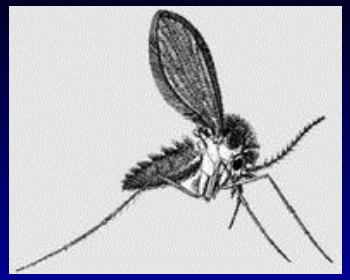



# Infezioni da virus West Nile ed altri patogeni emergenti

**Giovanni Rezza**
*Department of Infectious,*
*Parasitic Immuno-mediated Diseases*

# Mosquito-borne viruses

# WNV

- Mosquito-borne flavivirus of the JE virus complex
- Firstly identified in 1937 in a febrile patient in Uganda
- Several outbreaks in North-Africa, Europe, and the Middle East
- Epidemics in NYC in 1999 and virus migration from east to west in the US

# WNV cycle

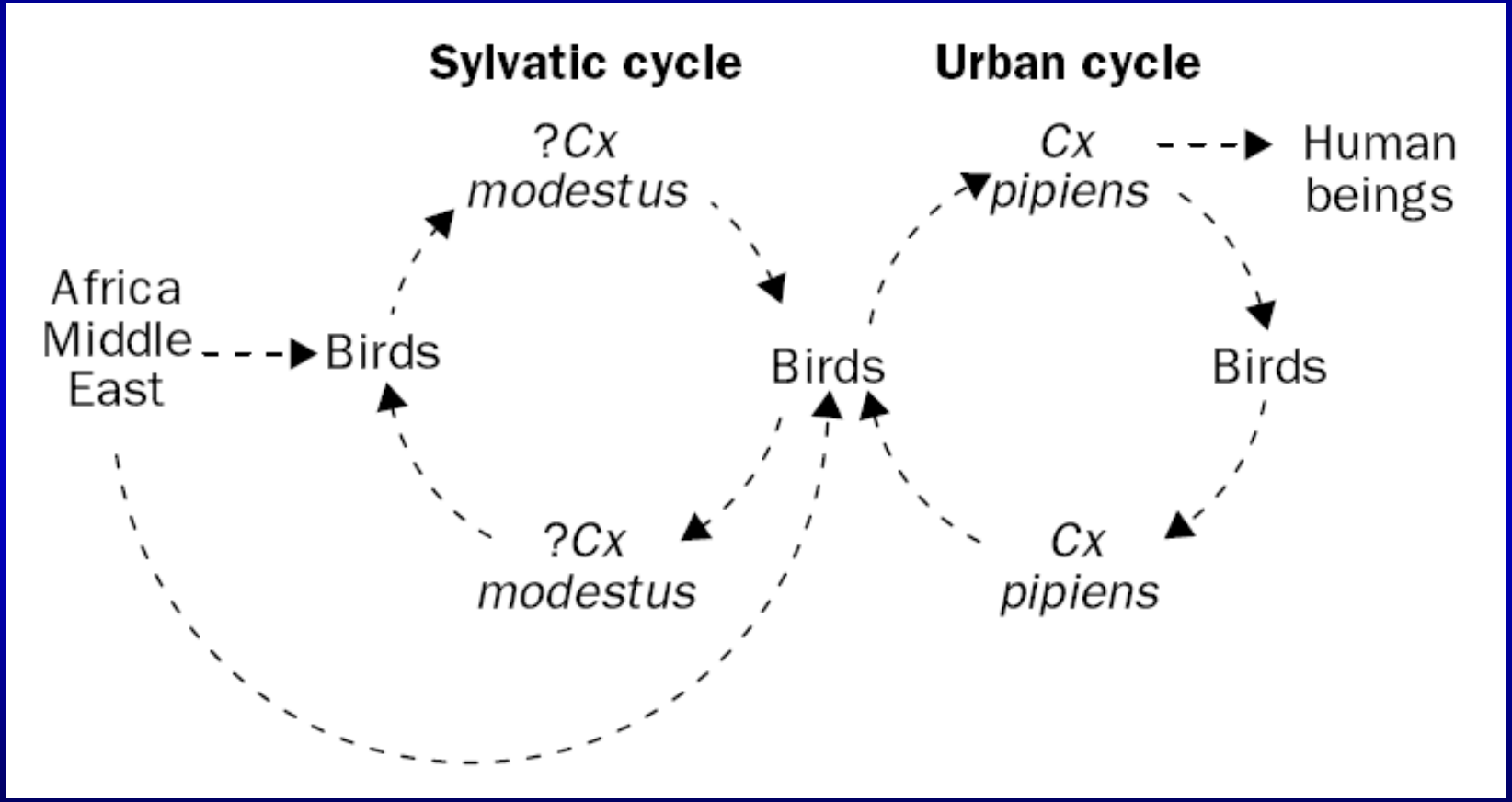

Sylvatic cycle
Urban cycle
?Cx
modestus
Cx
pipiens
Human
beings
Africa
Middle
East
Birds
Birds
Birds
?Cx
modestus
Cx
pipiens

