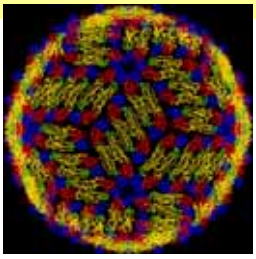
West Nile fever

2nd FAO-OIE-WHO Joint Scientific Consultation: Influenza and other Emerging Infectious Diseases at the Human Animal Interface

Verona, Italy, 27-29 April 2010

Hervé Zeller
European Centre for Disease Prevention and Control), Stockholm, Sweden

West Nile virus: the agent



Positive single strand RNA virus
Enveloped virus

Flavivirus genus, Flaviviridae family

Identified in humans and horses, birds, mosquitoes, ticks,

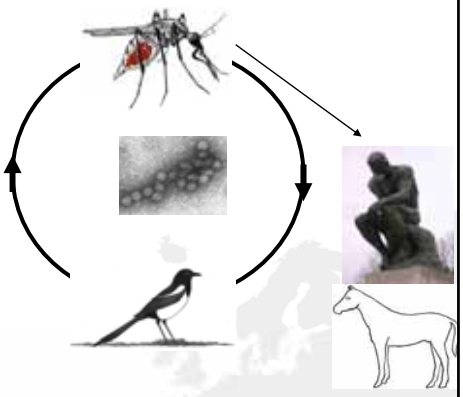
as well as during main outbreaks in cattle, sheep, goats, deer, dogs, cats, bats, pigs, squirrels, chipmunks, rabbits….

and in frogs…

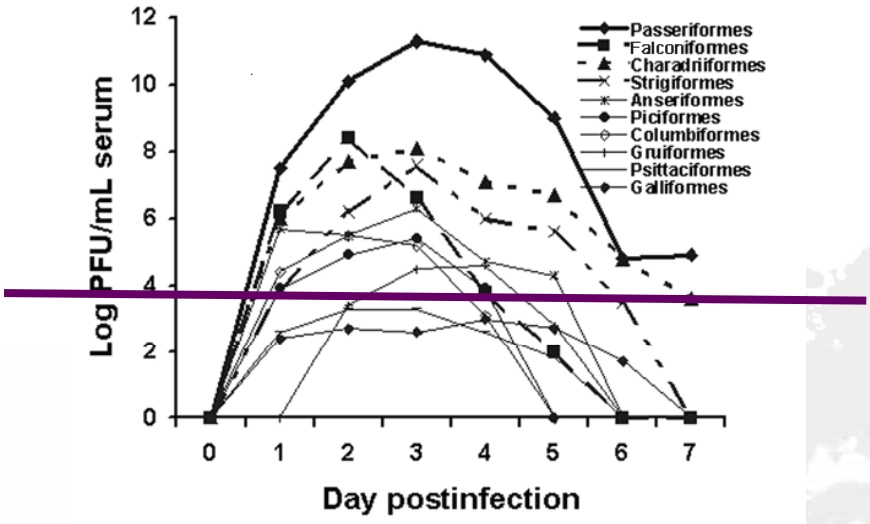
Infection induces immune response which can stay for several years

Transmission cycle

- Natural cycle between birds and mosquitoes
- Asymptomatic infections (>70%)
- Mild febrile illness
- Neuroinvasive illness in 1 out of 150-300 cases (mostly in elderly) with fatalities.
- Sporadic disease outbreaks in humans and horses in Africa, Europe, Asia and Australia
- Emergence in North America (1999)



Birds : amplifying host



Komar N et al. Emerg. Inf Dis 2003, 9: 311- 322

Cycle of transmission

- Competent mosquitoes able to replicate and transmit the virus
- Susceptible amplifying hosts (birds)
- Bird – mosquito – bird
  Mosquito bite: a complex figure: blood meal on a viremic amplifying host (bird)
  - Extrinsic incubation period: 7-14 days (duration varies according to environmental factors: temperature…)
- Mosquito - humans: Infection by biting infected bridge mosquitoes (multiple blood meals)

