Update su meningiti e meningoencefaliti non usuali

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La gestione delle emergenze/urgenze in malattie infettive
Roma, 29 settembre 2022

SISTEMA SANITARIO REGIONALE

IRCCS
LAZZARO SPALLANZANI

HOME CURARSI DA NOI STRUTTURA AZIENDALE L'ISTITUTO LA RICERCA

REGIONE LAZIO

Procedura per la funzione centrale di Bed Manager e per la valutazione sindromica nell'ambito della Rete di Malattie Infettive della Regione Lazio

Decreti del Commissario ad ACTA:

- DCA 58 - 12 luglio 2010 - rete malattie infettive
- DCA 452 29 settembre 2015 giubileo
- DCA 540 nov 2015 rete malattie infettive

Regione Lazio

Decreti del Commissario ad Acta

Decreto del Commissario ad Acta 27 aprile 2018, n. U00162

Approvazione del documento "Riorganizzazione della sorveglianza e miglioramento diagnostico delle sindromi neurologiche di sospetta origine infettiva nella Regione Lazio".

www.inmi.it/bedmanager

Rete regionale di Malattie Infettive

Punti di forza

- Accettazione strutturata con procedure standardizzate, e rintracciabili
- Unico pool con comportamenti omogenei
- Trattamento adeguato pazienti infettivi in periferia
- Maggior tutela legale
- Piattaforma digitale molto friendly

Punti di debolezza

- Integrazione tra diverse UOC
- Resistenza al cambiamento
- Sovrapposizione organizzazione precedente e nuova
- Multidisciplinarietà nella gestione clinica
- Limitati pl isolamento in regime acuto / critico

Approccio sindromico

- Sindrome neurologica acuta
- Sindrome respiratoria acuta
- Sindrome febbrile di ritorno dai tropici
- Sindrome febbrile epatitica
- Sindromi febbrili dermatologiche
- *Sindrome febbrile only, ie setticemie incluse le infezioni del torrente circolatorio e le endocarditi*
- *Sindrome gastroenteritica*

- Criteri che guideranno l'ingresso nella rete:
  - Pertinenza infettivologica
  - Contagiosità
  - Gravità valutata con differenti score

Sindrome neurologica acuta

Criticità rilevate nella gestione delle meningoencefaliti presupposto per la definizione sindromica nella Rete Regionale

- Non tempestiva identificazione dei pazienti con sospetta meningoencefalite che comporta un ritardo nella appropriata gestione di pazienti:
  - collocazione non sempre adeguata del paziente con sindrome neurologica acuta
  - Mancata condivisione dei metodi di valutazione de i pazienti critici o sospettati tali
  - Caratteristiche del liquor non sempre indicative di interessamento neurologico da parte di malattie infettive come TB, arbovirus, lue o HSV1/2.
  - Sorprendente non omogeneità di esecuzione di coltura su liquor e sangue
  - Tardivo inizio di una terapia antibiotica e di supporto cardio circolatorio
  - Non tempestiva notifica del caso sospetto
  - Attuazione non adeguata delle misure di isolamento necessarie del paziente

Paziente adulto con sindrome neurologica acuta febbrile/1

Paziente con febbre e sintomi e segni neurologici (cefalea, rigidità nucale e/o alterazione stato di coscienza e/o segni focali)

SI

Trauma perforante, patologia cronica riacutizzata, altre patologie non prioritariamente infettive (infez shunt, ecc),

SI → Eventuale patologia infettiva associata non preminente

NO

BK sospetto: isolamento respiratorio (anamnesi, RX torace)
BK non sospetto: isolamento droplet

Pannello esami comuni, 2 emocolture, EGA- PaO2/FiO2, TC/RMN cranio

Idrocefalo da derivare, ascessi>3 cm, ictus, emorragia

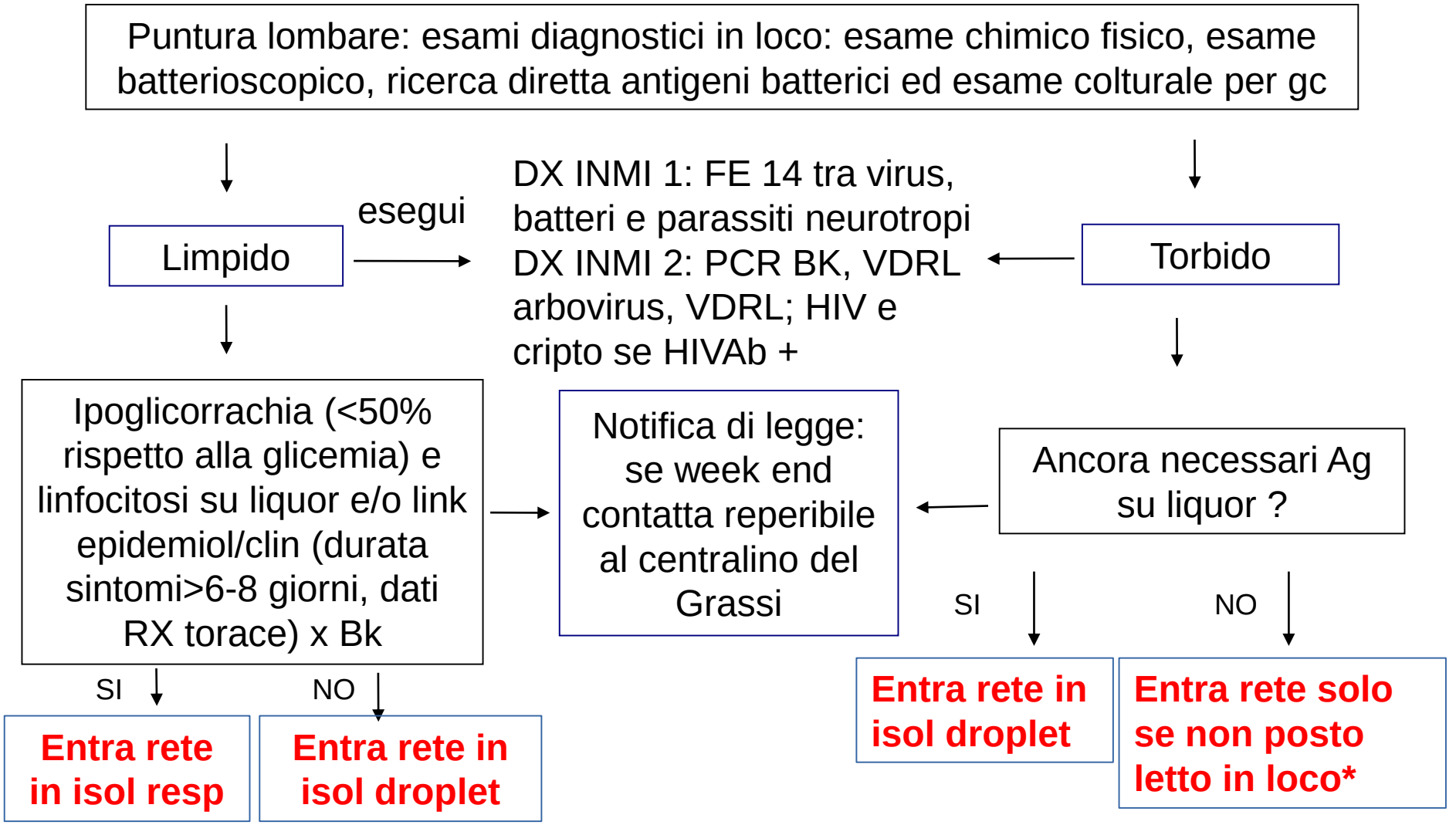
SI → Eventuale patologia infettiva associata non preminente ma considera eziologia tubercolare in caso di idrocefalo

NO

Puntura lombare

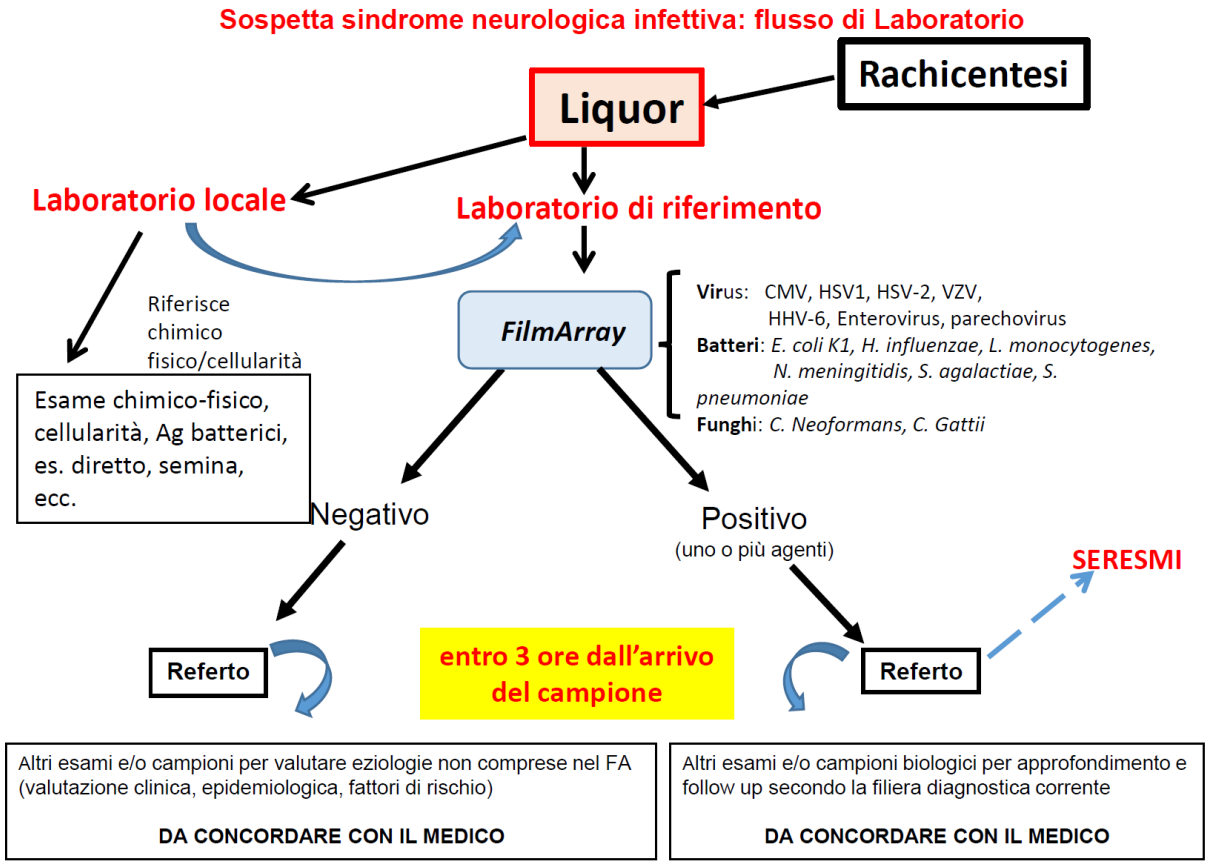
TX antibiotica entro 2 hr da arrivo

Paziente adulto con sindrome neurologica acuta febbrile/2

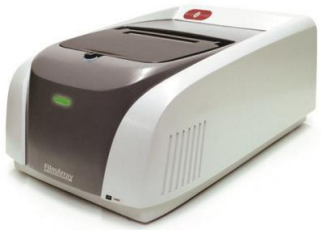


*Disporre trattamento in loco solo dopo aver escluso con certezza eziologia da meningococco/emofilo

Procedure diagnostiche presso l'INMI

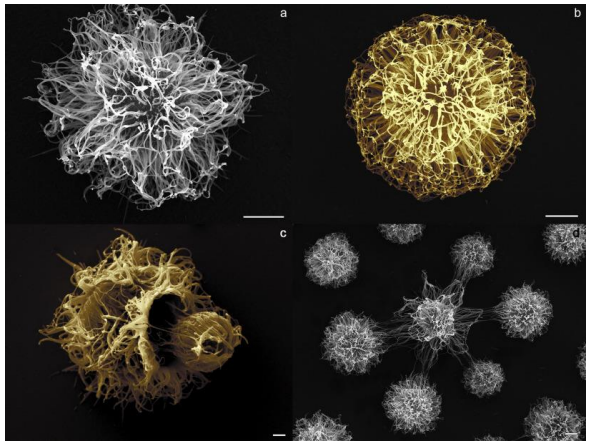


Meningitis-Encephalitis (ME) Panel (FilmArray)



- Test eseguibile in urgenza (piattaforma maneggevole, semplice)
- Risultati in 1 ora dal caricamento

Bacteria	Virus	Fungi
Escherichia coli K1	**Cytomegalovirus**	***Cryptococcus neoformans***
Haemophilus influenzae	**Enterovirus**	***Cryptococcus gattii***
Listeria monocytogenes	**Herpes simplex virus 1 (HSV-1)**	
Neisseria meningitidis	**Herpes simplex virus 2 (HSV-2)**	
Streptococcus agalactiae	**Human herpesvirus 6 (HHV-6)**	
Streptococcus pneumoniae	**Human parechovirus (HPeV)**	
	Varicella zoster virus (VZV)	

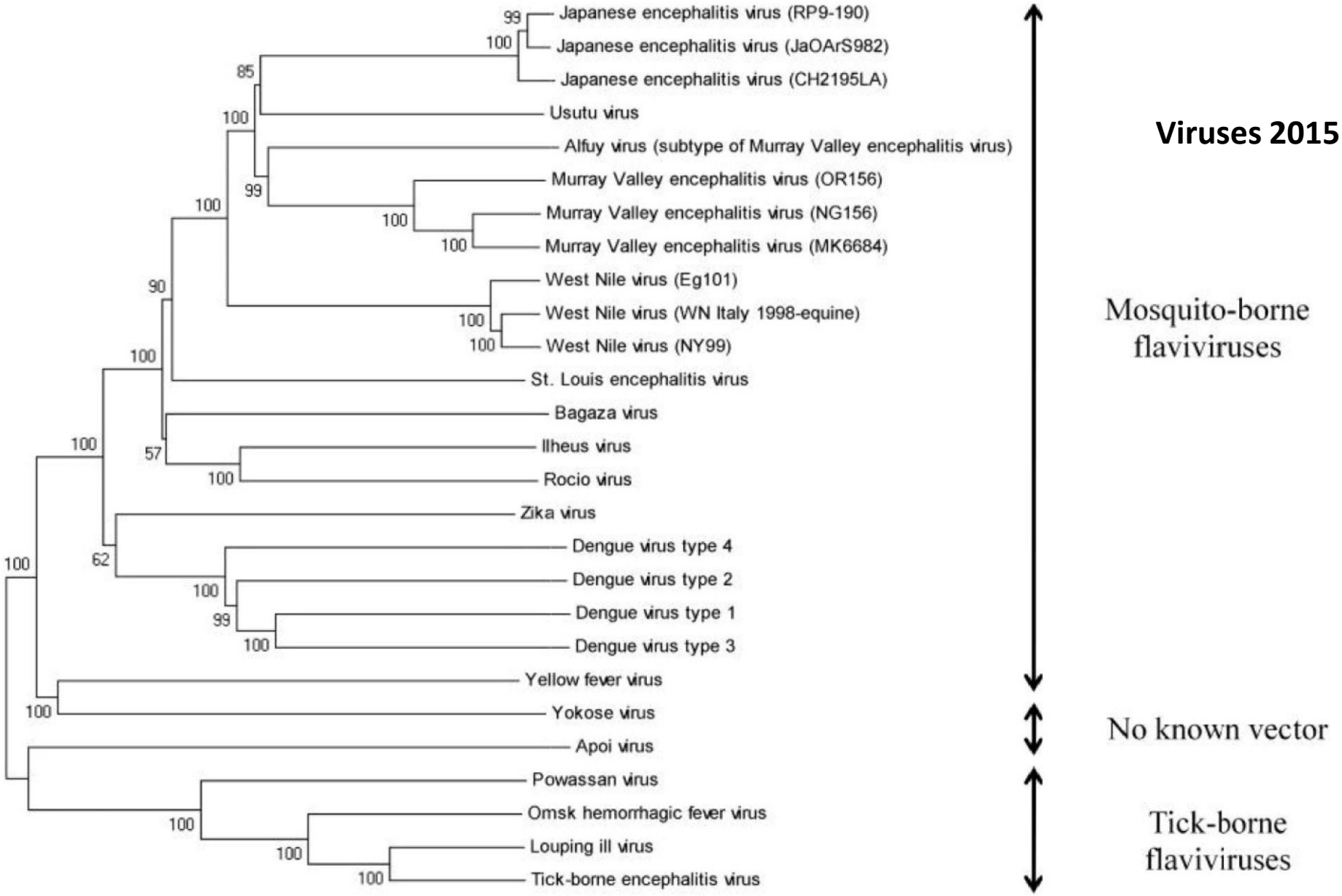


Electron microscopy images of *Cryptococcus gattii*

Major Arboviruses That Cause Encephalitis

- Flaviviridae
  - Japanese encephalitis
  - St. Louis encephalitis
  - Usutu
  - West Nile
- Togaviridae
  - Eastern equine encephalitis
  - Western equine encephalitis
- Bunyaviridae
  - La Crosse encephalitis

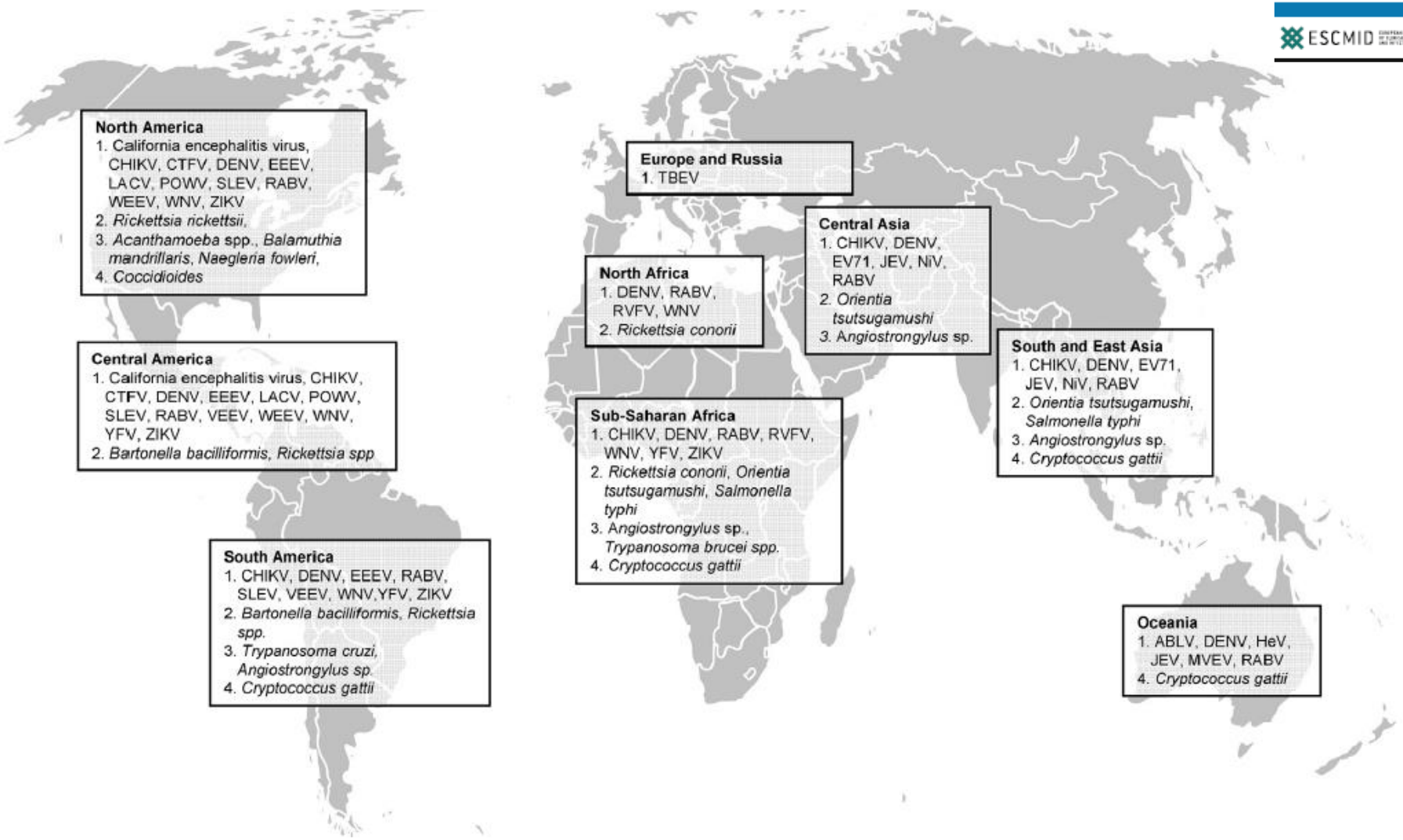
Phylogenetic tree based on complete flavirus genome sequence: This figure illustrates the close genetic relationship between Usutu, WNV, Dengue, TBE, Yellow fever, Zika, JE



Viruses 2015

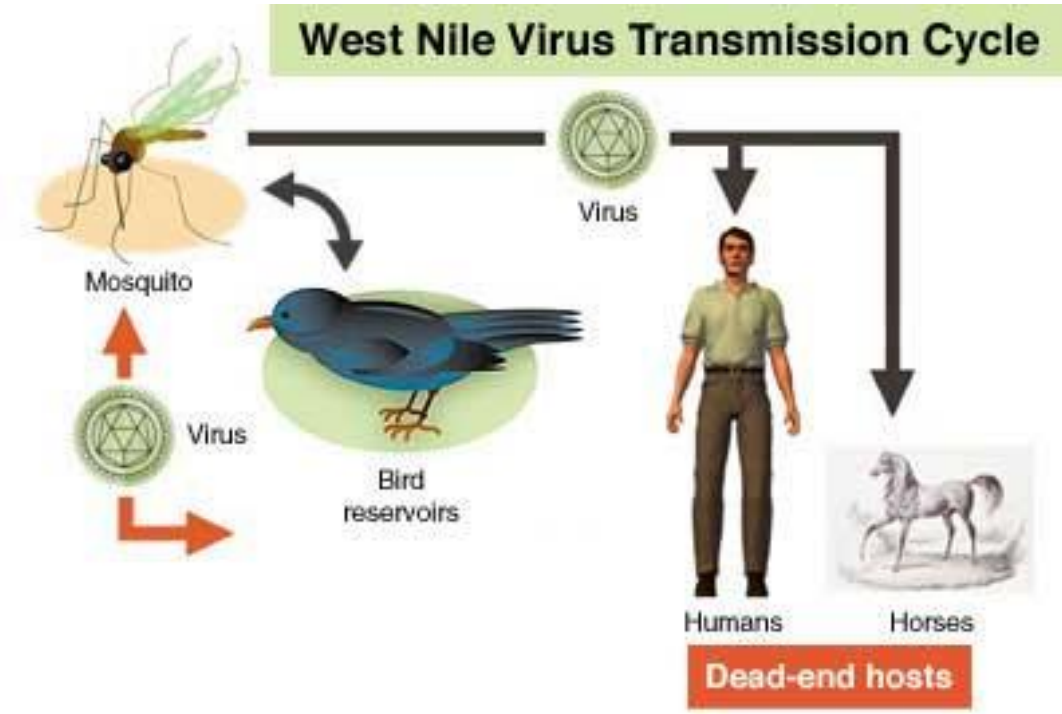
Diagnostic approach to encephalitis and meningoencephalitis in adult returning travellers

CMI CLINICAL MICROBIOLOGY AND INFECTION
ESCMID



West Nile Virus

- Flavivirus
- Primary host – wild birds
- Principal arthropod vector – mosquitoes
- Geographic distribution - Africa, Middle East, Western Asia, Europe, Australia, North America, Central America



http://www.walgreens.com/images/library/healthtips/july02/westnilea.jpg

History of West Nile Virus

- 1937 - West Nile virus isolated from woman in Uganda
- 1950s – First recorded epidemics in Israel (1951-1954, 1957)
- 1962 – Epidemic in France
- 1974 – Epidemic in South Africa. Largest ever West Nile epidemic.
- 1996 – Romanian epidemic with features similar to those of the North American outbreak. 500 cases and 50 deaths.
- 1999 – Russian outbreak. 40 deaths.