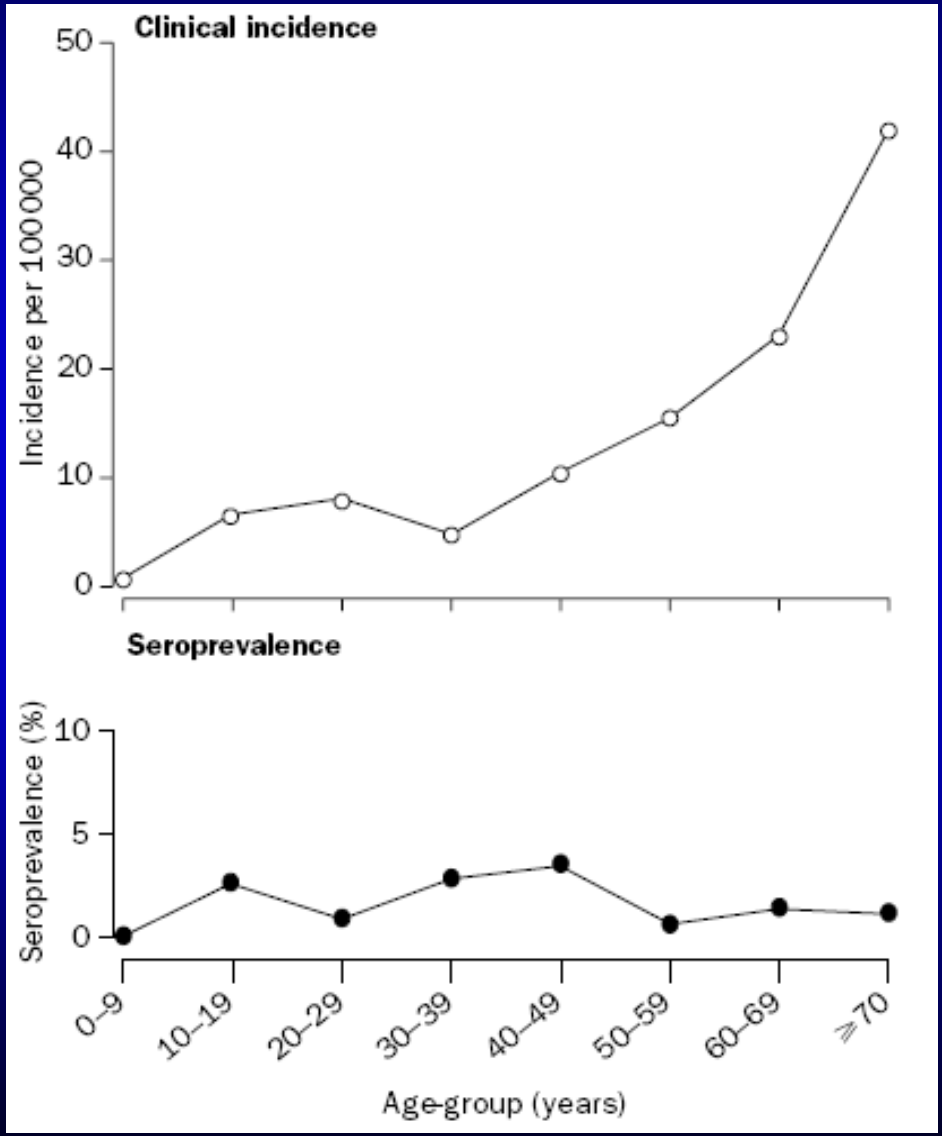
Table. Clinical features of disease in 76 horses with confirmed or probable West Nile virus infection

| Clinical signs | No. of horses (%) |
|---|---|
| Fever (>38.5°C) | 47 (62%) |
| Ataxia | 55 (72%) |
| Paresis/paralysis | 36 (47%) |
| Tremor | 7 (9%) |
| Hyperesthesia | 6 (8%) |
| Grinding teeth | 3 (4%) |
| Abnormal behavior | 2 (3%) |
| Hepatitis | 1 |

