Tick-borne Encephalitis

NVMM BVIKM VIZ NOV 2017

STEVEN VAN DEN BROUCKE

DISCLOSURE

(Potential) Conflict of interest	**None**
For this meeting possibly relevant relationships with companies	**None**
• Sponsoring or research funding • Fee or other (financial) compensation • Shareholder • Other relationship, namely …	• **None** • **None** • **None** • **None**

A 37-y old man

- March 2017 – mid August 2017: traveling in Cambodia, Thailand and Malaysia
- Before several countries in South-America
- Since 7 months pain in the left side hemicorpus: burning ++
- Spreading downward + towards neck/left ear/face (left)
- Lost 5 kg in 6 months
- Watery diarrhea and feverish feeling on-and-off
- Swollen lymph nodes: responsive to amoxicilline and clindamycine but relapse when stopping.

- Gastroscopy, chest X-ray and ultrasound: normal 6 months ago

- Slovenian origin

- Med history: Tooth abcess

Physical examination

- Lymph nodes : cervical anterior small but tender
- Heart : no murmurs, normal S1, S2, BP : 90/70 mmHg
- Lungs : normal vesicular sound
- Abdomen : no tenderness, no organomegaly
- Skin left hemicorpus painful on touching: **ALLODYNIA**
- 3 spider naevi on chest
- Mouth: irritated throat, not inflamed

- R/ Pregabaline: moderate effect, drowsiness

- CXR / Ultrasound abdomen: unremarkable

Lab exams

- Stools, tick smear: nl
- Hematology nl
- Biochemistry
- Urine: schisto neg

Treponema RPR	n
Negatief	
Treponema TPA	n
Cox.burneti fase I IgG	n
Negatief	
Cox.burneti fase II IgG	n
Negatief	
Cox.burneti fase I IgM	n
Negatief	
Cox.burneti fase II IgM	n
Negatief	
Bartonella henselae IgG	n
Negatief	
Bartonella quintana IgG	n
Negatief	
B.burgdorferi EIA IgG	n
Negatief	
B.burgdorferi EIA IgM	n
Negatief	
Brucella As(Rose Bengale)	n
Negatief	

Hepatitis A IgM	n
Negatief	
Hepatitis A Ig	n
Negatief	
Hepatitis B HBs antigen	n
Negatief	
Hepatitis B anti-HBs	n
Hepatitis C antistoffen	n
HIV screening ag/as	ntr
Niet reactief	
Dengue IgG (ELISA)	0,13
	n
Negatief	
Dengue IgM (ELISA)	0,24
	n
Negatief	
Zika IgG (ELISA)	0,07
	n
Negatief	
Zika IgM (ELISA)	0,04
	n
Negatief	
West Nile IgG (ELISA)	0,09
	n
Negatief	
West Nile IgM (ELISA)	0,03
	n
Negatief	
Japanse enceph.IgG (IFAT)	n
Negatief	
Japanse enceph.IgM (IFAT)	n
Negatief	

Chikungunya IgG (IFAT)	n
Negatief	
Chikungunya IgM (IFAT)	n
Negatief	
Cytomegalovirus IgG	129 ↑
Cytomegalovirus IgM	n
Mononucl.inf. slide test	n
Negatief	
Epstein-Barr IgG	251
Epstein-Barr IgM	n
Negatief	

Filaria (ELISA)	0,13
	n
Negatief	
Schistosoma (ELISA)	0,04
	n
Negatief	
Schistosoma (IHA)	n
Negatief	
Strongyloïdes (ELISA)	0,08
	n
Negatief	

Toxoplasma gondii IgG	n
Negatief	
Toxoplasma gondii IgM	n

Call from the lab

Tick-Borne Enc.IgG (IFAT)	>1/10 ↑		< 1/10
Tick-Borne Enc.IgM (IFAT)	n		< 1/10

TBE Virus neutr.test	>1/320

EUROIMMUN Medizinische Labordiagnostika AG

IIFT: Flavivirus Profile 2 (IgG)

Test system for in vitro determinations IVD of antibodies of the class IgG against TBEV, YFV, WNV, JEV, DENV (types 1-4) in human serum or plasma. Ready for use.

