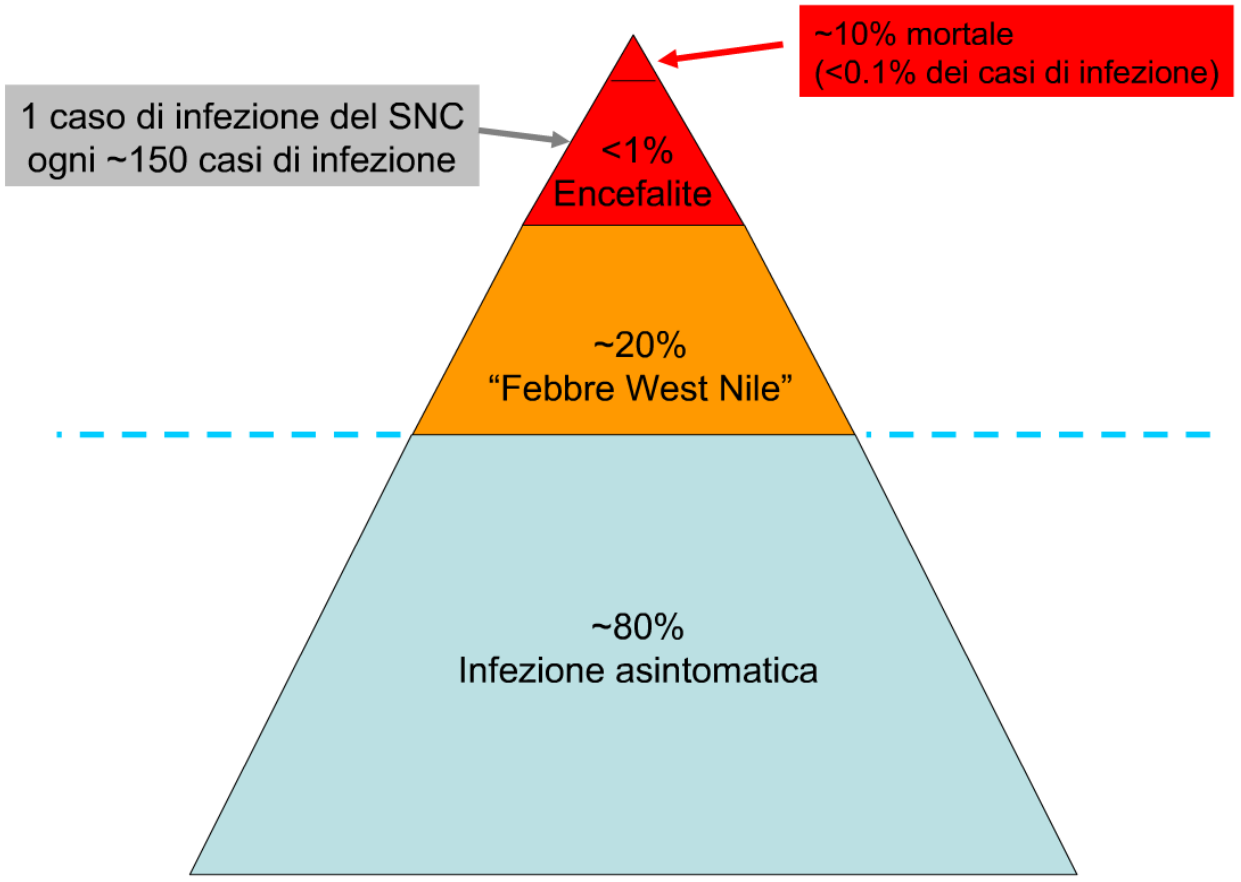
West Nile e Usutu virus: l'infezione nell'uomo

Azienda Ospedaliero-Universitaria Policlinico Modena

Antonella Grottola

Teramo 8 maggio 2015

Infezione da WNV nell'uomo: "Iceberg"



West Nile Fever

West Nile Fever (WNF)

- Incubazione da 3 a 15 giorni
- Evoluzione benigna, autolimitante in 7-10 giorni
- Sindrome febbrile ad esordio acuto
- Sintomi : febbre, mal di testa, mialgia, rash cutaneo (torace, dorso, arti, addome), sintomi gastroenterici, linfoadenopatia e astenia che può persistere per qualche mese

Campbell G, et al. Lancet Infect Dis2002;2:519 –529
Watson JT, et al. Ann Intern Med 2004;141:360 –365
ZouS, et al J Infect Dis2010; 202:1354-57

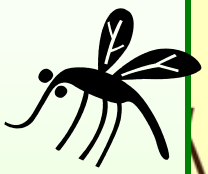
Esiti

- Inabilità studio e/o lavoro in media per 10 giorni
- Stanchezza persistente in media per circa 30 giorni
- Recupero del precedente stato di salute in 60 giorni

Watson et al. Ann Intern Med 2004; 141: 360-365

West Nile Neuroinvasive Disease

- Incubazione da 3 a 15 giorni
- Meningite
  Encefalite → Quadri misti
  Mielite
  Neurite (nervi cranici/periferici), neuropatie, Guillain-Barré)

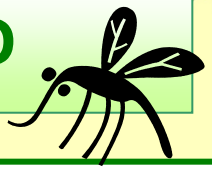


Sintomi generali: febbre, disturbi gastrointestinali, segni meningei, rash

Sintomi neurologici: differenti a seconda della sede colpita

Davis LE, et al. Ann Neurol2006;60:286–300

Complicanze e sequele della WNND



Complicanze

- Insufficienza respiratoria con necessità di VM
- Polmonite
- Batteriemia
- Eventi tromboembolici
- Decesso

Sequele

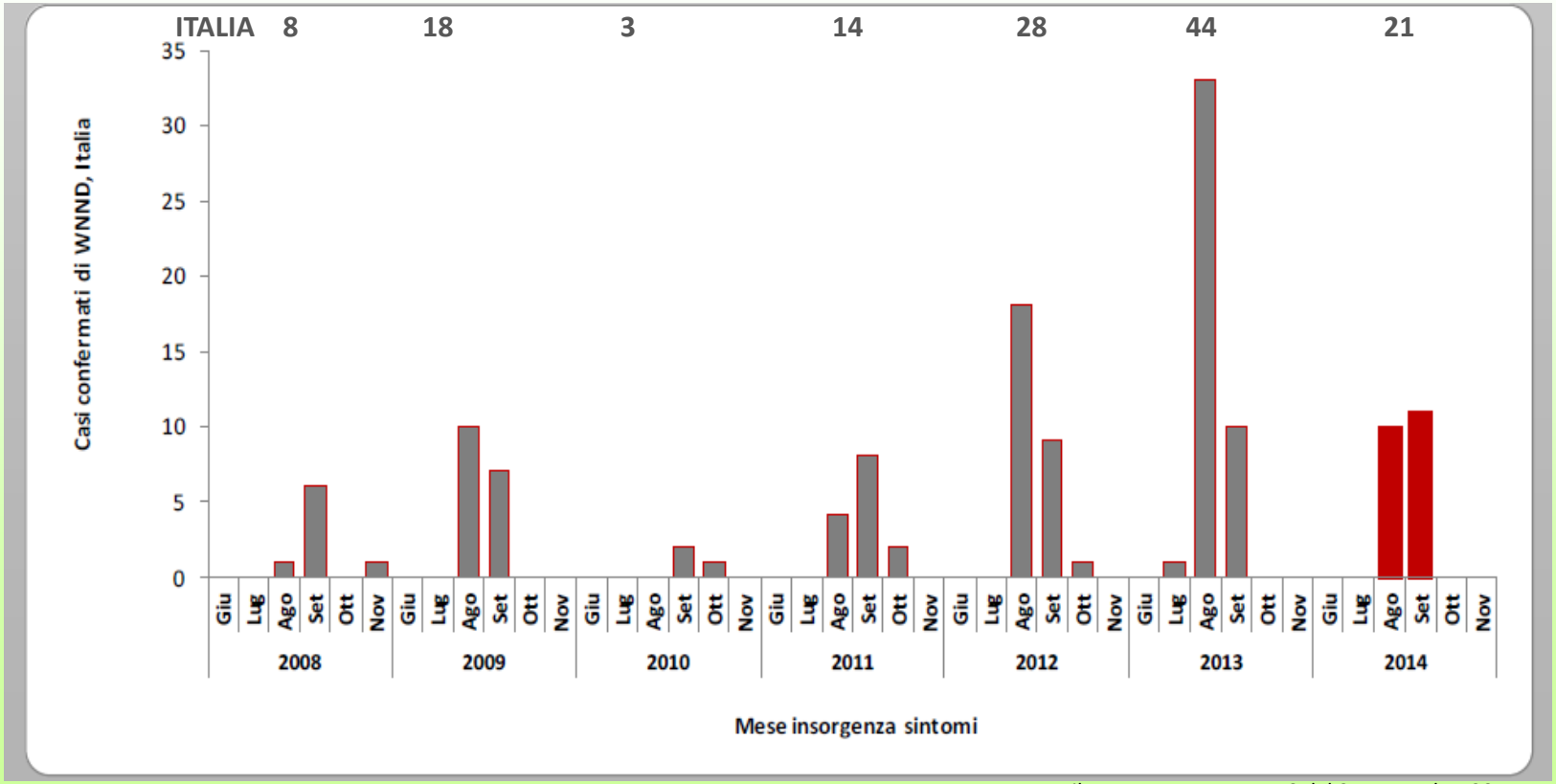
Dopo1 anno dall'infezione

- Stanchezza
- Deficit mnemonici
- Turbe della deambulazione
- Depressione
- Ipostenia muscolare