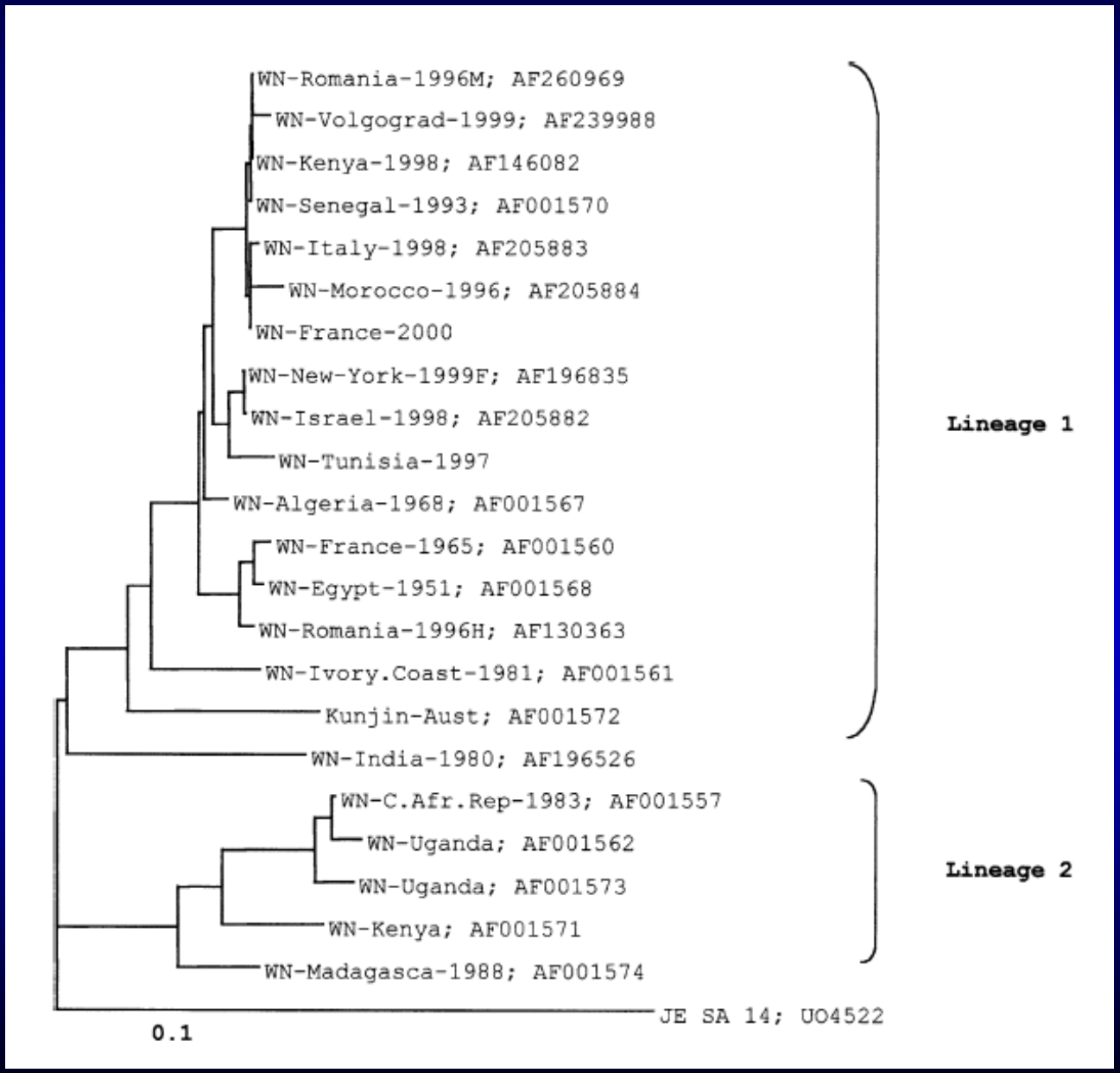
# West Nile Disease: signs and symptoms

- High fever
- Severe headache
- Stiff neck
- Disorientation or confusion
- Stupor or coma
- Tremors or muscle jerking
- Lack of coordination
- Convulsions
- Pain
- Partial paralysis or sudden weakness

