Flying and crawling encephalitis

Corinne Liesnard - Hôpital Erasme
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Flavivirus Genus (Flaviviridae family)

Vector	Disease	Virus	Geographic Distribution	Symptomatology
Mosquitoes	Dengue	Dengue type 1-4 Vir.	Tropical countries	- Fever - Hemorragic fever
	Encephalitis Yellow Fever	Japanese Enc.Vir. **West-Nile Vir.** St Louis Enc. Vir. Yellow Fever Vir.	S-E Asia Europe, Asia, Africa, America USA Africa South America	Encephalitis
Ticks	Encephalitis	**Tick-Borne Enc.Vir.** and related viruses	Europe, Central and Far East Asia UK, Canada, USA, Siberia, Asia	Meningitis, encephalitis

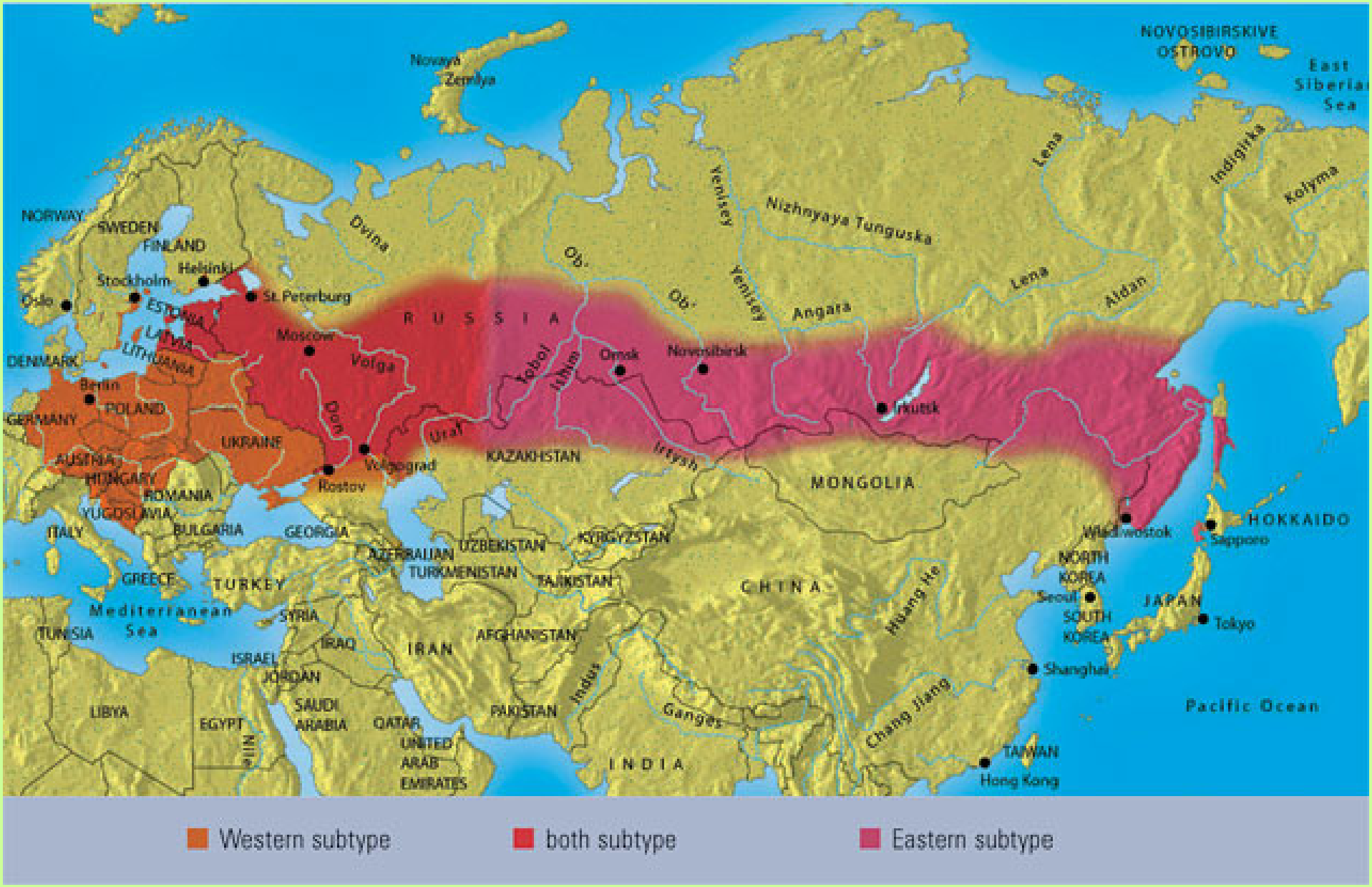
Tick-borne encephalitis virus (TBEV)

SS RNA virus - lipid enveloped

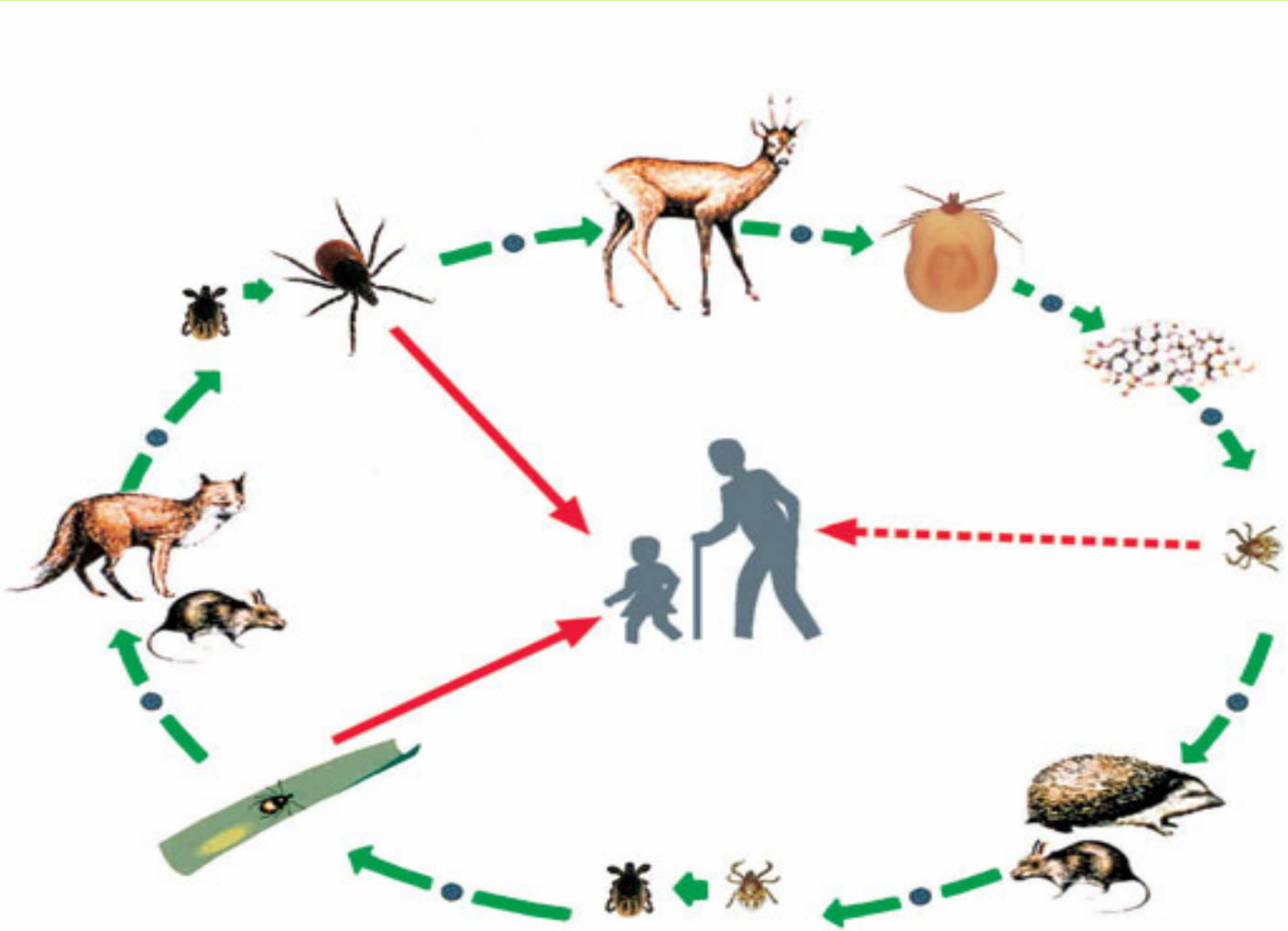
3 structural proteins - 7 NS proteins

2 or 3 subtypes closely related : 96% identity AA

Subtypes	**Vectors**
European	*I. ricinus*
Siberian	*I. persulcatus*
Far-eastern	*Haemophysalis concinna*