WNND in Italia

Andamento dei casi di WNND confermati per mese insorgenza sintomi, Italia 2008 - 2014

RER	3	9	0	0	0	20	7
MO	*0*	*2*	*0*	*0*	*0*	*7*	*2*
ITALIA	8	18	3	14	28	44	21



West Nile News-Rapporto N. 13 del 27 Novembre 2014
Reparto di Epidemiologia delle Malattie Infettive, CNESPS - ISS

USUV in humans

- In **1959** USUTU virus was first isolated in Swaziland (South Africa) from a woman exhibiting a fever and skin rash.

  (Adams F, Institut Pasteur de Dakar)

- In **1981** a case occurred in the Central African Republic in a patient with fever and rash. (Nikolai B et al., 2011)

- In **2004** in Burkina Faso, another case of a 10 year old patient with fever and jaundice was reported. (Nikolai B et al., 2011)

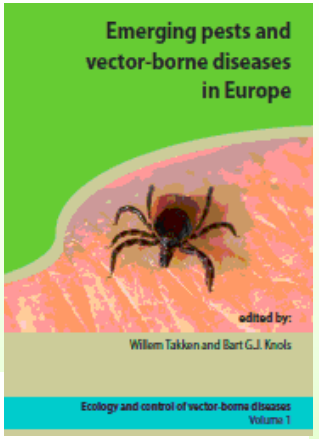
USUV human infection in Europe

Emergence of Usutu virus in Central Europe: diagnosis, surveillance and epizootiology

Herbert Weissenböck, Sonja Chvala-Mannsberger, Tamás Bakonyi and Norbert Nowotny

Emerging pests and vector-borne diseases in Europe

Wageningen Academic Publishers2007, 153-168



USUV-infections in humans

203 human blood samples from individuals exposed to mosquitoes in USUV-endemic areas were examined by RT-PCR for detection of USUV-specific nucleic acid and 208 human blood samples were investigated by HI test and by PRNT for the presence of antibodies to USUV. Many of the subjects included in this study exhibited rash of unknown origin, and they tested negative for Lyme-Borreliosis. In this pre-selected group, 83 individuals showed antibody titres to USUV between 1:20 and >1:160 in HI test, and 52 of them could be confirmed by PRNT, which results in an overall seroprevalence of 25% in this pre-selected group. In one 'fresh' case USUV nucleic acid was demonstrated by RT-PCR. These data indicate that USUV is able to infect humans without inducing severe disease; in particular, no association between neurological disease and USUV infection could be established in human beings. Transient rash, however, seems to be a clinical symptom associated with USUV infection in human beings (N. Nowotny, unpublished data, Weissenböck and Nowotny 2006).

USUV human infection in Italy

At the end of the summer of 2009 the USUV was associated with neurological disorders in two immunocompromised patients. They have been the first human cases of USUV neurological illness described worldwide.

www.eurosurveillance.org

CASE 1

Rapid communications

First human case of Usutu virus neuroinvasive infection, Italy, August-September 2009

M Pecorari (pecorari.monica@policlinico.mo.it)[1], G Longo[2], W Gennari[1], A Grottola[1], A MT Sabbatini[1], S Tagliazucchi[1], G Savini[3], F Monaco[3], M L Simone[4], R Lelli[3], F Rumpianesi[1]

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3. Department. of Virology, National Reference Centre for West Nile and Usutu disease, OIE Reference Laboratory for Bluetongue, Istituto Zooprofilattico Sperimentale dell'Abruzzo e Molise 'G. Caporale', Teramo, Italy
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This article was published on 17 December 2009.
Citation style for this article: Pecorari M, Longo G, Gennari W, Grottola A, Sabbatini AM, Tagliazucchi S, Savini G, Monaco F, Simone ML, Lelli R, Rumpianesi F. First human case of Usutu virus neuroinvasive infection, Italy, August-September 2009. Euro Surveill. 2009;14(50):pii=19446. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19446

Eurosurveillance, Volume 14, Issue 50, 17 December 2009

CASE 2

Rapid communications

USUTU VIRUS INFECTION IN A PATIENT WHO UNDERWENT ORTHOTROPIC LIVER TRANSPLANTATION, ITALY, AUGUST-SEPTEMBER 2009

F Cavrini[1,2], P Gaibani[1,2], G Longo[3], A M Pierro[1], G Rossini[1], P Bonilauri[4], G E Gerunda[5], F Di Benedetto[5], A Pasetto[6], M Girardis[6], M Dottori[4], M P Landini[1], V Sambri (vittorio.sambri@unibo.it)[1]

a. CASE 1

Clinical History

In May 2009: a 61 year old woman underwent right hemicolectomy because of diffuse large cell B lymphoma, CD20/L26+, CD3-, CD10+, bcl6+, bcl2+

Proliferative index MiB1 (95% neoplastic cells)

High International Prognostic Index (IPI) score (based on Performance Status, Clinical stage, N° of localizations, LDH serum level, symptoms) predisposed to a very aggressive form

Total body CT scan shows multiple lymph nodes regions in chest and pancreas, hypodense lesions in the liver, no bone marrow localization

b. CASE 1

Clinical history

In June 2009, chemotherapy was started (CHOP-R):

cyclofosfamide 750mg/mq, vincristine 1.4mg/mq, doxorubicine 50 mg/mq, steroids 80 mg/mq, Rituximab 375 mg/mq

after 4 treatments, CT showed:
Complete remission of lymphoma.

Treatment was completed on the 21st of August 2009 after 6 administrations.

c. CASE 1

On the 5th of September 2009

Clinical history

The patient was admitted to the hospital with a 10-days history of fever (T=39.5°C). At home the patient was treated with antibiotic therapy without results.

(moxifloxacine, amoxcilline/clavulanate, levofloxacine, fluconazole, tazobactam/piperacilline, meropenem + teicoplanine)

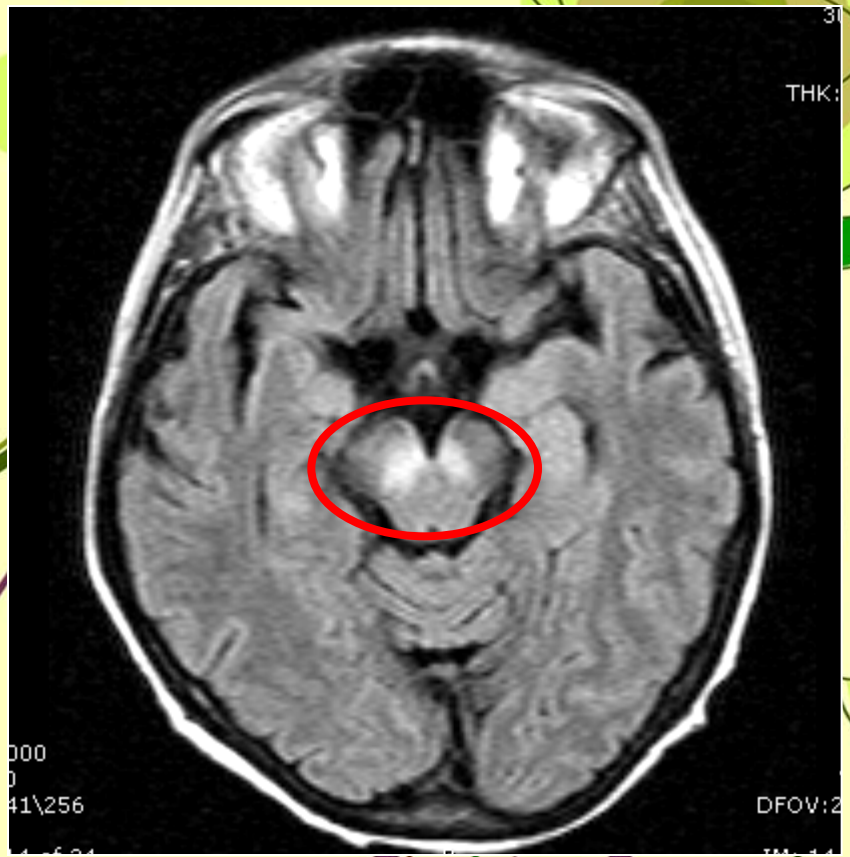
Total body CT scan: no other findings consistent with recurrent lymphoma

Neurologic examination showed generalized tremors, positivity to Romberg test, dysmetria and weakness of the limbs without cranial nerve affections. Meningoencephalitis?