# WNV: Clinical incidence and infection prevalence by age

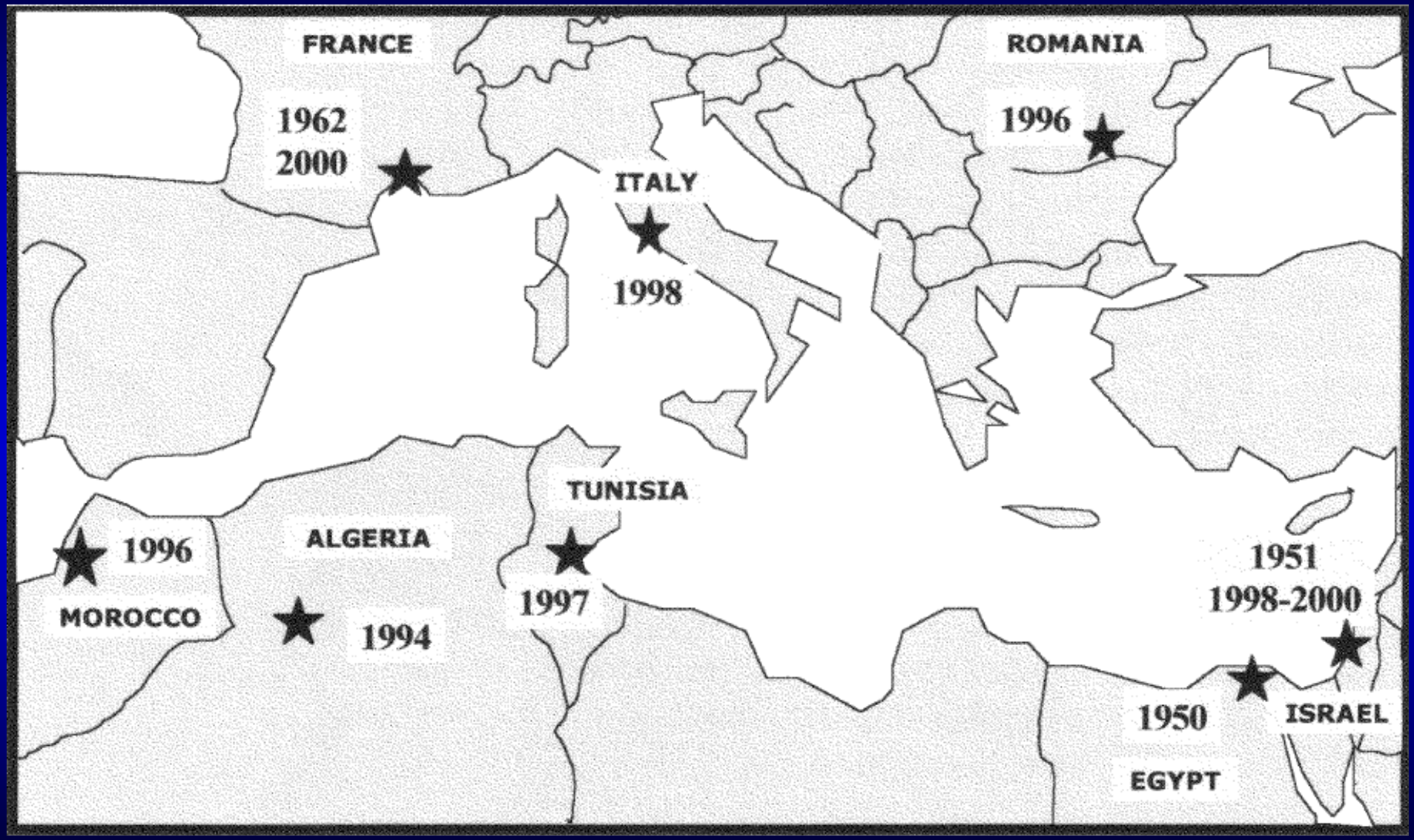


# WNV phylogenesis

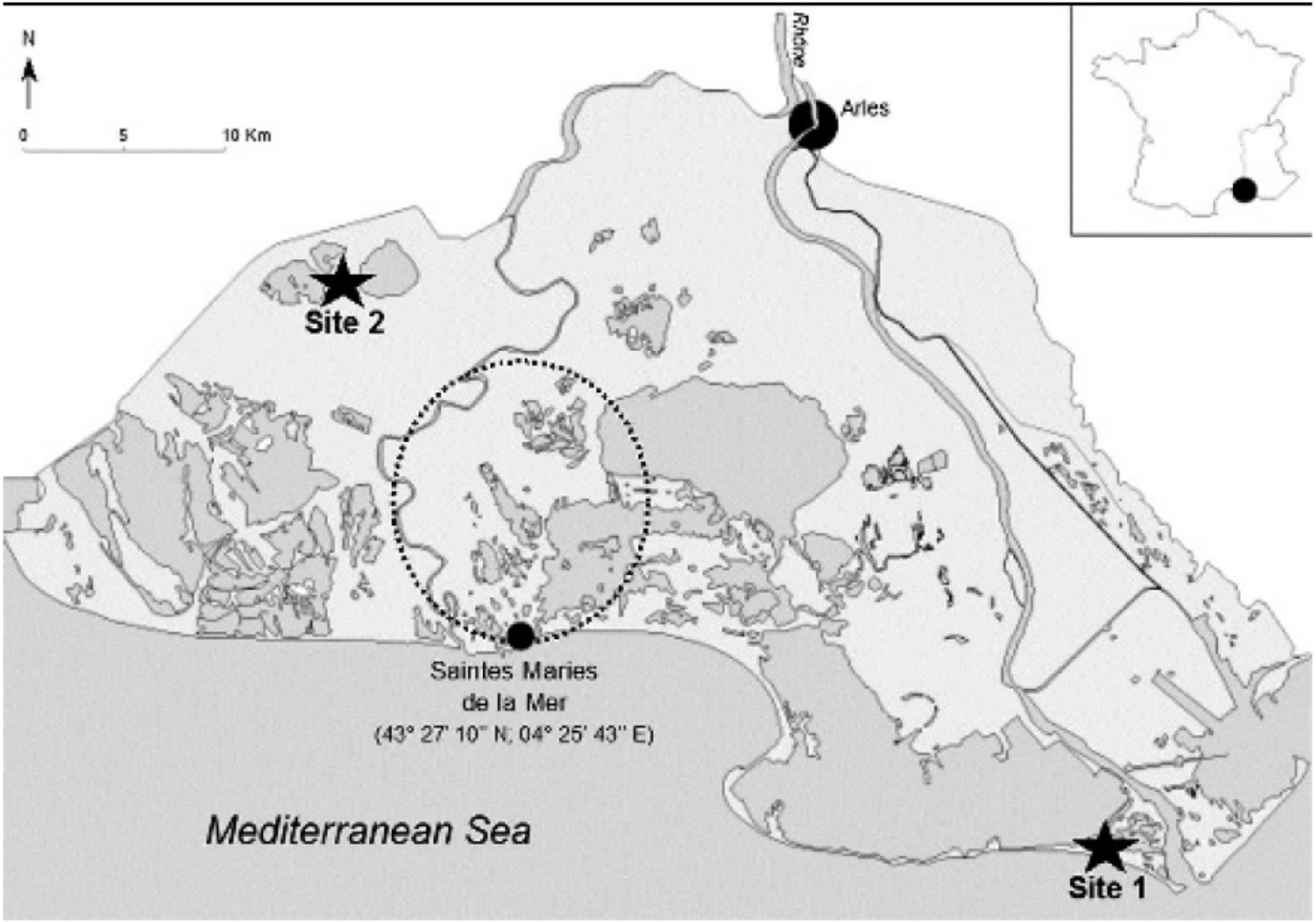



WEST NILE VIRUS
IN EUROPE