23 agosto 1999: WNV a New York

West Nile Virus: 1999 New York Outbreak

- Crows dying in and around Queens in late summer
- 27 deaths among captive birds in the Queens and Bronx zoos
- Concomitant human infection of apparent encephalitis in the same area
- Outbreak was first attributed to St. Louis encephalitis, but tissue samples from dead crows confirmed that it was West Nile virus
- 59 human cases requiring hospitalization, including 7 deaths

Alexander the Great and West Nile Virus Encephalitis

John S. Marr* and Charles H. Calisher†

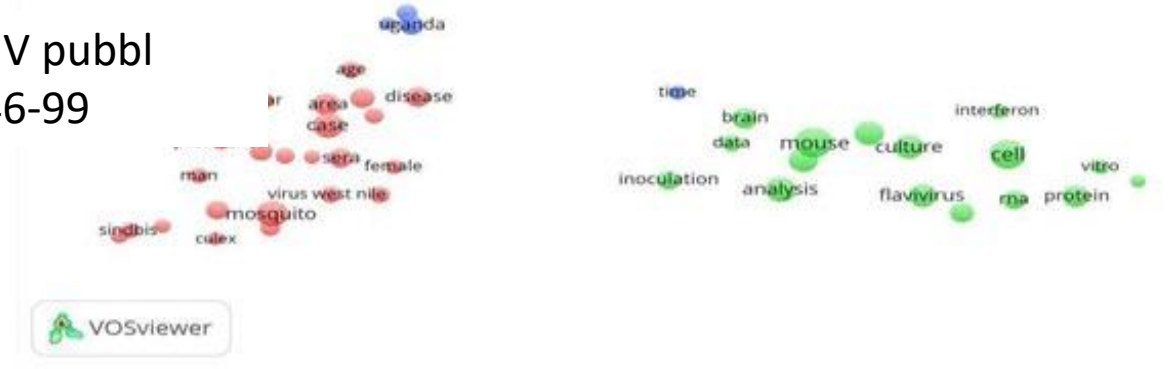
Table. Medical history and physical examination of Alexander the Great

Patient characteristics	Medical history	Clinical symptoms
Male	Ten years before death, traveled widely (Mediterranean, North Africa, and Middle East)	Escalating fever associated with chills
Born in Macedonia	Unexplained fever 5 years previously	Excessive thirst, diaphoresis
32 years of age	Penetrating right chest wound one year before final illness	Acute abdominal pain
Soldier	Onset of final illness May 29, 323 BC	Single episode of back pain at onset of fever
Heavy drinking	Death June 10, 323 BC	Increased weakness leading to prostration with intermittent periods of energy
Frequent bathing		Delirium
Married to many wives		Aphonia
One son		Terminal flaccid paralysis

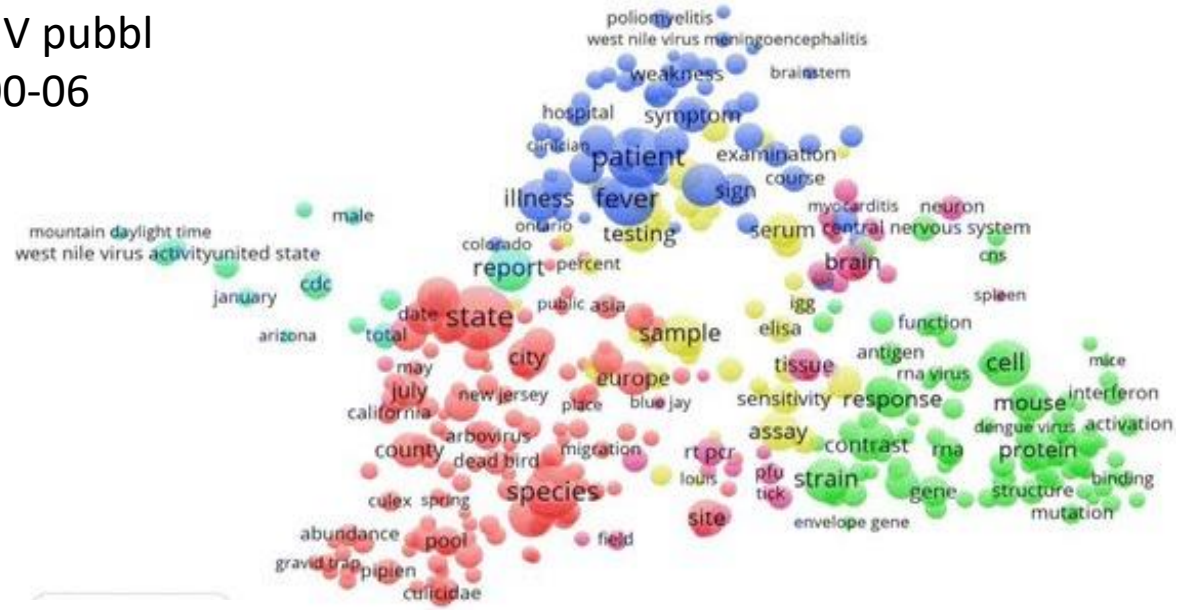
Diagnosi differenziale: tifo addominale, malaria o avvelenamento?

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 9, No. 12, December 2003

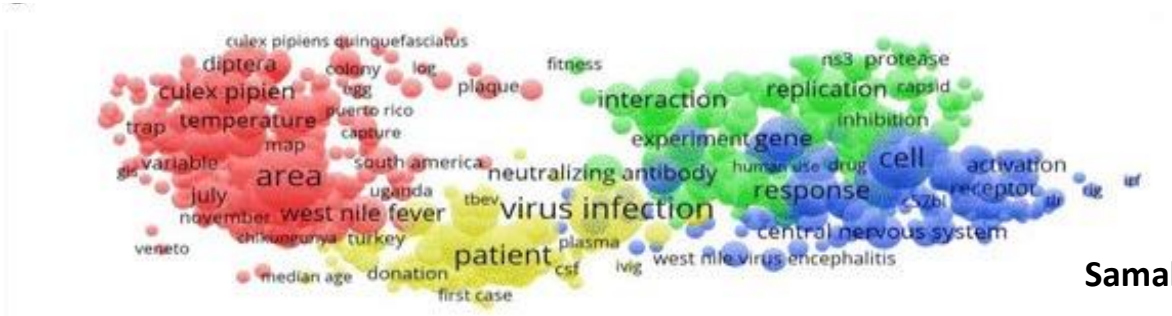
WNV pubbl
1946-99



WNV pubbl
2000-06



WNV pubbl
2006-16



Blue cluster contained terms related to phylogenesis

Green cluster contained terms related to transmission

Yellow cluster contained clinical terms

Red cluster contained terms related to ecology and epidemiology .

Samah W. Al-Jabi. Global Health. 2017;13:55

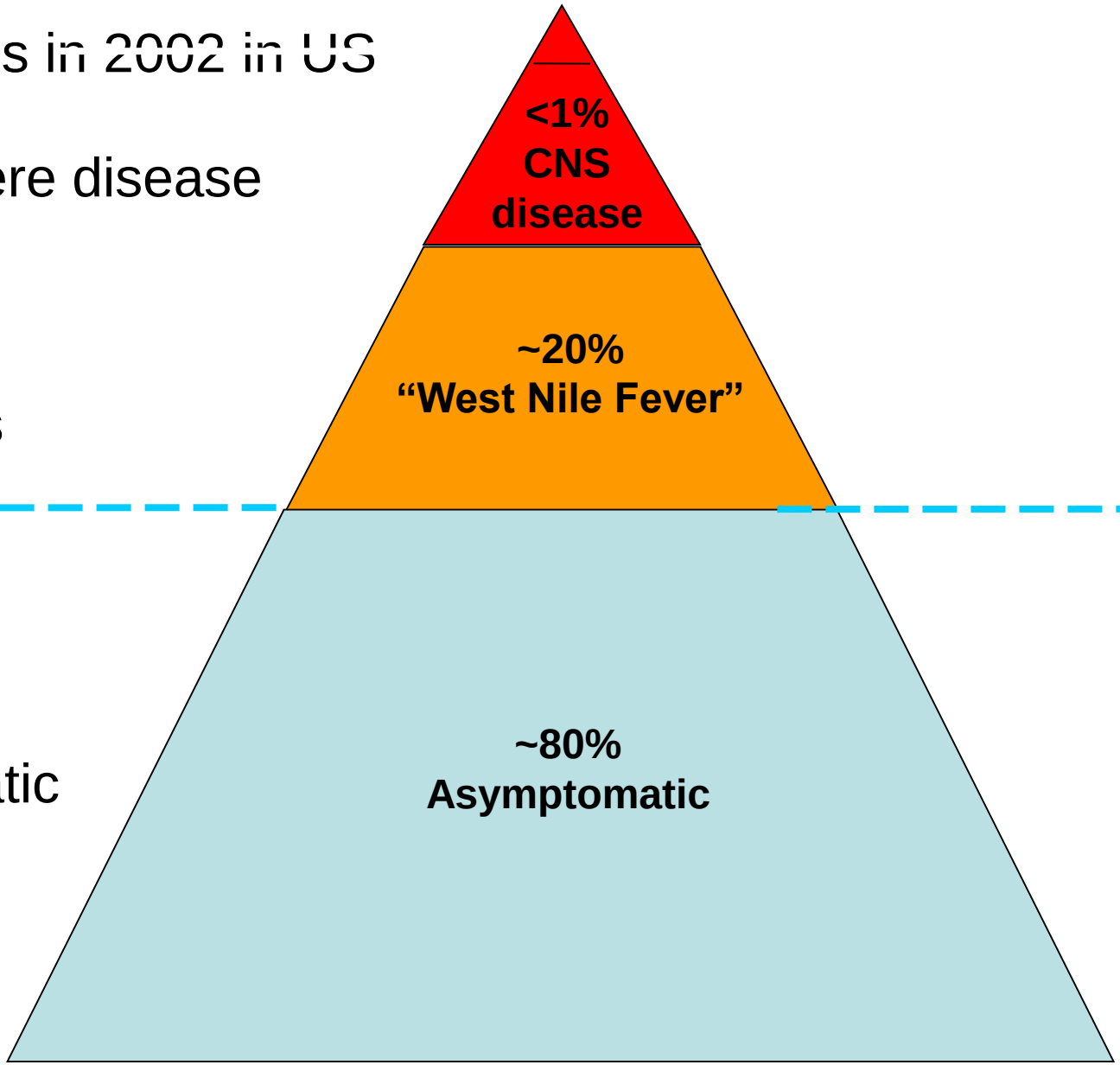
WNV Human Infection "Iceberg"

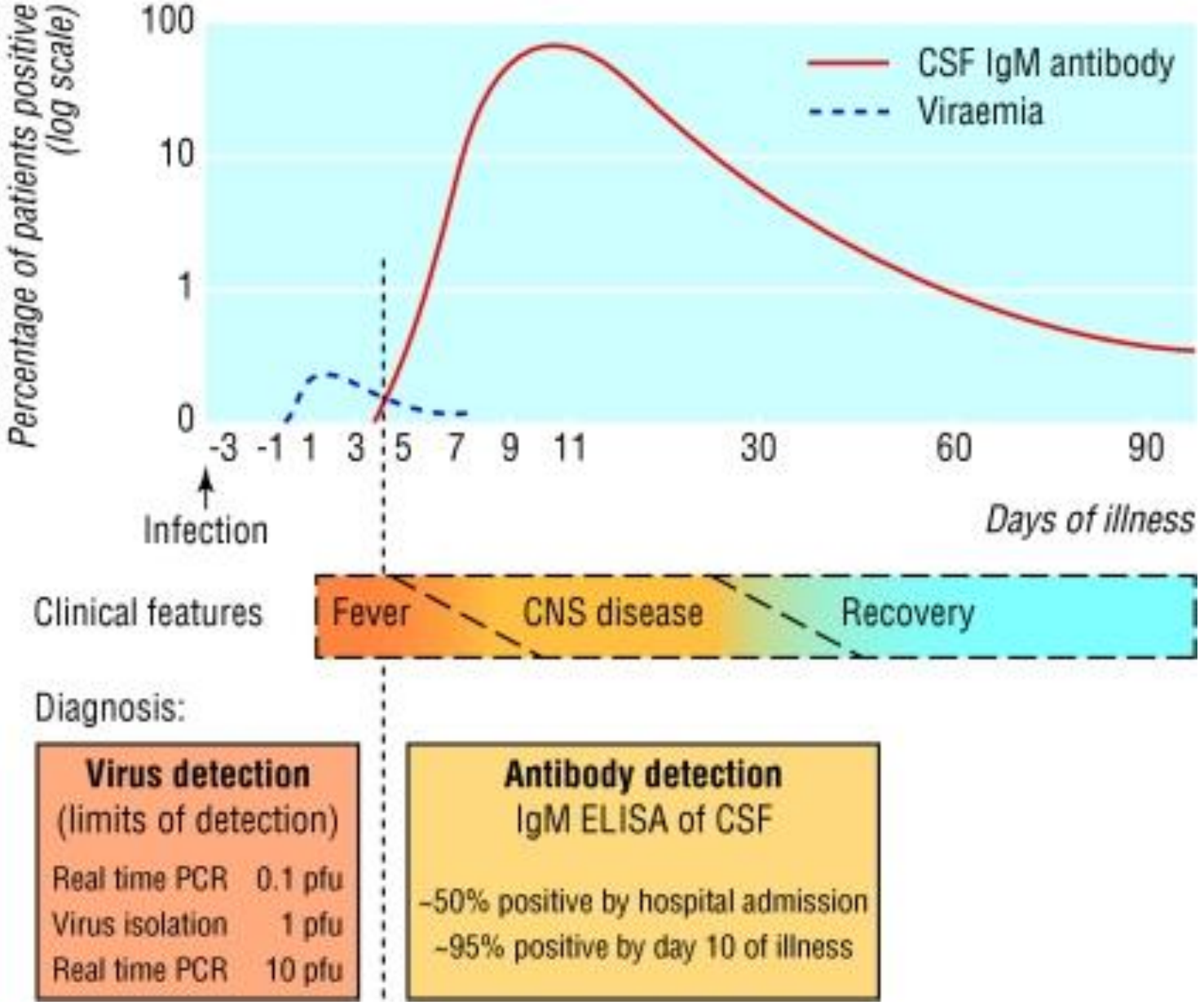
284 fatalities in 2002 in US

~ 3300 severe disease

~100,000
mild illness

~400,000
asymptomatic





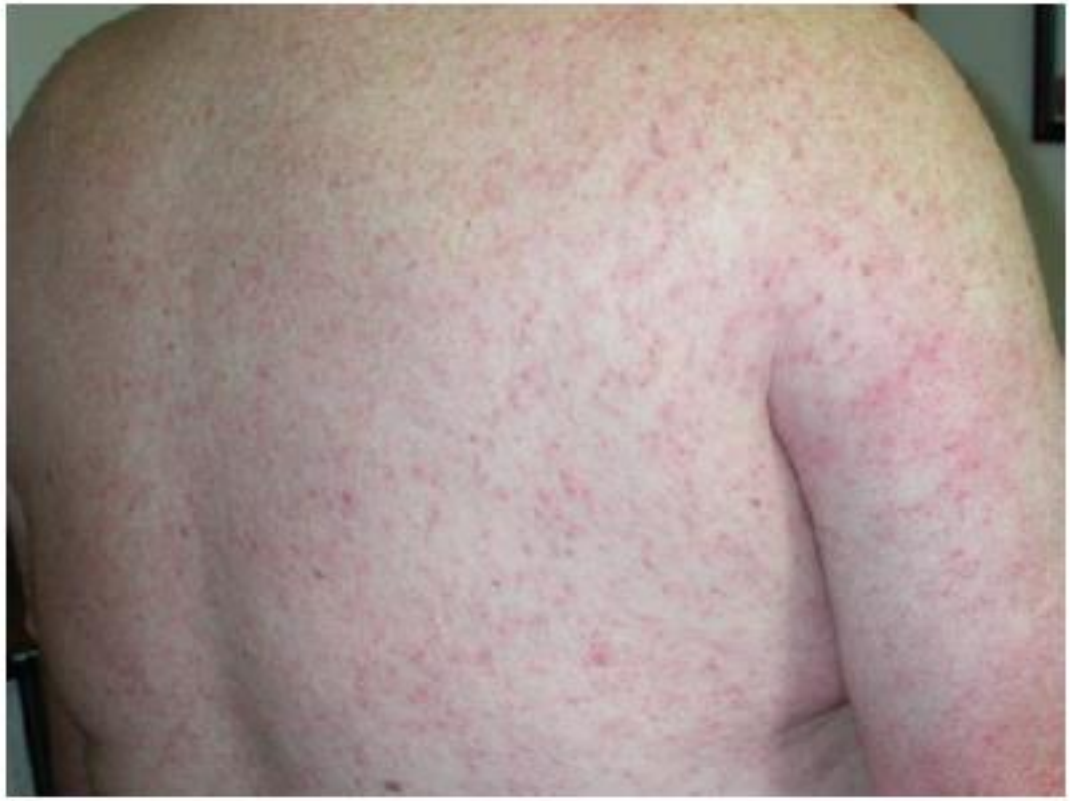
BMJ. 2003

Clinical course of WNV encephalitis: viraemia and antibody. Limits of virus detection are expressed as plaque forming units (pfu)/100 µl; viraemia is thought to be <10 pfu/100 µl. First day of fever is taken as first day of illness; most patients are not admitted until day 3-5

Clinical Manifestations and Outcomes of West Nile Virus Infection

Viruses 2014,

James J. Sejvar



Rash, morbilliform, maculopapular and non-pruritic and predominates over the torso and extremities, sparing the palms and soles, may be transient, lasting less than 24 hr.
It is more frequent in WN fever than in more severe manifestations, rash is more frequently observed among youngers. These findings raise the question as to whether the presence of a rash correlates with host immune or cytokine response to infection

Clinical Manifestations and Outcomes of West Nile Virus Infection

Viruses 2014,

James J. Sejvar

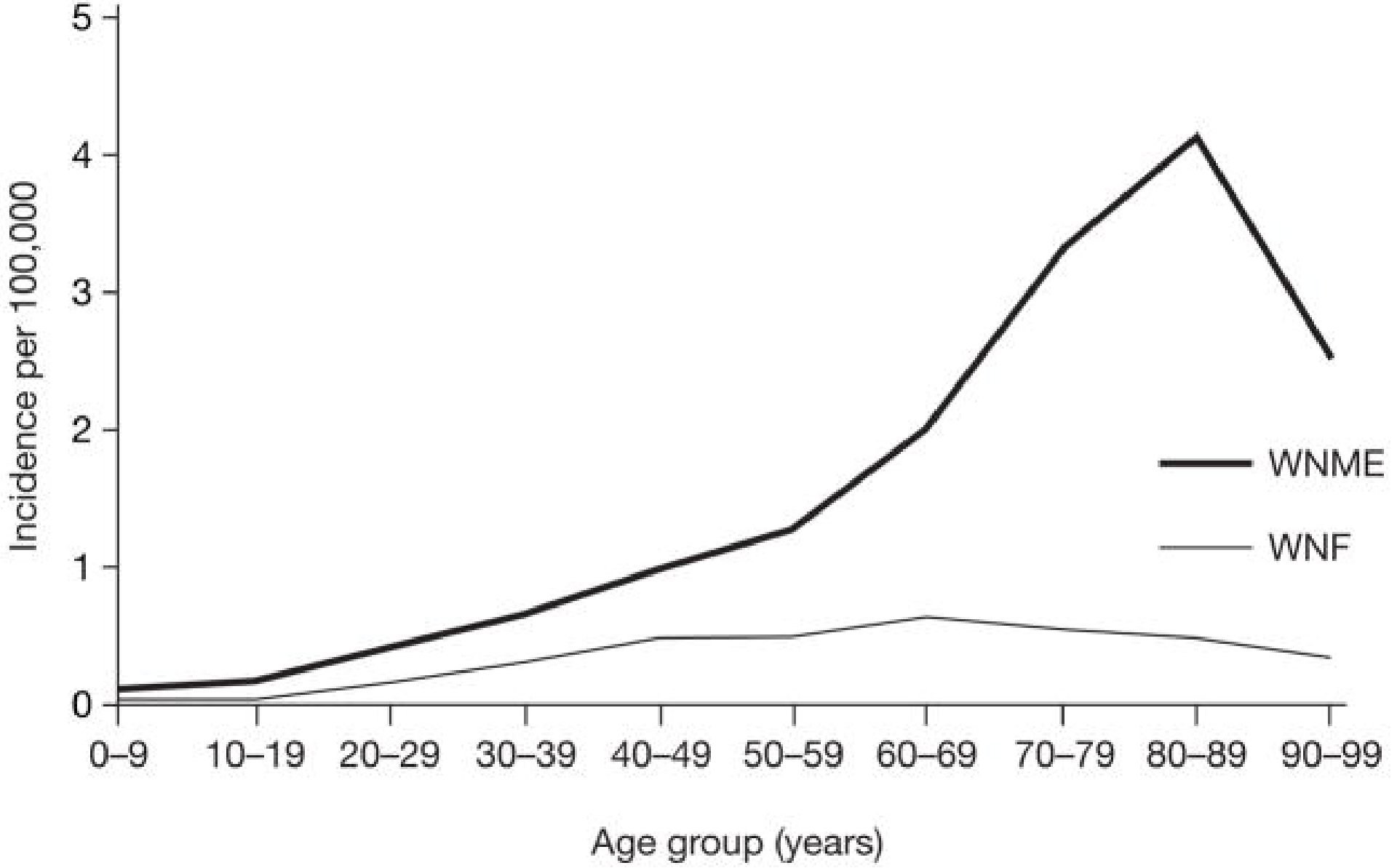
West Nile Meningitis (WNM)

WNM is indistinguishable from other viral meningitides with abrupt onset of fever and headache and meningeal signs, including nuchal rigidity, Kernig's and/or Brudzinski's signs and photophobia or phonophobia.

The associated headache may be severe, requiring hospitalization for pain control; associated gastrointestinal symptoms, such as nausea, vomiting and diarrhea, may result in dehydration, exacerbating head pain and systemic symptoms

WNM is generally associated with a favorable outcome, though, similar to WNF, some patients experience persistent headache, fatigue and myalgia

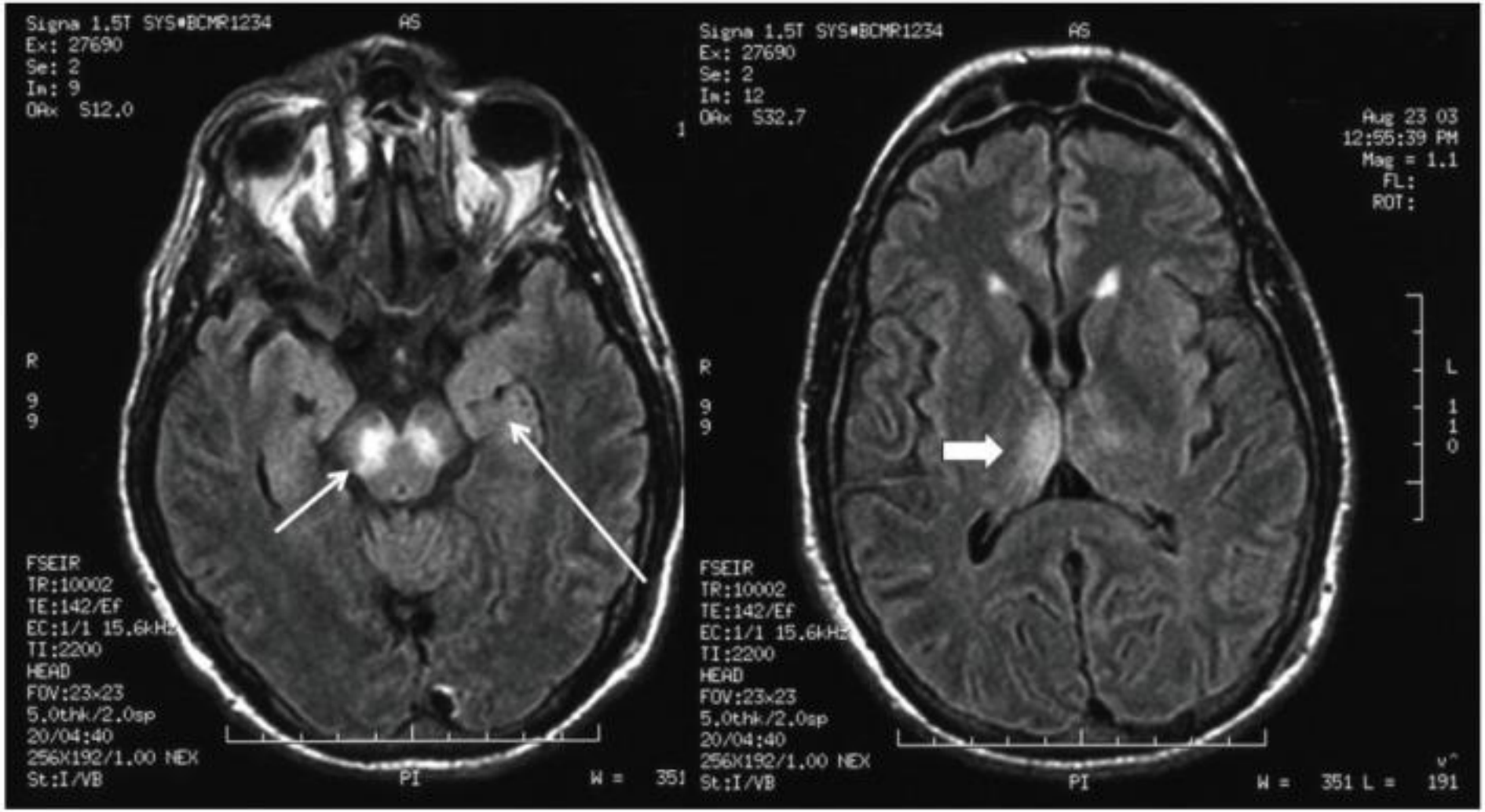
CSF is characterized by a modest pleocytosis, generally less than 500 cells/mm3, usually lymphocytic,



DeBiasi Nat Clin Pract Neurol. ;2013

Clinical Manifestations and Outcomes of West Nile Virus Infection

Viruses 2014,



West Nile virus encephalitis with associated parkinsonism and tremor, displaying signal abnormality in the substantia nigra (short arrow), the mesial temporal lobe (long arrow) and right posterior thalamus (thick arrow)

Clinical Manifestations and Outcomes of West Nile Virus Infection

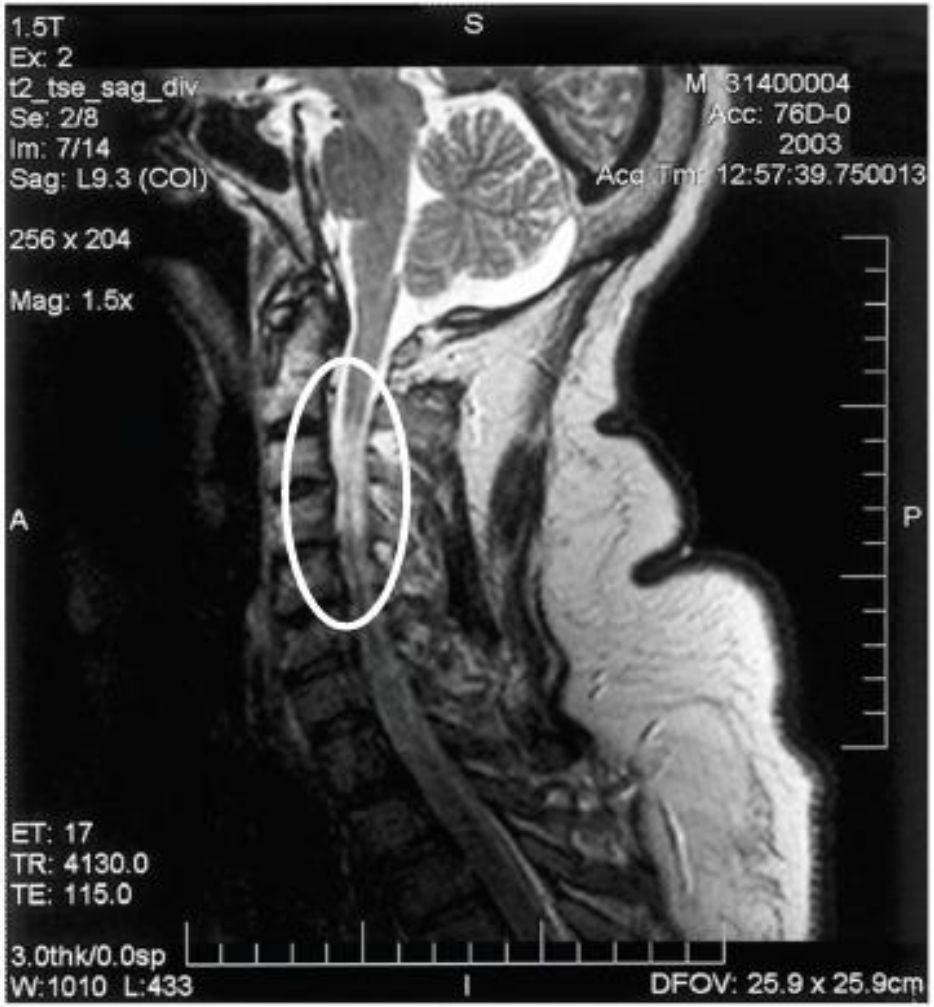
Viruses **2014**,

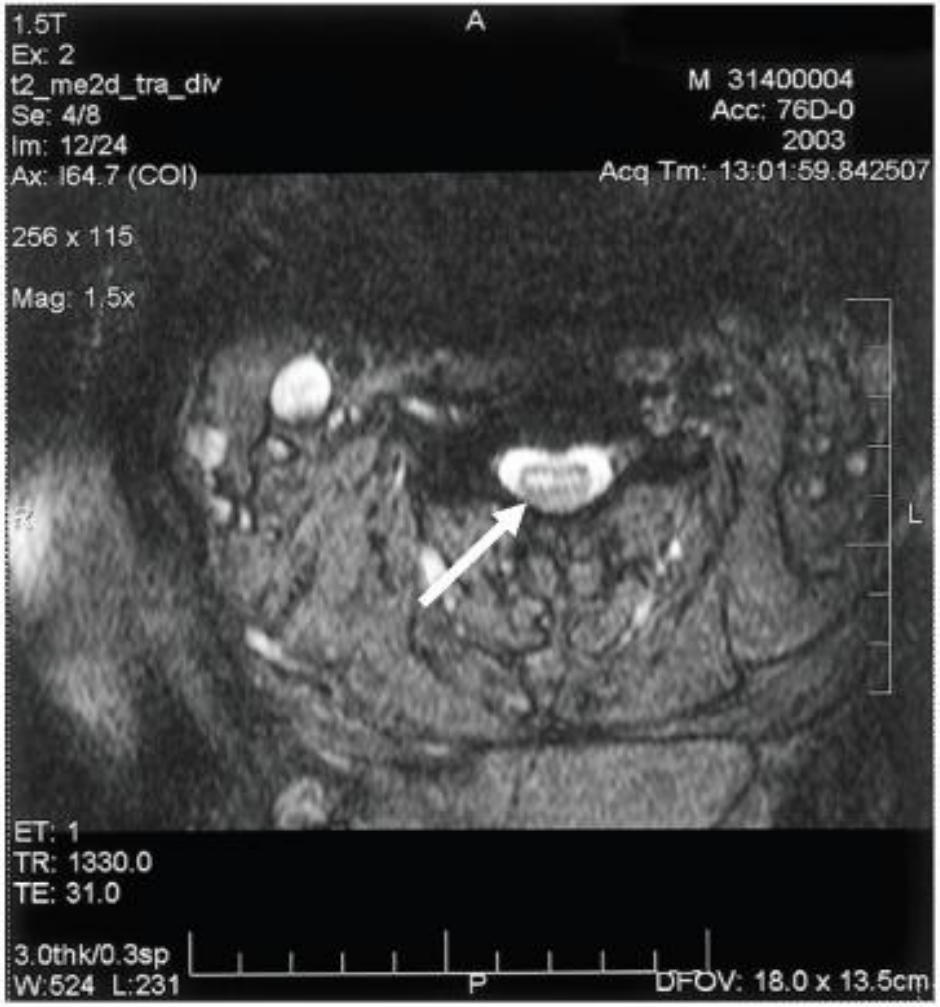
Table 1. Clinical and electrodiagnostic features of different types of weakness associated with West Nile virus infection.