WN in mosquitoes: Europe/Mediterranean Basin

Mosquito species	Country (No.)
Anopheles coustani	Israel (1)
maculipennis	Portugal, (3), Ukraine (2), Romania (1)
Aedes cantans	Slovakia (1) Ukraine (1), Bulgaria (2)
caspius	Ukraine (1)
excrucians	Ukraine (1), Russia (1)
Culex *antennatus**	Egypt (5)
modestus	France (2), Russia (1)
pipiens	Israel (2), Egypt (1), Romania (12) Czechland, (2), Bulgaria (1) Portugal (2)
perexiguus	Egypt
torrentium	Romania (2)
univittatus	Egypt (9), Israel (5), Portugal (2)
Uranoteania	Russia

Adapted from: Hubalek, 2000

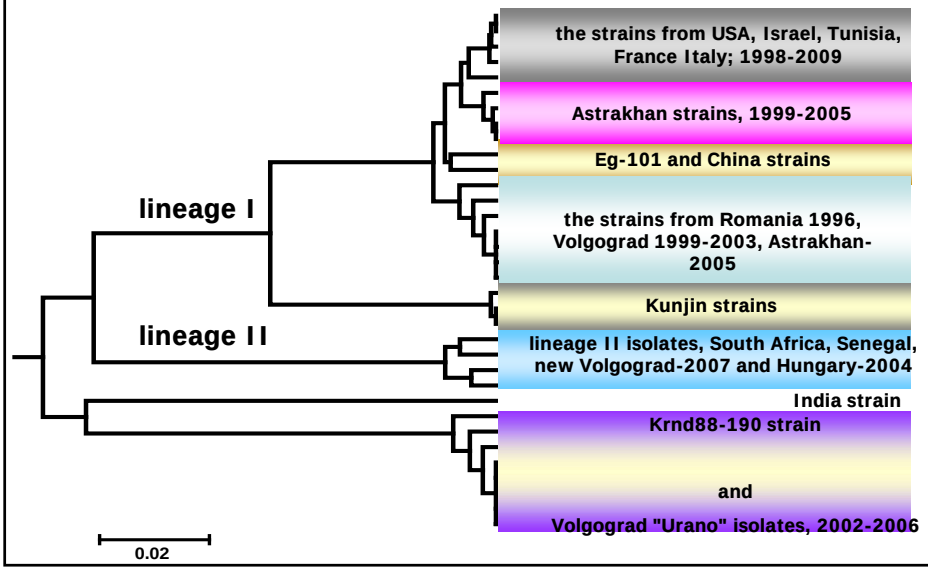
Modes of transmission to human

- Mosquito - human:
  but no transmission from human to mosquitoes (low viremia)
- Human - human infection
  - via blood products/organs:

    Numerous asymptomatic cases (up to 80%) with a low viremia for a median of 6.5 days up to 3 weeks

    From June to December 2003, 818 viremic blood donations in 6 million units
    (Source: MMWR 2004;53:281-4)
  - Others: Transmission of West Nile during horse autopsy. Emerg Infect Dis. 2010 Mar;16(3):573-5.