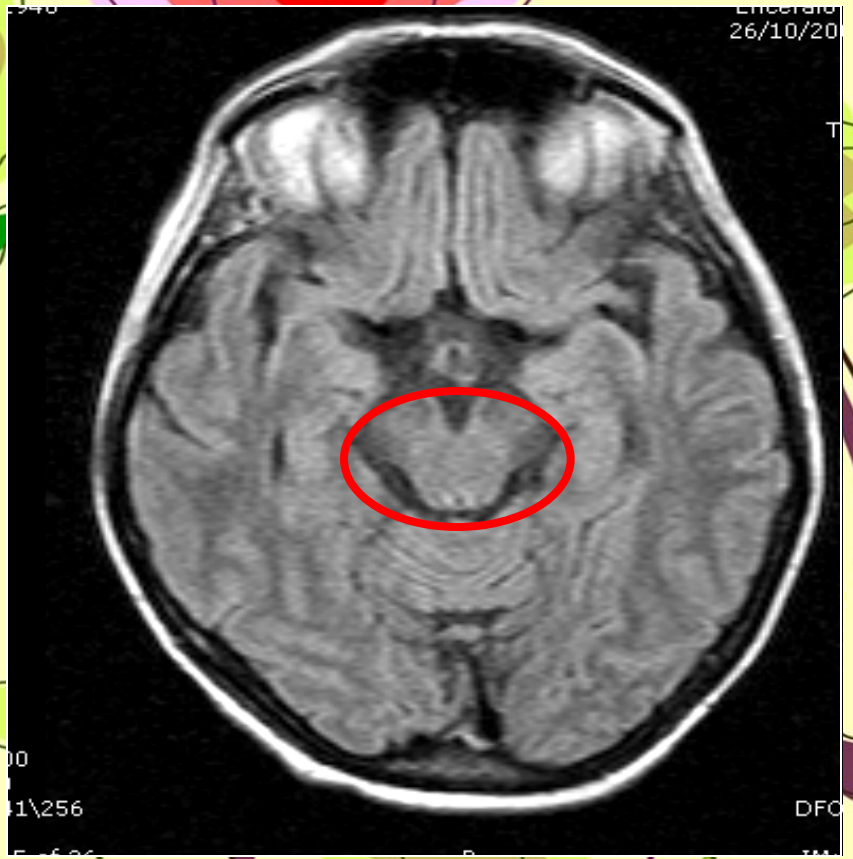
EEG: diffuse slow theta waves and slow spike in left frontal parietal areas

Brain MRI: a signal alteration of the *substantia nigra*

d. CASE 1



Brain RM on 10 September 2009



Brain RM on 16 October 2009

The picture on the left shows a degeneration of the *substantia nigra* with improvement (picture at right) of the MRI control after one month

e. CASE 1

On the 5th of September 2009

Microbiological and virological findings

Culture examinations of blood, urines and faeces were negative.

Molecular blood tests for the most common viruses (CMV, HSV1/2, EBV, adenovirus, parvovirus B19, polyomavirus JC, enterovirus) were negative.

f. CASE 1

On the 11th of September 2009

Cerebrospinal fluid (CSF) examination: limpid without any alteration detected in the chemical analysis.

Total proteins: 37mg/dl (normal values:12-60);
Glucose: 46mg/dl (normal values:45-80);
Clorure: 116 mEq/L (normal value:115-132)

Cells: 20/mmc
Cellular sediment showed population of mononuclear cells and few neutrophils

Cytology

several normal mononuclear cells, some activated lymphocytes, few neutrophils and monocytes

g. CASE 1

On the 11th of September 2009

Cerebrospinal fluid CSF virological findings

Molecular CSF tests for the most common viruses (CMV, HSV1/2, EBV, adenovirus, parvovirus B19, polyomavirus JC, enterovirus) mumps virus, West Nile Virus (specific RT-PCR) were negative, but CSF was positive to heminested RT-PCR for specific NS5 (214bp) region of "*Flaviviridae*" genomic (DENV, JEV, WNV, YFV, USUV and others).

The sequencing of amplified product has identified USUV. The alignment of the sequence shared an high nucleotide similarity with the Vienna 01 and the Budapest 05 strains.

PCR on serum confirmed the presence of RNA of USUV for three times during the acute phase of infection.

Serum and plasma specimens before and after the acute phase of infection were negative for USUV-RNA.

h. CASE 1

In May 2010

Total body CT scan: abdominal progression disease (peritoneum and liver localizations)

No bone marrow localization

Neurological symptoms improved by carbidopa and levodopa based therapy. A physiotherapy program was undertaken with progressive improvement of the global muscular strength. After approximately one month, the patient showed recovery of neurological functions.

a. CASE 2

Clinical History

In August 2009: a 45 year old woman showed persistent diarrhea a few days after returning from Egypt. She was admitted to the hospital, where she was diagnosed with Thrombotic Thrombocytopenic Purpura (TTP) (M. Moskowitz)

On admission to hospital:

PLT=11. 000/mmc; Hb=9.0 g/dl; LDH=1763 U/L; Bilirubin=1. 87 mg/dl; GOT=36 U/L; Dimer= 3270ng/ml

CT: Chest-Abdomen-Pelvis, esophagus-gastro-duodenoscopy and colonoscopy normal

b. CASE 2

Treatment program

Plasma exchange (PEX); methylprednisolone 60mg/day; blood transfusion after I and II PEX; Acetyl Salicylic Acid after III PEX

Overall the patient received 18 PEX (from August 10th to September 4th). After normalization of haematological indexes (PLT=185.000/mmc, GB=5.500/mmc, Hb=11.2 g/dl LDH=285 U/L) the woman was discharged because of TTP resolution.

c. CASE 2

On September 18th, 2009

The patient was admitted to the hospital for pneumonia, persistant fever (T= 38°C for 7 days), headache, skin rash, mild increment of cytolytic liver (GOT/GPT=306/277), increment of LDH=1112 U/L without signs of TTP relapse (CT total body negative).

She was treated with antibiotic without results.

PLT = 174.000/mmc

Blood Smear: negative for hemolysis, activated lymphocytes

Antibiotic therapy: moxifloxacin and amoxicillin clavulanate

d. CASE 2

Clinical history

On September 19th 2009, again persisting fever, headache, skin rash, further increment of cytolytic liver enzymes (GOT/GPT= 3119/1528) and further increment of LDH (8183 U/L). Within a few days, a fulminant hepatitis and impairment of neurological functions were observed and rapidly resulted in a coma.

On September 21st 2009 The molecular and serological laboratory tests for the most common viruses associated with hepatitis (hepatitis A, B, C viruses, CMV, EBV) gave negative results.

On September 24th 2009 a plasma specimen was positive for USUV RNA by hemisted RT-PCR (NS5 region).

Additional blood samples obtained during the following 15 days gave negative results for USUV.

e. CASE 2

Clinical history

On September 25th, 2009, the patient received an orthotropic liver transplant (OLT)

After liver transplant

Excellent recovery of liver function but only a low level of consciousness and limited motor functions were realized. The encephalopathy lasted for about a month with slow functional recovery from 3 to 6 months after transplant

USUV neuroinvasive infection
...about pathogenesis and transmission

In the clinical cases reported here, the immunodepressive status of the patients due to both the underlying diseases and treatments, may have played an important role in USUV infection and its pathogenicity.

- neoplastic disease
- prior chemotherapy/anti-CD20 Rituximab/steroids therapy
- liver transplant

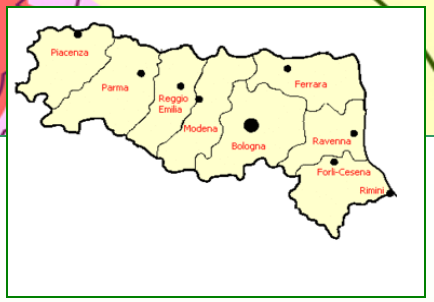
Vector-human transmission?