NOVOSIBIRSKIVE OSTROVO
East Siberian Sea
Novaya Zemlya
NORWAY
SWEDEN
FINLAND
Helsinki
Stockholm
Oslo
St. Peterburg
ESTONIA
LATVIA
LITHUANIA
DENMARK
Moscow
RUSSIA
Volga
Dvina
Ob
Yenisey
Nizhnyaya Tunguska
Lena
Indigirka
Kolyma
Tobol
Ishim
Omsk
Novosibirsk
Angara
Aldan
Irkutsk
Berlin
POLAND
GERMANY
Don
Ural
UKRAINE
Volgograd
Rostov
KAZAKHSTAN
Irtysh
MONGOLIA
AUSTRIA
HUNGARY
ROMANIA
YUGOSLAVIA
BULGARIA
ITALY
GEORGIA
UZBEKISTAN
KYRGYZSTAN
AZERBAIJAN
TURKMENISTAN
TAJIKISTAN
Vladivostok
HOKKAIDO
Sapporo
NORTH KOREA
Seoul
SOUTH KOREA
JAPAN
Tokyo
GREECE
TURKEY
CHINA
Huang He
Mediterranean Sea
SYRIA
IRAQ
IRAN
AFGHANISTAN
TUNISIA
ISRAEL
JORDAN
Shanghai
Indus
Ganges
Chang Jiang
Pacific Ocean
LIBYA
EGYPT
Nile
SAUDI ARABIA
QATAR
UNITED ARAB EMIRATES
PAKISTAN
INDIA
TAIWAN
Hong Kong
Western subtype
both subtype
Eastern subtype


The map is based on local reports of documented cases of TBE virus infection, screening for TBE antibodies in healthy unvaccinated populations, and regional screening for TBE virus in ticks and hosts.
Epidemiological information has been reported per district or region, e.g. Russia, Slovakia, Czech Republic, the Baltics and Germany; cities including reported locations, where infection occurred has been collected e.g. from Austria, Switzerland, Sweden and Denmark. For details please refer to the country specific references.
The extent of epidemiological assessment of TBE cases varies between countries. The data presented here may not therefore be entirely complete, nor can it be excluded that TBE viral infection - with subsequent development of the disease - won't occur in new areas.
Regions of TBE risk
more than 5 000 000 inhabitants
more than 1 000 000 inhabitants
more than 500 000 inhabitants
more than 100 000 inhabitants
other towns and villages
Basemap: Ed. Hölzel, Vienna

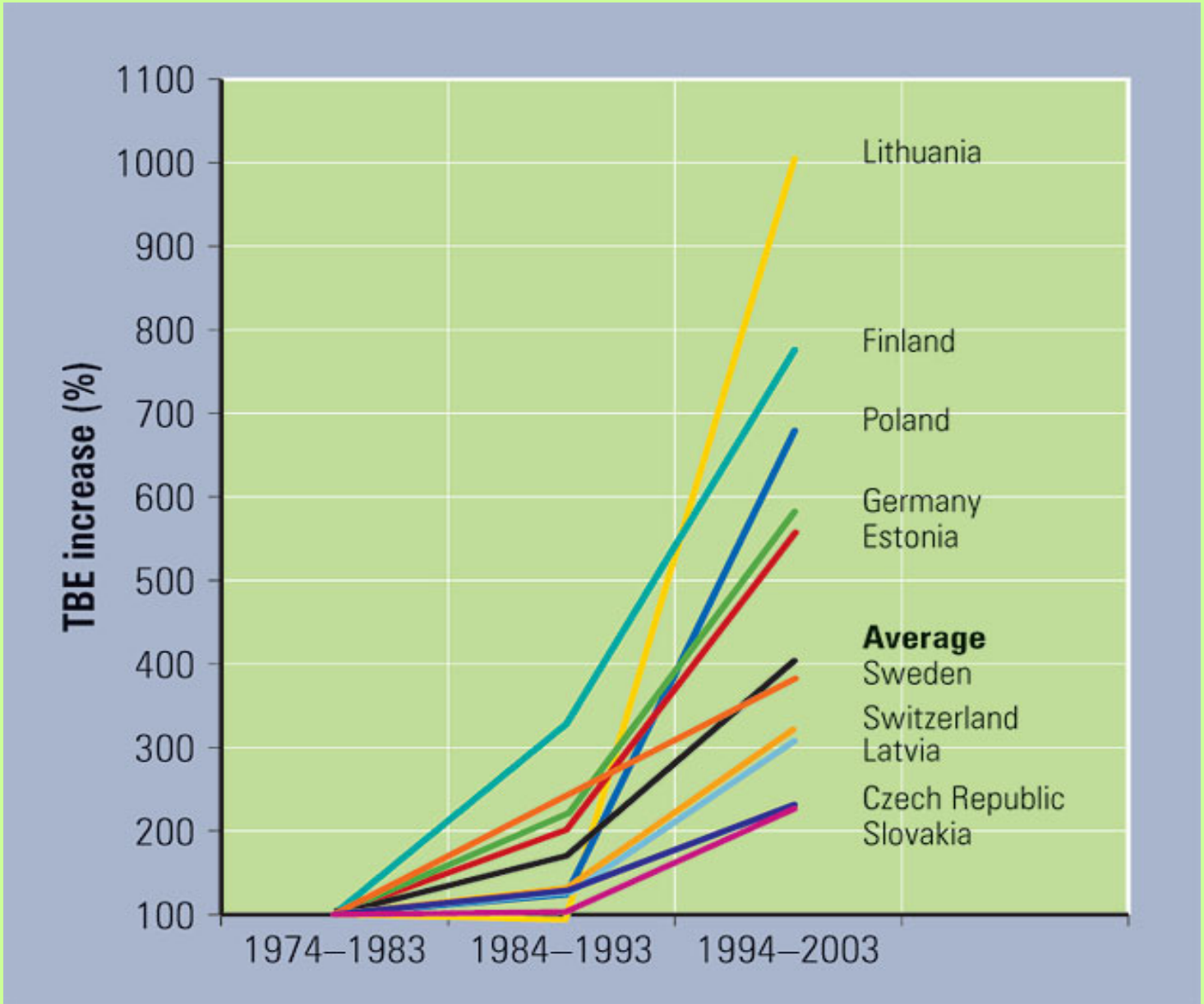


Ticks biotope

Factors governing the formation of TBE foci

- Population density and dynamics of infected ticks and their hosts (viremia)
- Susceptibility of individual host
- Proportion of immune hosts
- Properties of the biotope (92% humidity)
- Temperature (ex : Austria >90% foci at 7°C isotherm - up to 1300 m altitude)
- Sociological change