Characteristic	West Nile Poliomyelitis	Guillain–Barré Syndrome	Fatigue-Related "Muscle Weakness"
Timing of onset	Acute phase of infection	One to eight weeks following acute infection	Acute infection
Fever and leukocytosis	Present	Absent	Present
Weakness distribution	Asymmetric; occasional monoplegia	Generally symmetric; proximal and distal muscles	Generalized, subjective, but neurologic examination normal
Sensory symptoms	Absence of numbness, paresthesias or sensory loss; pain often present	Painful distal paresthesias and sensory loss	Generally absent
Bowel/bladder involvement	Often present	Rare	Not present
Concurrent encephalopathy	Often present	Generally absent	May be seen with fever, meningitis or encephalitis
CSF Profile	Pleocytosis and elevated protein	No pleocytosis; elevated protein (albuminocytologic dissociation)	Pleocytosis and elevated protein in the setting of meningitis/encephalitis

Clinical Manifestations and Outcomes of West Nile Virus Infection

Viruses 2014,





Sagittal (A) and axial (B) T2 MR imaging of the cervical spinal cord of a patient with bilateral upper extremity paralysis and respiratory failure from West Nile poliomyelitis, displaying the increased signal in the anterior spinal cord (circle and arrow).

No specific therapy

Only supportive care for severe infections

- Hospitalization
- IV fluids,nutrition
- Ventilator support
- Prevention of secondary infections
- Good nursing care
- *Ribavirin* in high doses and *interferon alpha-2b* show activity in vitro
- No clinical data yet - nor for other me including steroids, antiseizure drugs, c osmotic agents

BMC Infectious Diseases

BioMed Central

Research article

Open Access

Using high titer West Nile intravenous immunoglobulin from selected Israeli donors for treatment of West Nile virus infection

David Ben-Nathan*[1,2], Orly Gershoni-Yahalom[1], Itzchak Samina[2], Yevgeny Khinich[2], Israel Nur[3], Orgad Laub[3], Ahuva Gottreich[4], Michael Simanov[2], Angel Porgador[1], Bracha Rager-Zisman[1] and Nadav Orr[3]

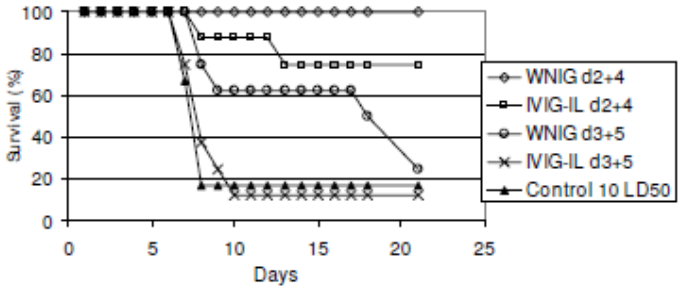


Figure 2
Therapeutic efficacy of WNIG. Groups of 5-week old BALB/c mice were treated i.p. with 2 mg/mouse IVIG-IL or WNIG on days 2 and 4, or days 3 and 5 after infection with 10 LD_{50} of West Nile virus. Mice were observed for mortality for 21 days. One group of infected mice received no treatment (control).

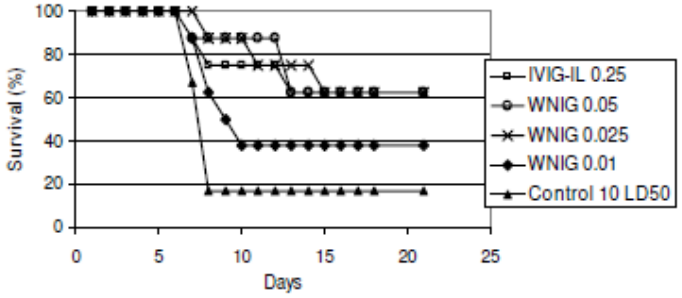


Figure 1
Dose-dependent protection by WNIG. Groups of 5-week old BALB/c mice were treated i.p. with IVIG-IL (0.5 or 0.25 mg/mouse) or with WNIG (0.01, 0.05, or 0.025 mg/mouse) 4 h after infection with 10 LD_{50} of WNV NY99. Mice were observed for mortality for 21 days. One group of infected mice received no treatment (control).

Lack of Efficacy of High-Titered Immunoglobulin in Patients with West Nile Virus Central Nervous System Disease

Table 7. Summary of unfavorable outcomes at day 90 after randomization of patients with confirmed West Nile virus in study of treatments for West Nile virus central nervous system disease*

Regimen	No. (%) patients			Odds ratio (95% CI)
	Favorable	Unfavorable	Missing	
Omr-IgG-am, n = 33	15 (45.5)	17 (51.5)	1 (3.0)	Referent
Polygam, n = 11	5 (45.5)	6 (54.5)	0	1.012 (0.198–4.975)
Normal saline, n = 11	8 (72.7)	3 (27.3)	0	3.238 (0.606–21.959)
Total confirmed, n = 55	28 (50.9)	26 (47.2)	1 (1.8)	

*Favorable/unfavorable determinations made on the basis of results of 4 standardized assessments of cognitive and functional status: Barthel Index (favorable ≥90, unfavorable <90), Modified Rankin Scale (favorable 0–3, unfavorable 4–6), Glasgow Outcome Score (favorable 4 or 5, unfavorable <4), and the Modified Mini Mental State Examination (favorable ≥78, unfavorable <78).

The Journal of Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

Primary Versus Nonprimary West Nile Virus Infection: A Cohort Study

Galia Rahav,[1,4,a] Michal Hagin,[1,a] Yasmin Maor,[1,4,b] Gilad Yahalom,[2] Musa Hindiyeh,[3,4] Ella Mendelson,[3,4,a] and Hanna Bin[3,a]

[1]Infectious Diseases Unit, [2]Department of Neurology, and [3]Central Virology Laboratory, Ministry of Health, Chaim Sheba Medical Center, Tel Hashomer, and [4]Sackler School of medicine, Tel Aviv University, Israel

Table 2. Factors at Admission Associated With Nonprimary West Nile Virus Infection

Variable	*P* Value	aOR (95% CI)	*P* Value
Psychiatric comorbidity	.008	13.73 (2.28–82.56)	.004
Season (winter or spring)	.002	8.82 (1.59–48.87)	.013
Fever	.036	0.61 (.39–.95)	.031
Abnormal result of LFT	.005	3.13 (.89–10.91)	.074
Age (per y increase)[a]	.43	1.03 (.99–1.06)	.085
Charlson comorbidity index[b]	.12	1.26 (.95–1.69)	.11
Encephalitis[a]	.85	0.21 (.83–1.71)	.34
Immunosuppression[a]	.42	1.35 (.43–4.29)	.60

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; LFT, liver function test.

Data are % (n) of patients, unless otherwise indicated.

[a] Variable was forced into the model.

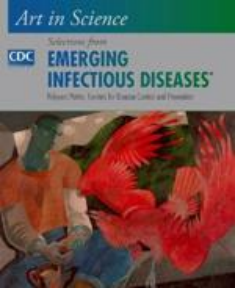
[b] Data are per unit increase in index.

Table 3. Outcome in Patients With Primary or Nonprimary West Nil Virus Infection

Outcome	Primary Infection (n = 68)	Nonprimary Infection (n = 50)	Overall	*P* Valu
In-hospital mortality	9 (6)	20 (10)	14 (16)	.080
Neurological sequelae	41 (28)	32 (16)	37 (44)	.30
Cognitive decline	23 (16)	20 (10)	22 (26)	.65
Length of stay, d	9.0 (1–244)	10.5 (2–132)	9.5 (1–244)	.96

Data are % (n) of patients or median value (range).

NPI, high IgG with a high avidity, absent or low IgM serum and CSF, and occasionally positive WNV PCR results may be an emerging clinical entity with a hig mortality rate must be considered seriously



Mutation in West Nile Virus Structural Protein prM during Human Infection

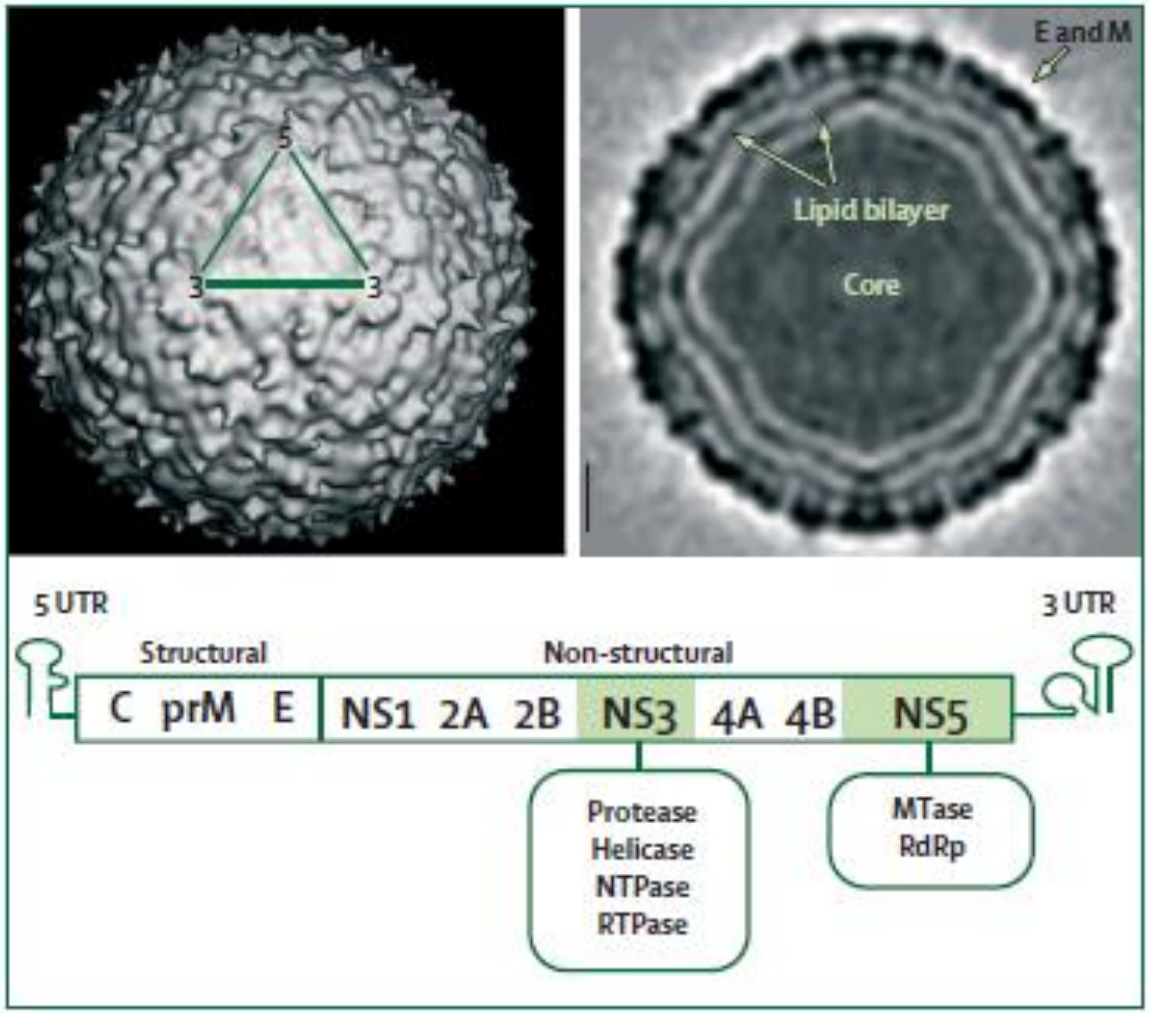


Figure 1: West Nile virion and genome

A key mutation in the prM protein occurred during persistent infection of an immunocompetent patient.

WNV RNA persisted in the patient's urine and serum in the presence of low-level neutralizing antibodies.

The results demonstrated persistent viremia for 47 days and viruria for 61 days after illness onset with persistence of WNV RNA and virus isolation, despite the development of IgM and IgG, as well as WNV neutralizing antibodies

WNV Patients

Physical and Cognitive Impairments

Missisipi 2002

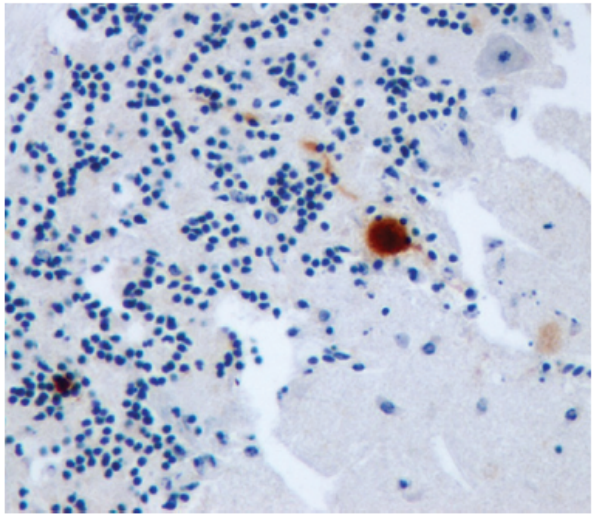
Frequency of physical and cognitive complaints before and after WNV illness

COMPLAINT	PRE (n=84)	POST (n=84)
Muscle Weakness	4.2%	56%
Difficulty walking	14.4%	50.6%
Fatigue	28%	65.5%
General malaise	21.5%	48.8%
Confusion	9.6%	27.4%

Usutu [*oo-soo'too*] virus

Usutu virus, named for the Usutu River in Swaziland, is a mosquito-borne flavivirus closely related to Japanese encephalitis virus, West Nile virus, Murray Valley encephalitis virus, and St. Louis encephalitis virus. Usutu virus was first isolated in 1959 from *Culex neavei* mosquitoes in South Africa. The first recognized infection in a human was in an African man with fever and rash in 1959 but was not reported until 1981.

In 2001, Usutu virus emerged in Europe, when it was identified as the etiologic agent of bird—mainly blackbird—mortality. Retrospective analysis of archived tissue samples from wild bird deaths in the Tuscany region of Italy in 1996, however, revealed an earlier introduction of the virus to Europe. It was not thought to be associated with severe or fatal disease in humans until a neuroinvasive infection was reported to have occurred in an Italian woman in 2009.



Immunohistochemical staining for Usutu virus antigen in a Purkinje cell of the cerebellum of a song thrush that died of encephalitis. Original magnification ×400.

Sources

1. Ashraf U, Ye J, Ruan X, Wan S, Zhu B, Cao S. Usutu virus: an emerging flavivirus in Europe. Viruses. 2015;7:219–38. http://dx.doi.org/10.3390/v7010219
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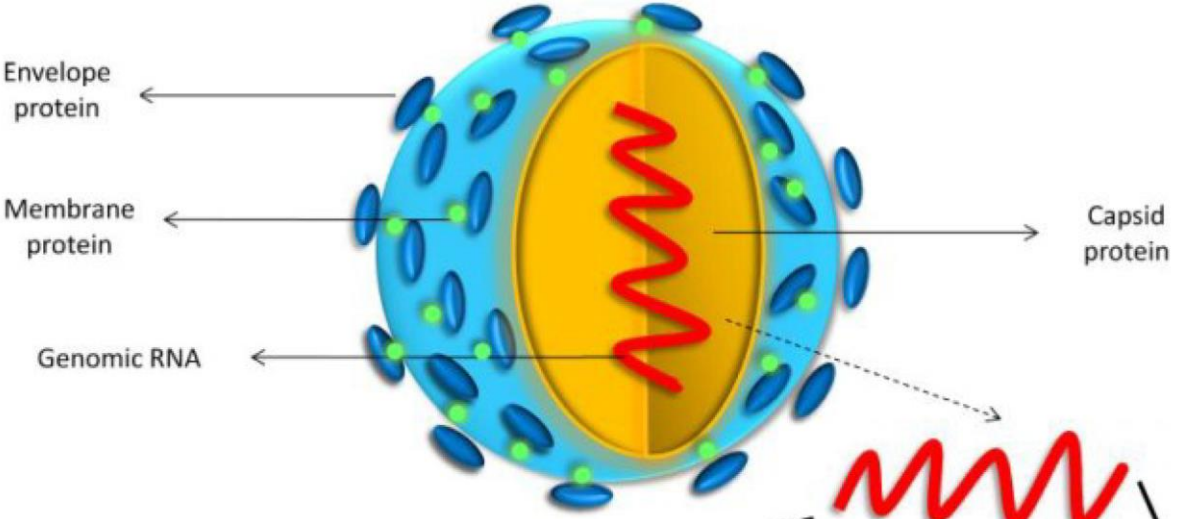
Usutu Virus: An Emerging Flavivirus in Europe

Usama Ashraf [1,2,3], Jing Ye [1,2,3], Xindi Ruan [1,2,3], Shengfeng Wan [1,2,3], Bibo Zhu [1,2,3] and Shengbo Cao [1,2,3,*]

Viruses **2015**, *7*, 219-238;



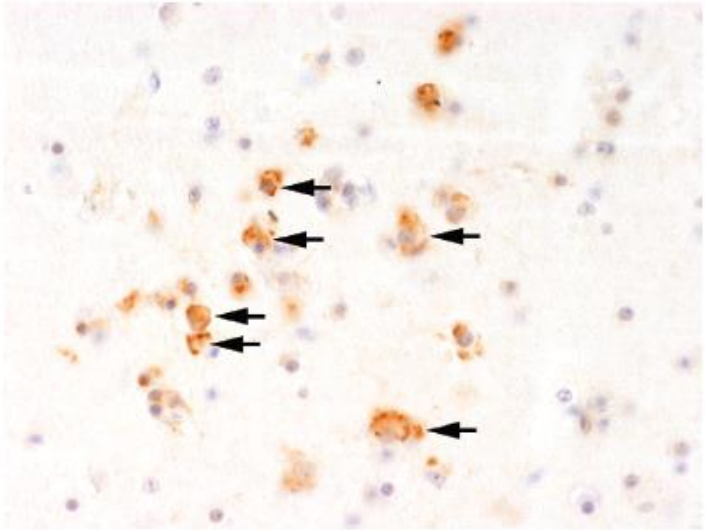
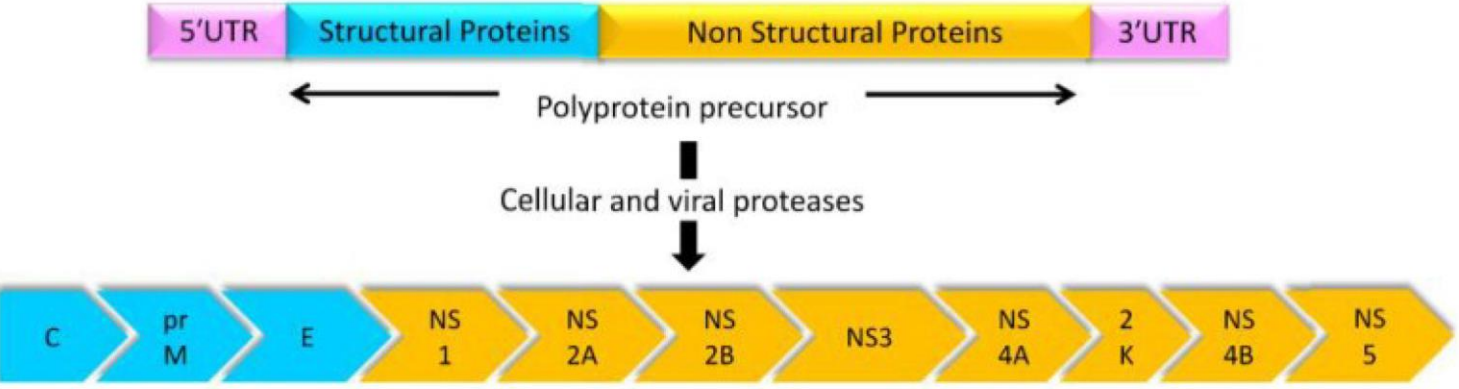


Figure 1. Immunohistochemical staining with Usutu virus–specific antibody showing virus antigen in the brain of a blackbird that died during an Usutu virus outbreak in Italy, 1996. Numerous neurons show characteristic, frequently coarsely granular cytoplasmic labeling (arrows). Original magnification ×390.



Usutu Virus: An Emerging Flavivirus in Europe

Usama Ashraf [1] ... an [1,2,3], Bibo Zhu [1,2,3] and Shengbo C...

...ses **2015**, *7*, 219-238;

Table 1. Avian species infected with USUV in Europe.