ORDER NO. FI 2661-1005-2 G

SLIDES x FIELDS (SIZE) 10 x 5 (50)

ANTIBODIES AGAINST	SUBSTRATE	SPECIES
TBE virus	infected cells	EU 14
Yellow fever virus	infected cells	EU 14
West Nile virus	infected cells	EU 14
Japanese encephalitis virus	infected cells	EU 14
Dengue virus type 1	infected cells	EU 14
Dengue virus type 4	infected cells	EU 14
Dengue virus type 2	infected cells	EU 14
Dengue virus type 3	infected cells	EU 14

CONTENTS

1. Slides with BIOCHIPs: TBEV/YFV/WNV/JEV+ DENV type 1/ 4/ 2/ 3	10	slides	SLIDE
2. FITC-labelled anti-human IgG, ready for use	2 x 1.5	ml	CONJUGATE
3. Pos. control: anti-Flaviviruses (IgG), ready for use	1 x 0.1	ml	POS CONTROL
4. Neg. control: anti-Flaviviruses negative, ready for use	1 x 0.1	ml	NEG CONTROL
5. Sample buffer (IIFT), ready for use	3 x 4.5	ml	SAMPLE BUFFER
6. Salt for PBS pH 7.2	2	pack(s)	PBS
7. Tween 20	2 x 2	ml	TWEEN 20
8. Mounting medium, ready for use	1 x 3	ml	GLYCEROL