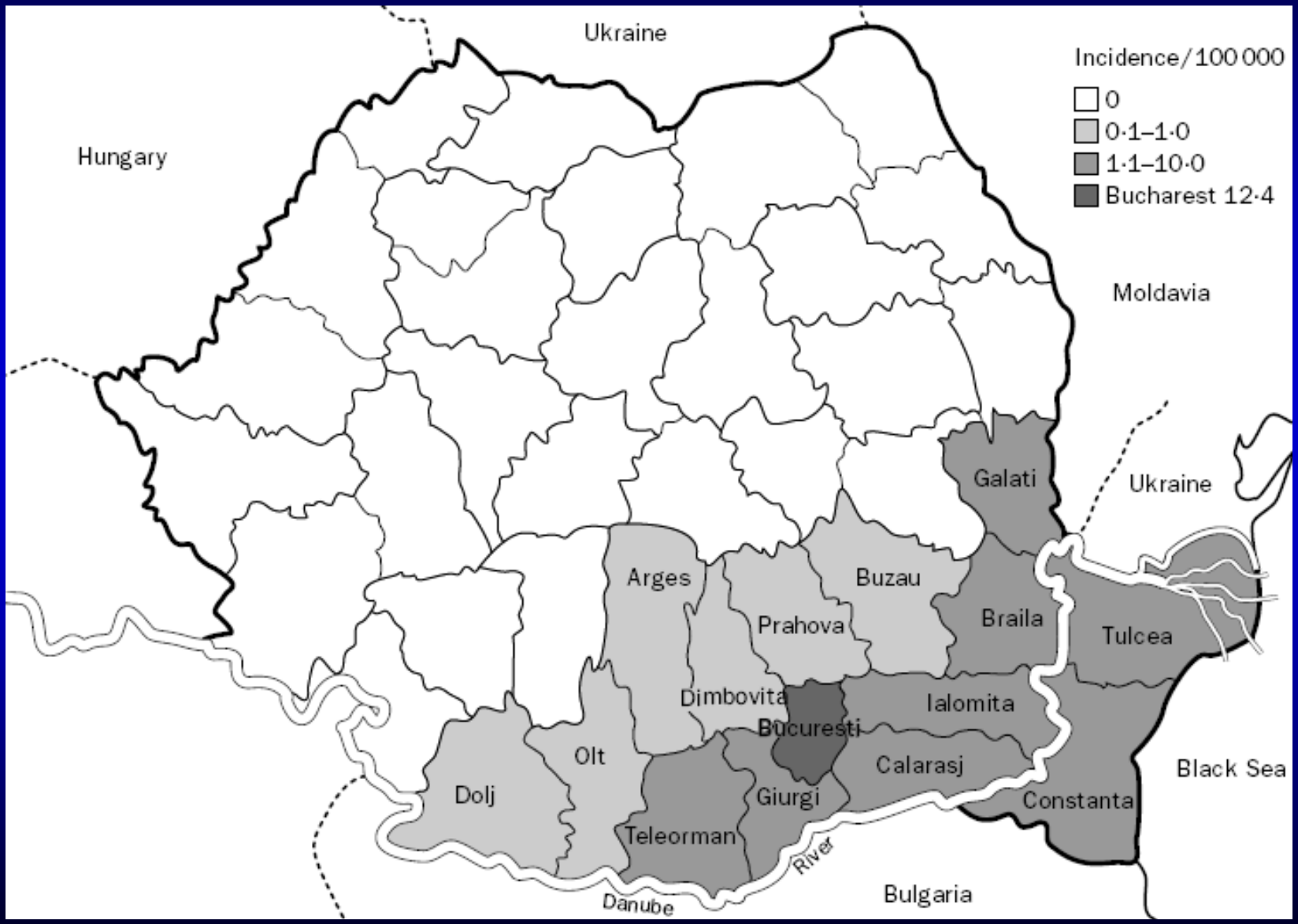
# WNV in the Mediterranean basin



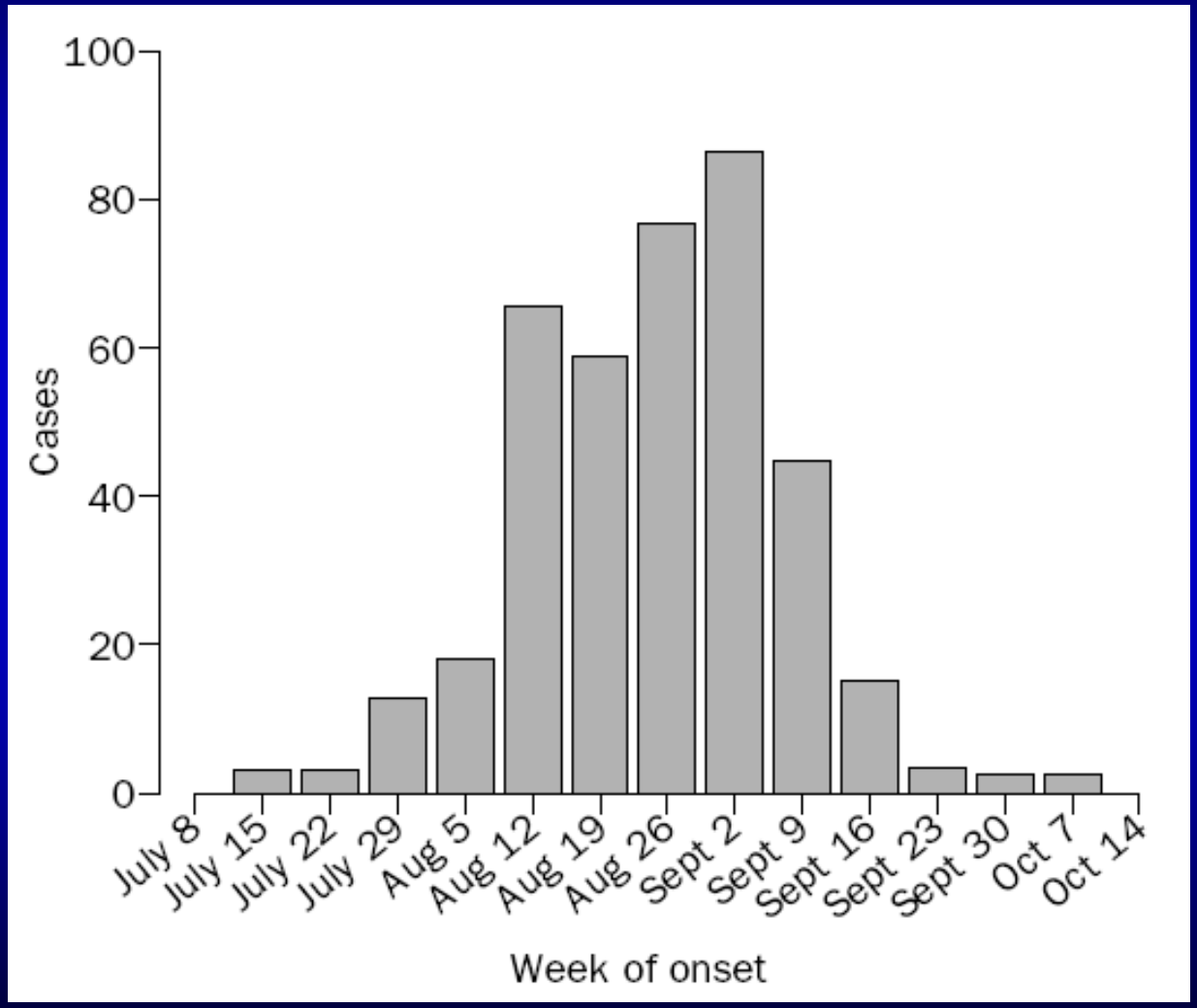
# WNV in Camargue, France: 1962-65 (cases in horses, 13 human cases) - 2000 (no cases in humans)