Species	Common Name	Country (year)	References
Dendrocopos major	Great spotted woodpecker	Belgium (2014)	[29]
Pyrrhula pyrrhula	Bullfinch		
Columba livia domestica	Domestic pigeon	Greece (2014)	[30]
Turdus philomelos	Song thrushes	Spain (2012)	[31]
Turdus merula	Eurasian blackbird	Italy (2010–2011) Germany (2011) Hungary (2003–2006) Austria (2001–2005)	[18,19,25–28]
Alcedo atthis	Common kingfisher	Germany (2011)	[26]
Serinus canaria domestica	Canary		
Alectoris rufa	Partridge	Italy (2010–2011)	[18,19]
Asio otus	Long-eared owl		
Caprimulgus europaeus	Nightjar		
Garrulus glandarius	Eurasian jay		
Larus michahellis	Yellow-legged gull		
Pica pica	Eurasian magpie		
Streptopelica decaocto	Eurasian collared dove		
Ardea cinerea	Grey heron	Germany (2011) Italy (2010–2011)	[18,19,26]
Merops apiaster	Eurasian bee-eater		
Passer domesticus	House sparrow		
Picus viridis	Eurasian green woodpecker		
Sturnus vulgaris	Common starling		
Strix nebulosa	Great grey owl	Germany (2011) Austria (2001–2002)	[26,27]
Gallus gallus domesticus	Chicken	Italy (2007–2009) Switzerland (2006–2007) England (2006)	[14,32–34]
Spheniscus humboldti	Humboldt penguin	Switzerland (2006–2007)	[34]
Phoenicopterus ruber	Greater flamingo		
Dacelo novaeguineae	Laughing kookaburra		
Ciconia ciconia	White stork	Austria (2006–2007)	[34]
Leptoptilos crumeriiferus	Marabou stork		
Neophron percnopterus	Egyptian vulture		
Bubo bubo	Eurasian eagle owl		
Bubo scandiacus	Snowy owl		
Strix uralensis	Ural owl		

Usutu Virus: An Emerging Flavivirus in Europe

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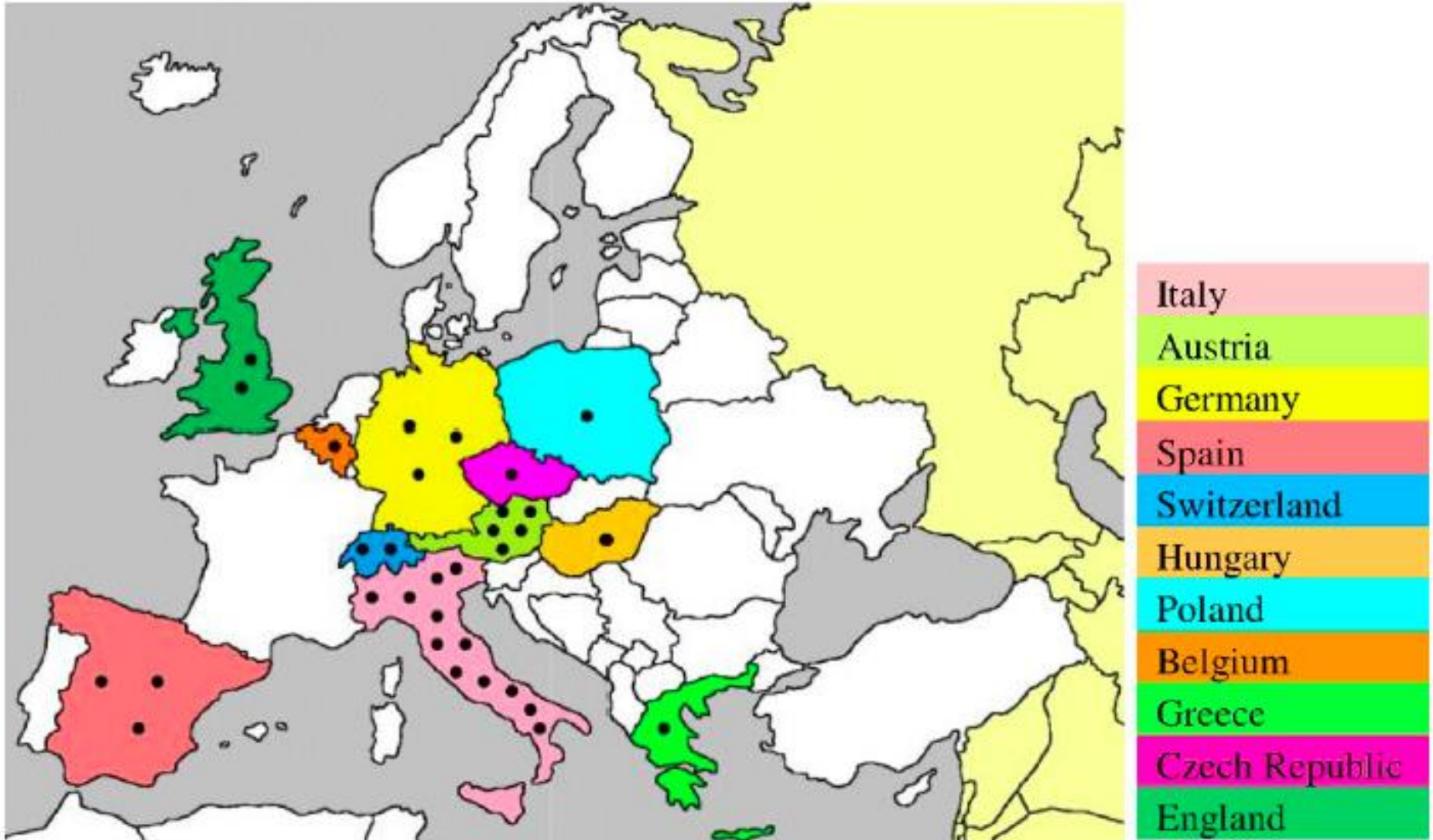


First human case of Usutu virus neuroinvasive infection, Italy, August-September 2009

A 60-yo women from Modena in 2009 with diffuse large B cell lymphoma had fever and neurological symptoms and was diagnosed with meningoencephalitits.

She had distal resting tremor, positivity to the Romberg test, dysmetry and weakness at four limbs without cranial nerve affection. Brain MR showed a signal alteration of the substantia nigra of the parietal and frontal subcortical areas that did not change after injection of contrast medium.

The CSF was limpid without any alteration detected in the clinical-chemical analysis, activated lymphocytes were evident in the sediment. It was positive for USUV, and USUV was also demonstrated in serum and plasma samples by RT-PCR

Eurosurveillance

Pecorari Eurosurveillance 2009

JOURNAL OF
MEDICAL VIROLOGY

Vol 90, 10,
October 2018

Prevalence of Usutu and West Nile virus antibodies in human sera, Modena, Italy, 2012

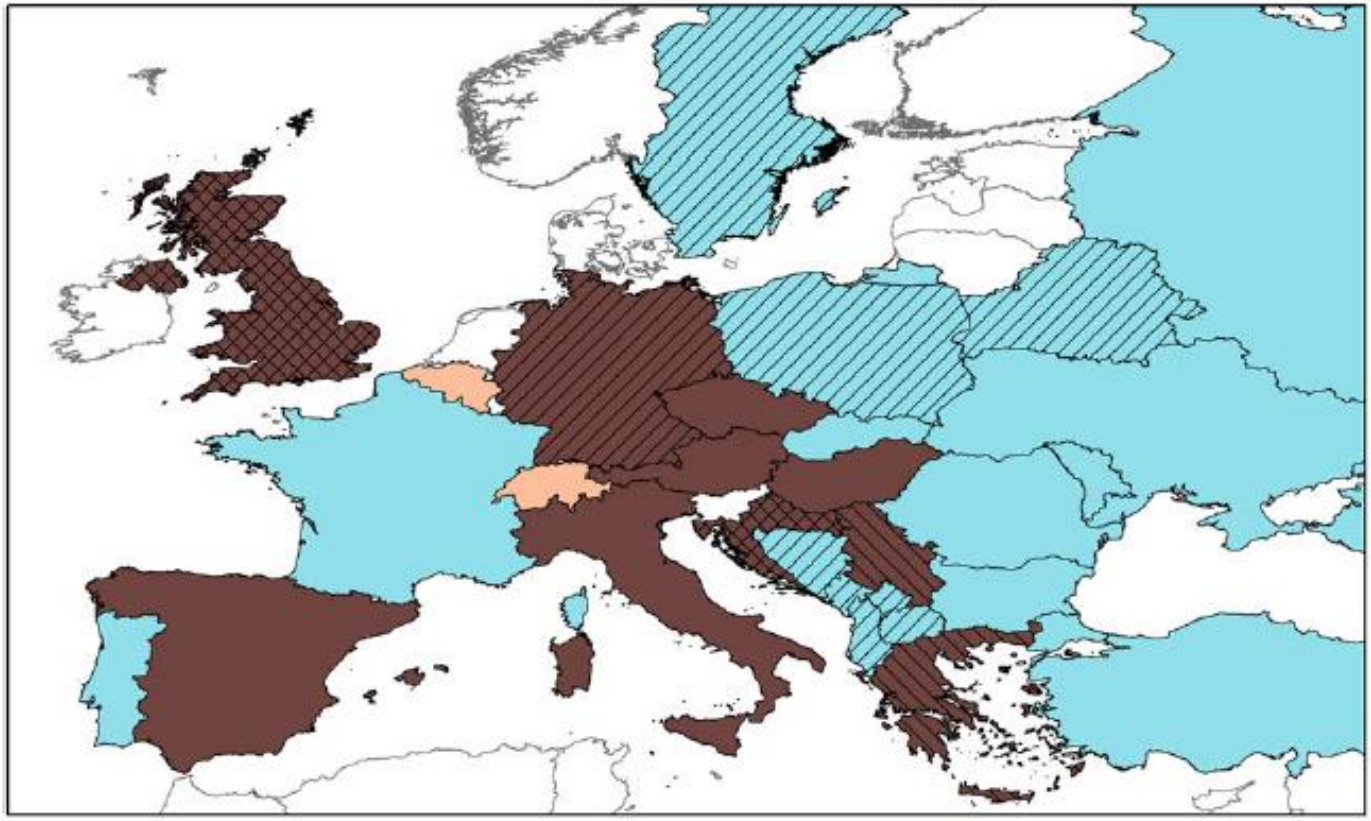
A collection of 3069 human sera collected in the area of the municipality of Modena, Emilia Romagna, Italy, was retrospectively investigated for specific antibodies against Usutu (USUV) and West Nile viruses (WNV).

All the samples resulting positive using a preliminary screening test were analyzed with the plaque reduction neutralization test.

Overall, 24 sera were confirmed as positive for USUV (0.78%) and 13 for WNV (0.42%). The results suggest that in 2012, USUV was circulating more than WNV in North-eastern Italy.

Trans R Soc Trop Med Hyg 2015; **109**: 609–618
doi:10.1093/trstmh/trv066 Advance Access publication 17 August 2015

A review of West Nile and Usutu virus co-circulation in Europe: how much do transmission cycles overlap?



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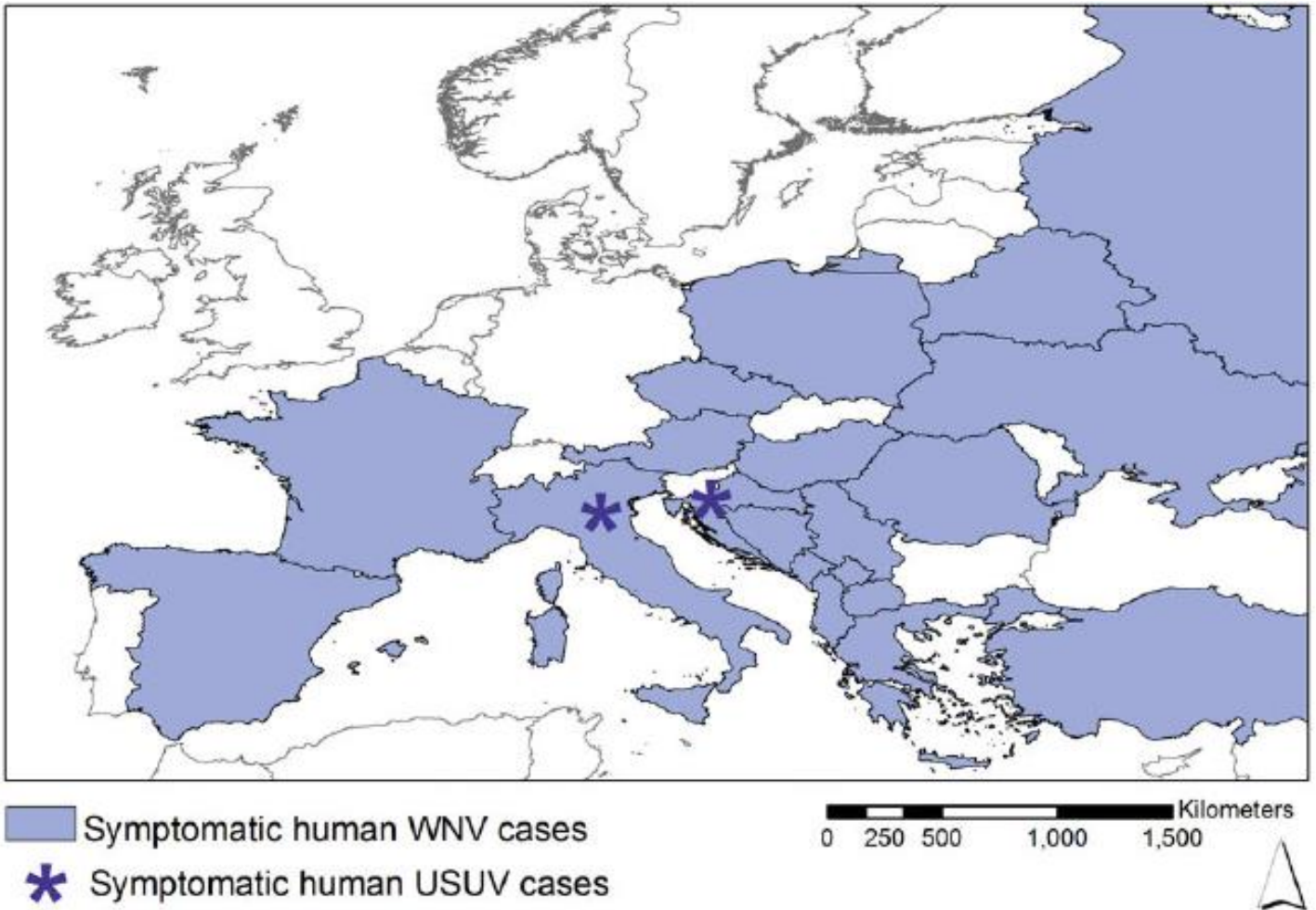

15/9/2022 - Mosquito Alert: un’app per tracciare le zanzare presenti in Italia

Mosquito Alert

Movement Ecology Lab

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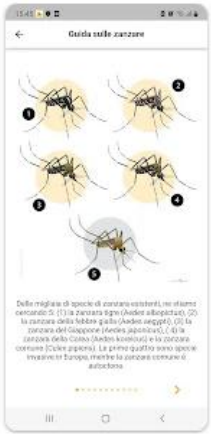


Contatto sviluppatore

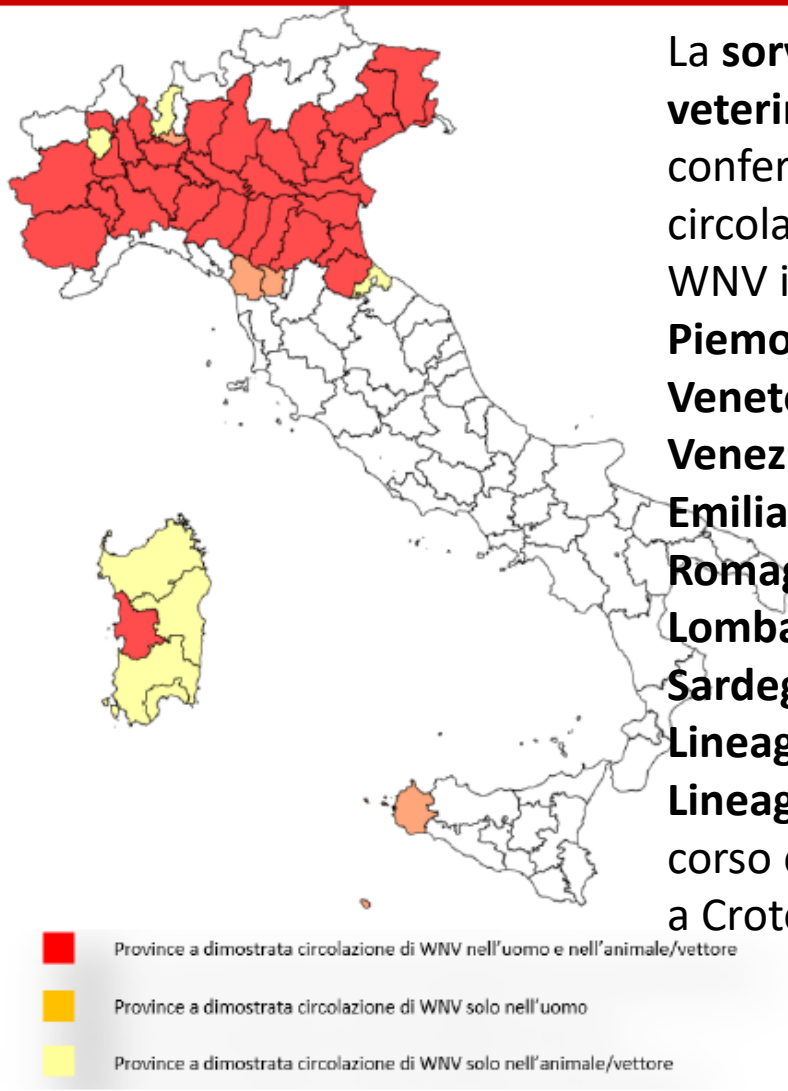
Informazioni su questa app →

Unisciti alla più grande rete di sorveglianza delle zanzare del mondo. Contribuisci allo studio e al monitoraggio delle zanzare invasive e

Sorveglianza integrata del WN e Usutu virus

Continua crescere il numero di casi umani di infezione da **West Nile Virus** nell'ultima settimana di sorveglianza. Dall'inizio di giugno 2022 sono stati segnalati in Italia **475** casi confermati di infezione da **West Nile Virus** (WNV) nell'uomo (440 nell'ultimo bollettino); di questi **234** si sono manifestati nella forma neuro-invasiva (28 Piemonte, 23 Lombardia, 112 Veneto, 4 Friuli-Venezia Giulia, 59 Emilia-Romagna, 3 Toscana, 1 in Sicilia, 4 Sardegna), **72** casi identificati in donatori di sangue (9 Piemonte, 21 Lombardia, 25 Veneto, 17 Emilia-Romagna), **159** casi di febbre (3 Piemonte, 10 Lombardia, 131 Veneto, 10 Friuli-Venezia Giulia, 2 Emilia-Romagna, 2 casi non nota la regione di esposizione e 1 caso importato dalla Spagna), **9** casi sintomatici (1 Lombardia, 7 Veneto, 1 Friuli-Venezia Giulia) e **1** caso asintomatico (1 Veneto). Il primo caso umano della stagione è stato segnalato dal Veneto nel mese di giugno nella provincia di Padova. Tra i casi confermati, sono stati notificati **25 decessi** (5 Piemonte, 4 Lombardia, 13 Veneto, 1 Friuli-Venezia Giulia, 2 Emilia-Romagna). Nello stesso periodo sono stati segnalati **5** casi di **Usutu virus** (3 Friuli-Venezia Giulia, 1 Piemonte, asintomatici in donatori di sangue) (1 Emilia-Romagna con febbre confermata).

Figura 1. *Province con dimostrata circolazione di WNV in vettori, animali e uomo (donatori asintomatici, febbri e casi neuroinvasivi confermati)*



La **sorveglianza veterinaria** ha confermato la circolazione del WNV in **Piemonte, Veneto, Friuli-Venezia Giulia, Emilia-Romagna, Lombardia** e **Sardegna WNV Lineage 1** e **Lineage 2. In** corso conferma a Crotone

Dati aggiornati al **13-9-2022**

Sorveglianza integrata del WN e Usutu virus

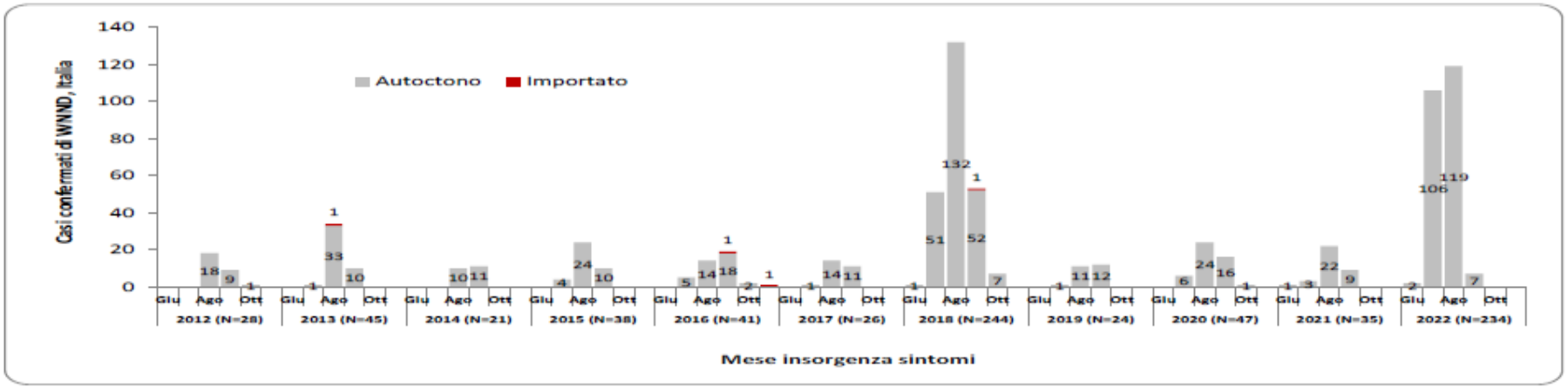
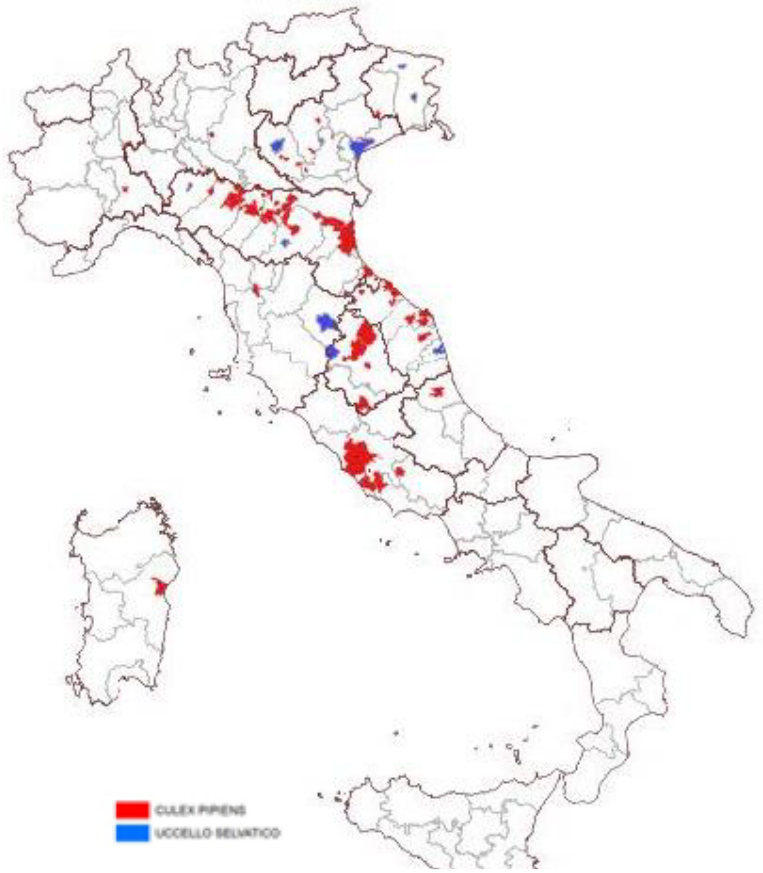


Figura 1. Andamento dei casi confermati di WNND per mese insorgenza sintomi. Italia: **2012 – 2022.**

Dati aggiornati al **13-9-2022**

Sorveglianza integrata del WN e Usutu virus

Il **virus Usutu** è stato identificato in **107 pool di zanzare e 51 uccelli in Abruzzo, Emilia Romagna, Lombardia, Marche, Friuli Venezia Giulia, Umbria, Toscana, Lazio e Veneto.**



Regione	Provincia	n.pool+
MARCHE	Pesaro e Urbino	6
	Ancona	3
	Ascoli Piceno	1
	Macerata	3
EMILIA ROMAGNA	Modena	13
	Ferrara	2
	Ravenna	4
	Bologna	13
	Reggio Emilia	18
	Parma	6
FRIULI VENEZIA GIULIA	Pordenone	1
LAZIO	Latina	5
	Roma	3
	Frosinone	1
LOMBARDIA	Milano	1
	Brescia	2
UMBRIA	Terni	1
	Perugia	4
VENETO	Verona	4
	Treviso	2
	Padova	2
	Vicenza	2
TOSCANA	Pistoia	1
	Firenze	1
PIEMONTE	Torino	1
	Novara	1
	Alessandria	3
SARDEGNA	Nuoro	1
ABRUZZO	Teramo	2
Totale	107	

Dati aggiornati al **13-9-2022**

Tick-borne encephalitis in north-east Italy: a 14-year retrospective study, January 2000 to December 2013

Characteristics		N (%)[a]
Nationality	Italians	355 (96.7)
	Others	12 (3.3)
Area of residence	Living in north-eastern Italy	364 (99.2)
	Living in other areas	3 (0.8)
Sex	Female	110 (30.0)
	Male	257 (70.0)
Age	Median (IQR)	56 (42–67)
Month of onset symptoms	January	2 (0.5)
	February	1 (0.3)
	March	3 (0.8)
	April	25 (6.8)
	May	50 (13.6)
	June	64 (17.4)
	July	79 (21.5)
	August	44 (12.0)
	September	32 (8.7)
	October	53 (14.4)
	November	11 (3.0)
	December	3 (0.8)

Descriptive characteristics of persons diagnosed with tick-borne encephalitis in 'Triveneto', north-eastern Italy, 2000–2013 (n=367)

Clinical syndrome	Encephalitis	175 (47.7)
	Meningoencephalitis	94 (25.6)
	Febrile illness only	60 (16.4)
	Aseptic meningitis	25 (6.8)
	Meningoencephalomyelitis	13 (3.5)
Vaccinated	–	3 (0.8)
Sequelae	–	60 (16.3)
Deaths	–	2 (0.5)

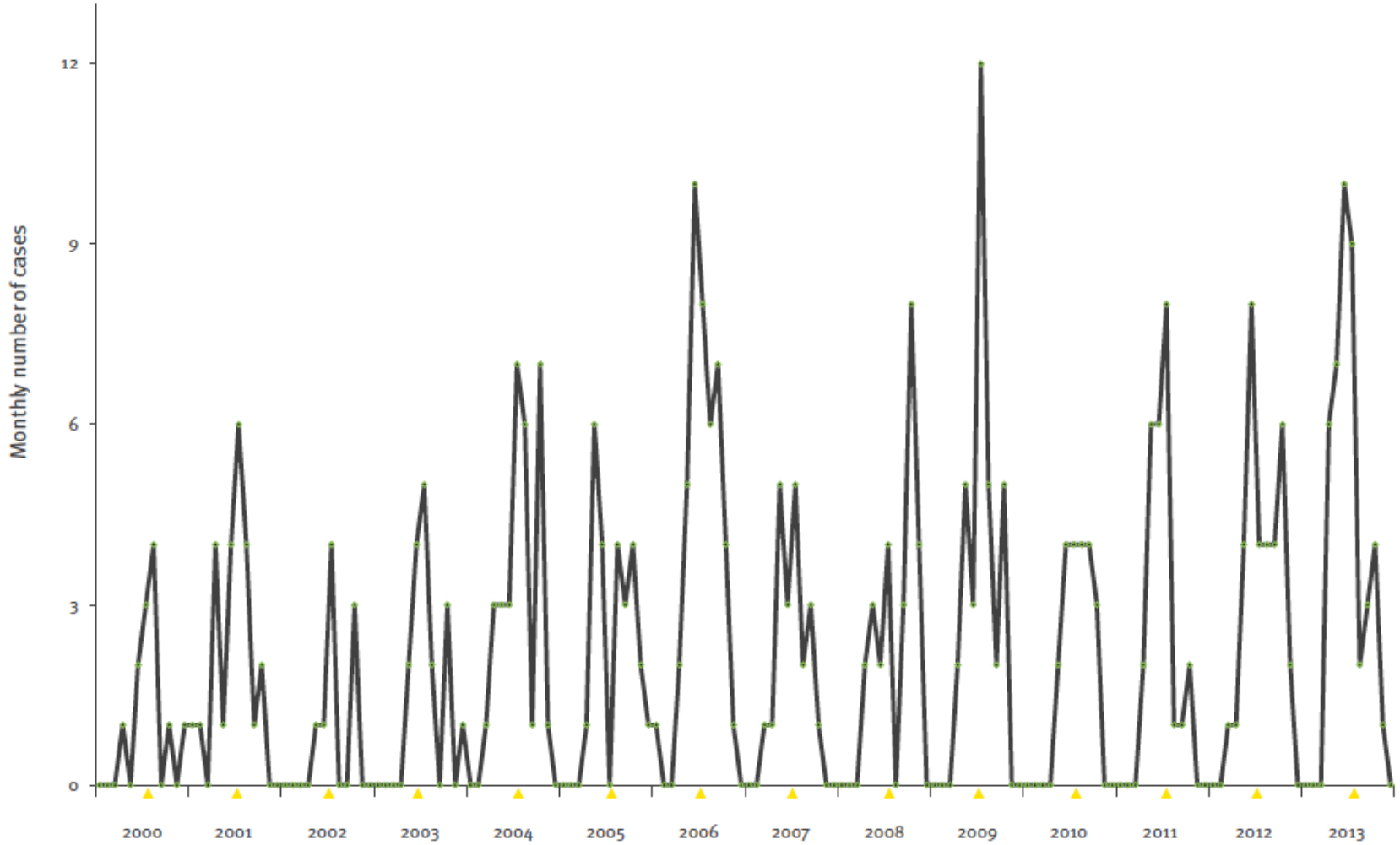
IQR: Interquartile range.