Increase (%) of the TBE incidence in Europe



TBEV prevalence in **tick** population of endemic areas in European countries

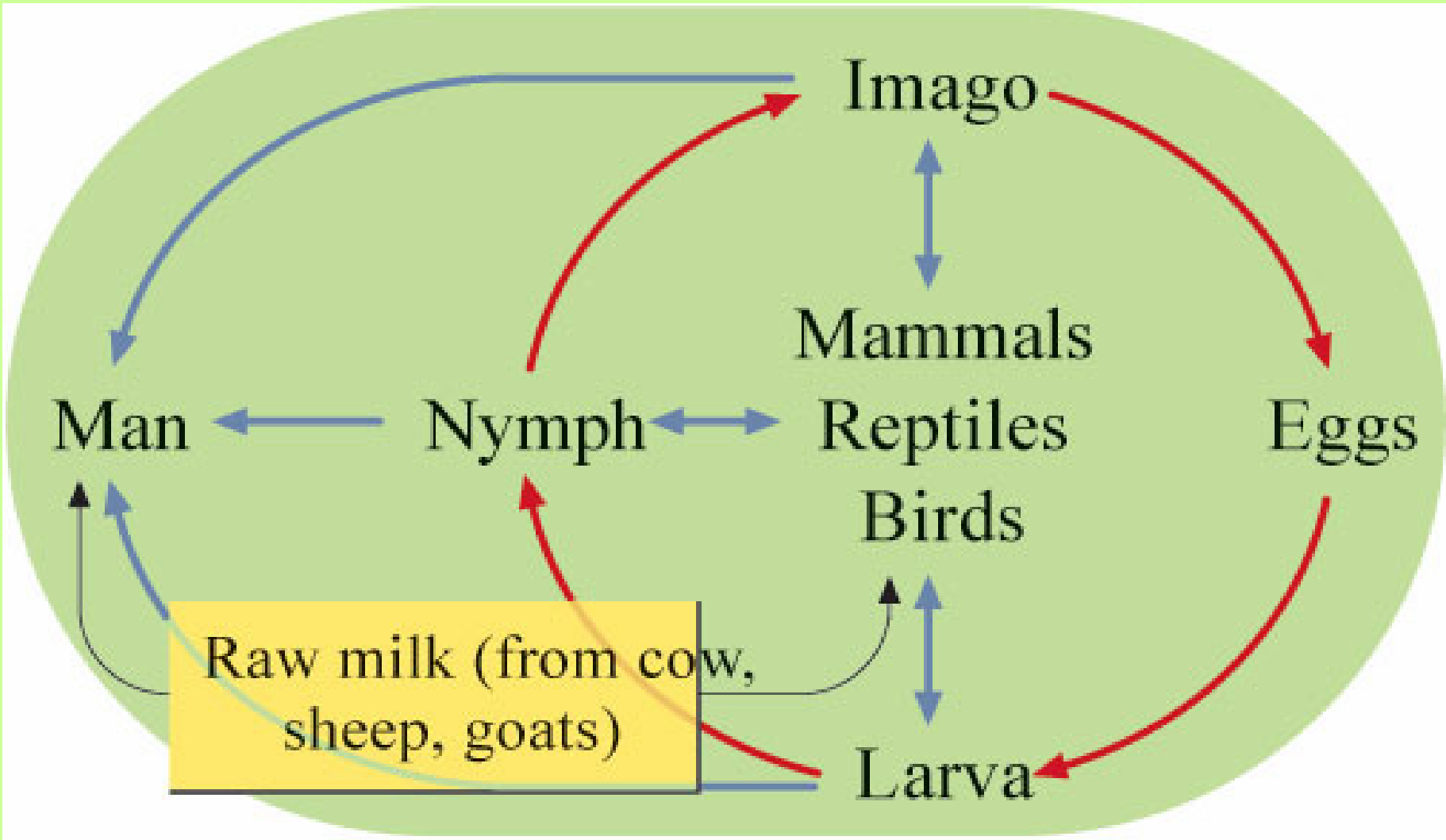
	Prevalence %
Austria	> 0.44 (max 6.2)
Germany	0.3 – 5.3
Switzerland	0.1 – 1.36
Sweden	0.1 – 1
Italy	0.05
Latvia	1.7 – 26.6 (*I. ricinus*) 0 – 37 (*I. persulcatus*)

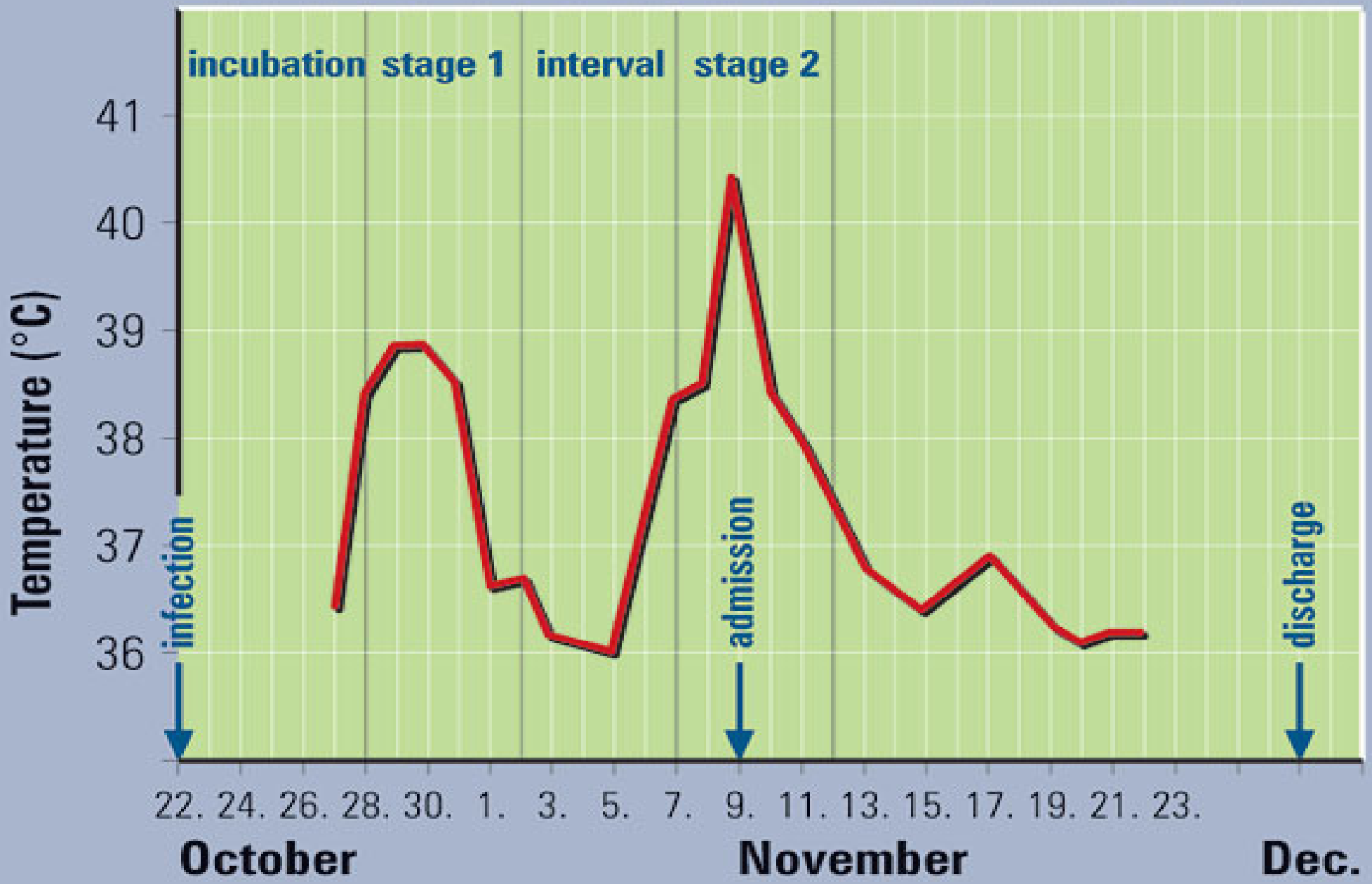
TBEV antibody prevalence in human population

	% population in endemic areas		
Austria	4-8	41	(risk groups)
Germany	0-43		
Sweden	4-22		
France	1	8	(risk groups)
Italy	-	0.6	(risk groups)
Switzerland		4-16%	(risk groups)
Czeck republic		15-64%	(risk groups)

Number of reported cases of TBE from various European countries and Russia [91]

Country	*1990*	*1991*	*1992*	*1993*	*1994*	*1995*	*1996*	*1997*	*1998*	*1999*	*2000*	*2001*	*2002*	*2003*	*2004*
Albania	8														
Austria	89	128	84	102	178	109	128	99	62	41	60	54	60	82	54
Belarus			2	20	50	66	97	67	78	26	23	61	18	25	
Croatia	23	60	27	76	87	59	57	25	24	26	18	27	30		41
Czech R.	193	356	338	629	613	744	571	415	422	490	719	411	647	606	500
Denmark									1	4	3	1	1	4	8
Estonia	37	68	163	166	177	175	177	404	387	185	272	215	90	237	182
Finland	9		14	25	16	23	10	19	17	12	41	33	38	16	31
France	2	1	2	5	4	6	1	1	2	5	0	0	2	6	7
Germany		44	142	118	306	226	114	211	148	115	133	253	226	278	274
Hungary	222	288	206	329	258	234	224	99	84	51	45	76	80	114	64
Italy			2	2	8	6	8	8	11	5	15	19	6	14	23
Latvia	122	227	287	791	1,366	1,341	716	874	1,029	350	544	303	153	365	251
Lithuania	9	14	17	198	284	426	309	645	548	171	419	298	168	763	425
Norway									1	1	2	1	2	1	4
Poland	8	4	8	249	181	267	257	201	209	101	170	205	126	339	262
Russia	5,486	5,225	6,301	7,893	5,593	5,982	9,548	6,539	6,987	9,955	5,931	6,339	5,150	4,770	4,156
Slovak R.	14	24	16	51	60	89	101	76	54	57	92	76	62	74	70
Slovenia	235	245	210	194	492	260	406	274	136	150	190	260	262	275	204
Sweden	54	75	83	51	116	68	44	76	64	53	133	128	105	105	185
Switzerland	26	37	66	44	97	60	62	123	68	112	91	107	53	116	137
Ukraine													12		


Imago
Mammals
Reptiles
Birds
Man
Nymph
Eggs
Raw milk (from cow, sheep, goats)
Larva


incubation
stage 1
interval
stage 2
Temperature (°C)
41
40
39
38
37
36
infection
admission
discharge
22. 24. 26. 28. 30. 1. 3. 5. 7. 9. 11. 13. 15. 17. 19. 21. 23.
October
November
Dec.