N
0
5
10 Km
Rhone
Arles
Site 2
Saintes Maries
de la Mer
(43° 27' 10'' N; 04° 25' 43'' E)
Mediterranean Sea
Site 1

# Romania, 1996



# Romania outbreak, 1996



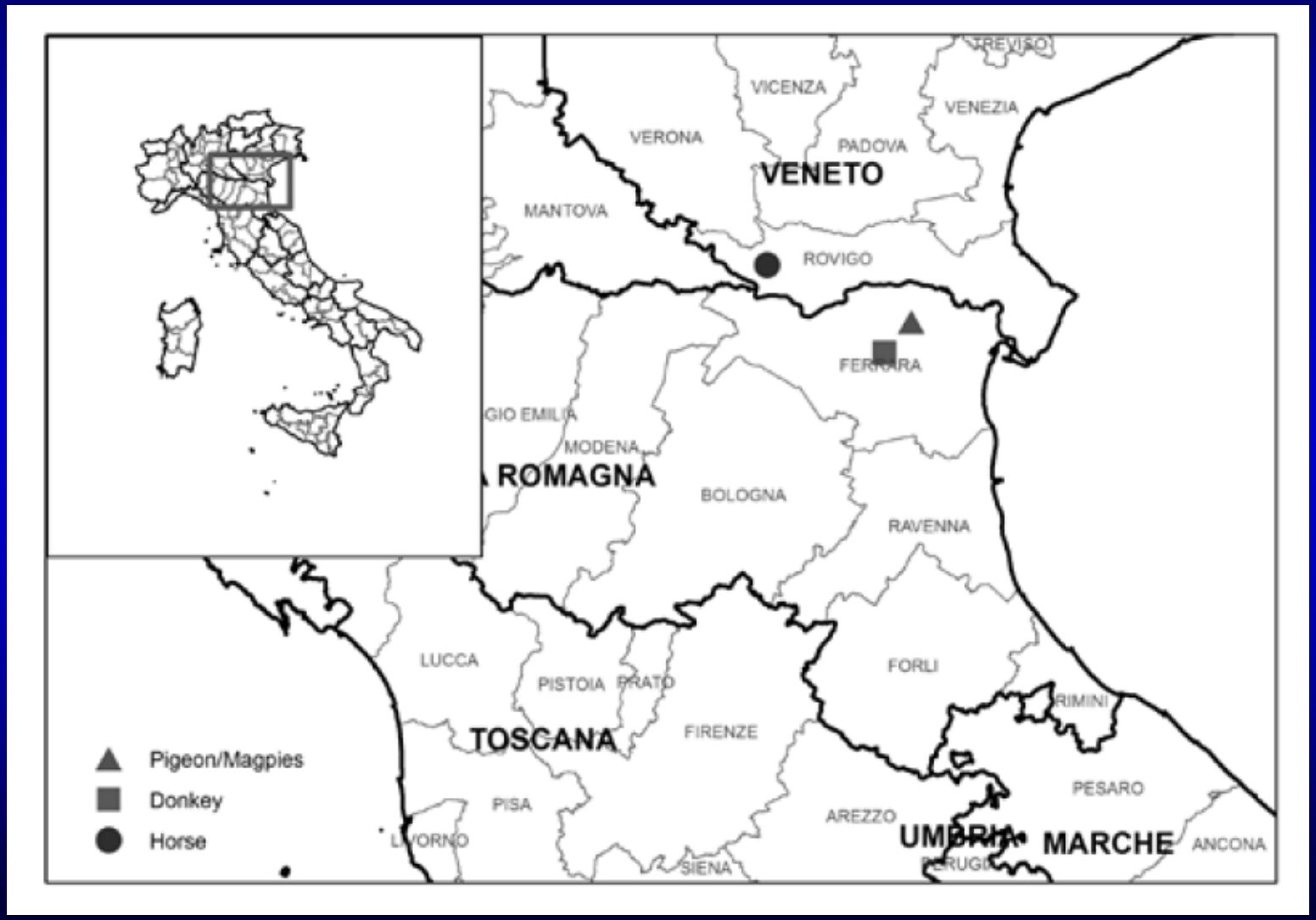
# Risk factors for West Nile infection Bucarest outbreak, 1996

| Factor | % of asymptomatically infected persons (no./total) | % of uninfected persons (no./total) | *P* | Odds ratio | 95% confidence interval |
|---|---|---|---|---|---|
| Mosquitoes in home | 97 (37/38) | 72 (36/50) | <.01 | 14.39 | 1.78–313.5 |
| Noted >5 mosquito bites/day | 34 (12/35) | 17 (7/42) | .08 | 2.61 | 0.79–8.8 |
| Flooded basement (apartment building residents only) | 63 (15/24) | 30 (11/37) | .01 | 3.94 | 1.16–13.7 |
| Full rainwater collection containers | 37 (14/38) | 22 (11/50) | .13 | 2.07 | 0.73–5.9 |
| Domestic fowl | 26 (10/38) | 26 (13/50) | .97 | 1.02 | 0.35–2.9 |
| Residence in apartment building | 63 (24/38) | 74 (37/50) | .28 | 0.60 | 0.22–1.6 |
| Home >20 years old | 50 (17/34) | 40 (19/48) | .35 | 1.53 | 0.57–4.1 |
| Residence in agricultural sector | 18 (7/38) | 8 (4/50) | .20 | 2.60 | 0.60–11.8 |
| Spent >6 h/day outdoors | 21 (8/38) | 28 (14/50) | .46 | 0.69 | 0.22–2.0 |
| Spent >6 h/day in garden | 8 (3/38) | 10 (5/50) | 1.00 | 0.77 | 0.13–4.1 |