Since the patient's area of residence is endemic for USUV vectors it is likely that the infection was transmitted through mosquito bites.

Blood transfusion?

The transfusions can not be excluded as a possible source of infection.

And after 2009?



1. VIROLOGICAL SURVEY in E. ROMAGNA, ITALY

Regional Reference Centre for Microbiological Emergencies (CRREM).

Journal of Clinical Virology 50 (2011) 221–223

A rapid and specific real-time RT-PCR assay to identify Usutu virus in human plasma, serum, and cerebrospinal fluid

Francesca Cavrini[a], Maria Elena Della Pepa[b], Paolo Gaibani[a], Anna Maria Pierro[a], Giada Rossini[a], Maria Paola Landini[b], Vittorio Sambri[a,b,*]

104 human specimens [cerebrospinal fluid (CSF), plasma, serum] collected in the summers of 2008 and 2009 from 44 patients with suspected meningoencephalitis WNV-negative.

3/40 patients were positive in CSF for USUV RNA while plasma and sera were negative.

2. SEROLOGICAL SURVEY in E. ROMAGNA, ITALY

Regional Reference Centre for Microbiological Emergencies (CRREM).

Detection of specific antibodies against West Nile and Usutu viruses in healthy blood donors in northern Italy, 2010–2011

Pierro, P. Gaibani, C. Spadafora1 D. Ruggeri, V. Randi, S. Parenti, A. C. Finarelli, G. Rossini, M. P. Landini and V. Sambri

Clinical Microbiology and Infection, Volume 19 Number 10, October 2013

- Between 1 September 2010 and 30 June 2011, 6.000 serum samples were collected from blood donors living in different districts of Emilia-Romagna, and tested for the presence of neutralizing antibodies against WNV and USUV (MNTA)

0.78% (47/6000)subjects positive for WNV

0.23% (14/6000)subjects positive for USUV

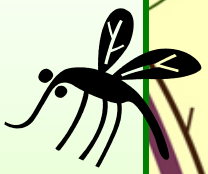
- USUV-specific neutralizing immune response
- USUV can be able to asymptomatically infect humans

3. SEROLOGICAL DIAGNOSIS OF USUV INFECTION IN CROATIA, 2013

First cases of human Usutu virus neuroinvasive infection in Croatia, August-September 2013: clinical and laboratory features.

Santini M[1], Vilibic-Cavlek T, Barsic B, Barbic L, Savic V, Stevanovic V, Listes E, Di Gennaro A, Savini G.

J Neurovirol. **2015 Feb;21(1):92-7.**



Case	Age (years)	Gender	Clinical diagnosis	Underlying disease	Outcome	Vaccination history
1	29	F	Meningoencephalitis	–	Recovered	No
2	61	M	Meningoencephalitis	Hypertension, cardiomyopathy	Recovered	No
3	56	M	Meningitis	Diabetes, hypertension	Recovered	No

Spread of USUV in humans in Northern Italy, Modena

Istituto Zooprofilattico Sperimentale of Teramo

Azienda Ospedaliero-Universitaria Policlinico of Modena

915 human samples analyzed for USUV and WNV infection

306 CSF from inpatients with neurological impairment

(sampling between June-November 2008-2009)

Onestep RT-PCR USUV-specific (NS5 region)

Real-time RT-PCR WNV (E region)

Nucleotide sequencig on positive samples

Origin and evolution of recent vector-borne virus incursions in the Mediterranean Basin

Italian Ministry of Health
Ricerca Finalizzata 2009

IZS of Teramo

609 sera from inpatients/outpatients with different anamnesis

(sampling between July-January 2008-2011)

Onestep RT-PCR USUV-specific (NS5 region)

Real-time RT-PCR WNV (E region)

Microneutralization assay (mNTA) for USUV/WNV

Serological results

Year	Neutralization test		Total tested samples	Positive samples (%)	CI(95%)
	Positive samples	Negative samples			
2008	14	230	244	5,74	3,47-9,40
2009	21	285	306	6,86	4,55-10,27
2010	4	41	45	8,89	3,62-20,79
2011	*1*	*13*	*14*	*7,14*	*1,66-31,95*
Total	40	569	609	6,57	4,87-8,82

Anti-USUV Ab

USUV 6.57%

WNV 2.96%

p<0.05%

Anti-WNV Ab

Blood donors seroprevalence (RER)

WNV **0.7-0.8%**
(2008-2011)

USUV **0.23%**
(2010-2011)

Year	Neutralization test		Total tested samples	Positive samples (%)	CI(95%)
	Positive samples	Negative samples			
2008	5	239	244	2,05	0,90-4,70
2009	11	295	306	3,59	2,04-6,32
2010	1	44	45	2,22	0,53-11,53
2011	*1*	*13*	*14*	*7,14*	*1,66-31,95*
Total	18	591	609	2,96	1,89-4,62

1. Virological results

WNV Real-time RT-PCR

all CSF and sera were negative

CSF = 0%; CI95%: 0%-0.97%; **Serum** = 0%; CI95%: 0%-0.49%

USUV Onestep RT-PCR

Human samples	RT-PCR		Total tested samples	Positive samples (%)	CI(95%)
	Positive samples	Negative samples			
CSF	7 *	299	306	2.29	1.13-4.64
SERUM	2 * *	607	609	0.33	0.10-1.18

* 6 CSF 2008 , 1 CSF 2009

** 2 Sera 2009

$\chi 2 = 8.03$; $p = 0.005$; $gdl = 1$

2. Virological results

USUV vs WNV

Virus	RT-PCR		Total tested samples	Positive samples (%)	CI(95%)
	Positive samples	Negative samples			
USUV	9	906	915	0.87	0.45-1.71
WNV	0	915	915	0	0-0.33

$p < 0,005$

PLoS One. 2010; 5 (12)

Evidence of Simultaneous Circulation of West Nile and Usutu Viruses in Mosquitoes Sampled in Emilia-Romagna Region (Italy) in 2009

Mattia Calzolari[1*], Paolo Bonilauri[1], Romeo Bellini[2], Alessandro Albieri[2], Francesco Defilippo[1], Giulia Maioli[1], Giorgio Galletti[1], Antoni Gelati[3], Ilaria Barbieri[1], Marco Tamba[1], Davide Lelli[1], Elena Carra[1], Paolo Cordioli[1], Paola Angelini[4], Michele Dottori[1]

Emilia Romagna regional surveillance on insect borne diseases plan

The PCR detections showed a stronger and longer USUV circulation in mosquitoes with respect to WNV, as displayed by the higher number of USUV positive pools detected …

PLoS One. 2012; 7 (5)

Mosquito, Bird and Human Surveillance of West Nile and Usutu Viruses in Emilia-Romagna Region (Italy) in 2010

Mattia Calzolari[1]*, Paolo Gaibani[2], Romeo Bellini[3], Francesco Defilippo[1], Anna Pierro[2], Alessandro Albieri[3], Giulia Maioli[1], Andrea Luppi[1], Giada Rossini[2], Agnese Balzani[1], Marco Tamba[1], Giorgio Galletti[1], Antonio Gelati[4], Marco Carrieri[3], Giovanni Poglayen[5], Francesca Cavrini[2], Silvano Natalini[6], Michele Dottori[1], Vittorio Sambri[2], Paola Angelini[6], Paolo Bonilauri[1]