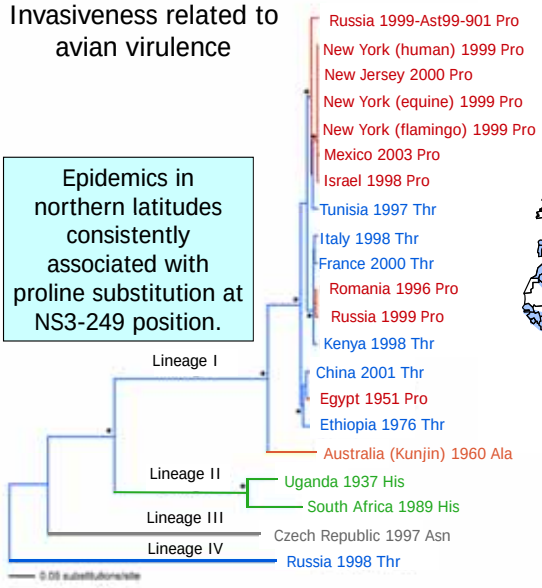
Virus phylogeny

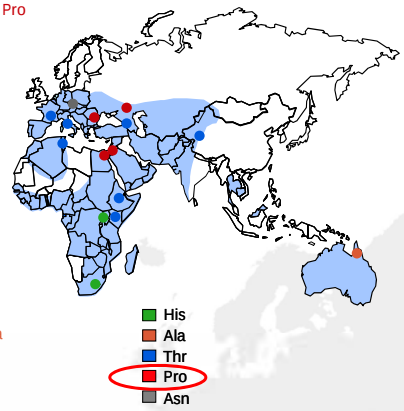


Brault et al. 2007. Nature genetics.

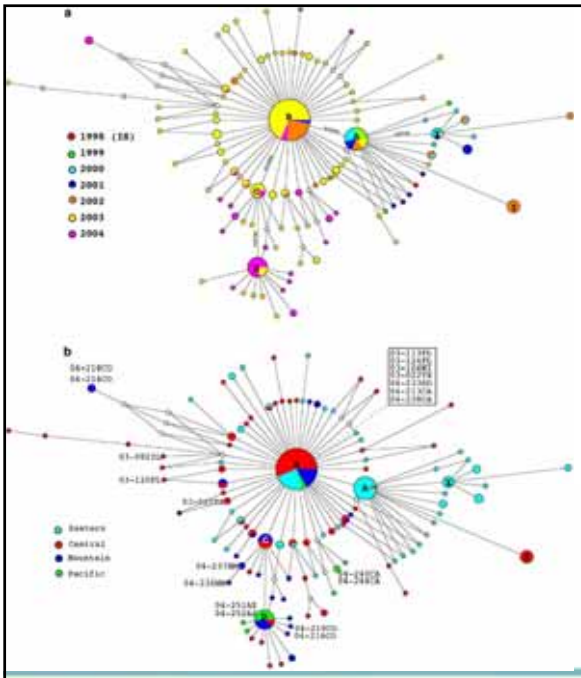
Invasiveness related to avian virulence

Epidemics in northern latitudes consistently associated with proline substitution at NS3-249 position.





Proline mutant imparts high virulence in American crows



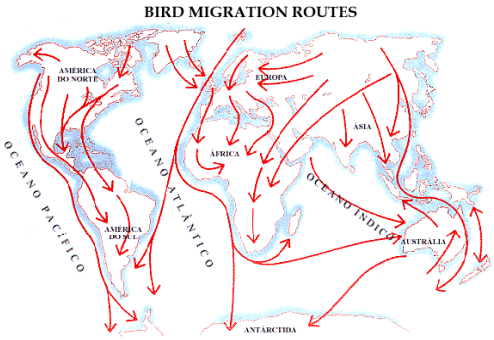
Genetic network analysis of E gene region of North American WNV.

Labeled by year of collection from 1998 (Israel) to 2004.

Labeled by time zone.

Multiple lines converging on a single peripheral variant indicate alternative mutational pathways.

Rossi, SL, et al Virol July 2007

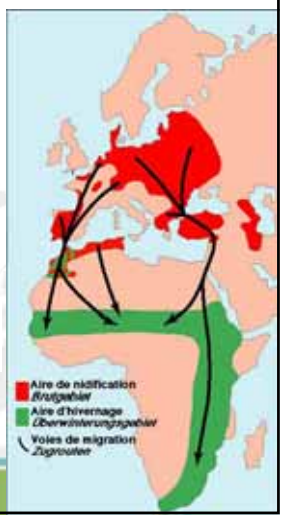


Israel

1997-98

Bird mortality

Storks, birds of prey, pigeons…



Source: M. Malkinson

and domestic geese...