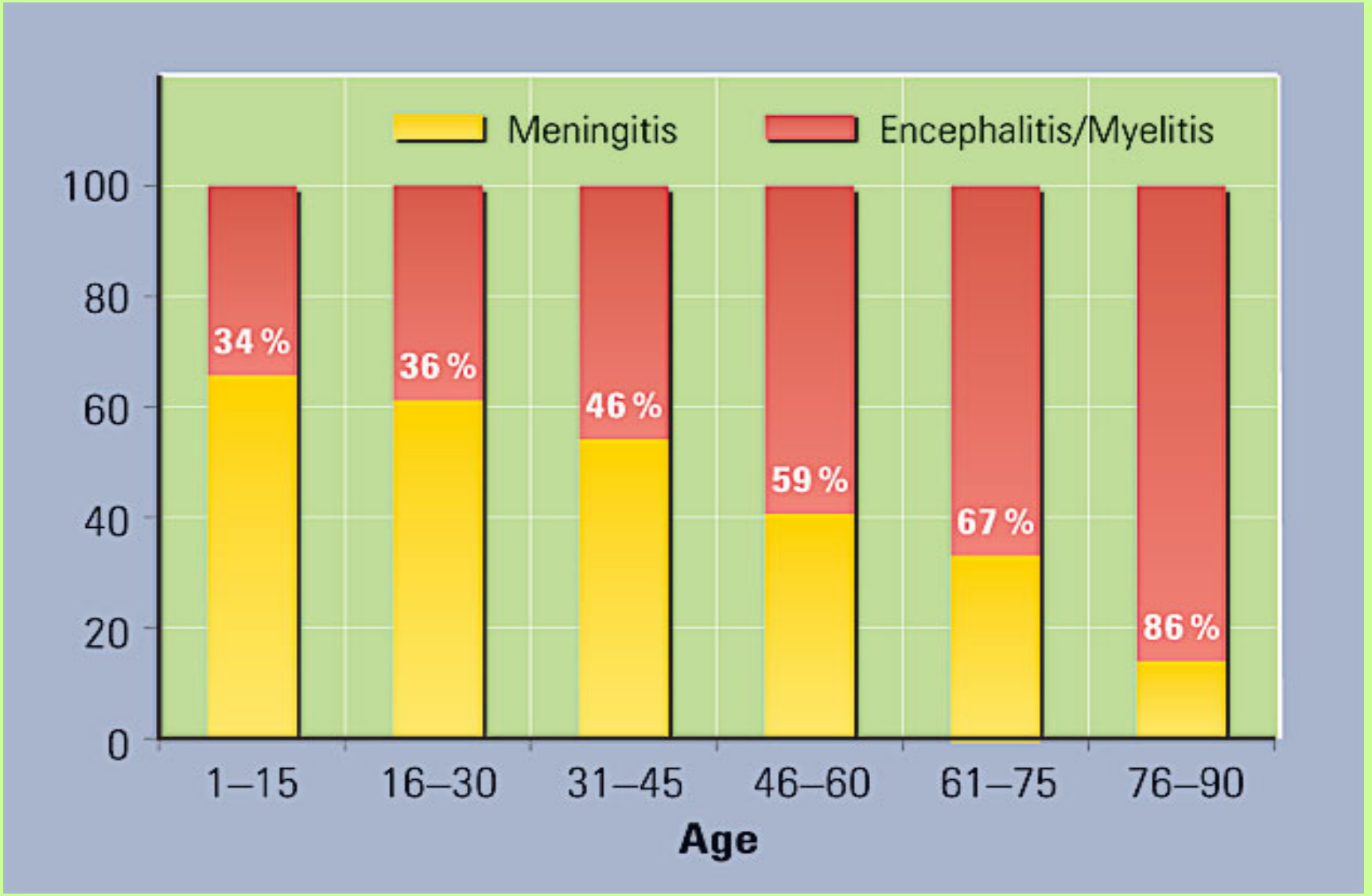
Clinical evolution : Second stage

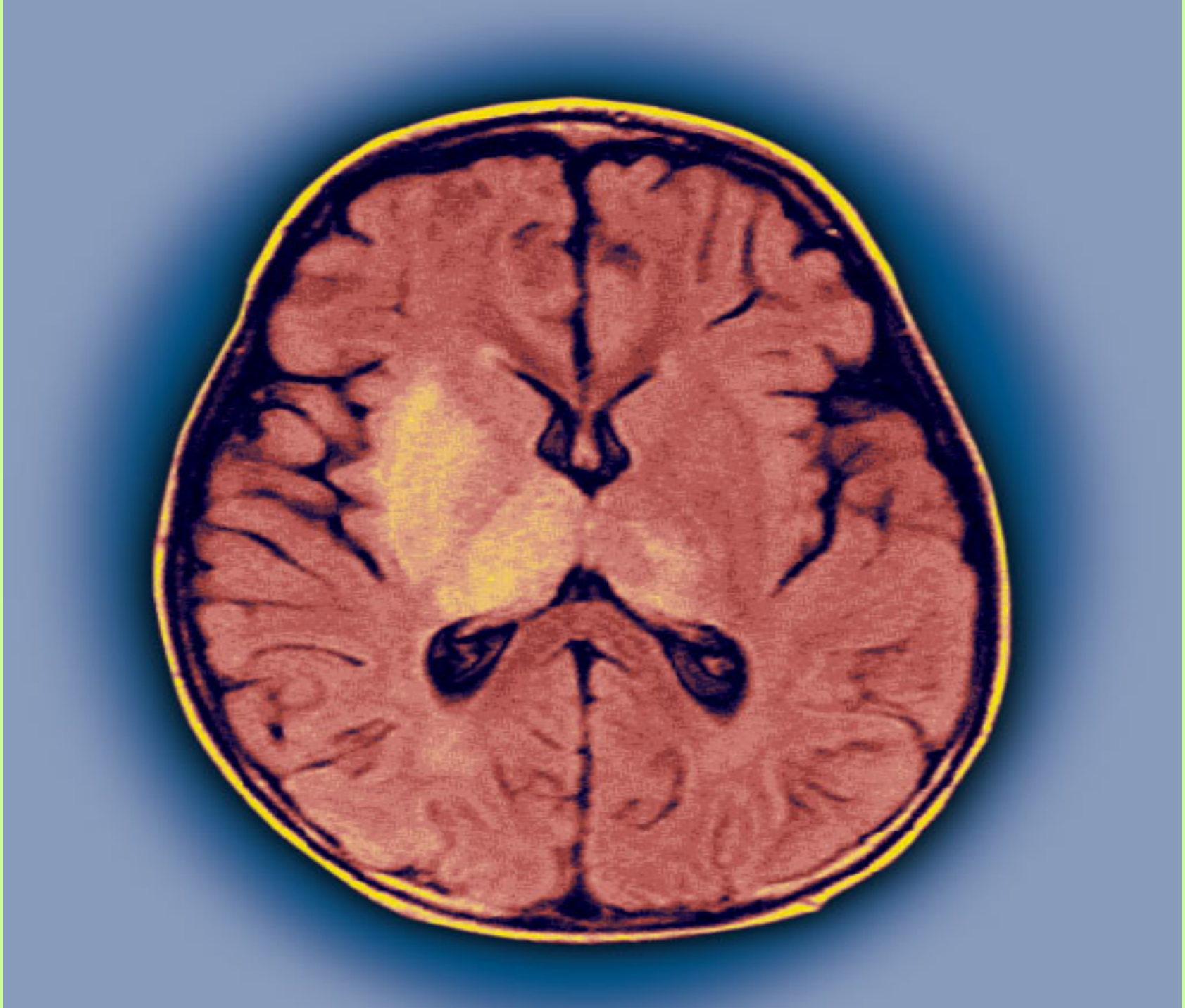
- 54% meningitis
- 37% meningoencephalitis
- 9% meningoencephalomyelitis
- Few cases of meningoencephaloradiculitis