# West Nile virus in Italy

- Between August and October 1998 an outbreak of equine encephalomyelitis occurred in Tuscany Region. 14 cases were registered, with 6 deaths.
- A strain of West Nile virus was isolated from the brain of a horse.
- Four asymptomatic infections were identified in asymptomatic humans at risk

# 2008: WNV is back!



# WNV in Italy: 2008-2010

- 9 human cases in 2008
- 16 human cases in 2009
- 3 casi umani nel 2010
- Most human cases identified in Emilia-Romagna and in Veneto
- Outbreaks identified among horses in Emilia-Romagna, Veneto and Lombardia

# Prevalence of IgM and IgG antibodies to West Nile virus among blood donors in an affected area of north-eastern Italy, summer 2009

**P Pezzotti (pezzotti@asplazio.it)[1], C Piovesan[2], L Barzon[3,4], R Cusinato[4], M Cattai[4], M Pacenti[4], A Piazza[4], E Franchin[3,4], S Pagni[3,4], S Bressan[4], T Martello[4], R Potenza[5], C Scipioni[5], R Ammendola[5], A Breda[6], G Palù[3,4], F Russo[2], G Rezza[7]**

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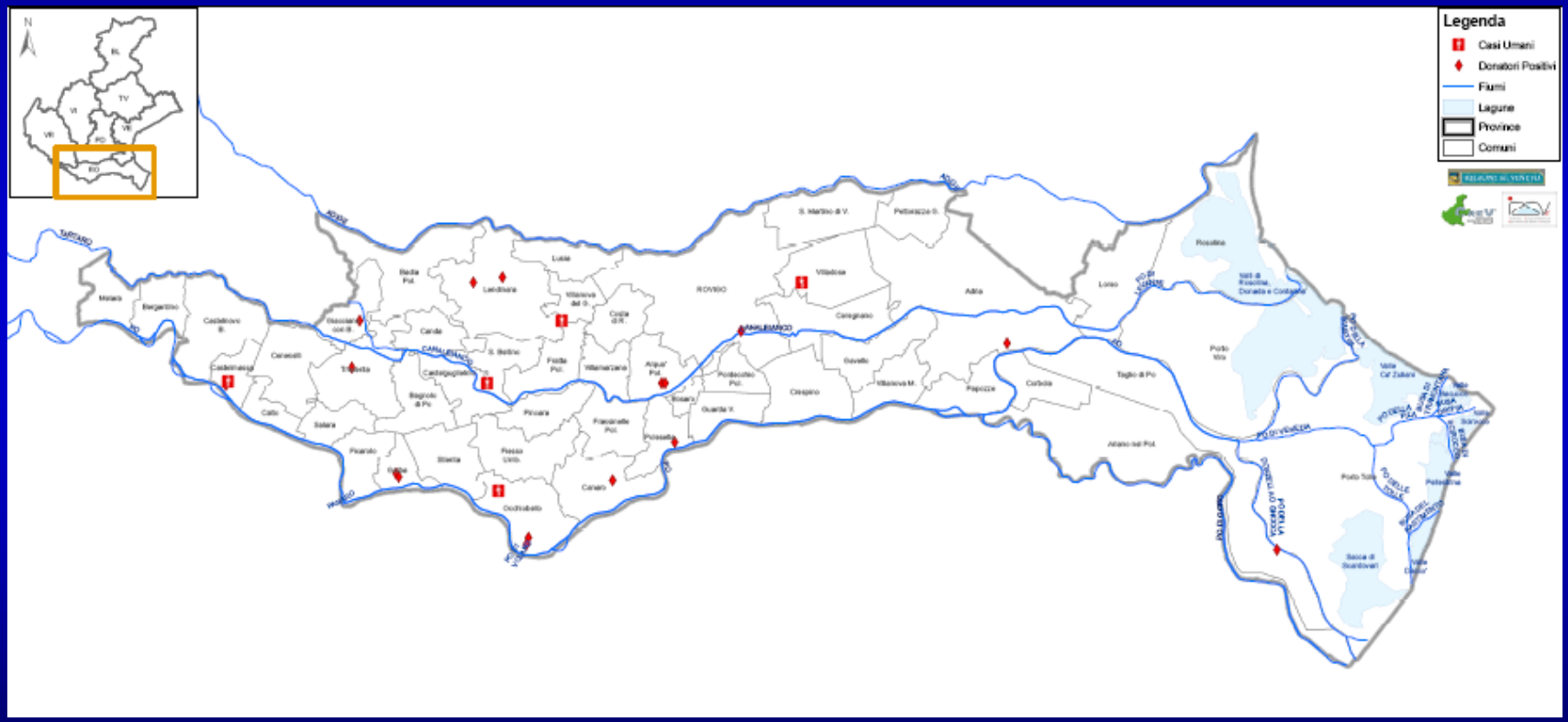
2. Direction of Prevention, Veneto region, Venice, Italy
3. Department of Histology, Microbiology, and Medical Biotechnologies, University of Padua, Padua, Italy
4. Regional Reference Centre for Infectious Diseases, Microbiology and Virology Unit, Hospital of Padua, Padua, Italy
5. Dipartimento Interaziendale di Medicina Trasfusionale (DIMT; Interinstitutional Department of Transfusion Medicine), Local Health Unit AUSL 18-19, Rovigo, Italy
6. Coordinamento Regionale per le Attività Trasfusionali (CRAT; Regional office for the coordination of blood transfusions), Pieve di Soligo, Italy
7. Department of Infectious Diseases, Istituto Superiore di Sanità, Rome, Italy