Emilia Romagna regional surveillance on insect borne diseases plan

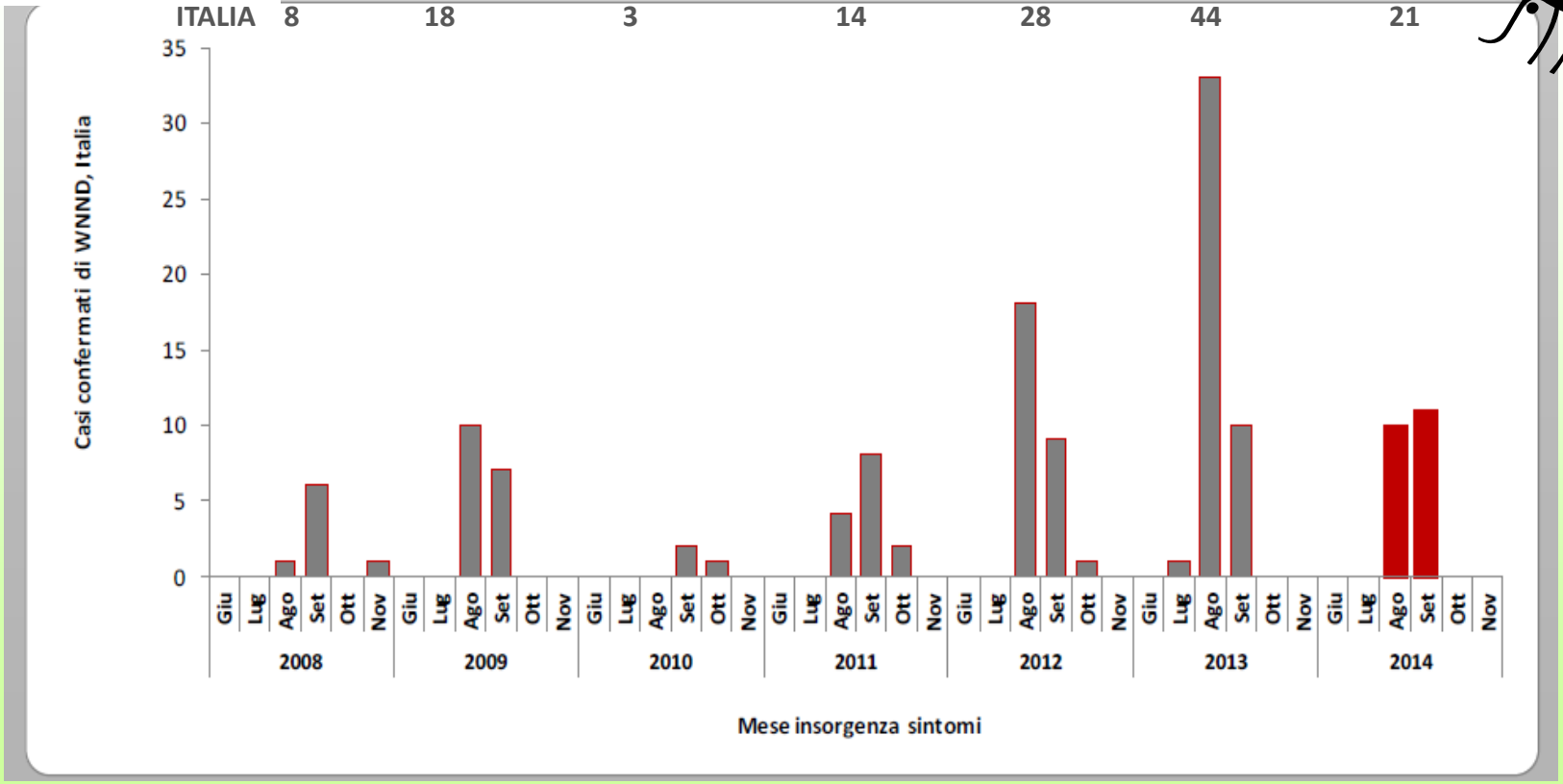
…the relevant 2010 USUV circulation did not correspond with the detection of symptomatic USUV infections in humans in the same study period….The discrepancy in the human epidemiologic data between USUV and WNV and the relevant level of USUV detected in the environment, suggest a lower capability of USUV to infect humans with respect to WNV

Clinical diagnosis in USUV-positive patients on admission

Year	ID Sample	Biological matrix	Diagnosis
2008	MO1_08_Hu_CSF	CSF	acute encephalitis
2008	MO2_08_Hu_CSF	CSF	unknown
2008	MO3_08_Hu_CSF	CSF	unknown
2008	MO4_08_Hu_CSF	CSF	unknown
2008	MO5_08_Hu_CSF	CSF	unknown
2008	MO6_08_Hu_CSF	CSF	unknown
2009	MO7_08_Hu_CSF	CSF	acute encephalitis/polyneuritis
2009	MO1_08_Hu_serum	Serum	dermatological infection
2009	MO2_08_Hu_serum	Serum	diabetes and neutropenia

Andamento dei casi di WNND e USUND, 2008-2009

WNND	RER	3		9		0		0		0	20	7	
WNND	MO	0		2		0		0		0	7	2	
USUND	RER/MO	6	3	3		?		?		0/?	0/?	0/?	
	ITALIA	8		18		3		14		28	44	21	



West Nile News-Rapporto N. 13 del 27 Novembre 2014
Reparto di Epidemiologia delle Malattie Infettive, CNESPS - ISS

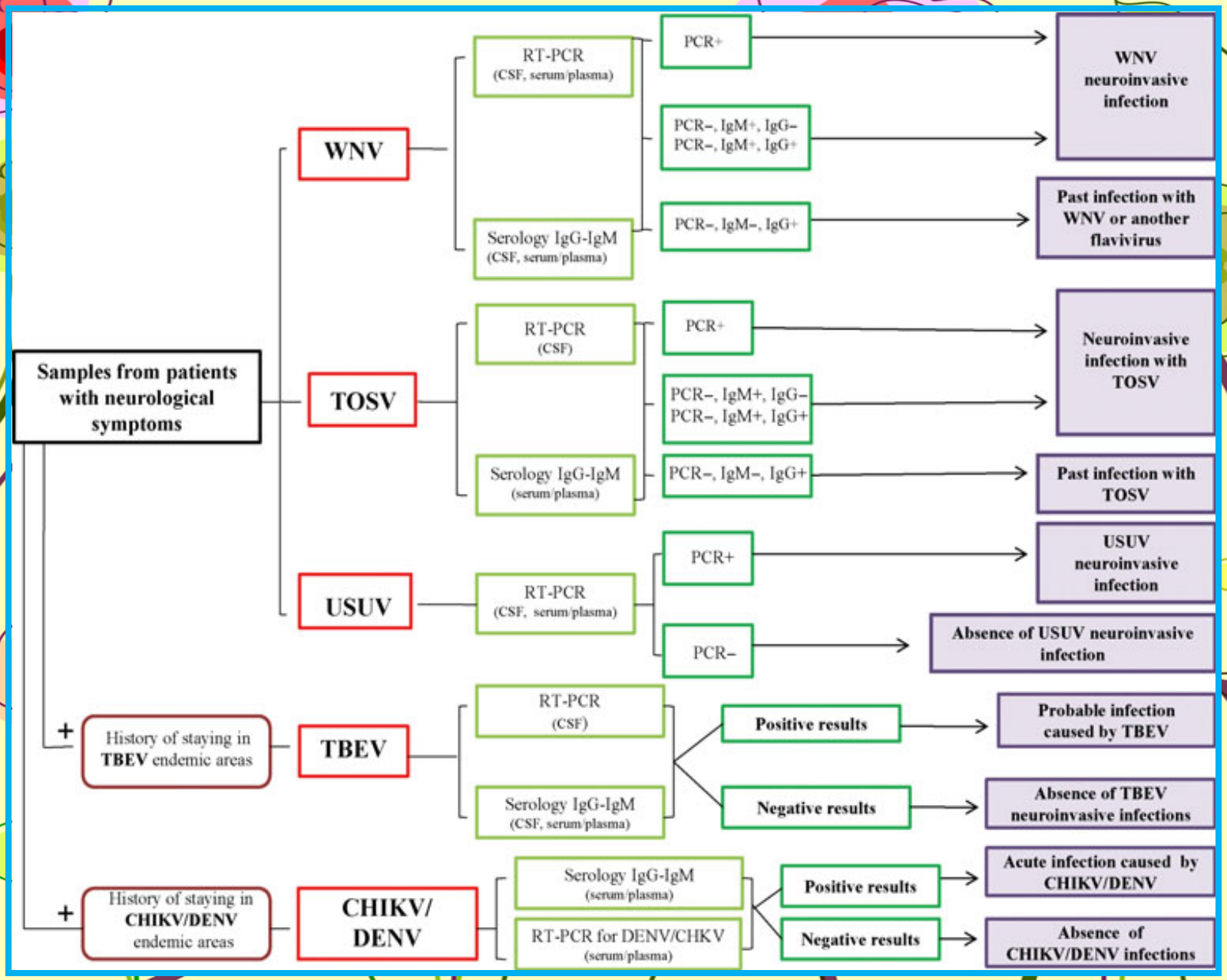
Conclusioni

- USUV e WNV compaiono in Italia nel 2008 con manifestazioni neuroinvasive nell'uomo; nella provincia di Modena USUV è presente prima di WNV
- La prevalenza dell'infezione da USUV è risultata maggiore rispetto a WNV nell'area e nel periodo studiati (Modena, 2008-2011)
- USUV sembra avere una preferenziale localizzazione a livello del SNC

Considerazioni

I test diagnostici per USUV dovrebbero essere presi in considerazione in tutti i casi di sospetta malattia virologica neuroinvasiva