+2 +8°C

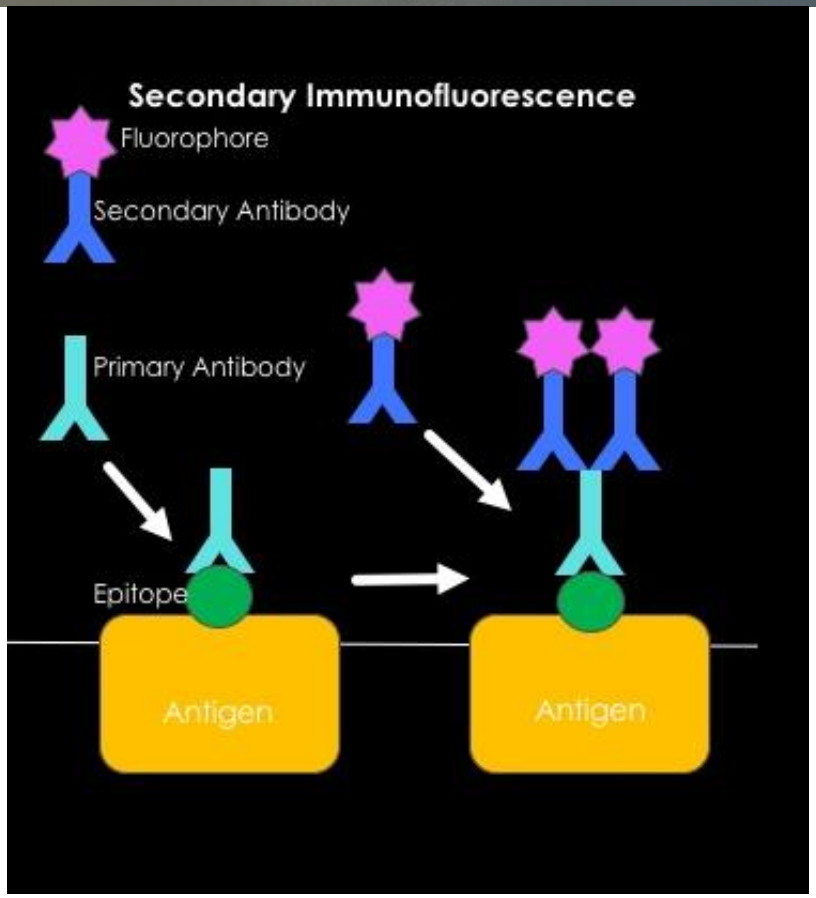
LOT F170515DH

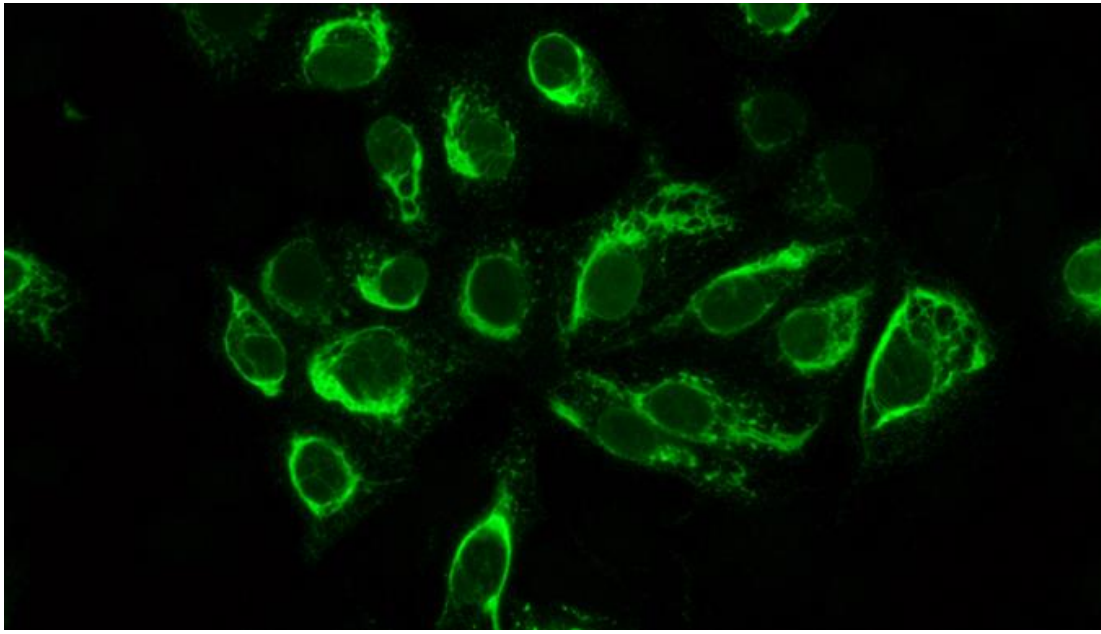
15.May 2017

CE

POTENTIAL BIOHAZARD!

14. Nov 2018


Secondary Immunofluorescence
Fluorophore
Secondary Antibody
Primary Antibody
Epitope
Antigen
Antigen



Is this a TBE case?

- Slovenia highest incidence in Europ 2013: 15/100,000 inh/y
- Malaysia? Thailand? Cambodia?
- Surely not vaccinated?
- What about other complaints (GI, LN's)?
- No clear history of 1st or 2nd phase

MRI and LP planned
LTFU: had to leave Belgium

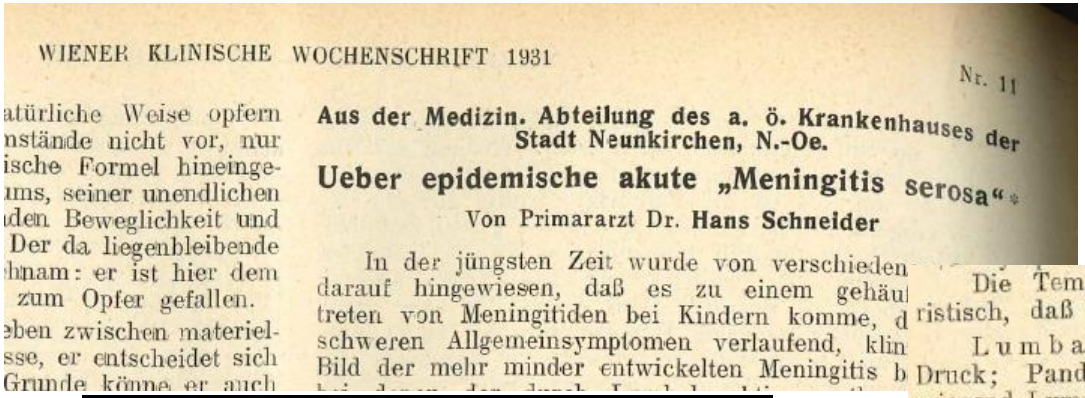
Outline

- Historical Note
- The Virus
- Epidemiology
- Transmission
- Clinical Presentation
- Diagnosis
- Treatment
- Prevention

Historical Note

- First description of TBE-like disease Scandinavian church records from 18th century (Island Aland, Finland)