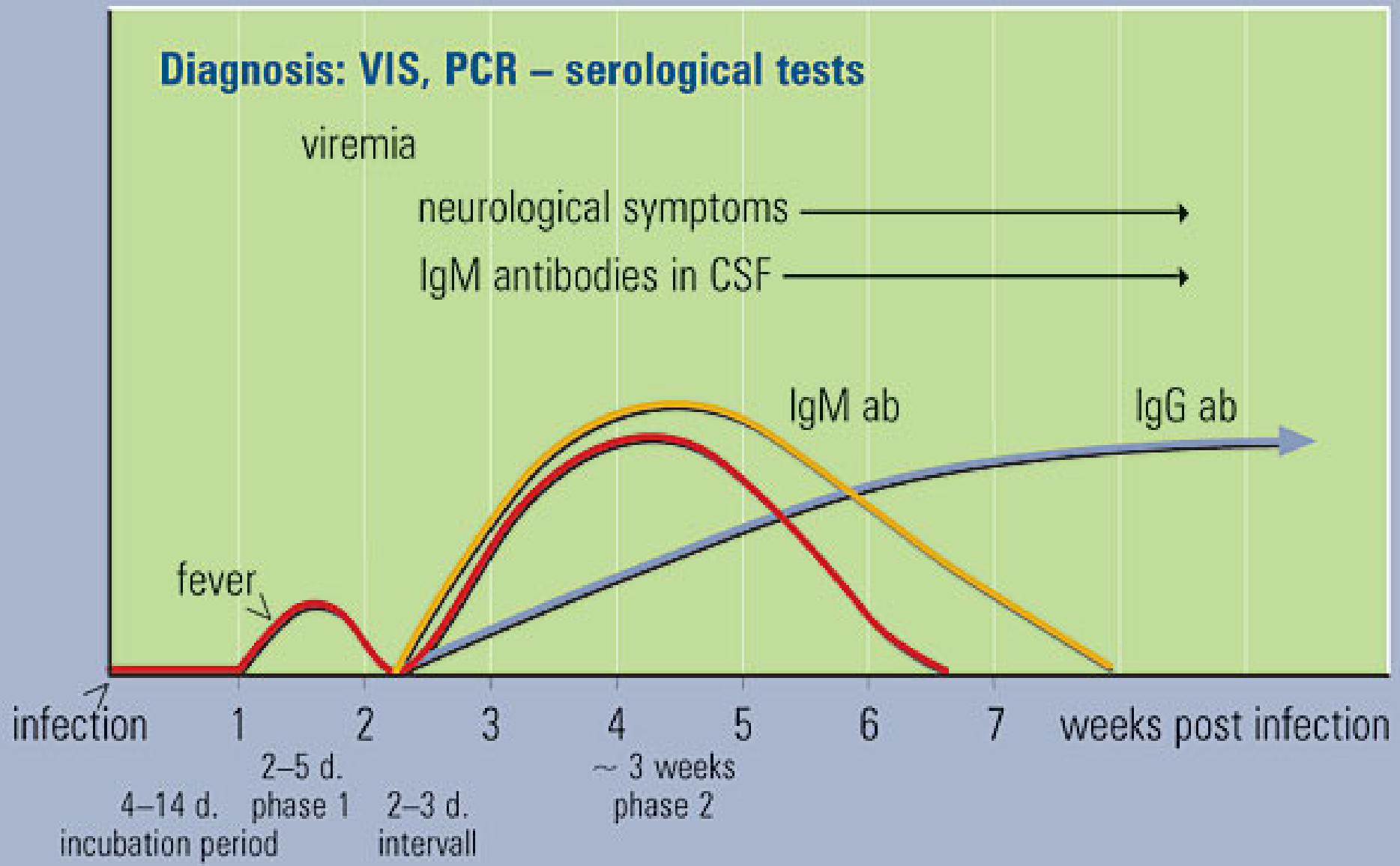
Mortality rate (Europe) : 1%

3% (among patients with severe course)

Post encephalitic syndrome : 10-20% of patients with severe course


Meningitis
Encephalitis/Myelitis
100
80
60
40
20
0
34 %
36 %
46 %
59 %
67 %
86 %
1–15
16–30
31–45
46–60
61–75
76–90
Age




Diagnosis: VIS, PCR – serological tests
viremia
neurological symptoms
IgM antibodies in CSF
IgM ab
IgG ab
fever
infection
1
2
3
4
5
6
7
weeks post infection
4–14 d.
incubation period
2–5 d.
phase 1
2–3 d.
intervall
~ 3 weeks
phase 2

Laboratory diagnosis

Serology

- TBEV IgG and IgM (ELISA) :
  - always positive at the second stage
  - cross-reactivity with yellow fever or Japanese enc. vaccination or dengue infections

⇨ immunoblot or neutralization assay for confirmation (reference lab)

RT-PCR or virus culture (L3 safety level) : initial stage

- not very useful

Prevention

- Control of vector : impossible
- Protective clothes, repellents

  ⇨ limited protection
- TBE immunoglobulin :

  possible antibody-dependent enhancement of infection

  ⇨ suspended

Prevention

- Vaccination (inactivated whole virus) (Encepur, FSME Immun)

basic immunization : 3 doses (0,1-3,9-12 months)

booster dosis : after 3 years

then every 3-5 years

accelerated vaccination schedule for travellers (0,7,21 days)

www.tbe-info.com (ISW-TBE)

Tourists at risk

Foreign Holiday-Makers (without winter months) in Endemic Regions - in millions.

Austria	10,6
Czech Republic	3,7
Slovakia	1,0
Hungary	4,5
Slovenia	1,0
Switzerland (in part)	4,7
Southern Germany	4,8

Additional countries with FSME risks can be found under www.tbe-info.com/epidemiology


Juchuuh!
Auf ihn!

West Nile Virus

2 genetic lineages :

- 1 : Europe, Africa, Asia, Australia, North America

  4 clades : Kunijn, India, A and B

  B : all are virulent in mice (USA)