# Meningoencephalitis cases and WNV positive samples



## Number of donations tested for WNV and seroprevalence by blood transfusion centre.

| Blood transfusion centre | Positive | | Negative | | Total |
|---|---|---|---|---|---|
| | N | % | N | % | N |
| Adria | 2 | 0,40 | 492 | 99,60 | 494 |
| Rovigo | 6 | 0,40 | 1503 | 99,60 | 1509 |
| Trecenta* | 9 | 1,79 | 495 | 98,21 | 504 |
| **Total** | **17** | **0,68** | **2490** | **99,32** | **2507** |

***OR for Trecenta compared to the other sites: 4.53, p<0.01**

# Serological results of serum samples positive in the West Nile virus ELISA screening, Rovigo province, Italy, 20 July–15 November 2009

| IgG ELISA | IgM ELISA | IgG IFA | IgM IFA | Number of samples |
|---|---|---|---|---|
| Confirmed positive by PRNT | | | | 17 |
| + | + | + | + | 7 |
| + | - | + | - | 9 |

Serological results of serum samples positive in the West Nile virus ELISA screening, Rovigo province, Italy, 20 July–15 November 2009 (n=94)

| | | | | |
|---|---|---|---|---|
| + | - | + | + | 3 |
| + | - | - | - | 19 |
| + | + | + | - | 1 |
| - | + | + | + | 2 |
| - | + | - | + | 1 |
| - | + | - | - | 5 |

ELISA: enzyme-linked immunosorbent assay; IFA: immunofluorescence assay; PRNT: plaque reduction neutralisation test.

# NAT screening, Veneto August-October 2009

One of 5,726 blood donations

(17.5 per 100,000 donation)

# Sensitivity, specificity, negative and positive predictive value of serological tests for West Nile virus, compared with PRNT, Rovigo province, Italy, 20 July to 15 November 2009 (n=2,507)

| | PRNT-positive | PRNT-negative | PPV | NPV | Sensitivity | Specificity |
|---|---|---|---|---|---|---|
| WNV ELISA | | | | | | |
| IgM-positive/IgG-positive | 8 | 1 | 88.9 | 99.6 | 47.1 | 100.0 |
| other | 9 | 2,489 | | | | |
| | | | | | | |
| IgM-positive/IgG-negative | 0 | 8 | 0.0 | 99.3 | 0.0 | 99.7 |
| other | 17 | 2,482 | | | | |
| | | | | | | |
| IgM-negative/IgG-positive | 9 | 68 | 11.7 | 99.7 | 52.9 | 97.3 |
| other | 8 | 2,422 | | | | |
| | | | | | | |
| ELISA-positive | 17 | 77 | 18.1 | 100.0 | 100.0 | 96.9 |
| ELISA-negative | 0 | 2,413 | | | | |
| WNV IFA [a] | | | | | | |
| IgM-positive/IgG-positive | 7 | 5 | 58.3 | 99.6 | 41.2 | 99.8 |
| Other | 10 | 2,485 | | | | |
| | | | | | | |
| IgM-positive/IgG-negative | 0 | 1 | 0.0 | 99.3 | 0.0 | 100.0 |
| other | 17 | 2,489 | | | | |
| | | | | | | |
| IgM-negative/IgG-positive | 10 | 47 | 17.5 | 99.7 | 58.8 | 98.1 |
| other | 7 | 2,443 | | | | |
| | | | | | | |
| IFA-positive | 17 | 53 | 24.3 | 100.0 | 100.0 | 97.9 |
| IFA-negative | 0 | 2,437 | | | | |

ELISA: enzyme-linked immunosorbent assay; IFA: immunofluorescence assay; NPV: negative predictive value; PPV: positive predictive value; PRNT: plaque reduction neutralisation test.

[a] WNV IFA is evaluated as a second line test for WNV ELISA-positive samples.

Note: It was assumed that all sera tested negative by ELISA would also have been negative in IFA and PRNT even when these tests were not performed.

# Adjusted odds ratios of being PRNT-positive for West Nile virus, associated with blood donor characteristics, conditional logistic model, Rovigo province, Italy, 20 July–15 November 2009 (n=17)

| | | PRNT-positive | | PRNT-negative[a] | | AOR | 95% CI | p |
|---|---|---|---|---|---|---|---|---|
| | | N | % | N | % | | | |
| Age (years) | <40 | 5 | 23,8 | 16 | 76,2 | 1.00 | | |
| | 40-46 | 4 | 18,2 | 18 | 81,8 | 0.42 | 0.08-2.14 | 0.30 |
| | 47-53 | 4 | 19,0 | 17 | 81,0 | 0.48 | 0.09-2.45 | 0.37 |
| | >53 | 4 | 19,0 | 17 | | 0.69 | 0.15-3.23 | 0.64 |
| | | | | | | | | |
| Sex | Male | 16 | 20,5 | 62 | 79,5 | 1.00 | | |
| | Female | 1 | 14,3 | 6 | 85,7 | 0.88 | 0.09-8.75 | 0.92 |
| | | | | | | | | |
| Indoor/outdoor working activity | Indoors | 5 | 16,2 | 57 | 83,8 | 1.00 | | |
| | Outdoors | 11 | 38,5 | 8 | 61,5 | 5.07 | 1.01-25.37 | 0.05 |
| | Unknown | 1 | 25.0 | 3 | 75.0 | 2.74 | 0.20-37.38 | 0.45 |

AOR: adjusted odds ratios; CI: confidence interval; PRNT: plaque reduction neutralisation test.

[a] PRNT-negative blood donors were matched to positive ones by day and centre of donation.

# Summer 2011, Greece and Russia

- Over 200 human cases
- Lineage 2
- Climate change effect?

# WNV and blood donations

- WNV infection may be transmitted through blood and solid organ donation
- Precautionary measures include NAT screening of donated blood in affected areas

# Other emerging pathogens

- Chikungunya
- Dengue
- Other?