Historical Note



WIENER KLINISCHE WOCHENSCHRIFT 1931 Nr. 11

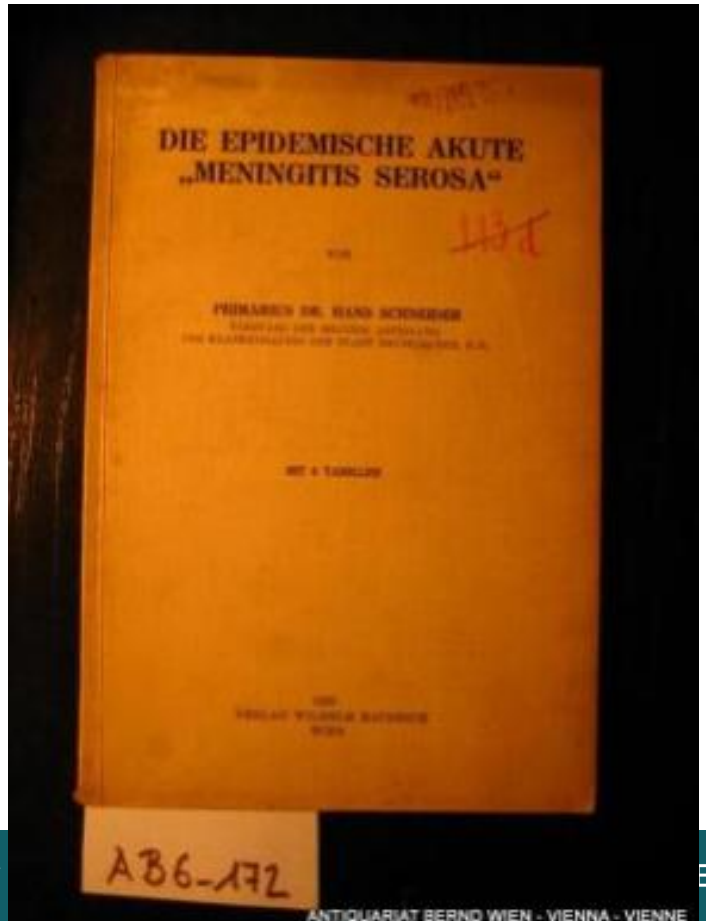
atürliche Weise opfern
nstände nicht vor, nur
ische Formel hineinge-
ıms, seiner unendlichen
ıden Beweglichkeit und
Der da liegenbleibende
hnam: er ist hier dem
zum Opfer gefallen.
eben zwischen materiel-
sse, er entscheidet sich
Grunde könne er auch

Aus der Medizin. Abteilung des a. ö. Krankenhauses der Stadt Neunkirchen, N.-Oe.

Ueber epidemische akute „Meningitis serosa“*

Von Primararzt Dr. **Hans Schneider**

In der jüngsten Zeit wurde von verschieden
darauf hingewiesen, daß es zu einem gehäu
treten von Meningitiden bei Kindern komme, d
schweren Allgemeinsymptomen verlaufend, klin
Bild der mehr minder entwickelten Meningitis b



Die Temperatur- und Pulskurve erscheint uns so charakteristisch, daß wir sie hierher setzen.

Lumbalpunktion: Leicht trüber Liquor unter mäßigem Druck; Pandy +++, Nonne-Apelt +. 1536/3 Zellen (überwiegend Lymphozyten; keine Bakterien nachweisbar. Kultur steril, Wa. R. in Blut und Liquor negativ. Rachenabstrich: keine Meningokokken.