[a] Unless otherwise specified.

Tick-borne encephalitis in north-east Italy: a 14-year retrospective study, January 2000 to December 2013

FIGURE 1

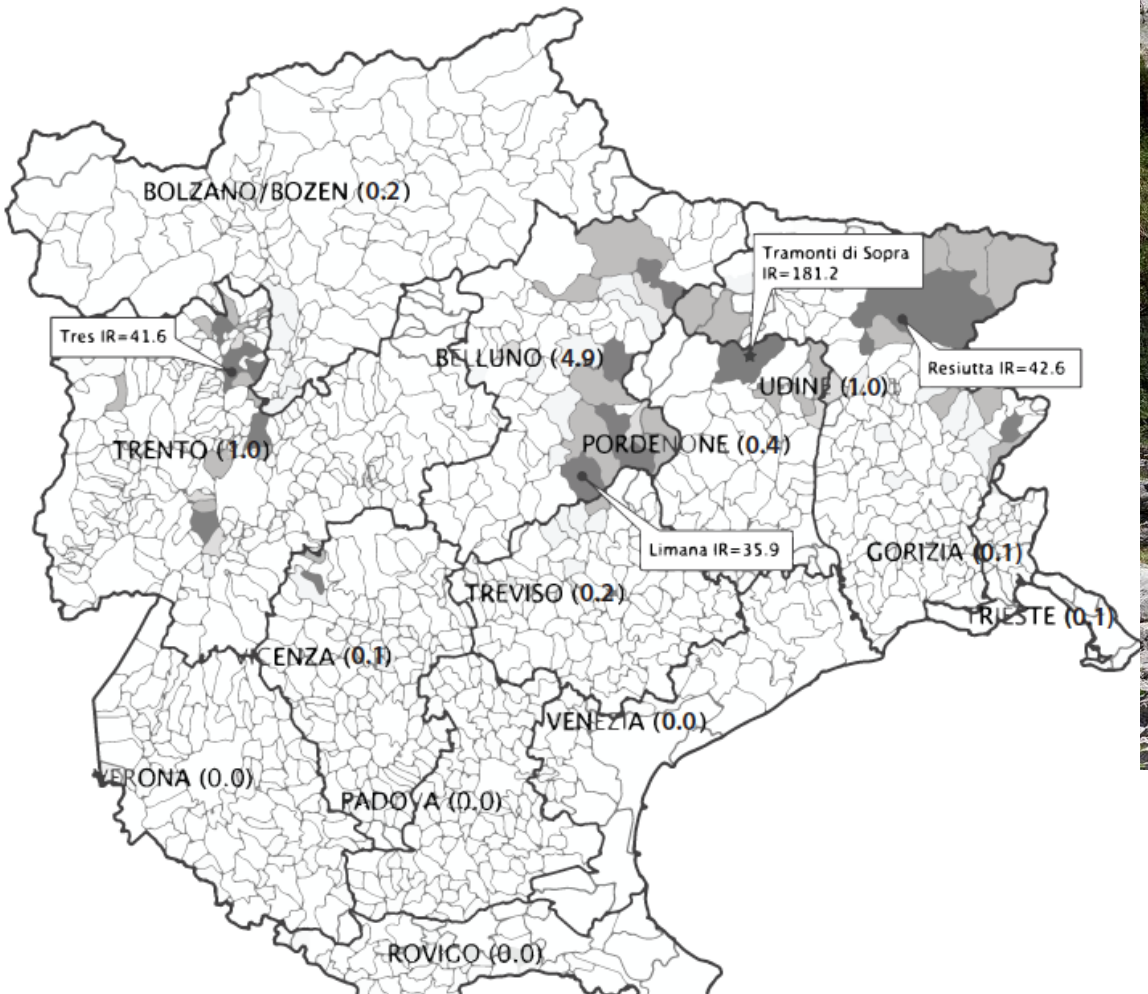
Monthly distribution of tick-borne encephalitis cases in 'Triveneto', north-eastern Italy, 2000–2013 (n=367 cases)

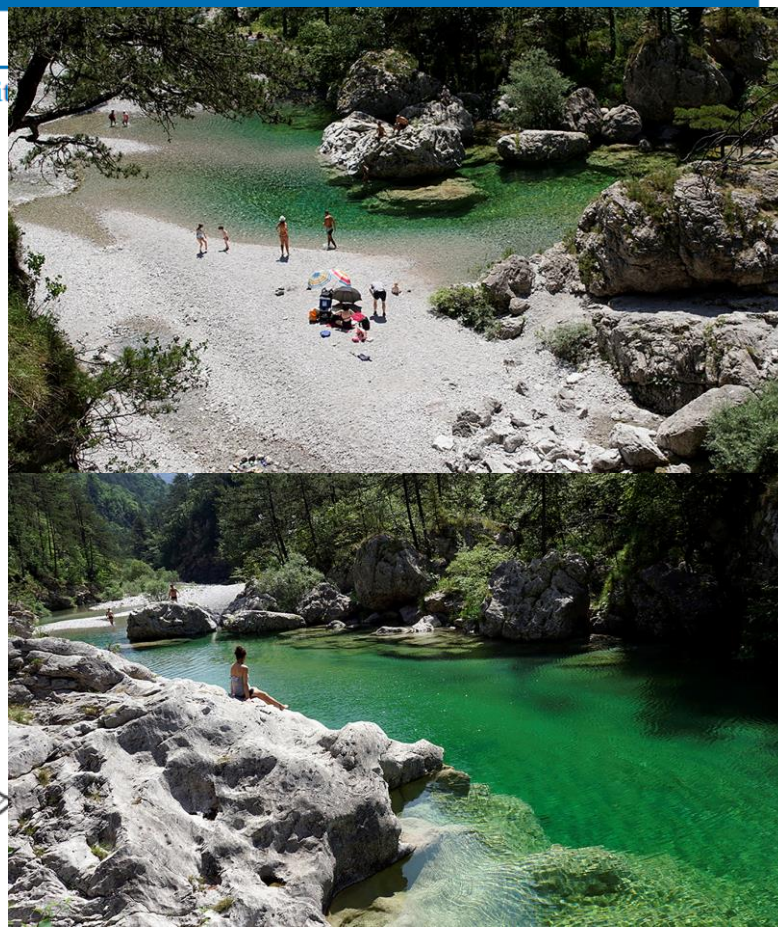


Tick-borne encephalitis in north-east Italy: a 14-year retrospective study, January 2000 to December 2013

FIGURE 2

Annual incidence rates (per 100,000 inhabitants) of tick-borne encephalitis cases by municipali
eastern Italy, 2000–2013





Tick-borne encephalitis in north-east Italy: a 14-year retrospective study, January 2000 to December 2013

TABLE 2

Incidence rates (IR) and incidence rate ratios (IRR) of tick-borne encephalitis (TBE) in 'Triveneto' according to the altitude of the municipalities of residence, north-eastern Italy, 2000–2013

Municipality altitude (metres)	Number of municipalities	Municipalities with at least one case N (%)	Total TBE cases	IR (per 100,000)	IRR (95% CI)	P-value[a]
0–200	589	44 (7.5)	78	0.10	1.00 (–)	<0.01
200–400	146	40 (27.4)	162	1.54	15.16 (11.57–19.86)	<0.01
400–600	101	22 (21.8)	70	2.41	23.81 (17.24–32.87)	–
600–800	103	15 (14.6)	28	1.27	12.52 (8.13–19.27)	<0.01
>800	196	17 (8.7)	26	0.55	5.42 (3.48- 8.45)	<0.01

[a] P-values refer to comparisons between IR in municipalities with a mean altitude between 400 and 600 m with that of the municipalities with another mean altitude.

Tick-borne encephalitis foci in northeast Italy revealed by combined virus detection in ticks, serosurvey on goats and human cases

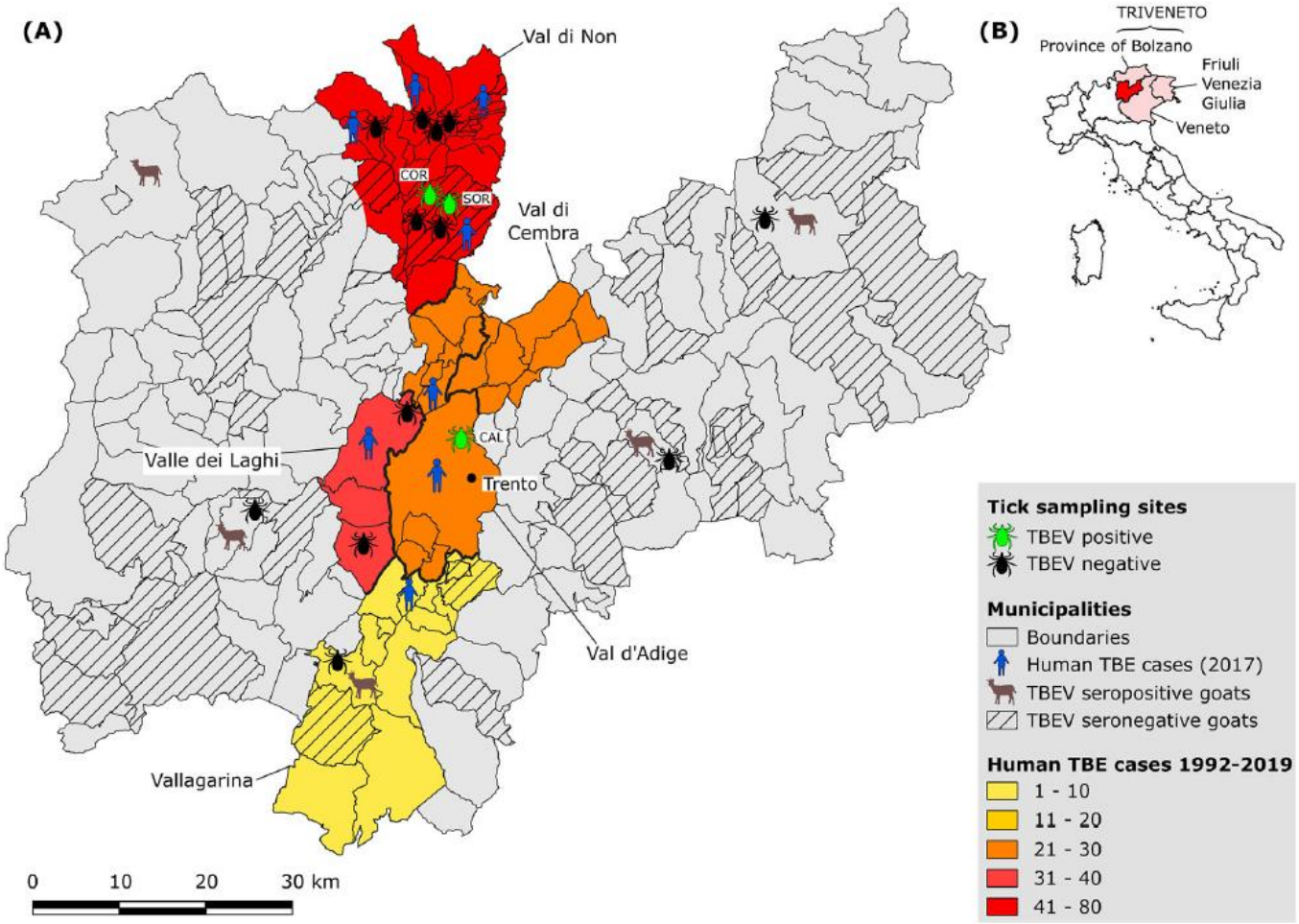


Figure 1. (A) Map of the Province of Trento reporting the locations of (i) the tick sampling sites; (ii) of the farms providing goat serum samples; (iii) of the human TBE cases. Thicker lines mark the borders between valleys. (B) Map of Italy showing the location of the Province of Trento within Triveneto.

Alfano EMI 2020

Tick-borne encephalitis foci in northeast Italy revealed by combined virus detection in ticks, serosurvey on goats and human cases

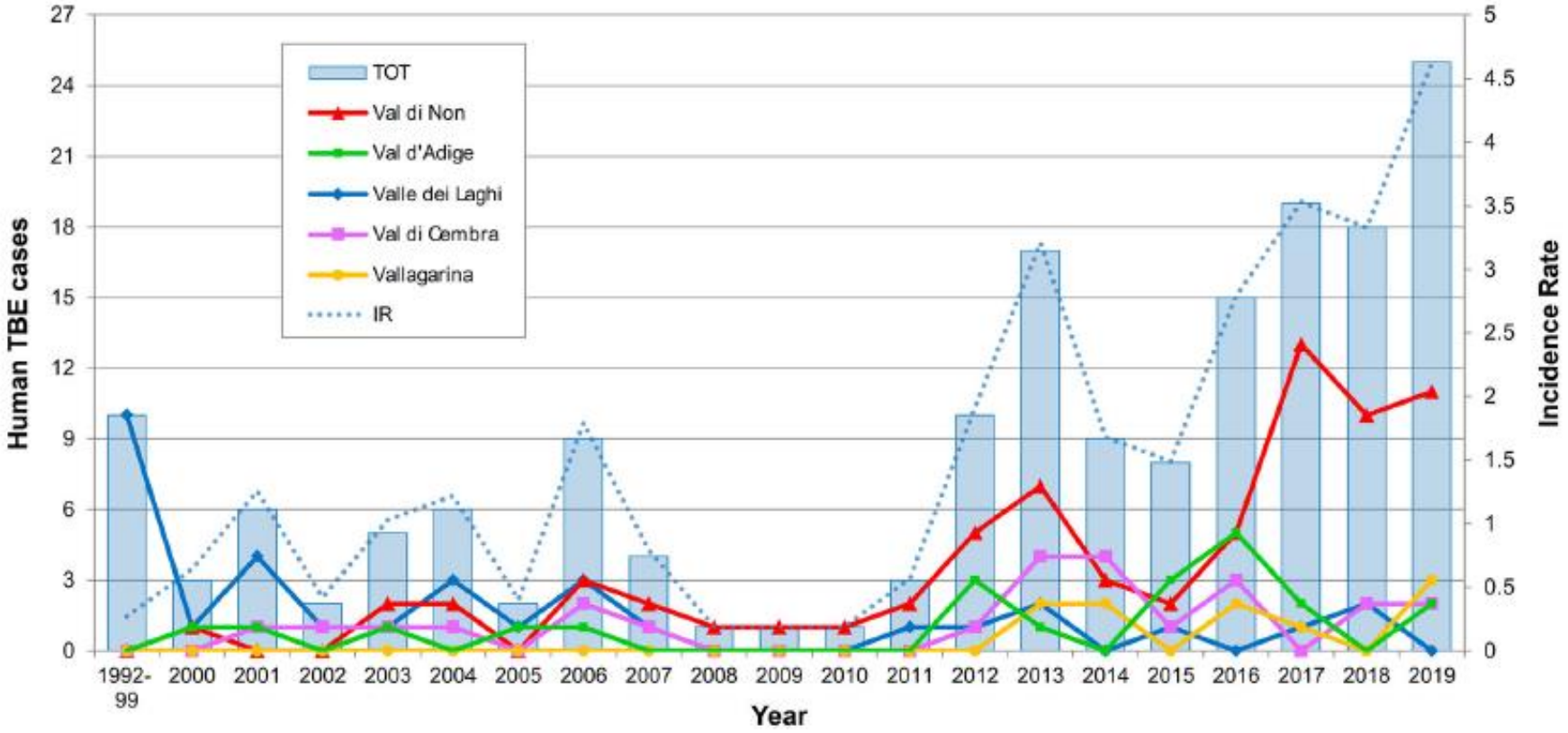
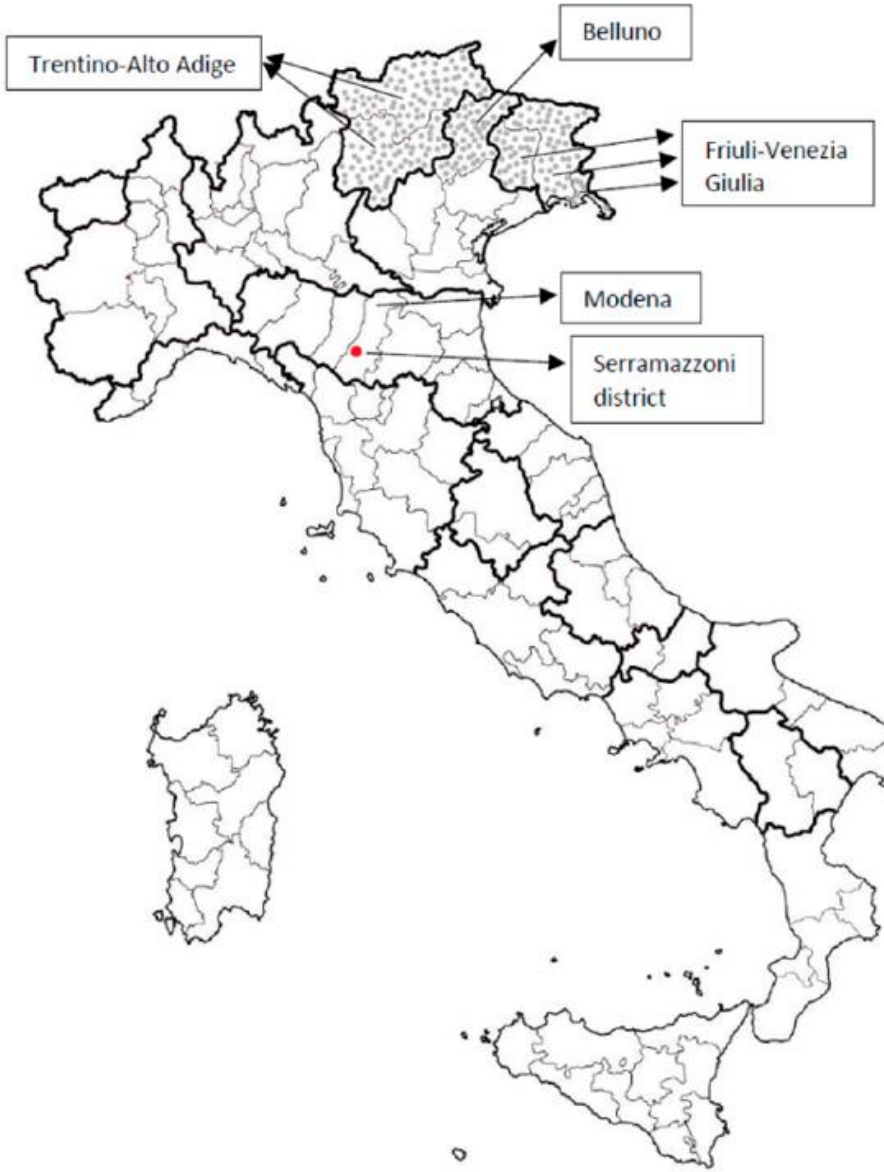


Figure 2. Human TBE cases reported by valley in the Province of Trento from 1992 to 2019. The incidence rate (IR) was calculated as the number of cases/resident population per 100,000 inhabitants.

Alfano EMI 2020

First Human Case of Tick-Borne Encephalitis in Non-Endemic Region in Italy: A Case Report

pathogens



Patients with suspicious cases of TBE may not be immediately tested for serology to TBEV in non-endemic regions.
Clinician should consider this differential diagnosis in patients with fever and neurological involvement, particularly in regions with high-tick density.

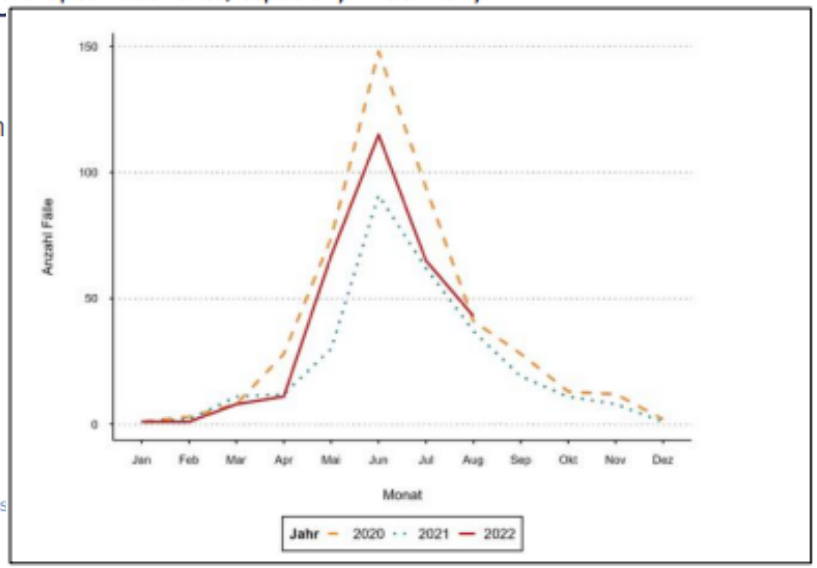
No reported tick bite but up 50% of patients with tick-borne disease ignore tick bites.

He had a typical biphasic course of TBE: first fever unspecific episode, the viremic phase, followed 9 days later by a second phase with neurologic symptoms and CSF clear, with high lproteins (57 mg/dL, 20–50) and 60 lymphocytes (cut off <4).

This first autochthonous case supports the concept of circulation of TBEV and the presence of a possible TBEV hot spot in Serramazzoni, Modena

Switzerland: Tick-borne diseases 2022

Tick-borne Encephalitis (TBE/FSME): Since the beginning of the year 2022 until the end of August, 311 TBE infections were reported, more than the reported 230 cases in the same period of 2021 and a bit less than in the same period of 2022 (n=384), see figure below. After the peak year of 2020, this year's case numbers are so far within the annually observed fluctuations. Over the past five years, the FOPH has observed an increase in the annual incidence of TBE. This increase has also been observed in several European countries, especially in Germany.



Published Date: 2022-09-21 03:09:51 CEST
Subject: PRO/AH/EDR> Tick-borne encephalitis - Switzerlan
Archive Number: 20220921.8705704

TICK-BORNE ENCEPHALITIS - SWITZERLAND
****

A ProMED-mail post
http://www.promedmail.org
ProMED-mail is a program of the
International Society for Infectious Diseases
http://www.isid.org

Date: Sun 18 Sep 2022
Source: Oi Canadian [edited]
https://oicanadian.com/infectious-disease-cases-of-tick-borne-encephalitis

The summer of 2022 saw a record number of tick-borne encephalitis infections. By early September [2022], more than 300 people had contracted the tick-borne meningoencephalitis virus [TBE] transmitted by the unwanted [tick]. There were fewer than 100 cases during the same period 10 years ago, reported our colleagues from the "SonntagsZeitung," which is already worth the title of "tick year" in 2022.

This disease is not to be taken lightly: if it is most often without consequence, it can sometimes cause serious neurological sequelae and cause death in 1% of cases. Especially since after infection, treatment is only symptomatic. The German-speaking Sunday newspaper thus gives the floor to [JR], a former high-level athlete, who was close to death due to this illness and who has been fighting since this summer to regain all his abilities.

In very hot years, ticks proliferate and the virus with it. In the event of a hot spring, it is estimated that one in a hundred ticks carries the [TBE] virus, while the proportion drops to one in a thousand if the same period is rather cool. But aside from these one-off effects, climate change has already compounded the problem.

While the regions at risk were still limited to certain sectors of the Plateau 10 years ago, all of Switzerland is now affected by the spread of this dangerous virus. Only Ticino and Geneva are still relatively spared. And the time when hikers who favored high altitude trails felt safe is over: you can find ticks up to 2000 meters [6500 ft] now.

If [JR] wanted to share his story in the newspaper it is because it could easily have been avoided: in the spring, he could have been vaccinated against this disease but he did not want to. "It was a huge mistake," he says today. Available in pharmacies, the vaccine, whose schedule is available in 3 doses, indeed offers very effective coverage against TBE, but the Swiss are relatively uninterested.

Barely 1/3 of the population has had recourse to the injection. "Given the danger of a bite, it's much too low," says Norbert Satz, a doctor in Zurich and tick specialist who points to "vaccine aversion" high in Switzerland. In Austria, 90% of the population is vaccinated, and the only cases of meningoencephalitis concern tourists.

Immunization is the best protection against tick-borne encephalitis

World Health Organization

19 February 2020 | Departmental news | Reading time: Less than a minute (241 words)

In a new position paper, published in the Weekly Epidemiological Record today, WHO recommends vaccination against tick-borne encephalitis in people of all ages where the disease is highly endemic. Where the prevaccination incidence of the disease is moderate or low or is limited to particular geographical locations or certain outdoor activities, immunization should target individuals in the most severely affected groups. People travelling from non-endemic areas to endemic areas should be offered vaccination if their visits will include extensive outdoor activities.