Nei paesi in cui circolano USUV e WNV, USUV dovrebbe essere incluso nel programma di sorveglianza della malattia da WNV così come altri neuro-arbovirus


Samples from patients with neurological symptoms
WNV
RT-PCR (CSF, serum/plasma)
Serology IgG-IgM (CSF, serum/plasma)
PCR+
PCR–, IgM+, IgG–
PCR–, IgM+, IgG+
PCR–, IgM–, IgG+
WNV neuroinvasive infection
Past infection with WNV or another flavivirus
TOSV
RT-PCR (CSF)
Serology IgG-IgM (serum/plasma)
PCR+
PCR–, IgM+, IgG–
PCR–, IgM+, IgG+
PCR–, IgM–, IgG+
Neuroinvasive infection with TOSV
Past infection with TOSV
USUV
RT-PCR (CSF, serum/plasma)
PCR+
PCR–
USUV neuroinvasive infection
Absence of USUV neuroinvasive infection
+
History of staying in TBEV endemic areas
TBEV
RT-PCR (CSF)
Serology IgG-IgM (CSF, serum/plasma)
Positive results
Negative results
Probable infection caused by TBEV
Absence of TBEV neuroinvasive infections
+
History of staying in CHIKV/DENV endemic areas
CHIKV/ DENV
Serology IgG-IgM (serum/plasma)
RT-PCR for DENV/CHKV (serum/plasma)
Positive results
Negative results
Acute infection caused by CHIKV/DENV
Absence of CHIKV/DENV infections

Mancata diagnosi di USUND in tempo reale?

Il programma regionale di sorveglianza è stato implementato per USUV nel 2012, tre anni dopo il primo caso di USUND

Costante sensibilizzazione dei clinici: per tutti i pazienti con sintomi neurologici, nel periodo di circolazione del virus, andrebbe formulato il sospetto di arbovirosi neuroinvasiva con l' immediato riscontro diagnostico di laboratorio

Auspicabile l'adozione, dove ancora assente, di programmi regionali di sorveglianza umana in tutte le aree di circolazione ambientale del virus

Integrazione con i sistemi di sorveglianza veterinaria

Impatto della malattia da WNV sulla salute pubblica

USUV?

- Promozione di misure protettive individuali ed ambientali
- Gestione di casi di malattia neuroinvasiva
- Screening delle donazioni di sangue e di organo

Grazie per l'attenzione!

Impact of WNV-and USUV-disease on Public Health

Perché fare il controllo sulle donazioni? Anche se non si conosce la cinetica replicativa di USUV né se effettivamente si può trasmettere con le trasfusioni, non dimentichiamo che per l'outbreak di Chikungunya del 2007, pur non essendo stata dimostrata la trasmissione con il sangue, si intraprese la campagna di controllo delle donazioni. Alla luce dei dati ottenuti dalla nostra indagine, sarebbe auspicabile fare la stessa cosa per USUV, un flavivirus tanto simile al WNV per il quale tutto ciò viene fatto

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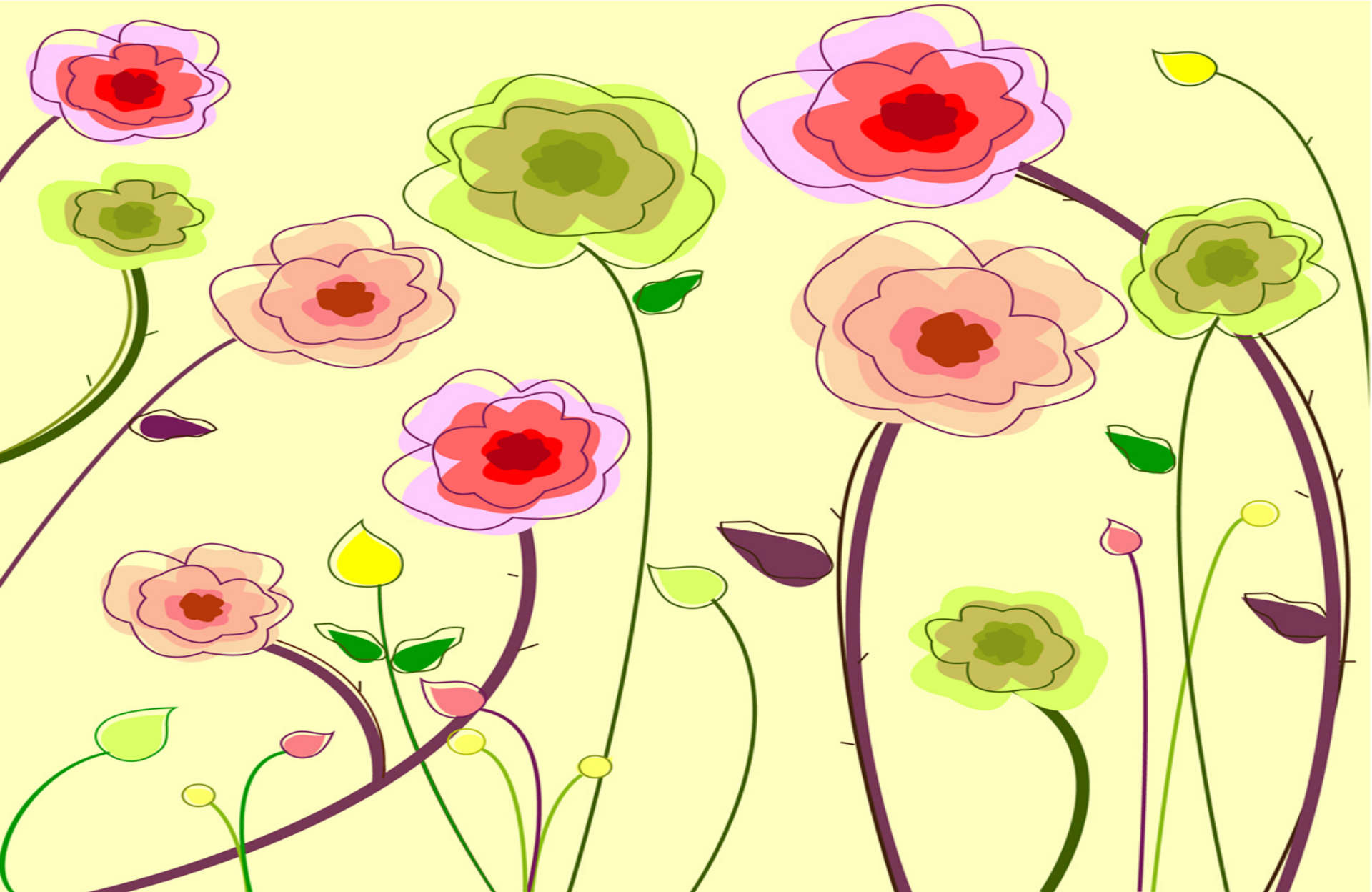