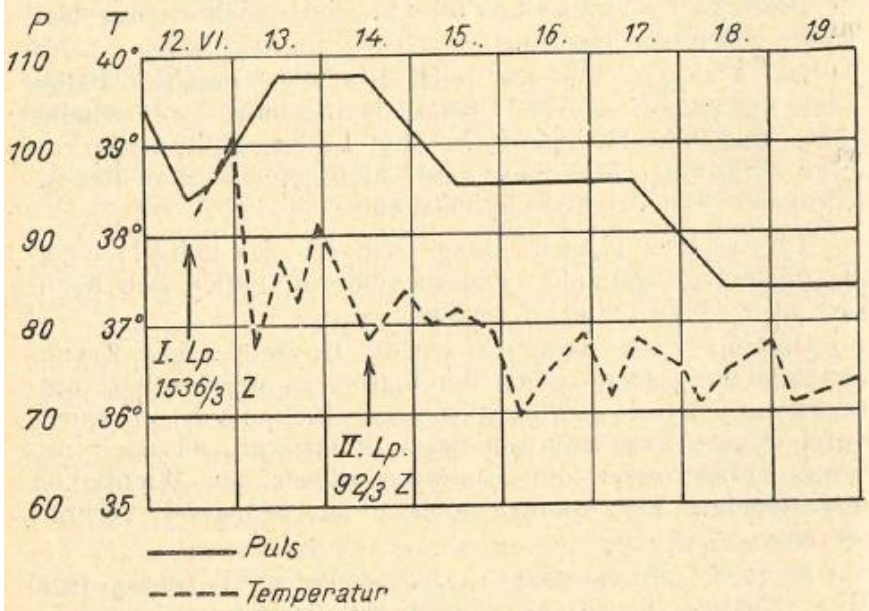


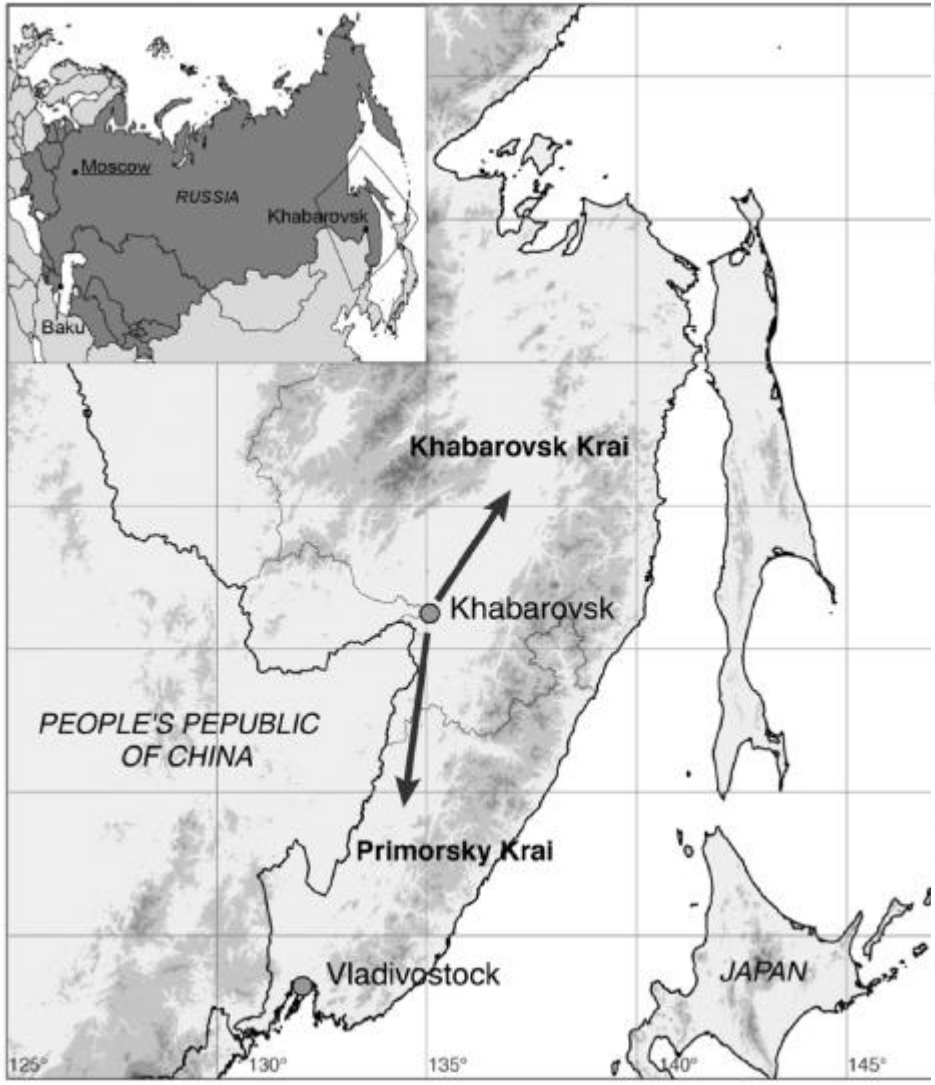
Abb. 1

13. Juni. Retentionsharnen.
14. Juni. Lumbalpunktion: Liquor klar, mäßiger Druck, Pandy ++, Nonne-Apelt +, 96/3 Zellen.
20. Juni. Lumbalpunktion: Klarer Liquor, normaler Druck; Pandy ++, Nonne-Apelt +, 62/3 Zellen.
Im weiteren Verlaufe klagte Pat. durch einige Tage über