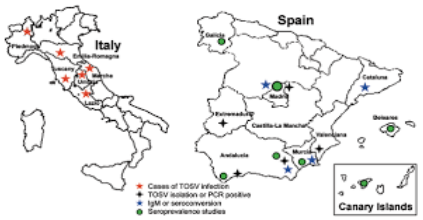
Richard Bartz

Since the incidence of tick-borne encephalitis may vary considerably between and even within geographical regions, public immunization strategies should be based on risk assessments conducted at country, regional or district level, and should be appropriate to the local endemic situation.

Immunization offers the most effective protection against tick-borne encephalitis. Currently, there are four widely used vaccines of assured quality: FSME-Immun and Encepur, manufactured in Austria and Germany respectively, and TBE-Moscow and EnceVir, manufactured in the Russian Federation. The four vaccines are considered to be safe and efficacious.

Tick-borne encephalitis virus is an important cause of viral infections of the central nervous system in eastern, central and northern European countries, and in northern China, Mongolia, and the Russian Federation.

Approximately 10 000–12 000 clinical cases of tick-borne encephalitis are reported each year, but this figure is believed to be significantly lower than the actual total. Most infections with the virus result from tick bites acquired during outdoor activities in forested areas.



TOSCV

- Arbovirus/Bunyaviridae firstly isolated in 1971 by Paola Verani
- Vectors: *Phlebotomus perniciosus* and *P. perfiliewi.*
- transmitted by sand flies (Naples and Sicily)
- Peaks in summer time
- High neurotropism (meningitis and encephalitis)
- Countries involved: Italy, Portugal, Spain, France, Greece, Croatia, Cyprus, Turkey
- Three most prevalent viruses in meningitis in warm seasons together with enteroviruses and herpes viruses
- Understimate agent due to aspecific symptoms
- ***Any physician should be consider TOSCV in diagnostic algorithms of CNS infection***

Signs and symptoms

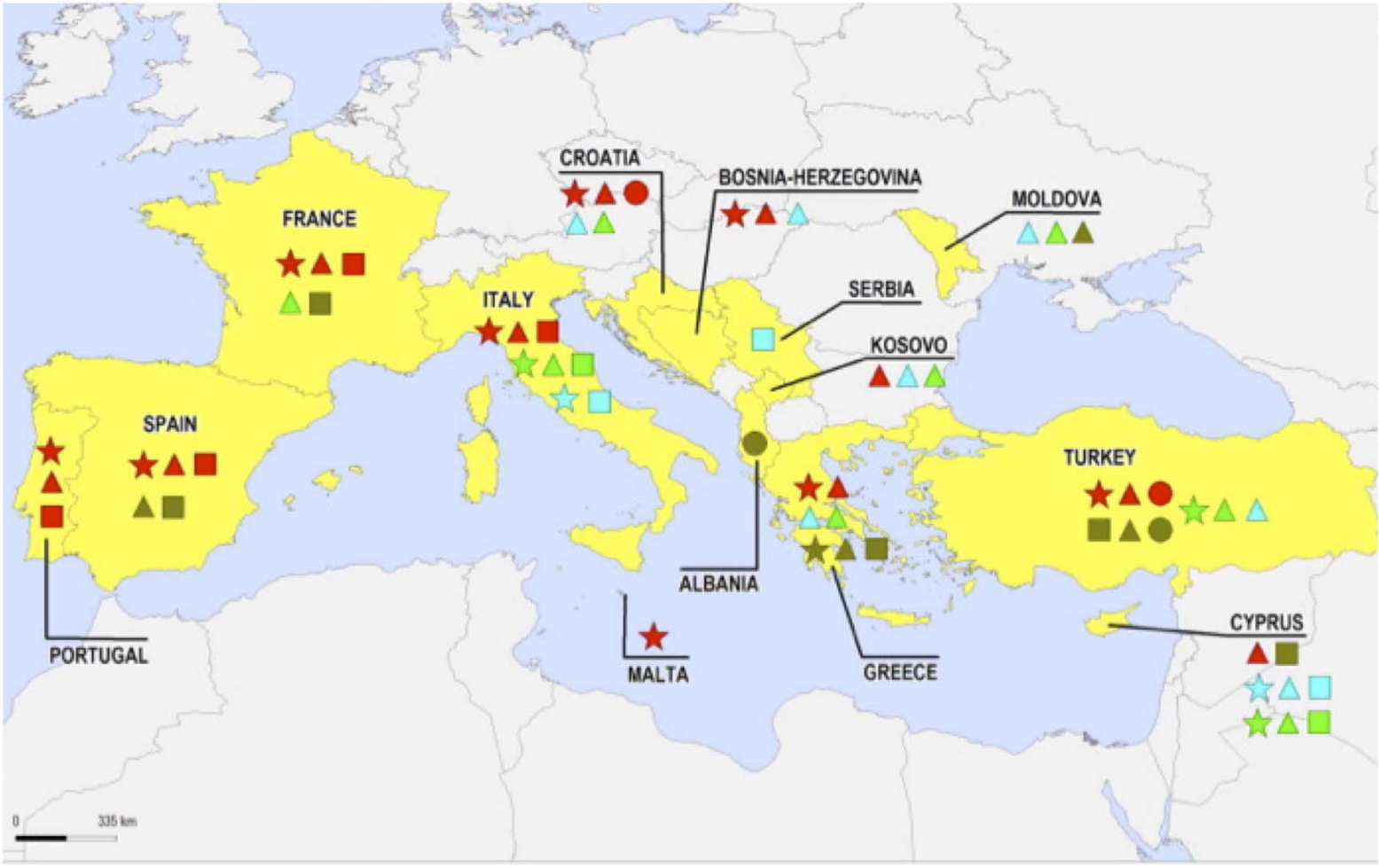
- short incubation (3d-2wks)
- headache 100%
- fever (76-97%)
- nausea and vomiting (67-88%)
- myalgias (18%)
- neck rigidity (53-95%)
- Kernig sign (87%)
- consciousness troubles (12%)
- tremors (2,6%)
- paresis (1,7%)
- nystagmus (5,2%)

The disease is usually favorable

Only few cases of meningo-encephalitis or meningitis

Highest risk of aquisition is in August then in July and September then in June and in October

Mediterran basin distribution



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AMERICAN SOCIETY OF TROPICAL MEDICINE & HYGIENE
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THE AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE
official Journal of the American Society of Tropical Medicine and Hygiene

Am. J. Trop. Med. Hyg., 38(2), 1988, pp. 433–439 (87-31)

ECOLOGY OF VIRUSES ISOLATED FROM SAND FLIES IN ITALY AND CHARACTERIZATION OF A NEW *PHLEBOVIRUS* (ARBIA VIRUS)

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**Laboratory of Virology, Istituto Superiore di Sanità, Rome, †Institute of Parasitology, "La Sapienza," University of Rome, ‡Department of Infectious Diseases, S. Maria Nuova Hospital, Florence, §Department of Neurology, University of Florence, and ¶Epidemiological Investigation Unit for Neurotropic Viruses, Toscana Region, Florence, Italy*

Abstract. A total of 84 virus strains was obtained from 16,374 male and female sand flies (*Phlebotomus perniciosus* and *P. perfiliewi*) collected in two localities of Tuscany region in Italy between 1980 and 1985. Thirty-seven (44%) were identified as Toscana virus (family Bunyaviridae, genus *Phlebovirus*) and 47 (56%) as a new member of the Phlebotomus fever serogroup, Arbia virus. The characteristics of this new serotype are described. The overall virus isolation rate from sand flies was 0.5 per 100 insects processed. Virus isolation rates for both viruses were similar in different years and in the two localities, suggesting that the two virus types were active in the sand fly population simultaneously. Each year, the largest number of isolates were obtained during July, corresponding to the period of maximal sand fly population density. Both viruses were repeatedly isolated from male sand flies, suggesting transovarial transmission in nature.

Serologic data showed no evidence of infection among domestic and wild animals. However, a strain of Toscana virus was isolated from the brain of a bat (*Pipistrellus kuhli*), indicating a possible involvement of this species in the ecology of the virus. Serologic tests did not provide definitive evidence for human infection by Arbia virus.

NEUROVIRULENT TOSCANA VIRUS (A SANDFLY FEVER VIRUS) IN SWEDISH MAN AFTER VISIT TO PORTUGAL

SIR,—The case described here and the accompanying letter draw attention to the possibility of contracting sandfly fever after summer visits to the Mediterranean.

In 1983 a Swedish couple with their 5-year-old son visited Albufeira, Portugal, during the last two weeks of August. On Sept 5 the man had a severe headache and slight fever. On Sept 9 he was referred to an infectious diseases clinic at Roslagstull's Hospital, Stockholm, as a possible case of encephalitis.

He was photophobic and had a severe headache, but was not stiff-necked. His temperature was 38·4°C. Peripheral white blood cells were normal. His erythrocyte sedimentation rate was 35 mm/h. His cerebrospinal fluid showed signs of an aseptic meningitis with 134 predominantly mononuclear cells. He recovered spontaneously without complications.

From his cerebrospinal fluid an ether-sensitive virus was isolated in green monkey kidney (GMK-AH1) cells. Electronmicroscopy revealed round, enveloped particles of about 115 nm diameter. Immunofluorescence of infected cells indicated the presence of a phlebovirus. Plaque-neutralisation showed it to be a strain of Toscana virus.

Sera were collected in September, 1983, in May, 1984 and in September, 1984. Sera from the wife and son were collected in September, 1984. The patient seroconverted to Toscana virus in a plaque-neutralisation test and to his own isolate by immunofluorescence and in a complement-enhanced neutralisation of cytopathic effect. The wife's serum but not the son's had low titre antibodies to the isolate on assay of cytopathic effect.

Toscana virus was isolated in Italy in 1971 from the sandfly *Phlebotomus perniciosus*.[1] It is closely related to sandfly fever Naples virus.[2,3] Toscana virus seems to be the most common phlebovirus in Italy now.[4] Insecticide spraying during the 1940s to control malaria seems in Italy to have more or less eliminated the previously more common sandfly fever Naples and Sicilian viruses, associated with *P papatasi*.[5] Naples and Sicilian viruses, both of which have been isolated from man, have been found also in Asia and Africa.[6] Toscana virus has hitherto only been found in Italy and a human isolate has not previously been reported. It has, however, been suspected of being neurovirulent as seroconversion has been observed in connection with CNS disease and Toscana virus has been isolated from the CSF in Italy (P. Verani and colleagues, personal communication).

THE LANCET, MAY 25, 1985

This case-report of a human isolate of Toscana virus from the CSF demonstrates that Toscana virus is present in Portugal and illustrates the neurovirulence of Toscana virus.

Central Microbiological Laboratory of Stockholm County Council, Stockholm S-101 22, Sweden — A. EHRNST

US Army Medical Research Institute of Infectious Diseases, Frederick, Maryland, USA — C. J. PETERS

US Army Medical Research Institute of Infectious Diseases; and National Bacteriological Laboratory, Stockholm — B. NIKLASSON

Central Microbiological Laboratory of Stockholm County Council — A. SVEDMYR

Roslagstull's Hospital, Stockholm — B. HOLMGREN

1. Verani P, Lopes MC, Nicoletti L, Balchussi M. Studies on phlebotomus-transmitted viruses in Italy I: Isolation and characterisation of a sandfly fever Naples-like virus. In: Vesenjak-Hirjan J, et al, eds. Arboviruses in the Mediterranean countries. *Zbl Bakteriol* 1980; suppl 9: 195–201.
2. Tesh RB, Peters CJ, Meegan JM. Studies on the antigenic relationship among phleboviruses. *Am J Trop Hyg* 1982; **31:** 149–55.
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Toscana virus meningo-encephalitis: an important differential diagnosis for elderly travellers returning from Mediterranean countries

BMC Geriatrics

Veater et al. BMC Geriatrics (2017) 17:193

An 87-year old gentleman presented with a three-day history of worsening confusion, lethargy, ataxia, and fevers following a trip to Spain, where he may have sustained a sandfly bite.

Clinical Case Report

Medicine®

OPEN

Guillain-Barré-like axonal polyneuropathy associated with Toscana virus infection

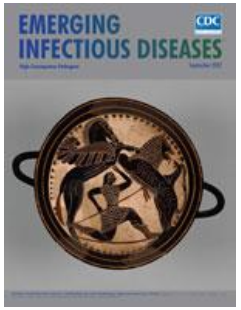
A case report

Rota et al. Medicine (2017) 96:38

Eugenia Rota, MD[a,b,*], Nicola Morelli, MD[a], Paolo Immovilli, MD[a], Paola De Mitri, MD[a], Donata Guidetti, MD[a]

A 40-year-old male patient from Alessandria was admitted for acute facial weakness, associated to numbness paraesthesias at lower and upper limbs: facial diplegia and reduced tendon reflexes. The nerve conduction studies documented an acute motor and sensory axonal neuropathy (AMSAN); the lumbar puncture detected albuminocytologic dissociation. Positivity for TOSV IgG antibodies was found on both CSF and serum. He was succesfully treated with plasma exchange but AMSAN relapsed 9 month later.

Infectious Toscana Virus in Seminal Fluid of Young Man Returning from Elba Island, Italy



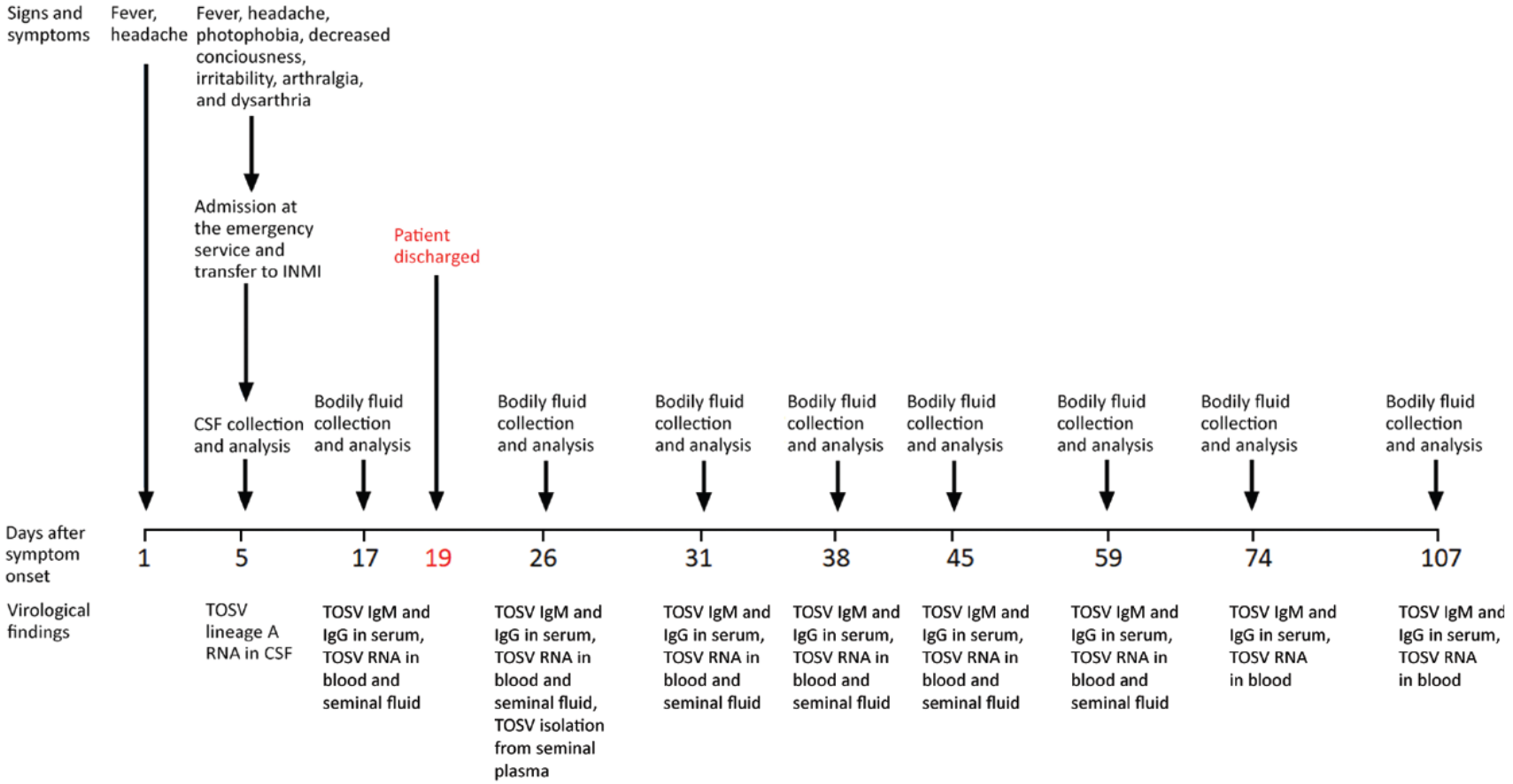


Figure 2. Clinical and laboratory findings during acute phase and follow-up treatment of man with infectious TOSV detected in seminal fluid, Italy. CSF, cerebrospinal fluid; INMI, National Institute for Infectious Diseases "Lazzaro Spallanzani"; TOSV, Toscana virus.

Matusali EID 2022

The Brief Case: *Tropheryma whipplei* Infection Resulting in Neurological Symptoms

Journal of Clinical Microbiology®

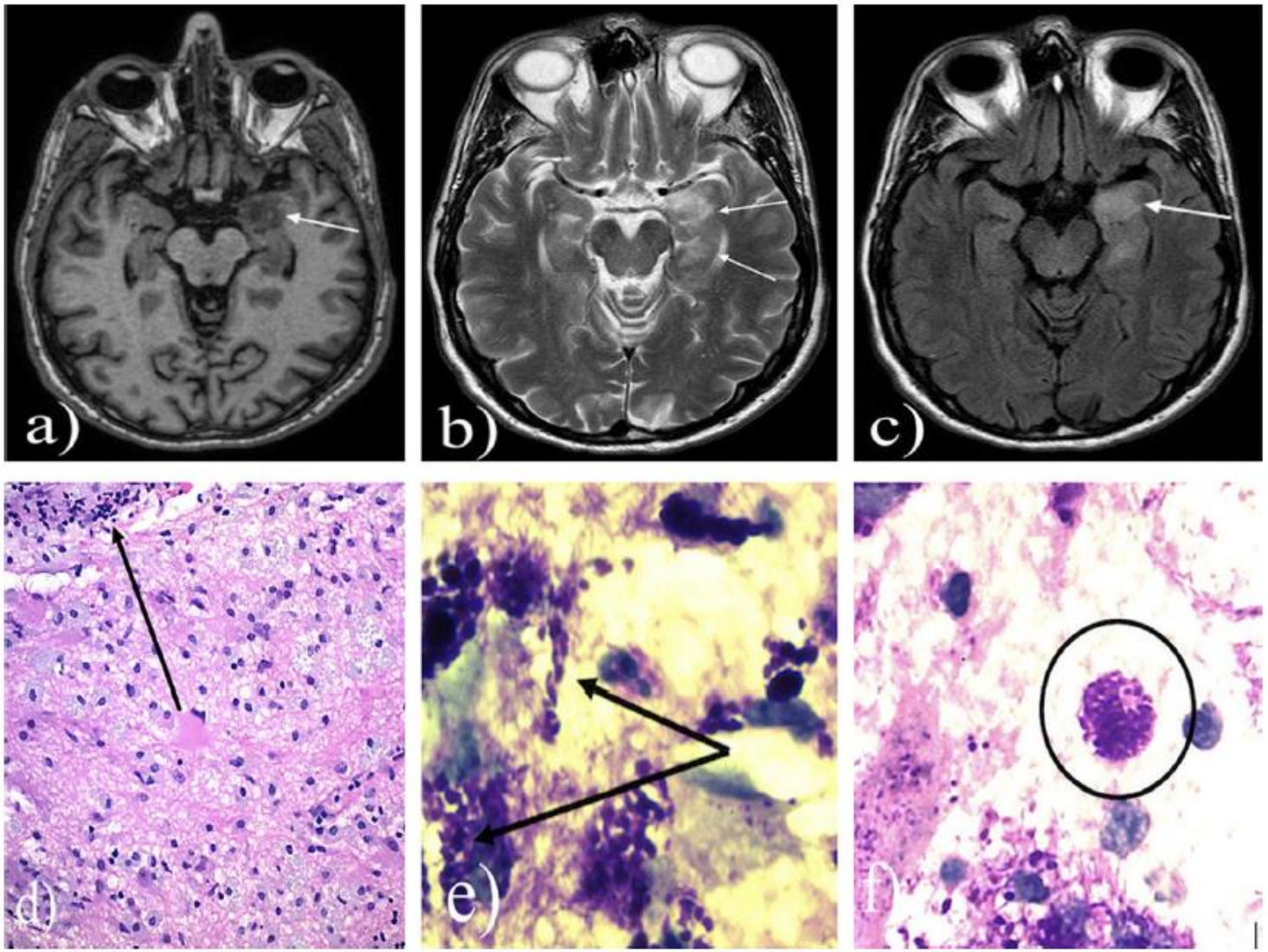
A 69-year-old Caucasian male with type 2 diabetes mellitus, anxiety, bipolar disorder, hypertension, seronegative rheumatoid arthritis, and prostate cancer presented to neurology for an evaluation of lightheadedness, poor balance, several falls, and a progressive deterioration in gait that had persisted for several months. The patient had confusion, worsening insomnia, word-finding difficulty, and long-standing joint pain. An unintended 30-pound weight loss over the last year was also noted. No history of toxic exposures, was identified.

MRI of the brain and spine were performed, and they revealed a signal abnormality on the medial left upper temporal lobe (Figure 1a–c). Findings were indeterminate for gliosis versus active inflammatory/neoplastic disease. CSF was negative, the patient underwent a left temporal lobe biopsy

Hyche JCM 08.22

The Brief Case: *Tropheryma whipplei* Infection Resulting in Neurological Symptoms

Journal of Clinical Microbiology®



(a) Axial T1 MRI low signal intensity (white arrow). (b) Axial T2 MRI high signal intensity (white arrow). (c) Axial FLAIR high signal intensity (white arrow). (d) Numerous macrophages with bluish-gray cytoplasm full of T. whipplei in small loose aggregates (e & f) The bacillary organisms within the macrophages are highlighted with a PAS-D stain

Hyche JCM 08.22

The Brief Case: *Tropheryma whipplei* Infection Resulting in Neurological Symptoms

Journal of Clinical Microbiology®

The patient was treated with 2 g ceftriaxone intravenously for 2 weeks, followed by 100 mg doxycycline twice daily and 200 mg hydroxychloroquine 3 times per day for 1 year. Response to therapy is being evaluated by improvements in weight gain, insomnia, arthritis, and neurological symptoms. Initially, slight improvements were reported in insomnia, mental acuity, and mood.