- 2 : Sub-Saharian Africa, Madagascar

other clades than B : virulent and attenuated strains

Transmission

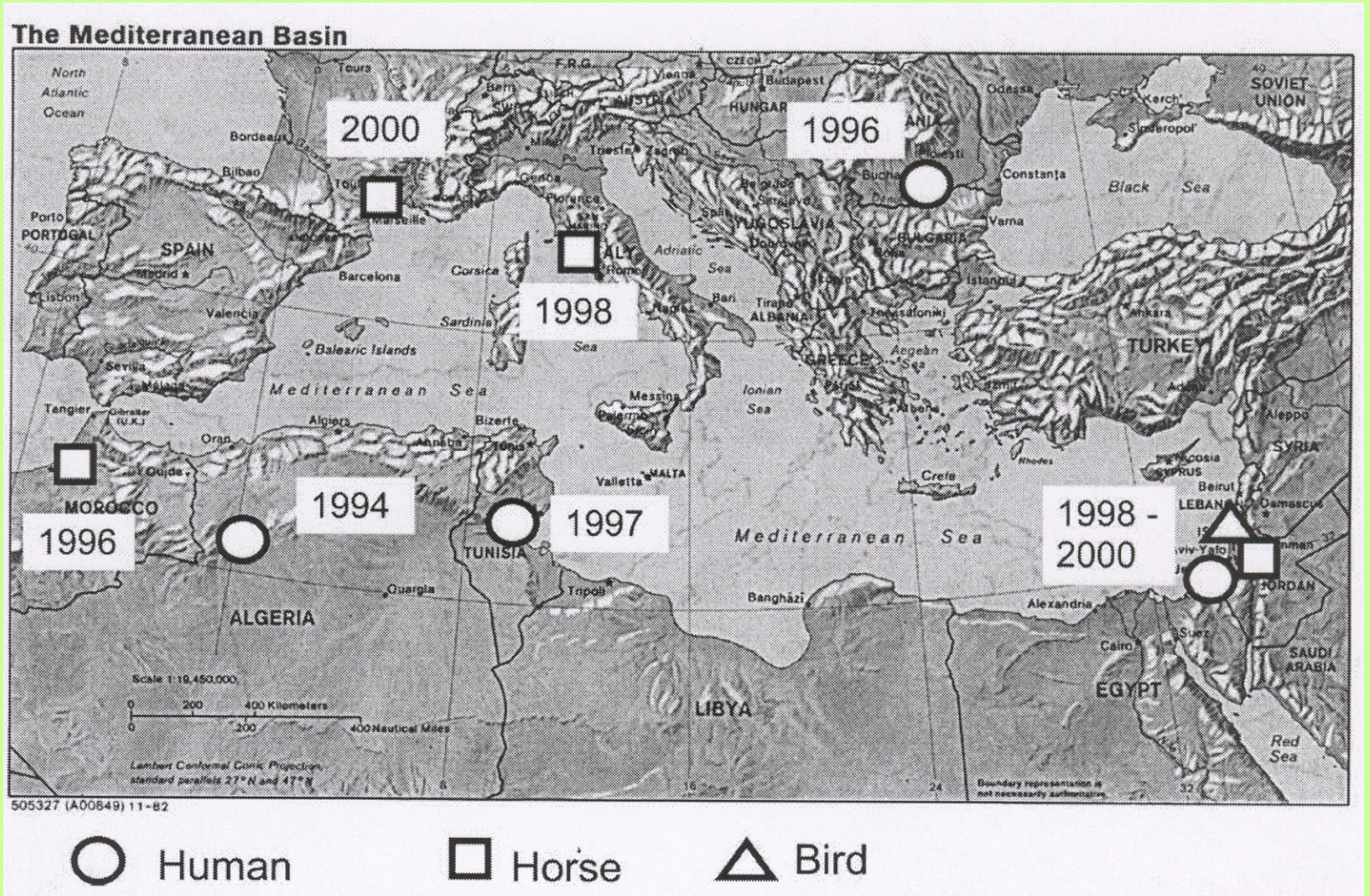
Mosquitoes : vector : *Culex sp* (also *Aedes*, *Anopheles*..)

Birds : amplifying hosts - high viremia

native or migrant, aquatic or terrestrial

Mammals, reptiles : can be infected

Outbreaks of West Nile virus infections reported in the Mediterranean bassin, 1994-2002



West Nile virus outbreaks in Europe and the Mediterranean basin since 1994-2002

Year	Country	No. in humans		No. in horses		Date	Reference
		Cases	Deaths	Cases	Deaths		
1994	Algeria	50	2			Aug–Sept	[77]
1996	Morocco	1	1	94	42	Aug–Oct	[11]
1996	Romania	393	17			mid July–mid Oct	[70]
1997	Tunisia	173	8			Sept–Nov	[7]
1998	Italy			14	6	mid Aug–early Oct	[12]
1999	Russia	318	40			end July–Sept	[71, 72]
1999	Israel	2	2			end Aug	[20]
2000	France			76	21	mid Aug–early Nov	[13]
2000	Israel	417	35	76		Aug–Oct	[14, 39]
2000	Russia	56					[73]
2001	Russia	64	(5–10%)				[73]

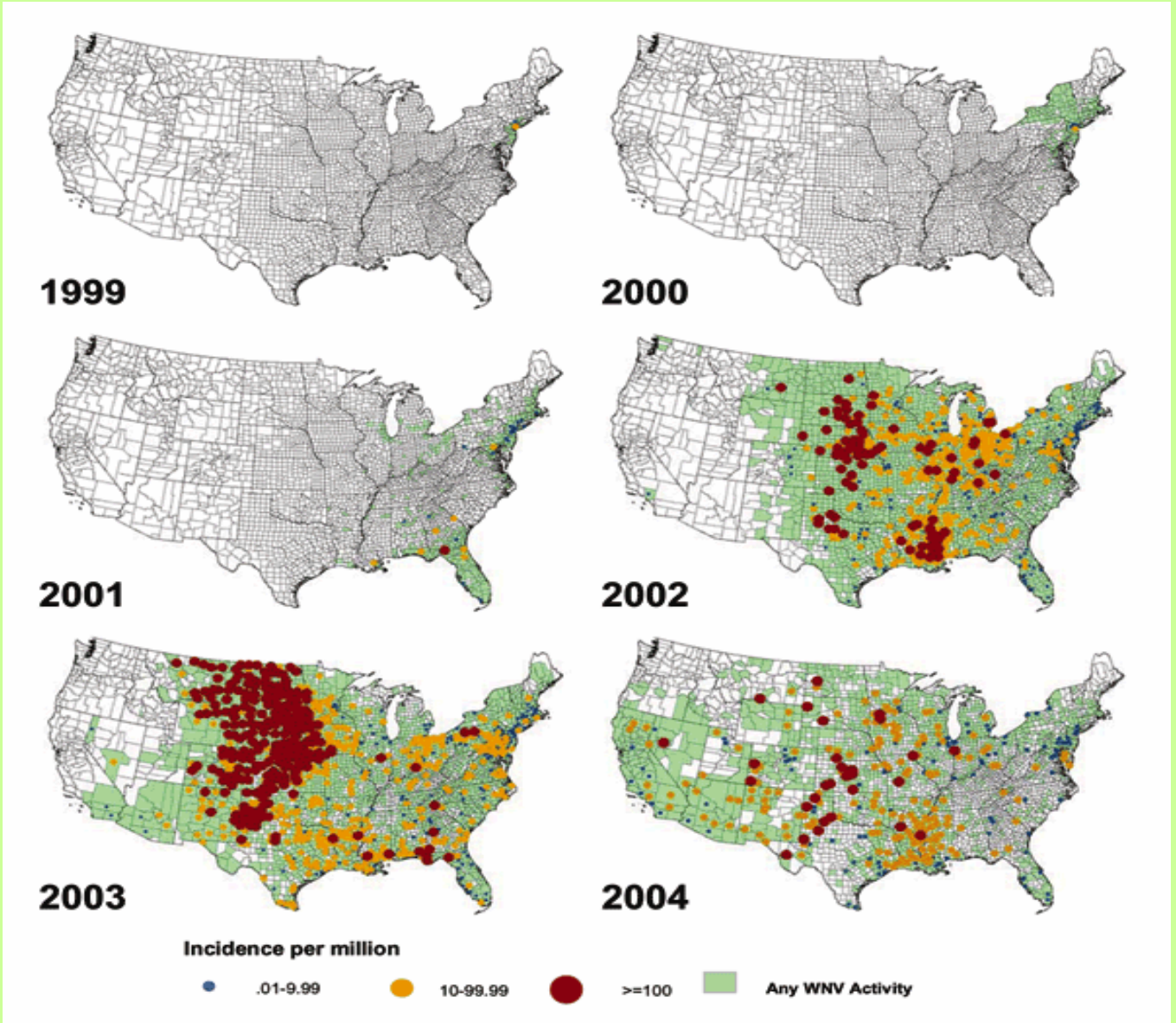
Emergence of WNV in N-Y (USA) 1999

- 1999-2001 : 149 cases, 18 deaths (24 states)
- → 2004 : > 16.000 cases, > 660 deaths
  (USA → Canada)

Deaths of thousands of native and exotic birds (indicator of WNV spread)

Transmission by blood transfusion and organ transplantation

Incidence of neuroinvasive WNV disease by county, USA, 1999-2004



Clinical manifestations

- 80 % asymptomatic
- 15-20% self-limited West Nile fever :

  flu-like symptoms, fatigue, rash

  muscle weakness (→ 2 months)