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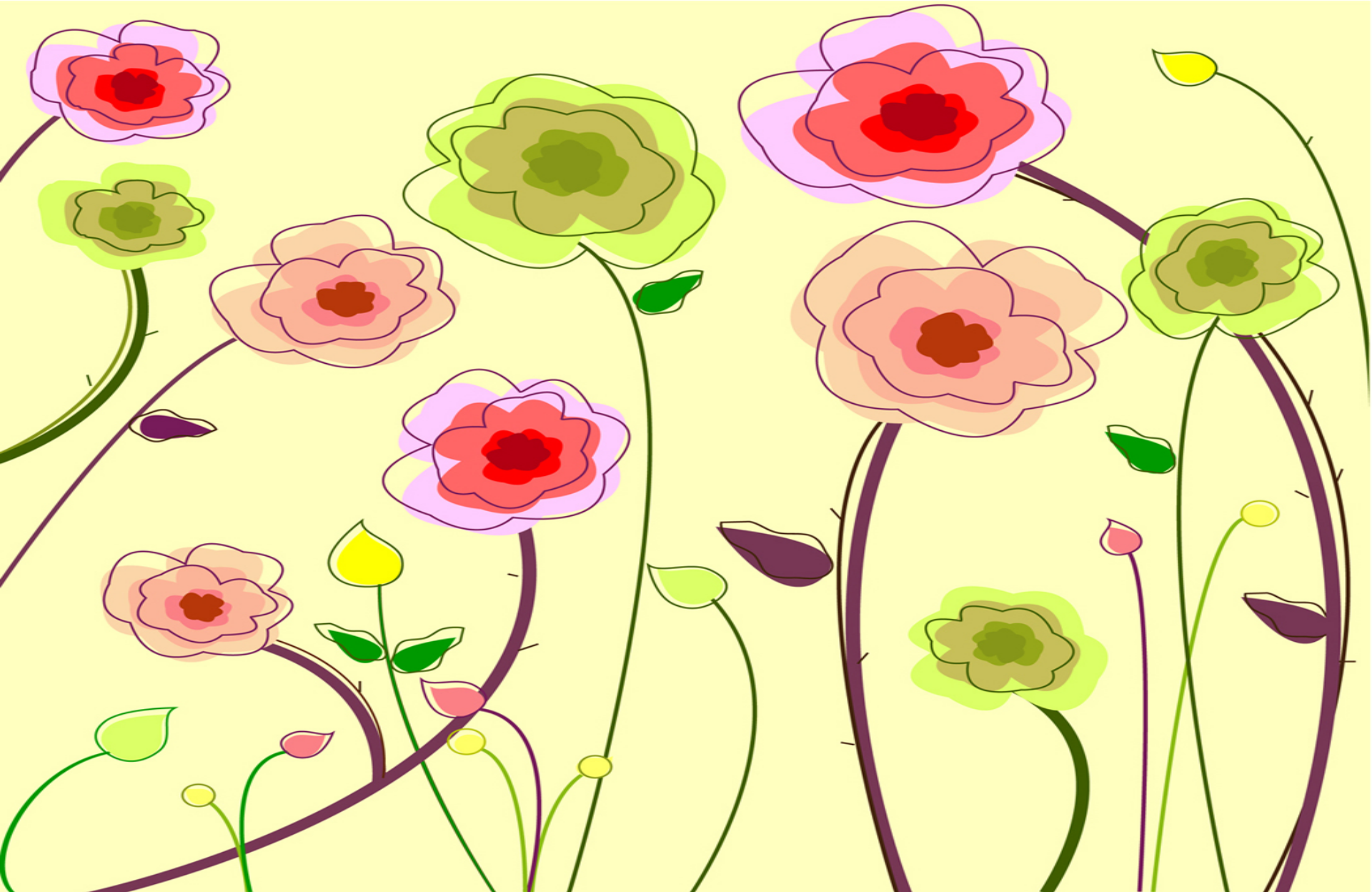

Epidemiol Infect. 2011 Jun;139(6):818-25. doi: 10.1017/S0950268810001871. Epub 2010 Jul 30.

West Nile virus circulation in Veneto region in 2008-2009.

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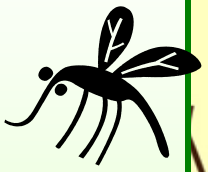

West Nile virus (WNV) was detected in Italy, in late summer 2008 in horses and birds in the Po valley. As a consequence, an intense WNV surveillance was implemented in that area involving Emilia-Romagna, Veneto and Lombardy. This paper presents the results of the September 2008-November 2009 surveillance on equines, mosquitoes, wild birds, dogs and cattle in Veneto. WNV was detected in equines and dogs, and, to a lesser extent in cattle and wild birds. Simultaneous circulation of Usutu virus was detected by testing wild birds found dead. Usutu virus but not WNV was also found in mosquitoes monitored during 2009. Equine practices monitoring allowed the definition of an area of WNV circulation and the 2008-2009 westward and northward spread of the infection. Although a relatively low number of human cases and a low virus circulation in vectors and birds detected in Veneto region could be considered favourable conditions for a limited risk of human exposure, it remains difficult to predict the possible evolution of the epidemiological situation.

Veterinary Microbiology 151 (2011) 264–274

Usutu virus in ITALY: An emergence or a silent infection?

Giovanni Savini [a,*], Federica Monaco [a], Calogero Terregino [b], Annapia Di Gennaro [a], Luca Bano [b], Chiara Pinoni [a], Roberta De Nardi [b], Paolo Bonilauri [c], Monica Pecorari [d], Luigina Di Gialleonardo [a], Lebana Bonfanti [b], Andrea Polci [a], Paolo Calistri [a], Rossella Lelli [a]

WND National Surveillance plan

A two year study (2008–2009) was carried out to monitor the Usutu virus (USUV) circulation in Italy. Sentinel horses and chickens, wild birds and mosquitoes were sampled and tested for the presence of USUV and USUV antibodies within the WND National Surveillance plan. Seroconversion evidenced in sentinel animals proved that in these two years the virus has circulated in Tuscany, Emilia Romagna, Veneto and Friuli Venezia Giulia regions. In Veneto USUV caused a severe blackbird die-off disease involving at least a

PLoS One. 2010; 5 (12)

Evidence of Simultaneous Circulation of West Nile and Usutu Viruses in Mosquitoes Sampled in Emilia-Romagna Region (Italy) in 2009

Mattia Calzolari[1*], Paolo Bonilauri[1], Romeo Bellini[2], Alessandro Albieri[2], Francesco Defilippo[1], Giulia Maioli[1], Giorgio Galletti[1], Antoni Gelati[3], Ilaria Barbieri[1], Marco Tamba[1], Davide Lelli[1], Elena Carra[1], Paolo Cordioli[1], Paola Angelini[4], Michele Dottori[1]

Emilia Romagna regional surveillance on insect borne diseases plan

The PCR detections showed a stronger and longer USUV circulation in mosquitoes with respect to WNV, as displayed by the higher number of USUV.positive pools detected …

PLoS One. 2012; 7 (5)

Mosquito, Bird and Human Surveillance of West Nile and Usutu Viruses in Emilia-Romagna Region (Italy) in 2010

Mattia Calzolari[1]*, Paolo Gaibani[2], Romeo Bellini[3], Francesco Defilippo[1], Anna Pierro[2], Alessandro Albieri[3], Giulia Maioli[1], Andrea Luppi[1], Giada Rossini[2], Agnese Balzani[1], Marco Tamba[1], Giorgio Galletti[1], Antonio Gelati[4], Marco Carrieri[3], Giovanni Poglayen[5], Francesca Cavrini[2], Silvano Natalini[6], Michele Dottori[1], Vittorio Sambri[2], Paola Angelini[6], Paolo Bonilauri[1]

…the relevant 2010 USUV circulation did not correspond with the detection of symptomatic USUV infections in humans in the same study period.…The discrepancy in the human epidemiologic data between USUV and WNV and the relevant level of USUV detected in the environment, suggest a lower capability of USUV to infect humans with respect to WNV

OGGETTO: Sorveglianza dei casi umani delle malattie trasmesse da vettori con particolare riferimento a Chikungunya, Dengue, Zika virus e West Nile Disease – 2014.

Sorveglianza epidemiologica dei casi umani di malattia neuro-invasiva (WNND) da West-Nile Virus (area di sorveglianza)

La sorveglianza sui casi umani di WNND consente, insieme alla sorveglianza animale ed entomologica, di evidenziare la circolazione del virus in un determinato ambito territoriale e di avere una stima della sua entità, attraverso l'individuazione sistematica dei casi clinici emergenti.

Ambito di applicazione della sorveglianza:

- casi importati, tutto l'anno;
- casi autoctoni, nelle aree a dimostrata circolazione di WNV negli animali e aree limitrofe (in base ai criteri sotto riportati) dal 15 giugno al 30 novembre di ogni anno. Tali date potranno essere modificate sulla base delle evidenze epidemiologiche ottenute fino a quel momento sia in ambito umano che animale. La sorveglianza dei casi autoctoni avviene anche in aree che l'anno

Aree a dimostrata circolazione di WNV negli animali e aree limitrofe

Al fine di ottimizzare le azioni di sanità pubblica da intraprendere, nel caso in cui sia dimostrata la circolazione di WNV negli animali in un'area, vengono identificate le "aree affette" (con le province come unità geografica) e le "aree di sorveglianza" (con le Regioni come unità geografica) per la sorveglianza della WNND nell'uomo.

OGGETTO: Sorveglianza dei casi umani delle malattie trasmesse da vettori con particolare riferimento a Chikungunya, Dengue, Zika virus e West Nile Disease – 2014.

Per **"area affetta"** si intende un'area identificata che soddisfi almeno una delle seguenti situazioni:

1) positività nelle sorveglianze veterinarie ed entomologiche (come disposto dal D.M. del 29 novembre 2007 e successive modifiche e integrazioni e dall'Ordinanza Ministeriale del 4 agosto 2011 e successivo aggiornamento del 13 luglio 2012);

2) presenza di casi di encefalomielite di tipo West Nile negli equidi (secondo le definizioni ex D.M. 29 novembre 2007 e Ordinanza 4 agosto 2011, la cui efficacia è stata prorogata dall'Ordinanza 6 agosto 2013);

3) presenza di casi autoctoni confermati di malattia neuro-invasiva e/o di infezioni recenti umane autoctone.