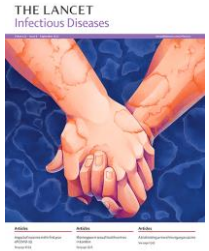
The patient was referred to physical therapy and speech therapy. As of this report, progress in therapy has slowed, and the patient has again experienced confusion, falls, and worsening neurological symptoms similar to his presenting complaints

In alternativa alla biopsia stereotassica si sarebbe potuta richiedere PCR su liquor e su 3 campioni di feci per Tropheryma whippelii che si esegue a INMI Spallanzani

Hyche JCM 08.22

Whipple's disease and *Tropheryma whipplei* infections: from bench to bedside

Asma Boumaza TLID 09.22



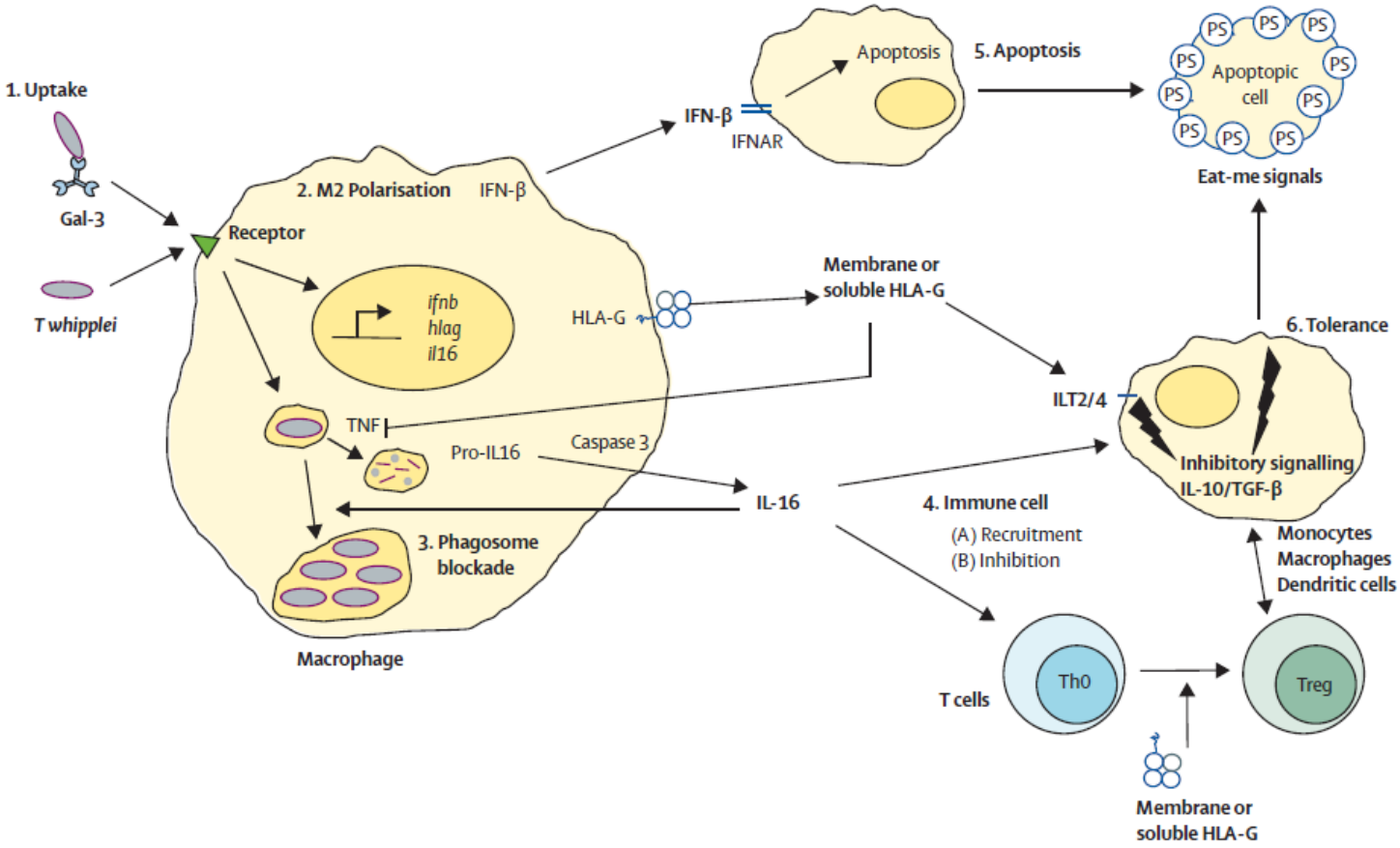
Panel 1: Spectrum of *T whipplei* infections and main clinical manifestations

Classical Whipple's disease
- Weight loss
- Arthralgia or arthritis
- Diarrhoea
- Fever
- CNS manifestations

Chronic localised infections
- Endocarditis
- Isolated encephalitis
- Polyarthritis
- Uveitis

Acute infections
- Pneumonia
- Gastroenteritis
- Bacteraemia

Asymptomatic carriage
- Saliva
- Stools



T whipplei, is opsonised by Gal-3 interacts with a yet unknown macrophage receptor, induces an unusual M2 polarisation associated with the expression of IL-16, IFN-β, and HLA-G-encoding genes. IL-16 interferes with phagosome maturation and favours bacterial replication. IL-16 also induces the recruitment and differentiation of CD4-expressing cells into tolerogenic cells. IFN-β induces macrophage apoptosis. Expression of eat-me signals such as phosphatidyl serine by these apoptotic cells promotes the phagocytosis of apoptotic cells and contributes to the local immunotolerance. Finally, tolerance is also strengthened by membrane or soluble HLA-G, which regulates the expression of TNF, inhibits immune cell activation after engagement of ILT2 or ILT4, and favours the generation of regulatory T cells

JAMA Neurology | Review

Neurologic Complications of Smallpox and Monkeypox
A Review

B. Jeanne Billioux, MD; Oliver Tshiani Mbaya, MD; James Sejvar, MD; Avindra Nath, MD

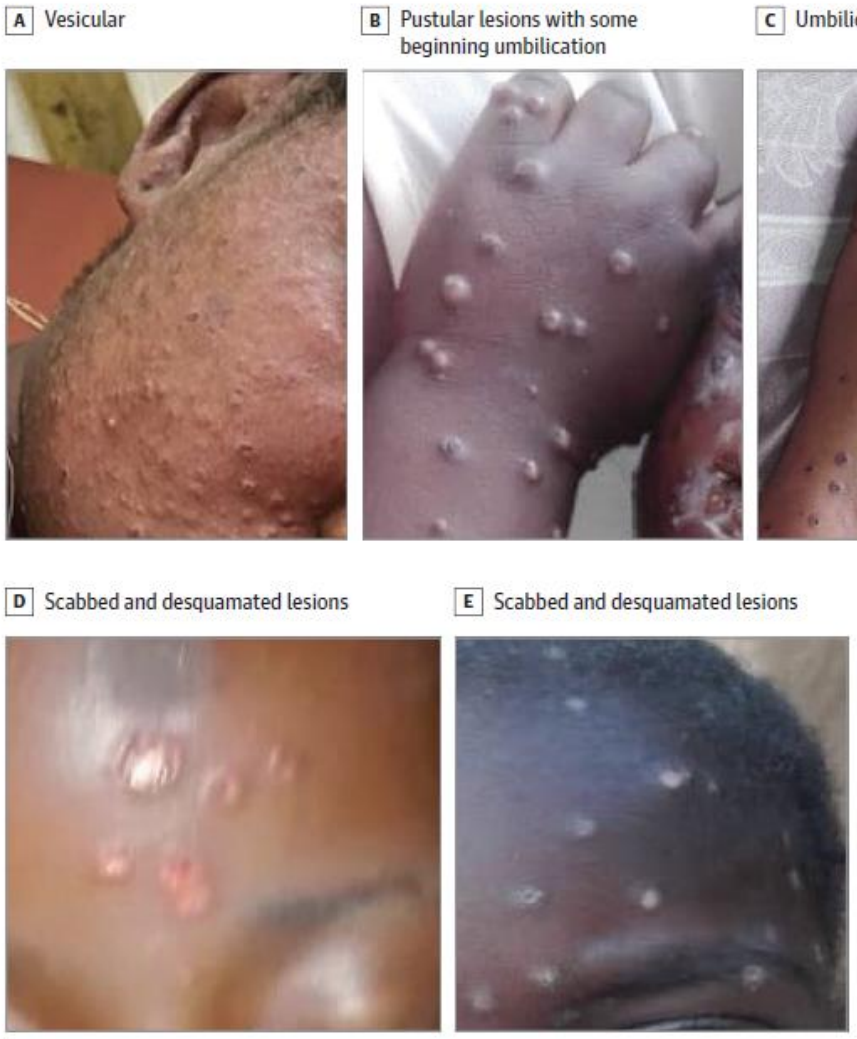
IMPORTANCE Orthopox viruses include smallpox virus, a once feared but now eradicated virus, as well as monkeypox virus. Monkeypox is an emerging virus initially isolated in 1958, previously unrecognized outside sub-Saharan Africa until a worldwide outbreak in May 2022. It is important to review known neurologic consequences of both these viruses, as complications of smallpox may be relevant to monkeypox, though complications of monkeypox may be rarer and perhaps less severe.

OBSERVATIONS This was a literature review of the known neurologic complications of smallpox, which include encephalitis, transverse myelitis, and acute disseminated encephalomyelitis among others; historical complications of smallpox vaccination, including postvaccinal encephalomyelitis; and the known neurologic complications of monkeypox, which include headaches and mood disturbances, as well as rare presentations of encephalitis, transverse myelitis, and seizures. Of concern is the possibility of viral persistence and systemic complications in immunocompromised individuals. Also provided were considerations for diagnosis, current treatment, and prevention of monkeypox.

CONCLUSIONS AND RELEVANCE Monkeypox should be considered in high-risk populations who present with neurologic syndromes. Diagnosis may require serology and polymerase chain reaction testing of blood and spinal fluid. Antiviral therapy should be initiated early in the course of the illness.

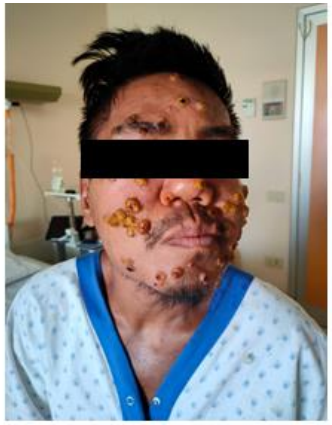
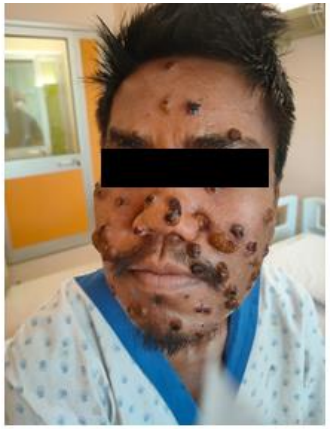
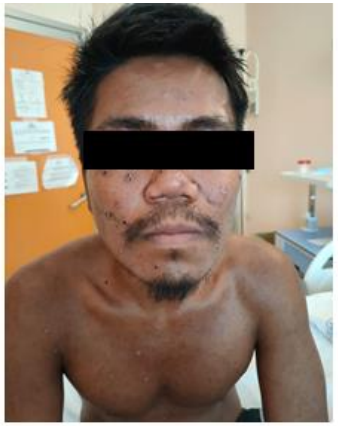
Neurologic Complications of Smallpox and Monkeypox

Figure 2. Stages of Monkeypox Rash



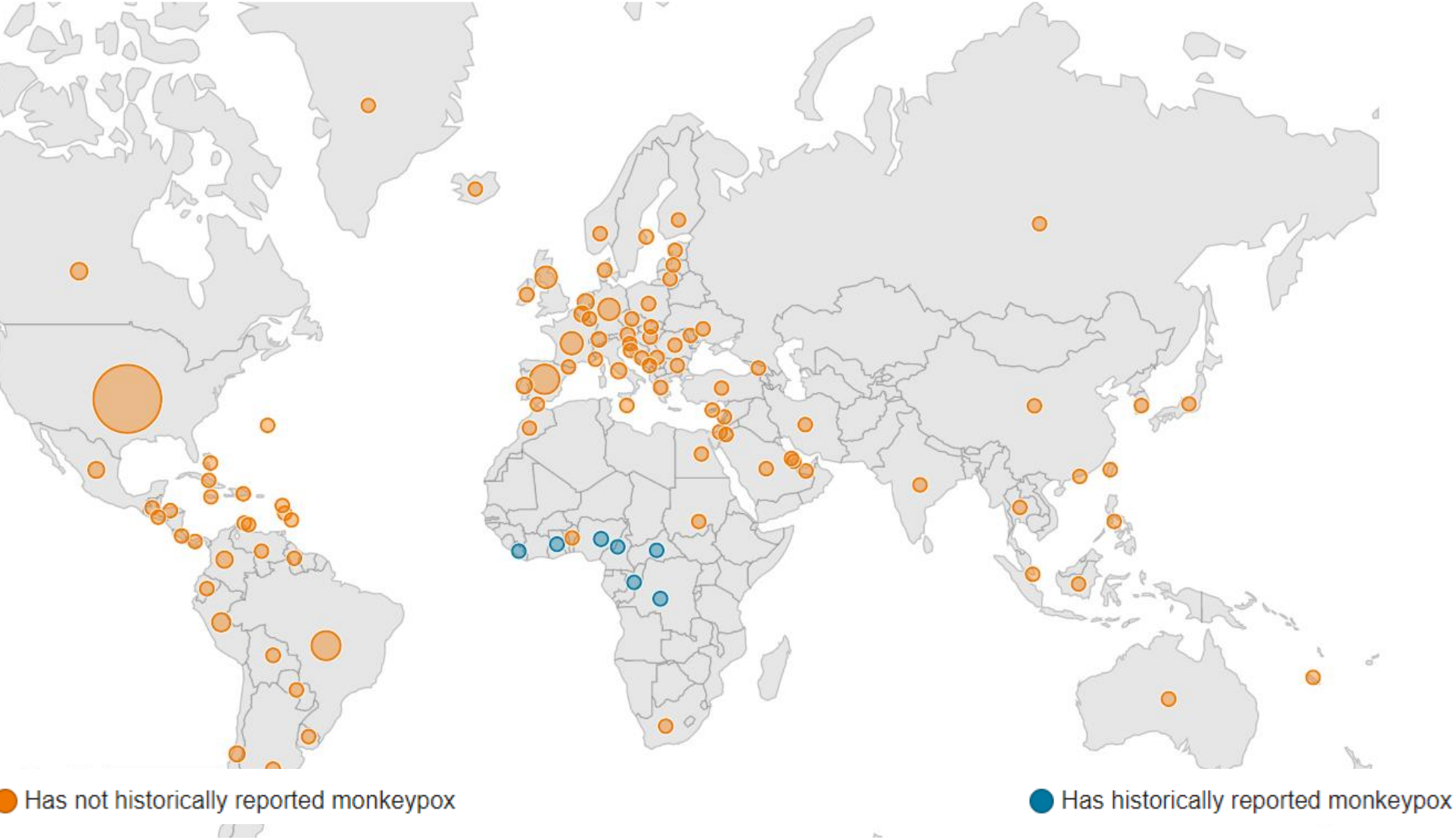
The stages of the monkeypox rash are depicted: vesicular (A), pustular lesions with beginning umbilication (B), umbilicated and ulcerated lesions (C), early-stage scabbed and desquamated lesions (D), and later-stage scabbed and desquamated lesions (E).

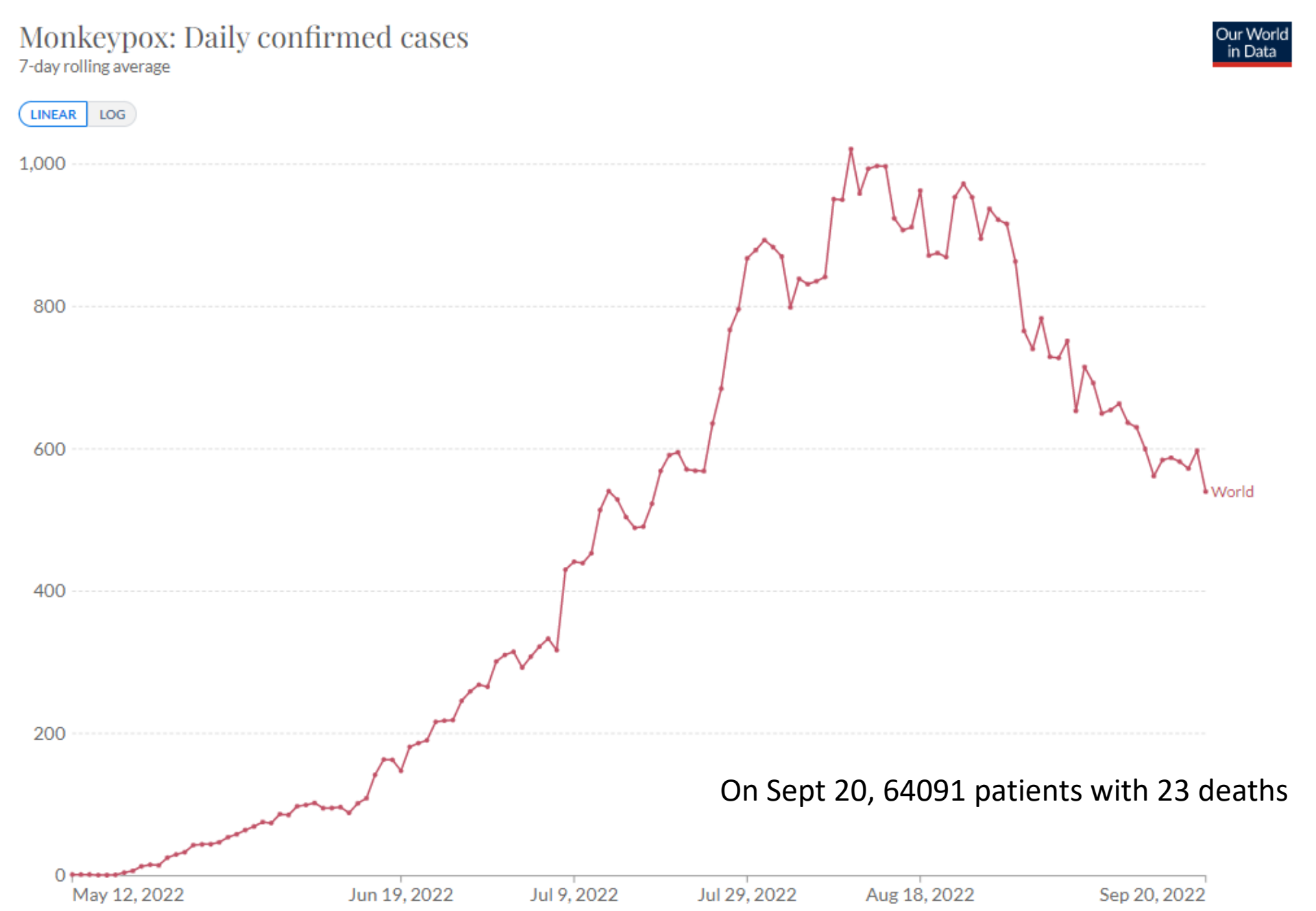
Monkeypox in immunocompromised patient with recent HIV infection at low CD4 cells and MDR TB : a severe smallpox-like clinical presentation.


Vita S submitted

2022 Monkeypox Outbreak Global Map by CDC



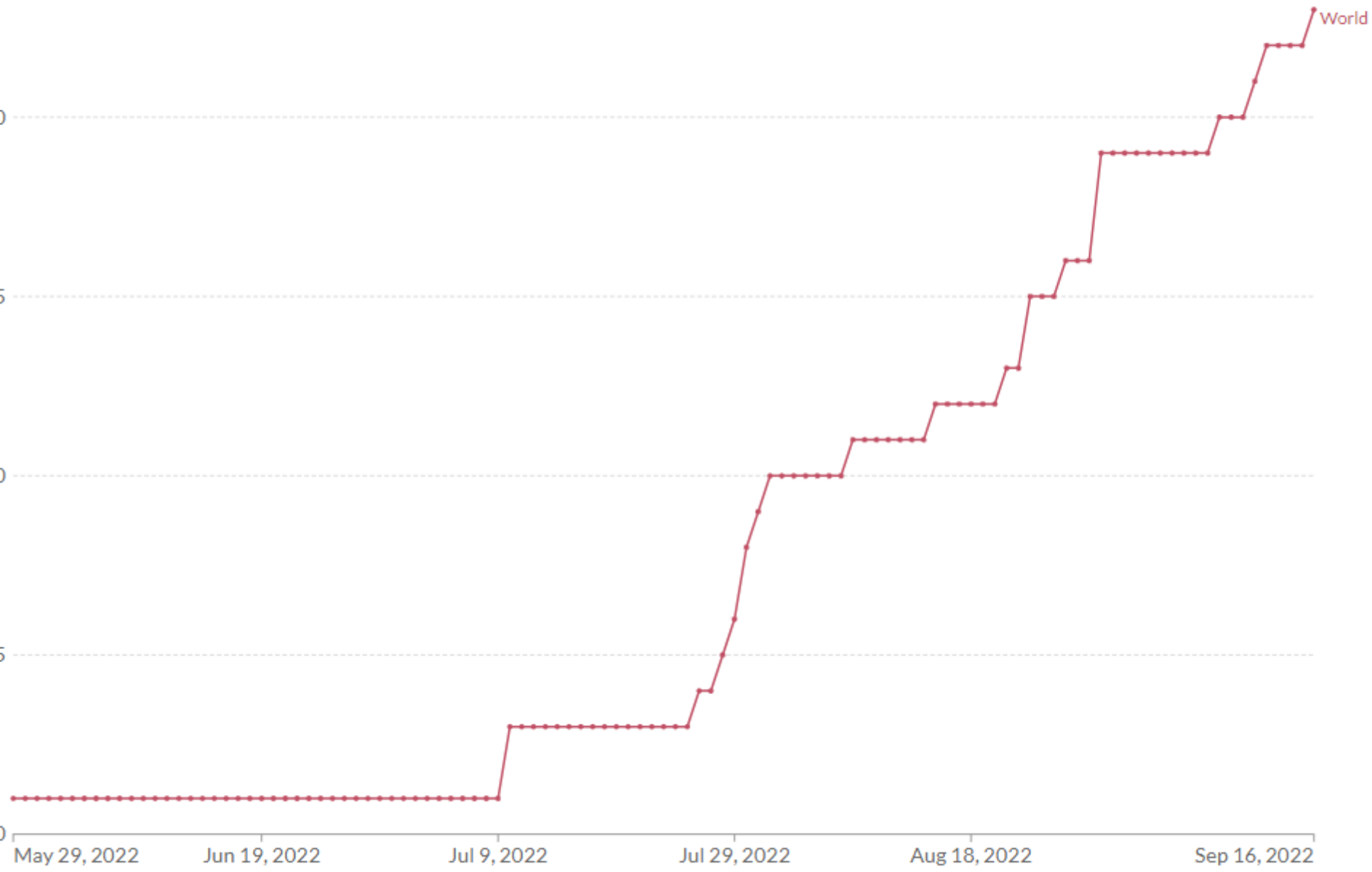


On Sept 20, 64091 patients with 23 deaths

Monkeypox: Cumulative confirmed deaths

Our World in Data

LINEAR LOG



Source: Data produced by the 'Global.health' team — available at github.com/globaldothealth/monkeypox

CC B

JAMA Neurology | Review

Neurologic Complications of Smallpox and Monkeypox

Table 1. Orthopox Viruses That Infect Humans

Virus	Human-to-human transmission	Animal-to-human transmission	Major animal host
Variola (smallpox)	Yes	No	None
Monkeypox	Yes	Yes	Rodents
Vaccinia	Yes	Yes	Cattle
Cowpox	Yes	Yes	Cats, rodents, cattle
Buffalopox	Yes	Yes	Cattle
Akhmeta virus	No	Yes	Small mammals, cattle
Alaskapox	No	Yes	Small mammals
Camelpox	No	Yes	Camels
Horsepox	No	Yes	Horses, cattle

Table 2. Neurologic Manifestations of Orthopox Viruses

Symptom	Smallpox	Vaccinia vaccine	Monkeypox
Headaches	+[a]	+	+
Mood disorder	–	–	+
Febrile seizures/encephalopathy	+	+	–
Viral encephalitis[b]	+	–	+
ADEM	+	+	–
Cranial neuropathy	–	+	–
Transverse myelitis	+	+	–
Acute flaccid paralysis	+	+	–
Guillain-Barré syndrome	+	+	–
Post viral cerebellar signs	+	–	–
Neuropathic pain	–	–	+

Monkeypox rarely causes encephalitis.

During Zaire outbreak, a 3-yo girl, developed encephalitis, became comatose, and died 2 later.

During US 2003 outbreak in pet prairie dog, a 6-yo girl developed 7 d after so decreased responsiveness, rigidity, dilated pupils, disc edema, and bilateral Babinski signs. MRI revealed meningeal enhancement, right parietal and left thalamic signal abnormality, and diffuse edema. CSF: 21 cells/mm3 (60% N) and normal protein and glucose, negative for MPXV. She improved and 2w after admission. 3 cases with seizures occurred in a cohort of 40 monkeypox cases in Nigeria died.

During 2022, 3 male cases: 2 Spanish and 1 Indian patients, all died. MPXVDNA in CSF of 2 Spanish

The first case of meningitis associated to SARS-Coronavirus-2 BA.2 variant infection with persistent viremia

Figure 1. The T2-weighted images shows two hyperintense lesions in the right corona radiata (a, b) and left trigone of the lateral ventricle (c).

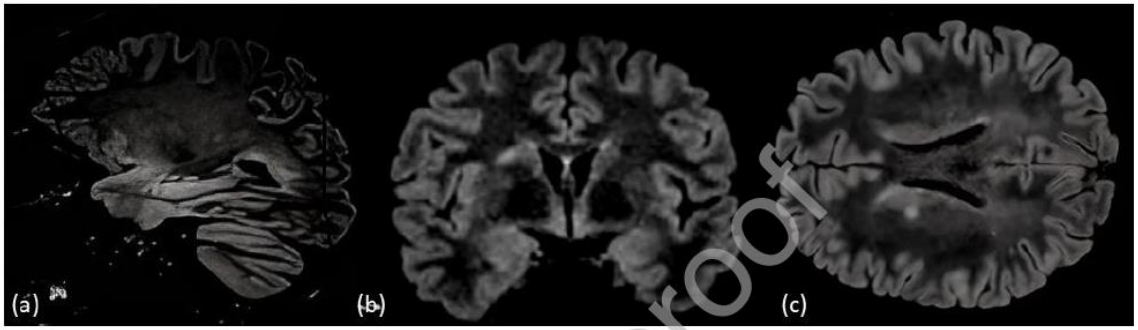


Table1. Patient's laboratory findings

		Plasma	CSF
IL-8 (pg/ml)		4.57	1722
IL-1β (pg/ml)		0	0.3
IL-6 (pg/ml)		3.5	7.3
TNF-α (pg/ml)		4.2	1.5
SARS-COV-2 RNA CT	March 12	30.6	39
	March 15	34	NA
	March 28	negative	NA

IL: Interleukin, SARS-CoV-2: Severe Acute Respiratory Syndrome-CoronaVirus-2, CT: cycle threshold, NA: not available

Severe neurological disorders and vascular events during COVID-19 have been described. Here, we describe the first case of a Italian 40 yo female patient with *Omicron* SARS-CoV-2 BA.2 VoC meningitis with newly diagnosed central demyelinating disease.