  31% hospitalized

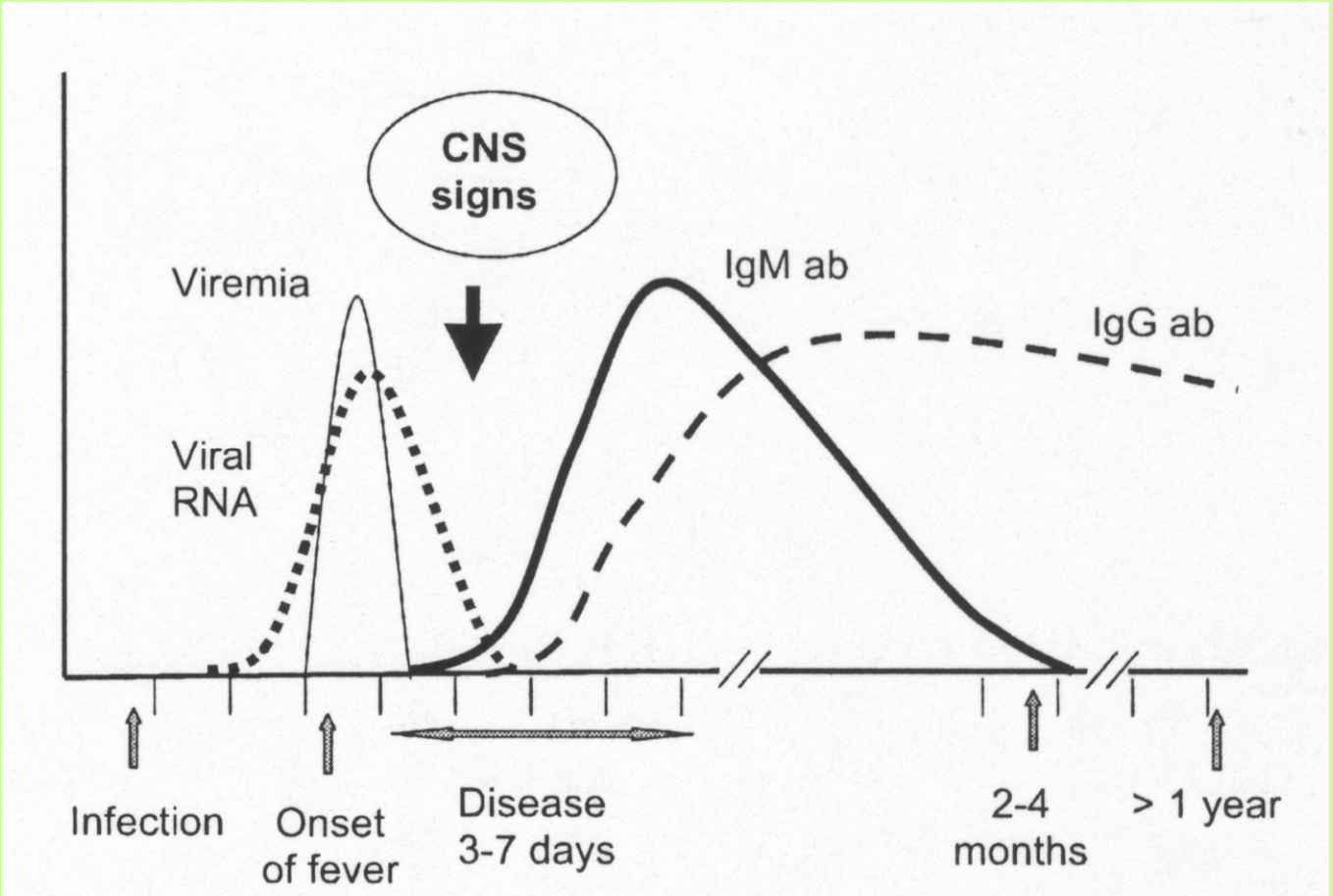
  79% missed work or school

  chorioretinitis, hepatitis, pancreatitis, myocarditis, …
- < 1% : meningitis, encephalitis, myelitis

  ↗ age, organ transplant patients

  mortality ± 10%

Viremia and antibody kinetics in West Nile virus infection



Diagnosis

- Viral blood culture or RT-PCR

  not useful

  low and short viremia
- RT-PCR on CSF : sensitivity 57%
- Serology : IgG and IgM (ELISA)

  IgM present with the CNS symptoms

  IgM in CSF

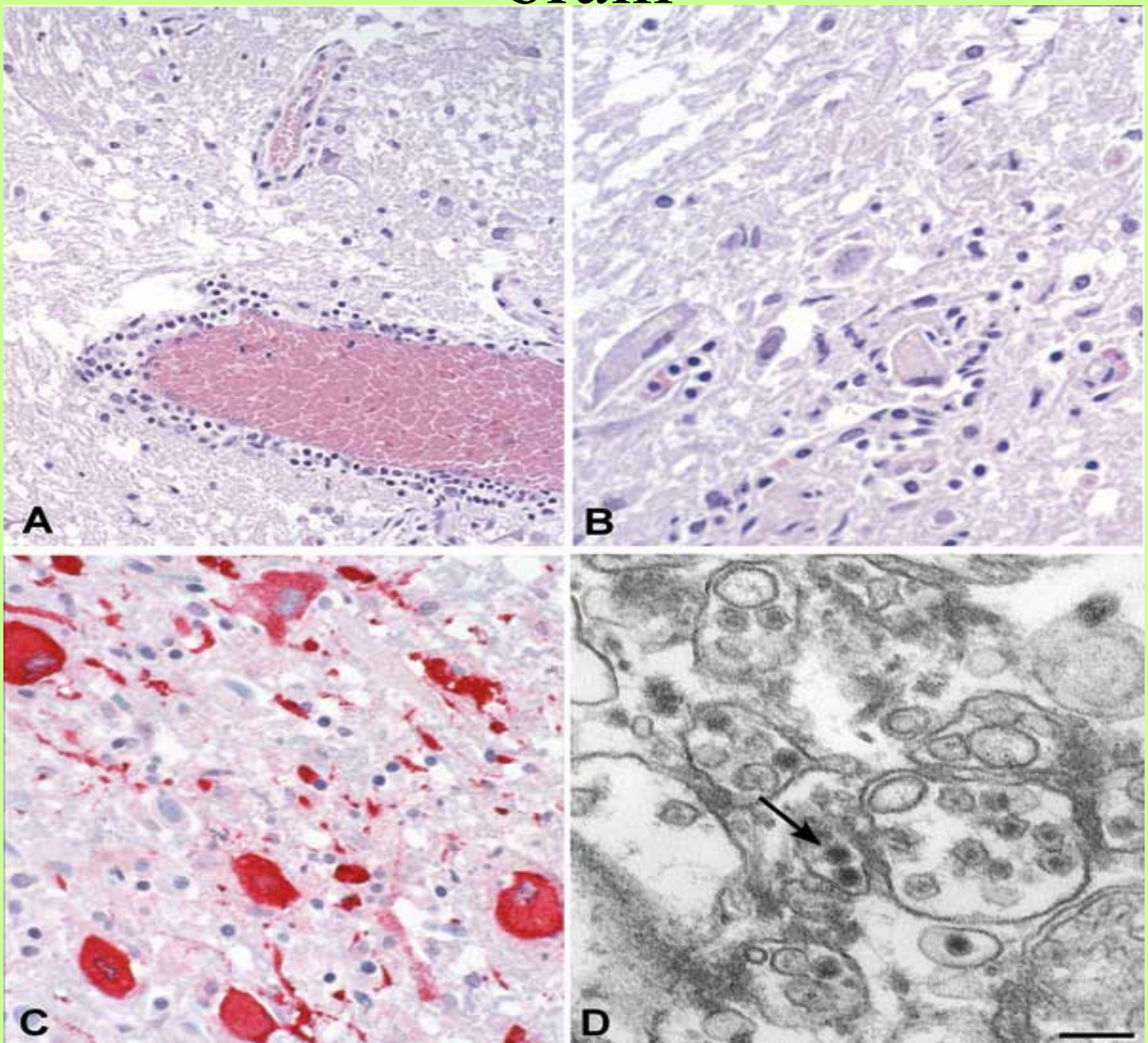
but cross reactivity with other flavivirus

persistence (low value) > 12 months

⇨ neutralisation assay (possible cross reactions)