V.I. Zlobin et al., *Ticks and Tick-borne Diseases 8 (2017) 813–820*

A brief history of the discovery of tick-borne encephalitis virus in the late 1930s (based on reminiscences of members of the expeditions, their colleagues, and relatives)☆

Vladimir I. Zlobin[a], Vanda V. Pogodina[b], Olaf Kahl[c,*]



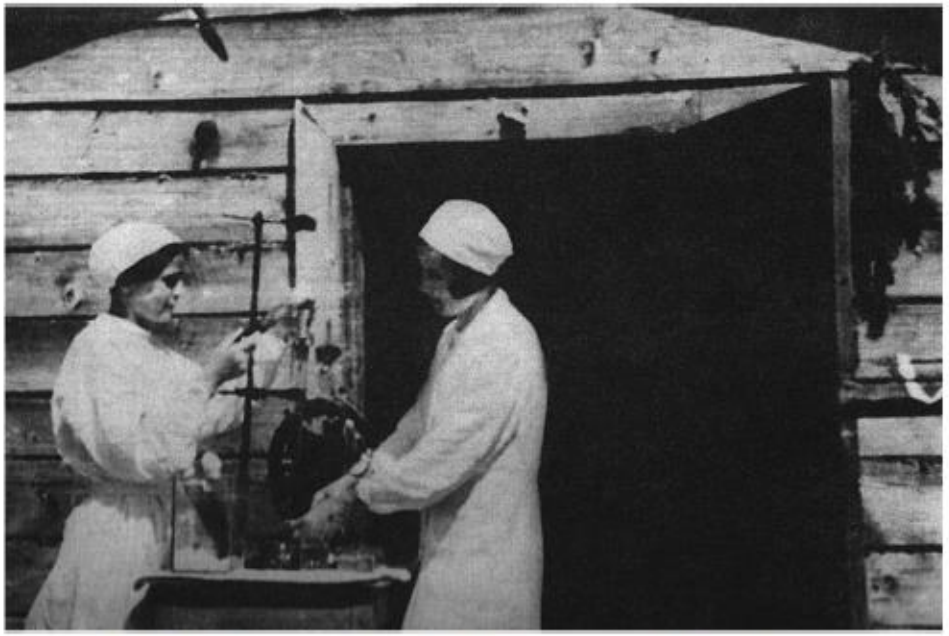
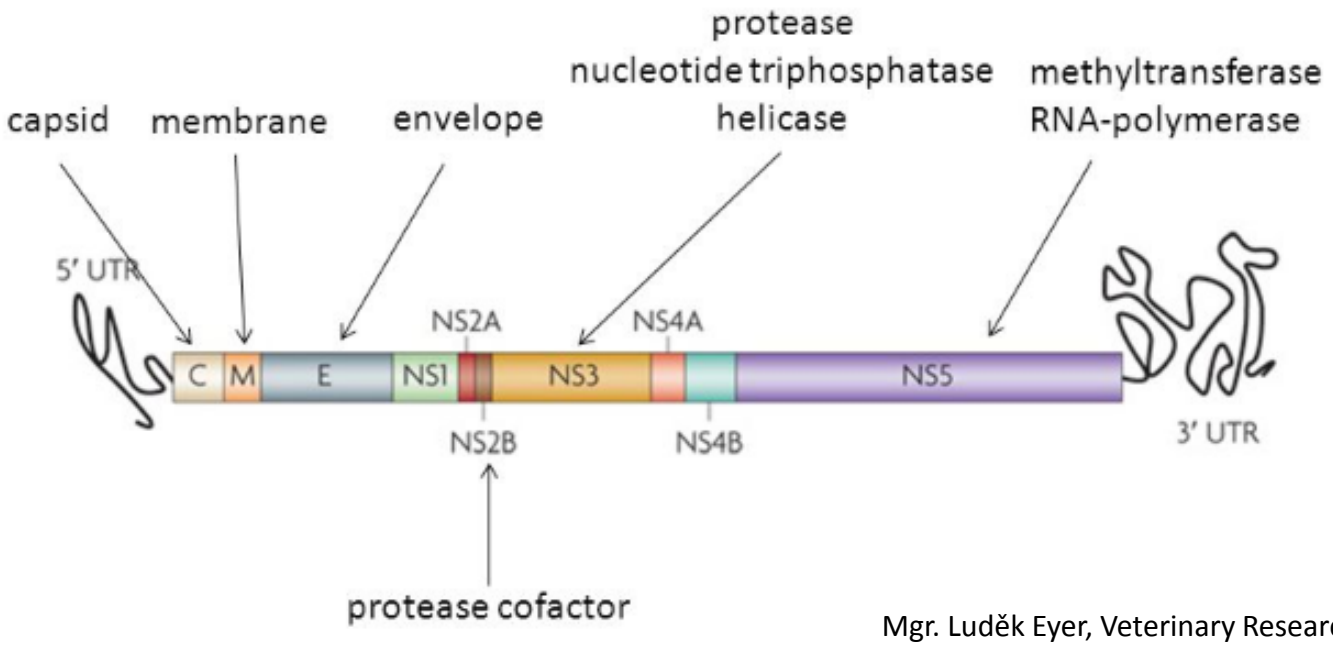