Crows

Blue jays

Arrival in North America…

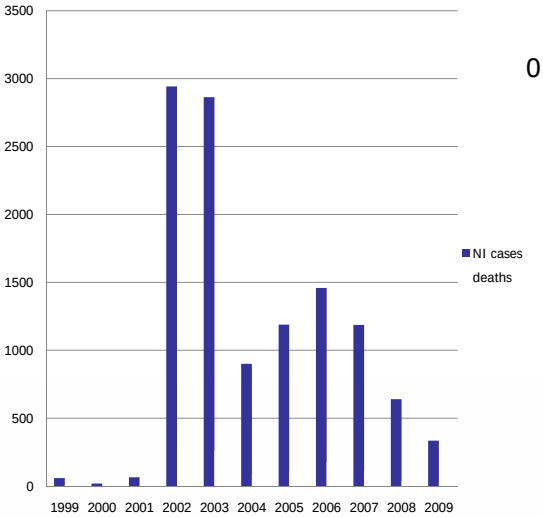
=

commotion

Source : L. Petersen

USA: West Nile – Neuroinvasive human cases 1999-2009

11657 cases CFR 9.6%



Canada 2001-2009

800 NI cases

Estimates

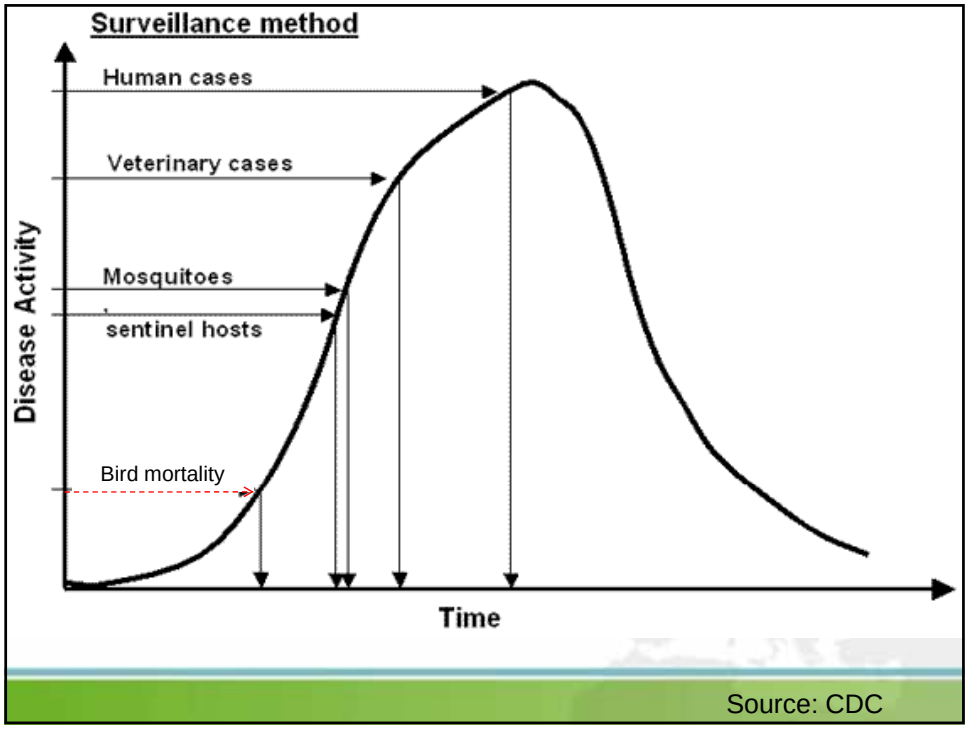
0.11-0.25 millions human infections

Horses, USA:

More than 27,000 cases since 2001

with a case fatality rate of about 33%

Estimate: 1.6-3.7 millions human infections



Sustainability of transmission

Bird - bird transmission

Isolation of WNV from a Red-tailed hawk that died in NY during Feb 2000.