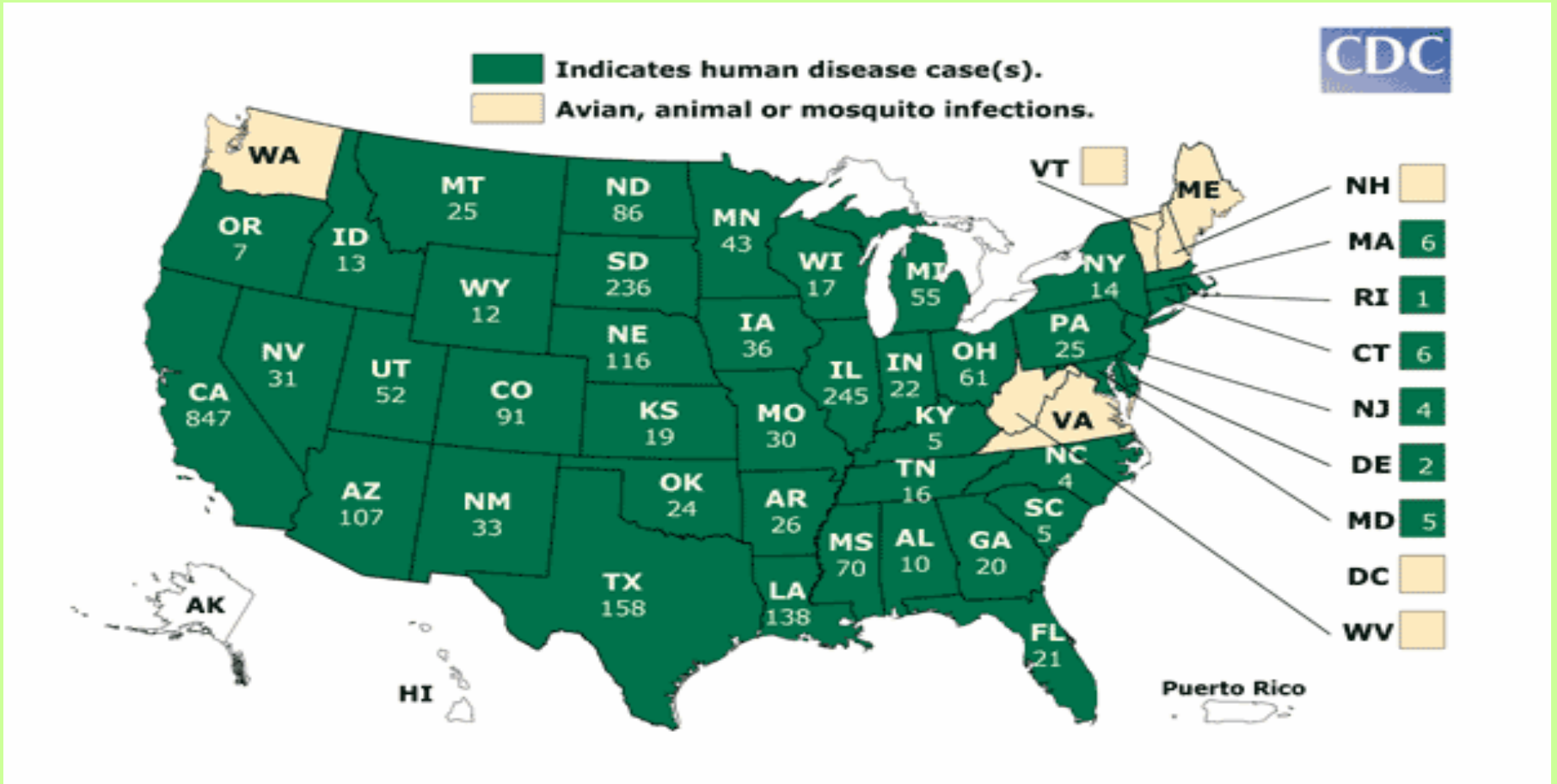
⇨ new assays in development

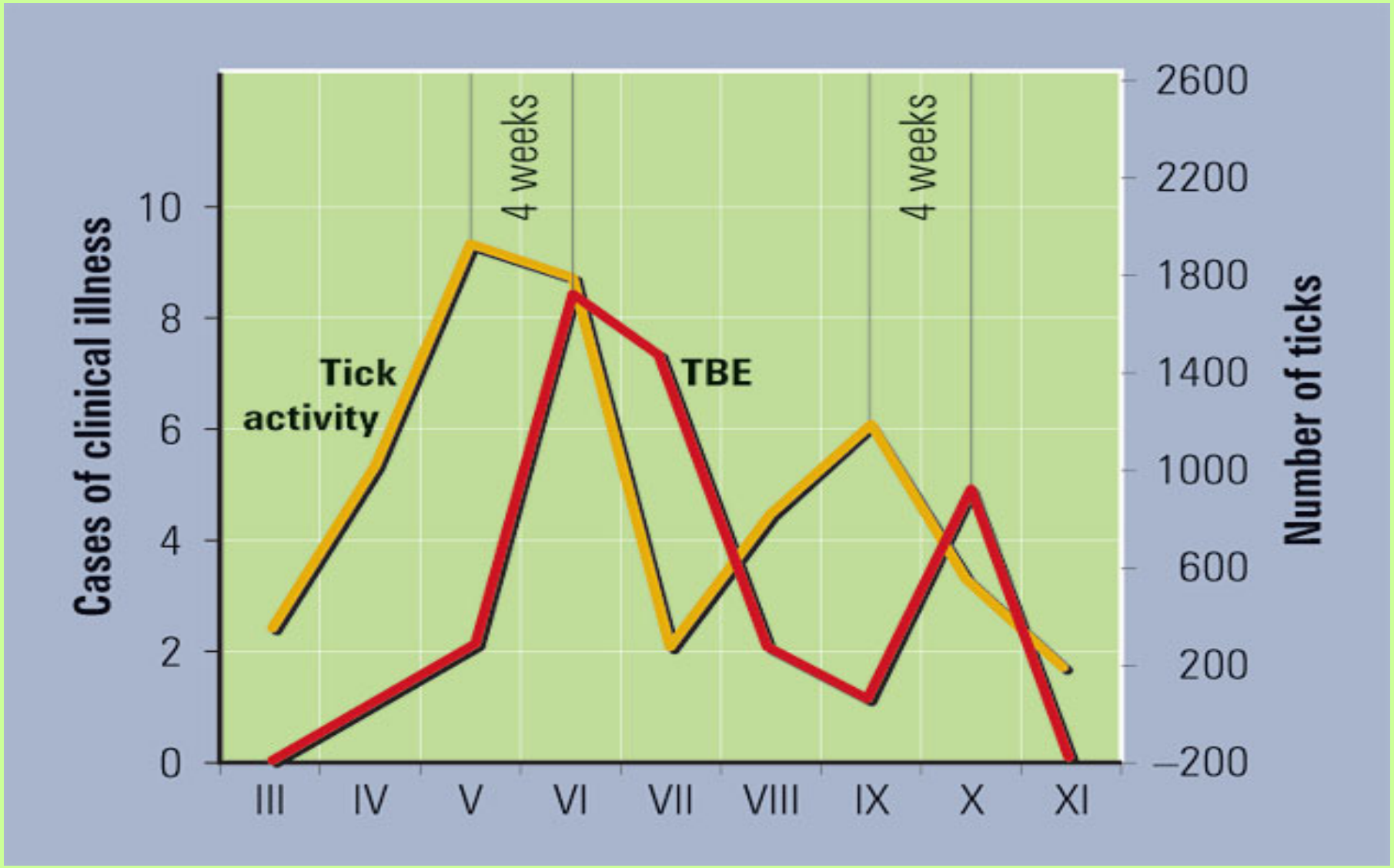
Histopathologic features of WNV in human brain



Prevention

- Vector control : pesticides
  larvicides
  source reduction
- General prevention measures :
  - repellent on skin and clothes (permethrin, DEET)
  - avoid being outdoors during dusk to dawn
  - screening of blood donations in endemic areas using RT-PCR (but false + and false -)


Indicates human disease case(s).
Avian, animal or mosquito infections.
CDC
WA
OR 7
CA 847
ID 13
NV 31
MT 25
WY 12
UT 52
AZ 107
CO 91
NM 33
ND 86
SD 236
NE 116
KS 19
OK 24
TX 158
MN 43
IA 36
MO 30
AR 26
LA 138
WI 17
IL 245
MS 70
MI 55
IN 22
KY 5
TN 16
AL 10
OH 61
GA 20
SC 5
NC 4
VA
PA 25
NY 14
VT
ME
NH
MA 6
RI 1
CT 6
NJ 4
DE 2
MD 5
DC
WV
FL 21
AK
HI
Puerto Rico


Cases of clinical illness
Number of ticks
4 weeks
4 weeks
Tick activity
TBE
0
2
4
6
8
10
–200
200
600
1000
1400
1800
2200
2600
III
IV
V
VI
VII
VIII
IX
X
XI