Fig. 8. E.N. Levkovich and G.N. Zorina-Nikolaeva. Filtration of the first samples of the TBE vaccine.

The Virus, TBEV

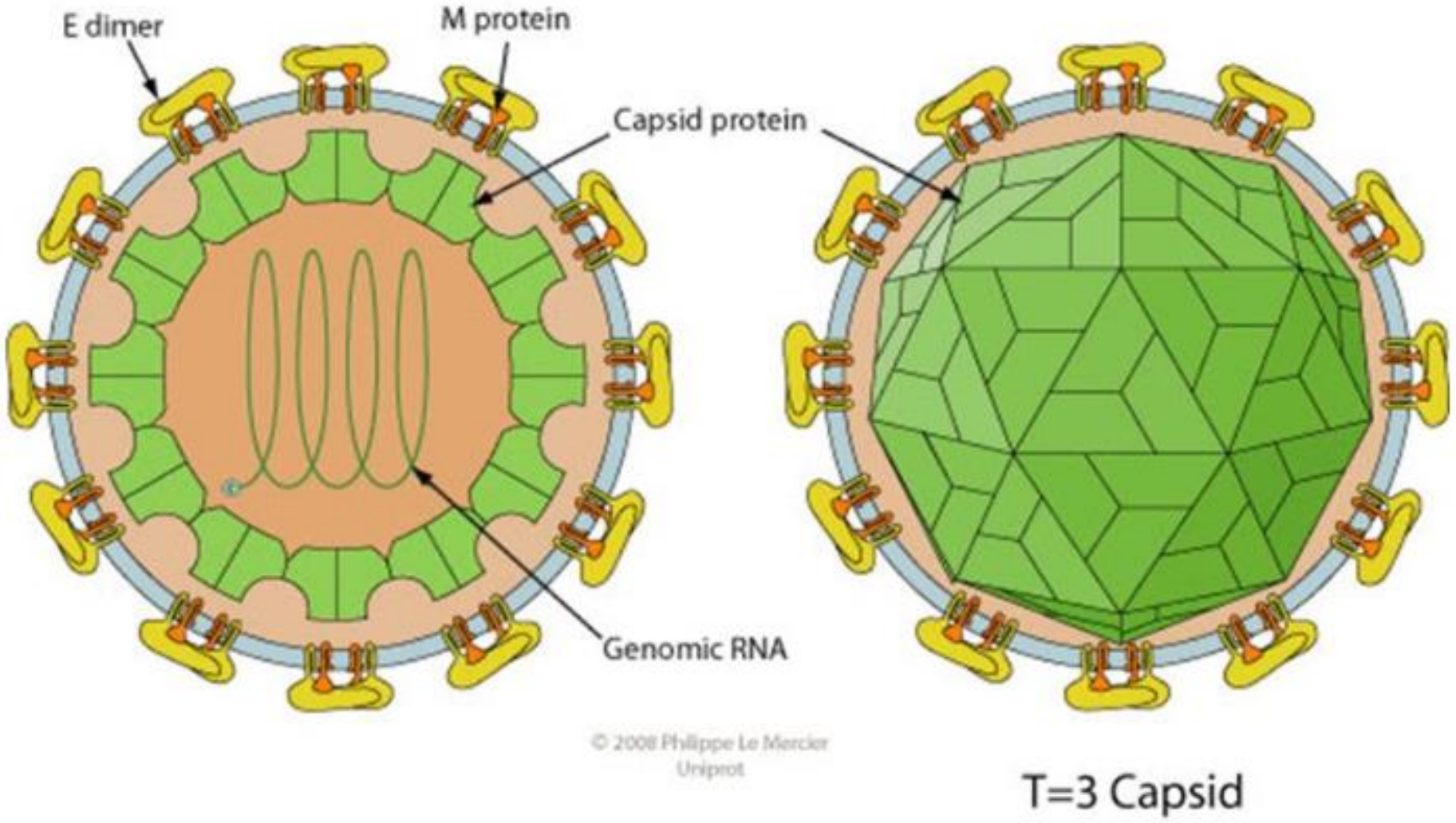
Genome of the tick-borne encephalitis virus