Una volta identificata l'area affetta, è necessario valutare l'avvio di azioni dirette alla riduzione del rischio di trasmissione, che includano sia azioni mirate contro il vettore che misure precauzionali finalizzate a prevenire la trasmissione dell'infezione attraverso la trasfusione di sangue ed emocomponenti (incluse le cellule staminali emopoietiche) e i trapianti di organi e tessuti infetti (vedi provvedimenti stabiliti dal Centro Nazionale Sangue e dal Centro Nazionale Trapianti).

OGGETTO: Sorveglianza dei casi umani delle malattie trasmesse da vettori con particolare riferimento a Chikungunya, Dengue, Zika virus e West Nile Disease – 2014.

Per **"area di sorveglianza"** si intende un'area identificata attorno ad un'area affetta in base ad entrambe le informazioni seguenti:

- presenza del vettore, competente per il WNV, nel territorio regionale, considerando le peculiarità geografiche (esempio: zone montane o zone umide) che possono limitare o favorire la presenza del vettore stesso;
- presenza di casi umani o veterinari confermati nelle aree provinciali (aree affette) come precisato precedentemente.

DEFINIZIONE DI CASO DI MALATTIA NEURO-INVASIVA DA VIRUS DI WEST NILE

•**(nota circolare Ministero della salute 15 giugno 2011, prot. 14381)**
•• **CASO POSSIBILE**: qualunque persona con febbre alta (> 38,5 °C) e manifestazioni
•neurologiche di tipo encefalite, meningite a liquor limpido o poliradicoloneurite (simil
•Sindrome di Guillain Barré) o paralisi flaccida acuta.
•• **CASO PROBABILE**: la sintomatologia sopra descritta **e/o** uno dei seguenti criteri di
•laboratorio:
•• presenza di anticorpi IgM anti-WNV nel siero testato;
•• presenza di anticorpi IgG anti-WNV nel siero testato;
•• sieroconversione da negativo a positivo o aumento di 4 volte del titolo di anticorpi
•anti-WNV su due prelievi consecutivi di siero.
•• **CASO CONFERMATO**: la sintomatologia sopra descritta **e/o** il rispetto di almeno
•uno dei seguenti parametri, riscontrato da un laboratorio di riferimento:
•• isolamento del virus WN nel sangue o nel liquor;
•• presenza di anticorpi IgM nel liquor;
•• PCR positiva per virus WN nel sangue o liquido cefalo-rachidiano;
•• identificazione di un titolo elevato di anticorpi IgM e IgG contro il virus WN,
•confermati con un test di neutralizzazione.

SORVEGLIANZA EPIDEMIOLOGICA CASI DI MALATTIA NEURO-INVASIVA DA WNV

Definizione di caso

Criteri clinici

Qualsiasi persona che presenti febbre

e

almeno una delle seguenti manifestazioni cliniche:

- encefalite
- meningite a liquor limpido
- poliradicolo-neurite (simil Guillain-Barré)
- paralisi flaccida acuta

Criteri epidemiologici

Almeno una delle seguenti due correlazioni epidemiologiche:

- trasmissione da animale a uomo (che risieda o abbia viaggiato in zone in cui il WNV è endemico nei cavalli o negli uccelli o che sia stato esposto a punture di zanzare in tali zone);
- trasmissione interumana (trasmissione verticale, trasfusione sanguigna, trapianti).

Criteri di laboratorio

per caso probabile:

- Risposta anticorpale specifica al WNV nel siero
- Positività esame PCR nelle urine.

per caso confermato:

Almeno uno dei seguenti quattro criteri:

- isolamento del WNV nel sangue o nel liquor
- identificazione dell'acido nucleico del WNV nel sangue o nel liquor
- risposta anticorpale specifica al WNV (IgM) nel liquor
- titolo elevato di IgM WNV e identificazione di IgG WNV nel siero e conferma mediante neutralizzazione.

I risultati di laboratorio vanno interpretati in funzione della presenza o meno di vaccinazione contro i flavivirus.

In base alla valutazione dei criteri sopra esposti le definizioni di caso sono le seguenti:

CASO POSSIBILE: N.A.

CASO PROBABILE: qualsiasi persona che soddisfi i criteri clinici precedentemente indicati e almeno uno dei seguenti due criteri:

- una correlazione epidemiologica;
- un risultato positivo a un test di laboratorio per caso probabile.

CASO CONFERMATO: qualsiasi persona che soddisfi i criteri clinici e/o il rispetto di almeno 1 dei criteri di laboratorio per caso confermato[3].

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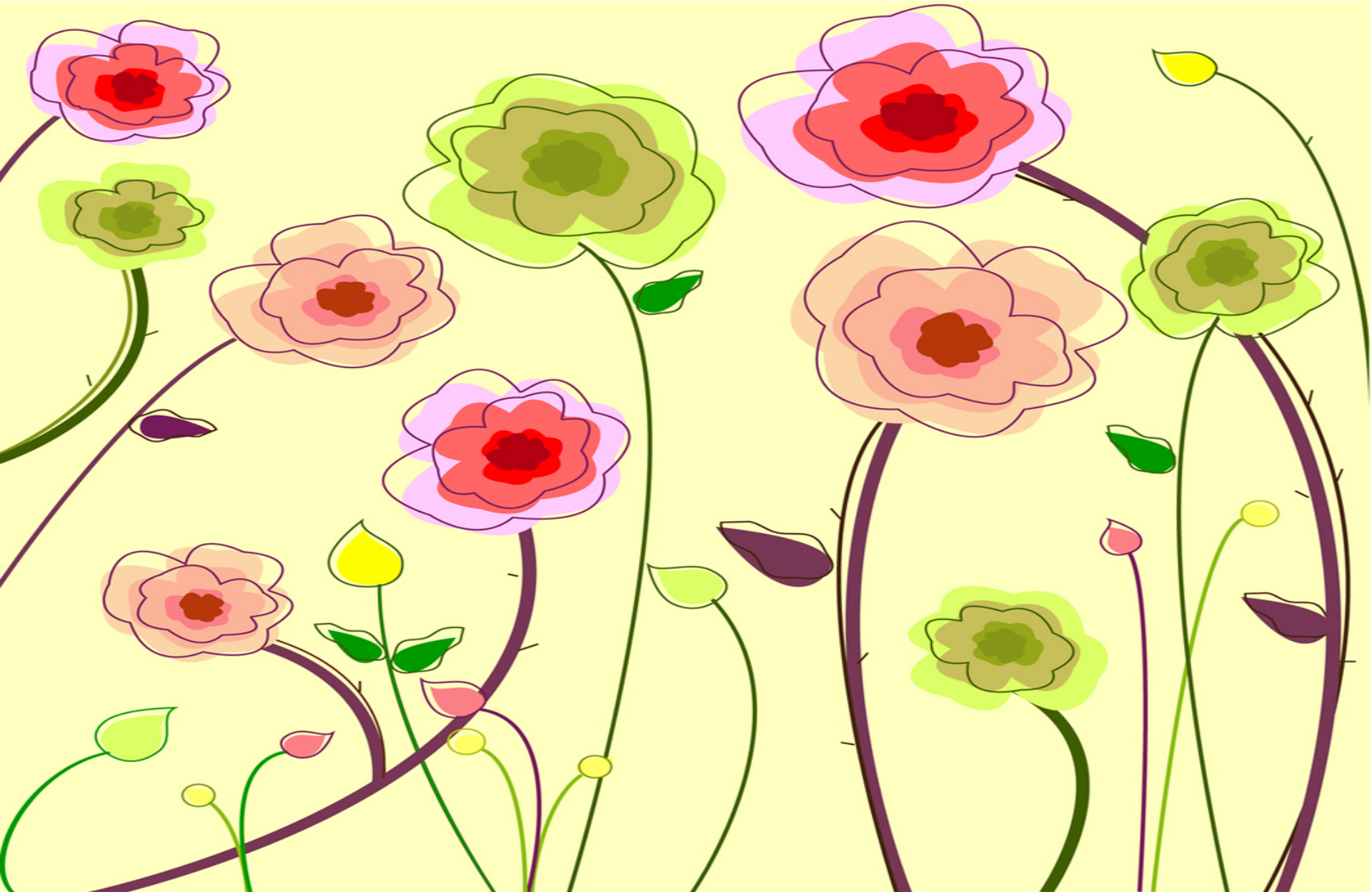

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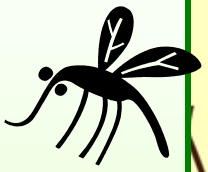

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