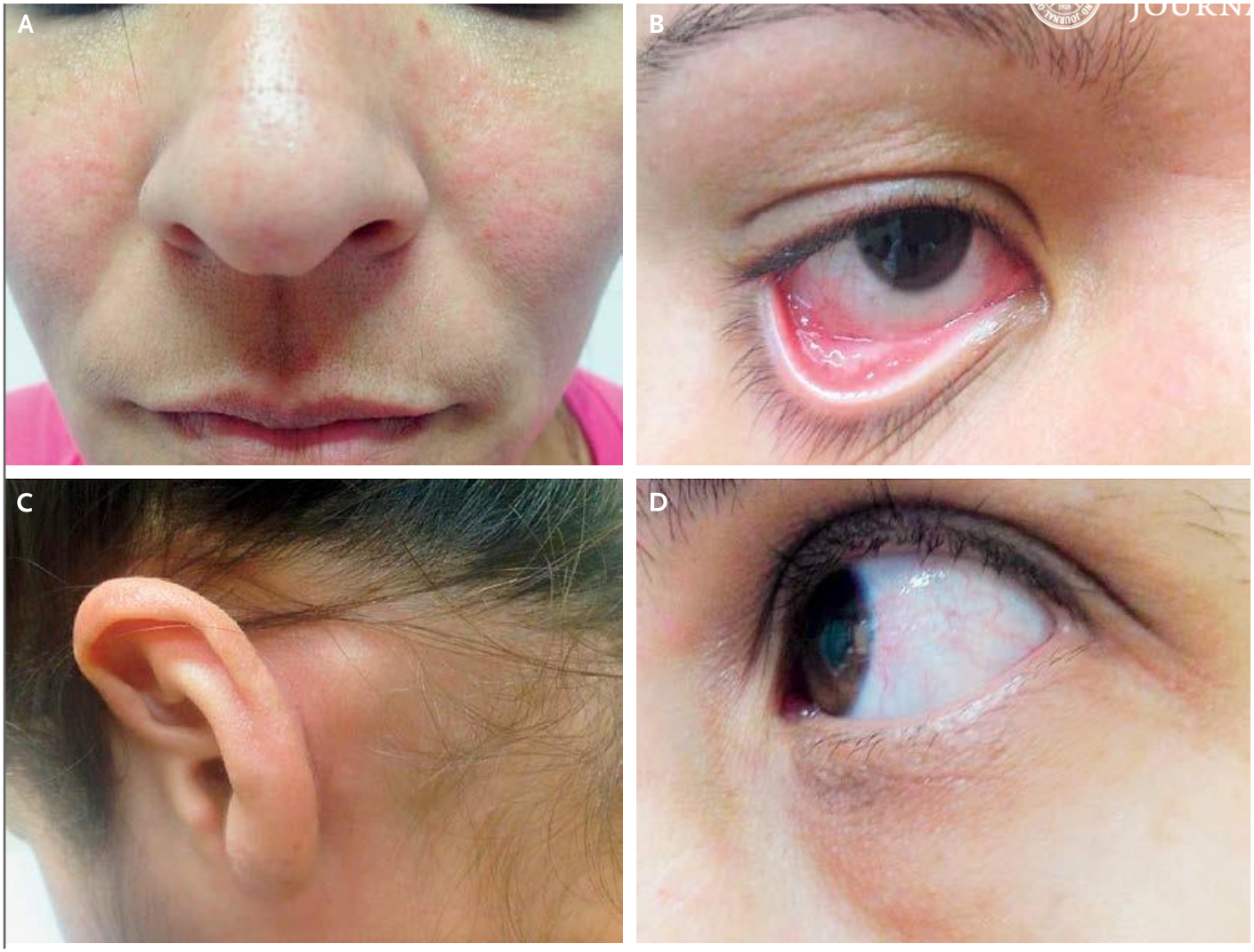
A d'Abramo IJID 09.22

Case April 2016

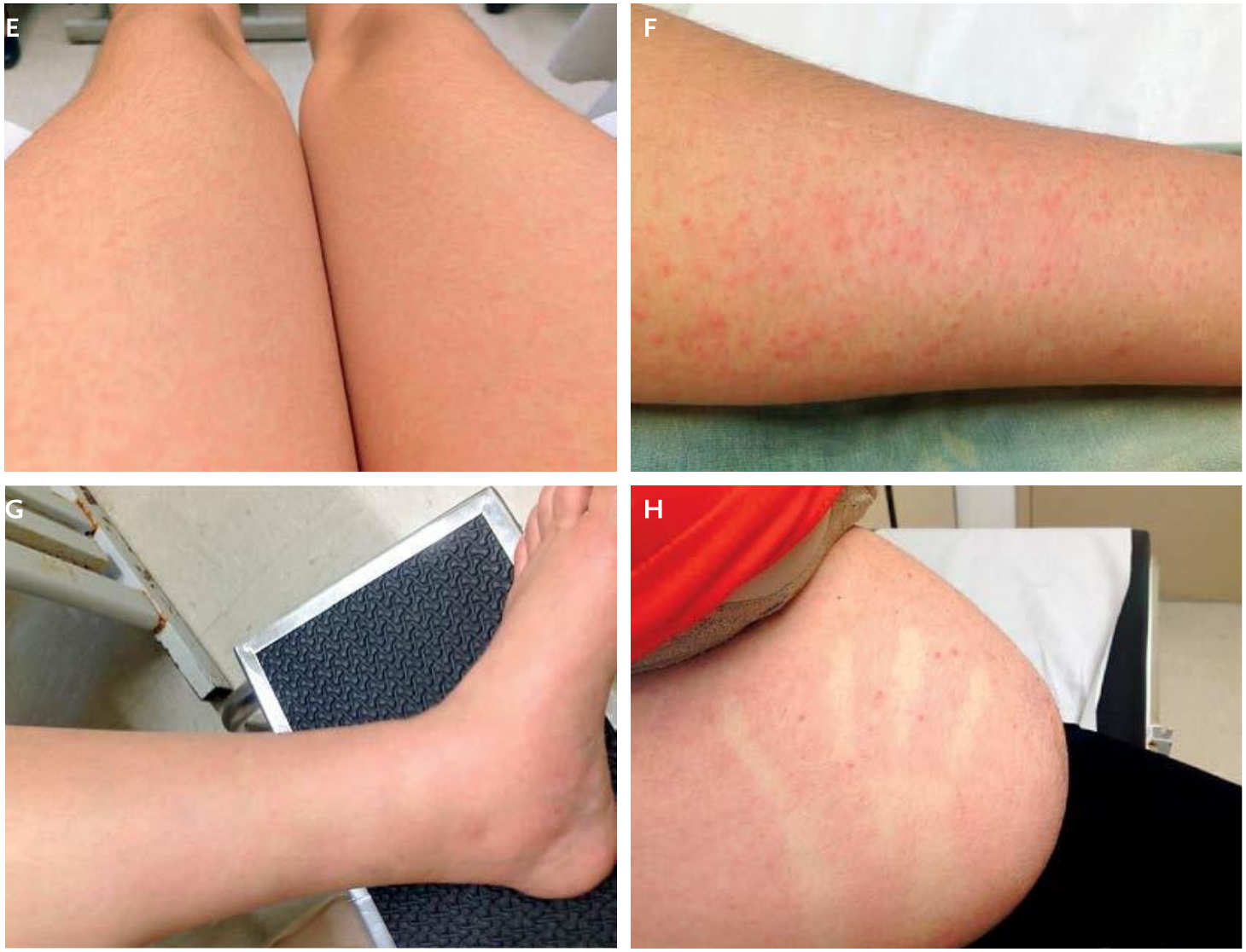
- A 32-year-old woman travelled to Santo Domingo Republic from April 9 to 17, 2016.
- She was admitted to the Spallanzani Institute in Rome on April 27, 2016 for a febrile syndrome with rash, generalised headache, and weakness, which started on April 21.
- On admission, she had gait abnormality, deep asthenia and disseminated pruritic rash involving the face, abdomen, chest and arms, without fever.
- She was alert and fully oriented. Temperature was 36.9°C, pulse rate 90 beats per minute, blood pressure 100/60 mm Hg and respiratory rate 20 breaths per minute.

Case April 2016

- Diffuse erythematous macular rash and bilateral non-purulent conjunctival hyperaemia without meningeal signs.
- Muscular strength was reduced in both legs (left>right) while tendon reflexes and sensory modalities were normal.
- A contrast-enhanced MRI of the brain and spinal cord (d6), nerve conduction studies and electromyography (d8), electroencephalogram (d15) was normal.
- LP on d6 showed normal cell counts, normal glycorrachia and a slight increment in protein concentration (0.48 g/l)
- A complete neuropsychological examination (on d8) showed mild deficits in attention and mental processing speed and mental flexibility, and moderate deficits in verbal and non-verbal memory tasks



Brasil P et al. N Engl J Med 2016. DOI: 10.1056/NEJMoa1602412



Brasil P et al. N Engl J Med 2016. DOI: 10.1056/NEJMoa1602412

Case April 2016

- Viral meningitis
- Bacterial meningitis
- Heat stroke
- Arbovirosis with neurological involvement
- Epilepsy
- Drug intoxication
- Tick borne encephalitis

Case 3 April 2016

Parameters	1st sample (day 5)*	2nd sample (day 6)*	3rd sample (day 9)*	4th sample (day 12)*	5th sample (day 16)*	6th sample (day 27)*
ZIKV RT-PCR [a] serum	Positive (32.9)	Negative	Negative	Negative	Negative	Negative
ZIKV RT-PCR [a] urine	Positive (34.2)	Positive (31.8)	Positive (32.4)	Positive (29.8)	Positive (32.1)	Positive (32.2)
ZIKV RT-PCR [a] saliva	ND	Positive (29.9)	Positive (33.5)	Positive (34.1)	Negative	Negative
ZIKV RT-PCR [a] liquor	ND	Positive (37.0)	ND	ND	Negative	ND
ZIKV RT-PCR [a] cervical swab	ND	Positive (31.1)	Negative	Positive (34.3)	Negative	Negative
IFA [b] IgM	<1:20	1:40	1:160	1:80	1:320	1:1280
IFA [b] IgG	<1:20	<1:20	1:40	1:320	1:320	1:320
MNT [c] Ab	ND	ND	1:40	ND	1:160	>=1:640
IFA IgM [b] (Liquor)	ND	ND	ND	ND	<1:2	ND
IFA IgG [b] (Liquor)	ND	ND	ND	ND	1:8	ND

Figure

	April 29, 2016	May 6, 2016
• Attention and speed of mental processing		
Trail Making Test A	❖	□
WAIS-R Digit Span	□	□
WAIS-R Digit Symbol	□	□
Corsi's block tapping test	□	□
Stroop colour denomination	□	□
Stroop word lecture	□	□
• Mental Flexibility		
Trail Making Test B	❖	□
Stroop (Colour-Word)	❖	□
Controlled Oral Word (FAS)	❖	❖
• Memory		
Rey Auditory Verbal Learning (total)	◆	◆
Rey Auditory Verbal Learning (after 15')	◆	◆
Rey-Osterrieth Complex Figure (delayed)	◆	◆
• Fine Motor Functining		
Lafayette Grooved Pegboard Test (dominant hand)	❖	□
Lafayette Grooved Pegboard Test (non-dominant hand)	□	□
Finger Tapping Test	❖	□
• Visuospatial and Costructional Abilities		
Rey-Osterrieth Complex Figure (copy)	□	□
• Self-report anxiety and depression questionnaires		
Zung Self-rating Anxiety Scale	❖	□
Zung Self-rating Depression Scale	□	□

□ normal ❖ mild deficit ◆ moderate deficit

Case 3 April 2016

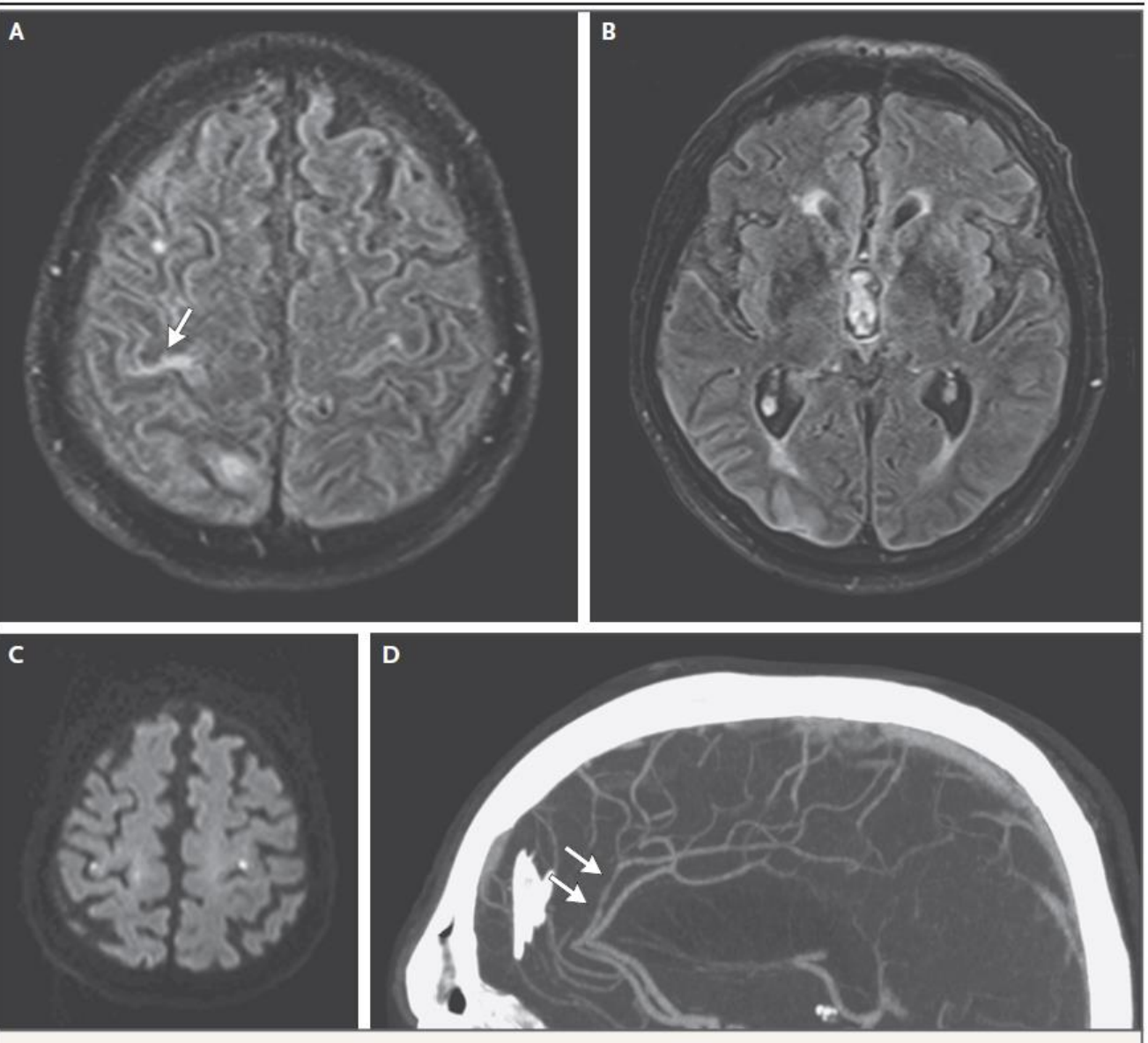
- Since d6 iv immunoglobulins were administered (0.4 g/kg/day for five days). A second neuropsychological examination was performed on day 15 with the evidence of a persistent impairment in memory performances and an improvement in mental concentration and flexibility tasks (Figure).
- The second lp (on d16) showed an increased cell count (70 cells/ml, mostly lymphocytes), detectable ZIKV IgG and negative PCR for ZIKV RNA.
- She was discharged home on day 20 with a progressive neurological recovery since day 16.
- At 60-days follow-up visit, no neurological deficits are reported.

Zika Virus Infection in the Central Nervous System and Female Genital Tract

Emanuele Nicastri, Concetta Castilletti, Pietro Balestra, Simonetta Galgani, Giuseppe Ippolito

Zika Virus Associated with Meningoencephalitis

TO THE EDITOR: Zika virus (ZIKV) is currently spreading widely, while its clinical spectrum remains a matter of investigation. Evidence of a relationship between ZIKV infection a birth abnormalities[1,2] is growing.[3] An incidence of some peripheral nervous syndromes



Subcortical white-matter hyperintensities in the right frontal region, the right parietal region (Panel A), the right temporo-occipital region (Panel B), and bilateral rolandic regions (Panel A).

The slight hyperintensity of the right rolandic fissure (Panel A, arrow) is suggestive of meningitis.

The multiple punctuated hyperintensities on diffusion-weighted sequences are suggestive of ischemic foci (Panel C).

The computed tomographic angiogram shows an irregular narrowing of the right callosomarginal artery (Panel D, arrows).

RAPID COMMUNICATIONS

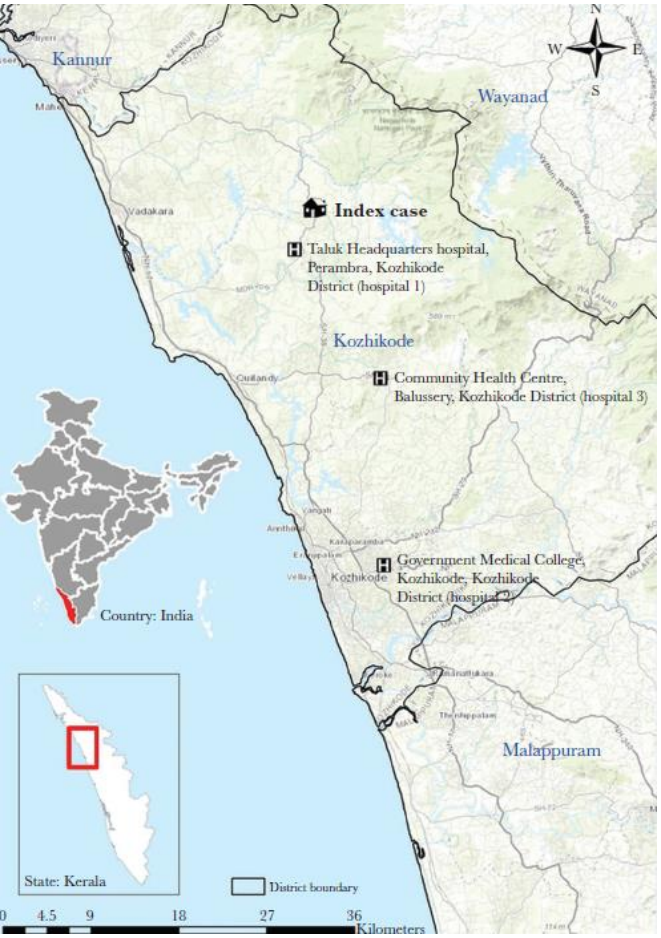
Zika virus detection in cerebrospinal fluid from two patients with encephalopathy, Martinique, February 2016

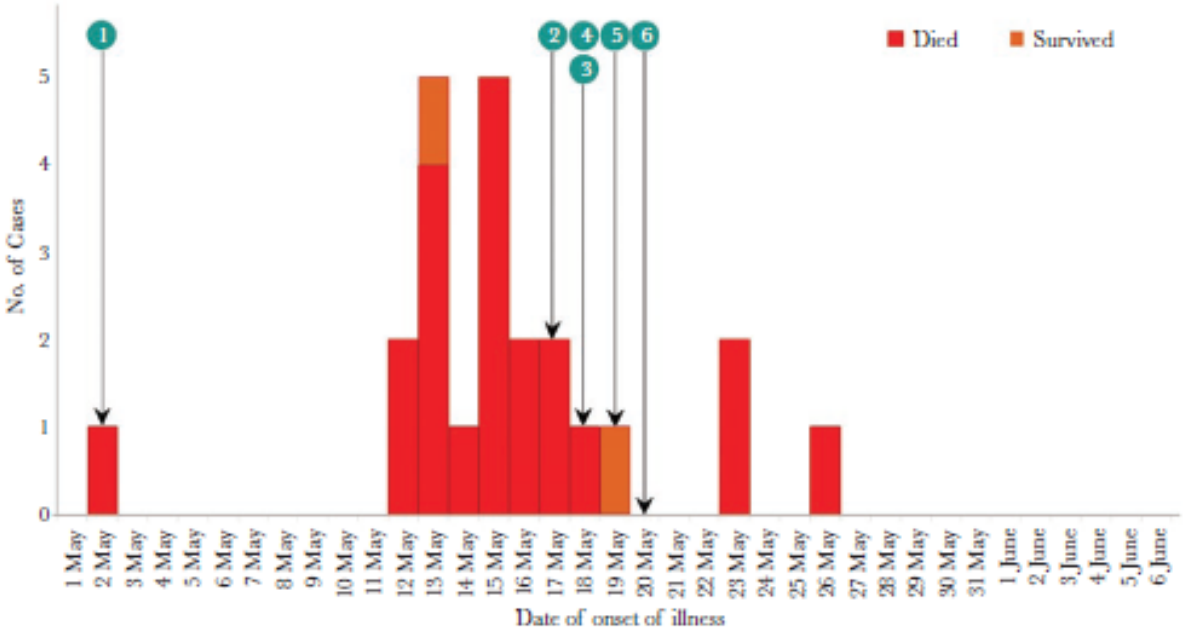
B Rozé [1], F Najioullah [2,3], A Signate [4], K Apetse [5], Y Brouste [6], S Gourgoudou [6], L Fagour [2], S Abel [1,3], P Hochedez [1,3], R Cesaire [3], A Cablé [3,7], on behalf of the Neuro-Zika Working Group of Martinique [8]

The Journal of Infectious Diseases

MAJOR ARTICLE

Outbreak Investigation of Nipah Virus Disease in Kerala, India, 2018





1. 2 May, 2018 - Onset of illness in index case
2. 17 May, 2018 - Cases 2, 5, and 6 admitted to hospital
3. 18 May, 2018 - MCVR, Manipal confirms Nipah virus disease in cases 2, 5, 6
4. 18 May, 2018 - State public health activates Rapid Response Team (RRT)
5. 19 May, 2018 - Isolation of cases initiated
6. 20 May, 2018 - Offical declaration of Nipah virus disease outbreak

Outbreak Investigation of Nipah Virus Disease in Kerala, India, 2018

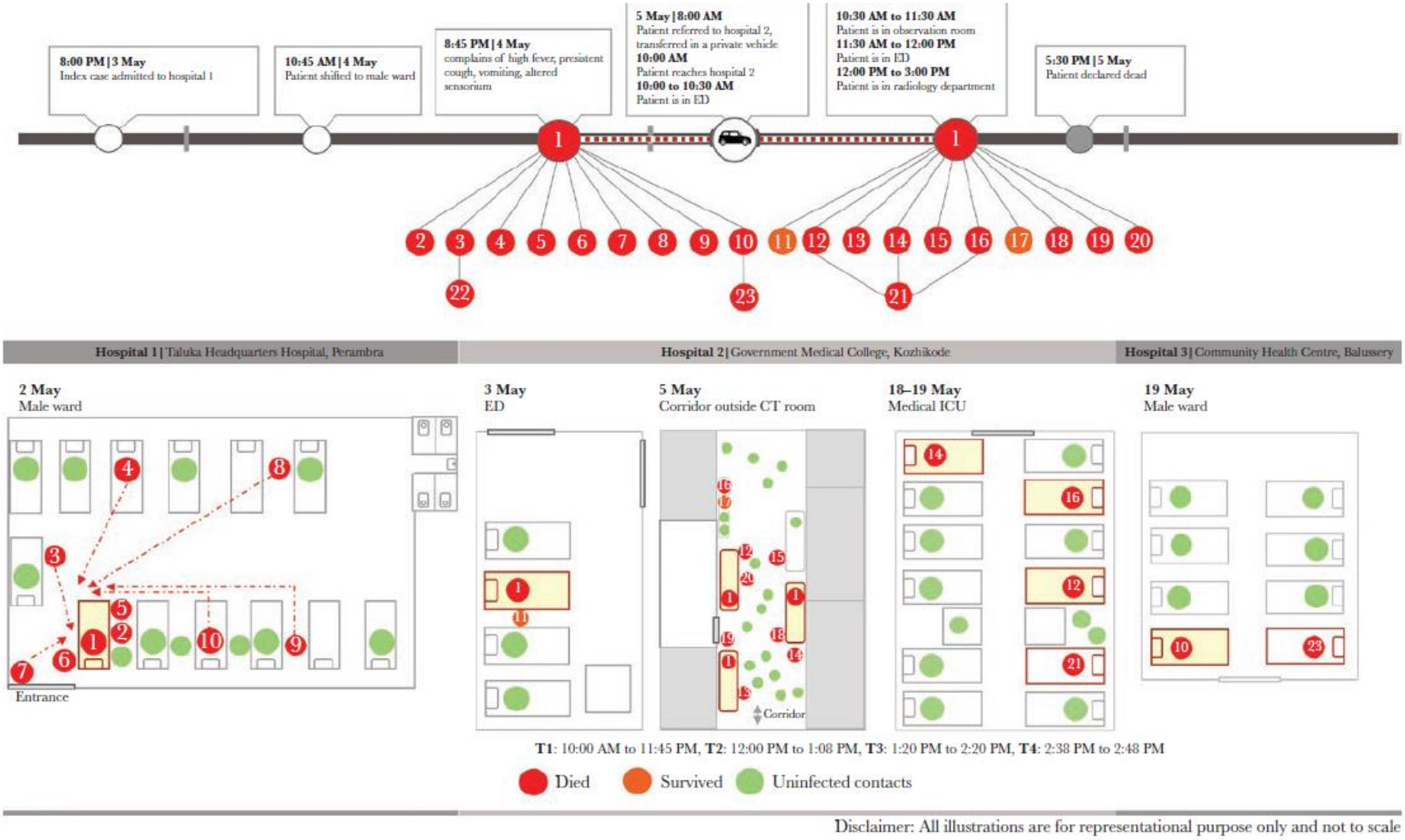


Figure 4. Transmission dynamics in the Nipah virus disease outbreak in Kozhikode District, Kerala State, India, 2018, depicting the chain of transmission between the index case and other cases in 3 hospitals. CT, computed tomography; ICU, intensive care unit.

Animal models of disease shed light on Nipah virus pathogenesis and transmission

Zoonotic transmission cycles of Nipah in Malaysia and Bangladesh. Pteropus species fruit bats are the natural reservoir of Nipah virus.

In Malaysia (left), Nipah istransmitted from bats roosting in fruit trees on pig farms to pigs. Pigs transmitted Nipah virus to people in close contact with the pigs.

In Bangladesh (right), Nipah is transmitted raw date palm sap. While date palm sap is collected, bats drink from the sap stream and contaminate the sap with Nipah virus through their saliva or urine. People become infected with Nipah virus after drinking contaminated date palm sap. These infected people can transmit Nipah virus to others via close contact.


PREPARING FOR ANOTHER TERRORIST ATTACK, MR. JOHNSON ?
NO...JUST THE MOSQUITOES.
WEST NILE VIRUS
ROTH ©2002 PITTSBURGH POST-GAZETTE

Grazie per la attenzione

Bebe Vio ha deciso di posare insieme ad altri atleti, per la fotografa Anne Geddes, autrice di "Win for Meningitis", la campagna di sensibilizzazione diffusa a livello internazionale per promuovere la vaccinazione contro la meningite.

Take home message - 1

- Isolare il paziente (droplet >95% dei casi) al semplice sospetto
- Iniziare terapia antibiotica entro 2 hr dall'arrivo del paziente al DEA
- Eseguire PL con conta cellule e coltura, ed emocolture a prescindere dalla risposta molecolare ora centralizzata c/o INMI
- Appena evidenza di sindrome neurologica a esami diretti e conta cellule liquor, trasferire il paziente in MI/TI senza ritardi
- In caso di paziente in condizioni critiche la messa in sicurezza PRECOCE delle vie aeree e del SNC con intubazione precoce è necessaria per evitare complicanze tardive
- Coinvolgere gli altri specialisti, infettivologi, rianimatori, neurologi, neurochirugi e/o ORL

Take home massage - 2

- Coinvolgere gli altri specialisti, infettivologi, rianimatori, neurologi, neurochirugi e/o ORL
- In caso di meningiti batteriche, specie se da pneumococco o emofilo, è necessario eseguire valutazione ORL dopo TC cranio x seni per effettuare una toilette chirurgica precoce
- La diagnostica molecolare rapida ha portato vantaggi nella tempestività di diagnosi ma impatto clinico non chiaro con >80% delle diagnosi indeterminate. Ruolo futuro metagenomica
- Notificare il caso alla ASL appena possibile (<12hr) e attivare anche telefonicamente il reperibile del SISP chiamando ilcentralino del Grassi specie se notte o week end

Many thanks to…

Francesco Vaia & Giuseppe Ippolito

INMI High Isolation UNIT

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