Garmendia et al. 2000. J. Clin. Micro 38: 3110

Persistent avian infection: Experimentally infected birds positive for WNV RNA at necropsy 6-8 wks post infection

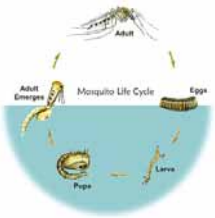
Reisen et al. 2006. JME 43: 344

Predation and/or scavenging: possible mechanism for WNV infection in raptors during winter

Sustainability of transmission

WNV probably overwinters by multiple mechanisms:

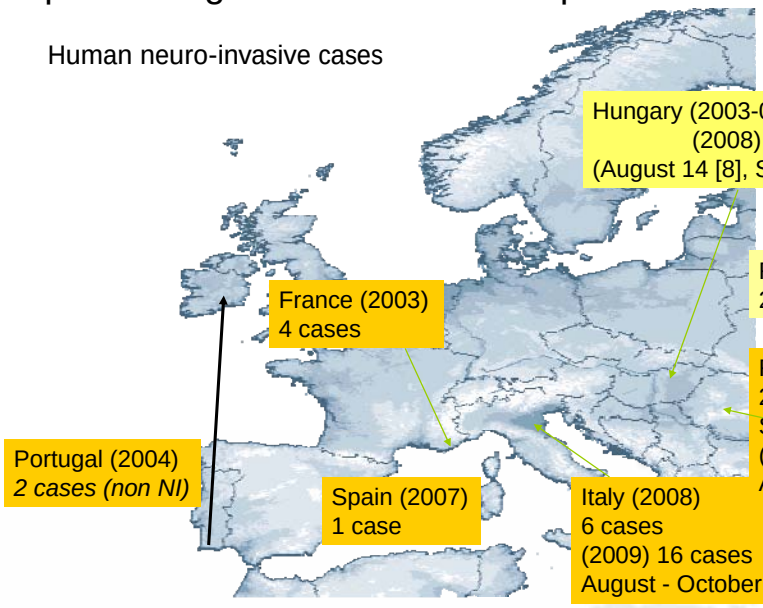
- Vertical infection of diapausing *Culex* females
- Vertical transmission in *Culex* :
  Cx pipiens overwintering mosquitoes (USA, Czech Republic) (PCR 4, isolation 1 out of 4)
  Virus also isolated from male *Cx. pipiens* in US, and from larvae of *Cx. univittatus* Kenya
- Chronic avian infections [no evidence for relapse]
- Migrating birds [results mostly negative]



Reiter P. West Nile virus in Europe: understanding the present to gauge the future. Euro Surveill. 2010;15(10):pii=19508.

Epidemiological situation in Europe 2000-2009

Human neuro-invasive cases



Hungary (2003-07) 14 cases
(2008) 14 cases
(August 14 [8], Sept 24 [6])

Romania (1997-2007): x cases

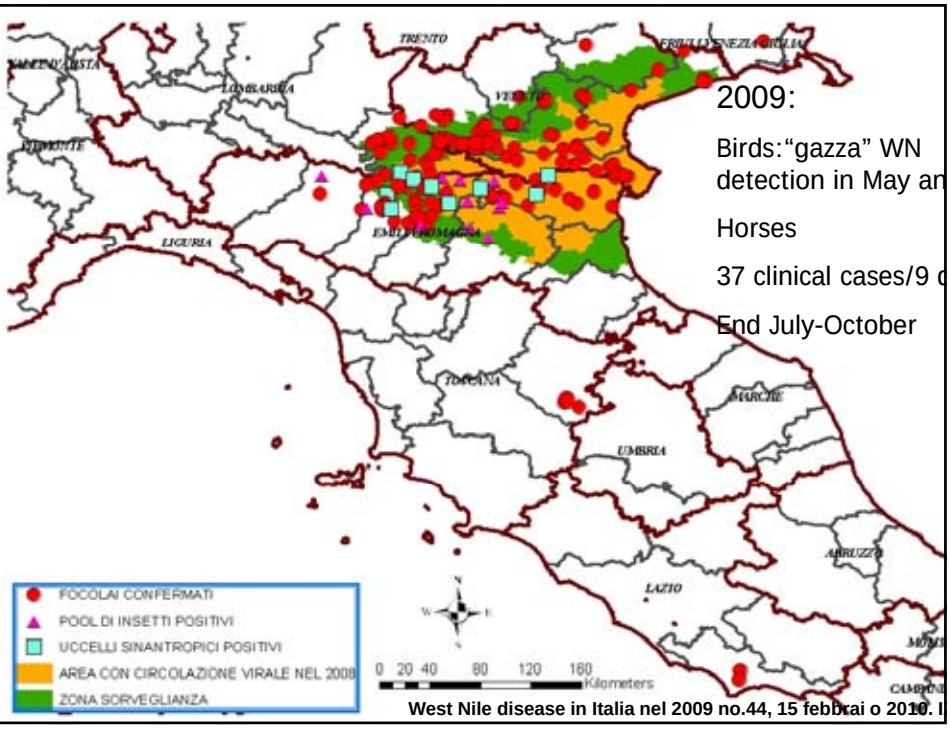
Romania (2008) 2 cases August-Sept ember (2008) 2 cases August

France (2003) 4 cases

Portugal (2004) *2 cases (non NI)*

Spain (2007) 1 case

Italy (2008) 6 cases (2009) 16 cases August - October



2009:

Birds:"gazza" WN detection in May an

Horses

37 clinical cases/9 c

End July-October

West Nile disease in Italia nel 2009 no.44, 15 febbrai o 2010. I

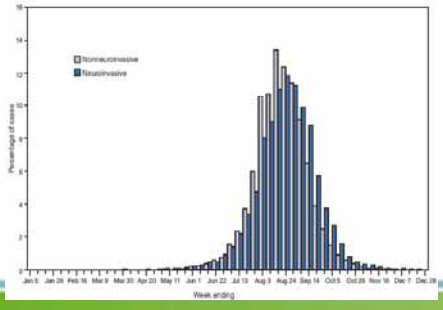
Interface aspects affecting evolution, exposure, or transmission

Climate impact: Seasonality for transmission

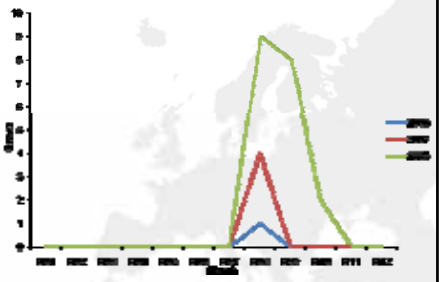
Mosquitoes activity is dependent on temperature and humidity

Do mosquitoes change host preference habits over the season: switching from birds to mammals?

West Nile virus disease cases (N = 28,961), by week of illness onset --- US, 1999—2008

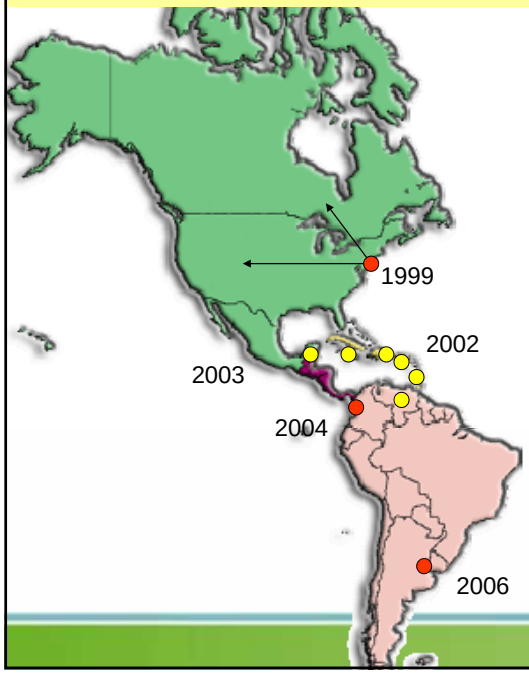


Cases in Europe from 2006 to 2009 (mid-July to mid-October)



Lindsey NP et al, *Surveillance Summaries* April 2, 2010 / 59(02);1-17

Epidemiological situation in the Americas



1999	New York
2001	Cayman islands, Canada
2002	Guadeloupe, Dominican Republic, Jamaica
2003	Mexico, Bahamas, Puerto Rico, Cuba
2004	Colombia, Trinidad
2006	Argentina
	also reported in Venezuela

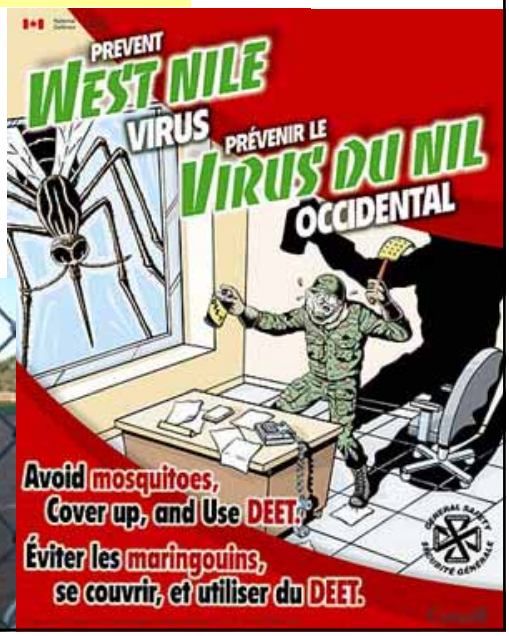
Vaccine: for humans

Cost-effectiveness of West Nile Virus Vaccination

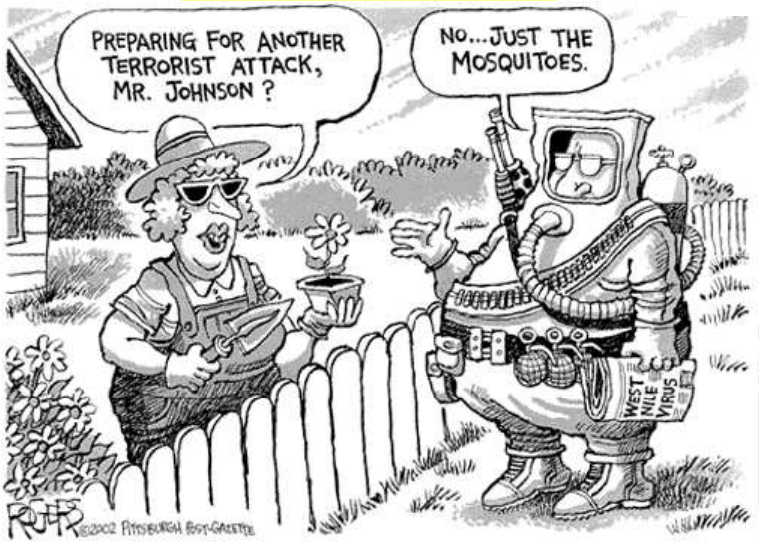
Zohrabian A et al EID 12, No. 3, March 2006

"Analysis indicated that universal vaccination against WNV disease would be unlikely to result in societal monetary savings unless disease incidence increases substantially over what has been seen in the past 6 years"

Vector control



Vector control



New approaches needed

Uncertainties

West Nile persistence in temperate climate:

In Europe, data collected in wild birds and horses suggest that a recurrent circulation of West Nile virus could exist in some areas.

Whether this circulation is permanent (due to overwintering mechanisms) or not remains unknown?

Climate changes:

Model predictions: example:

"Based on the climatologically characteristic drought occurrence in the past and on climate model predictions for climate change and potentially greater drought occurrence in the future, we suggest that the frequency and relative risk of WNV outbreaks could increase.".

Wang G, et al . BMC Infect Dis. 2010 Feb 24;10:38.

More Challenges

Yesterday: West Nile

- Lack of resources
- Learning to live with WNV does not mean complacency
- Creative (and cost efficient) strategies needed to mitigate an omnipresent risk

Tomorrow: Usutu?

Saint-Louis Encephalitis may reach the old world?

Imaginative scenario:

to assess the unpredictable and the Public Health impact?

One perspective:

to get a comprehensive approach of the ecology of the environment constantly modified by humans

Environmental and human behaviour "surveillance" is crucial…