+ssRNA (11 kb)
single ORF – single polyprotein



Mgr. Luděk Eyer, Veterinary Research Institute, Brno

TBEV, Structure



Arboviruses

- Togaviridae
  - Alphavirus : EEE, WEE, VEE, Ross River, Chikungunya
- Flaviviridae
  - Yellow Fever, Dengue, Japanese Encephalitis, West Nile
  - TBEV, Omsk HF, Kyasanur FD (sim. Alkhurma virus)
- Bunyaviridae
  - Bunyaviruses : California Encephalitis, Hantavirus
  - Nairoviruses : CCHF
  - Phleboviruses : Rift Valley, Phlebotomus Fever

Table 1. Mammalian tick-borne flavivirus group

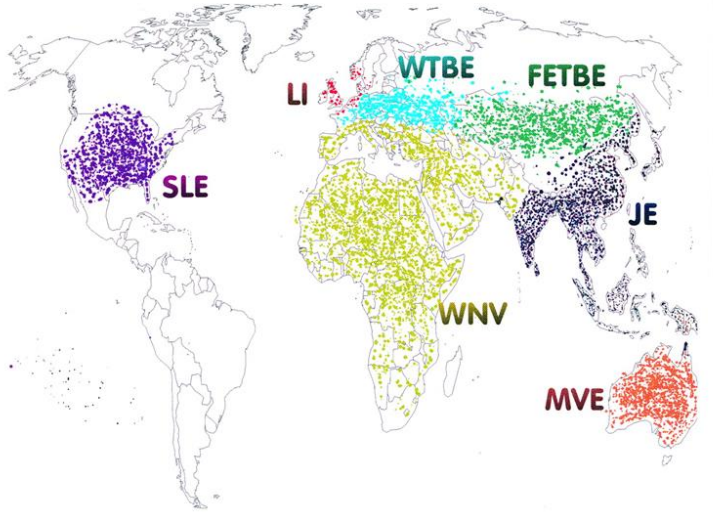
Data are adapted from the following references: Calisher & Gould (2003); Gritsun *et al.* (2003b); Gould & Solomon (2008); Grard *et al.* (2007).

Virus name	Abbreviation	Principal tick vector	Geographical distribution
Tick-borne encephalitis virus (European subtype)	TBEV-Eu	*I. ricinus*	Central/western Europe, Scandinavia, Korea
Tick-borne encephalitis virus (Siberian subtype)	TBEV-Sib	*I. persulcatus*	Russia, Finland
Tick-borne encephalitis virus (far-eastern subtype)	TBEV-Fe	*I. persulcatus*	Russia, Far East (China, Japan)
Louping ill virus	LIV	*I. ricinus*	UK, Ireland, Norway
Spanish sheep encephalomyelitis virus	SSEV	*I. ricinus*	Spain
Turkish sheep encephalitis virus	TSEV	*I. ricinus*	Turkey
Greek goat encephalitis virus	GGEV	*I. ricinus*	Greece
Powassan virus	POWV	*Ixodes cookei*, *Ixodes marxi*	USA, Canada, far-eastern Russia
Kadam virus	KADV	*Rhipicephalus pravus*	Uganda, Saudi Arabia
Omsk hemorrhagic fever virus	OHFV	*Dermacentor reticulatus* (*Dermacentor marginatus*)	Western Siberia
Kyasanur Forest disease virus	KFDV	*Haemaphysalis spinigera* (*Ixodes* spp., *Dermacentor* spp., *Haemaphysalis* spp.)	India
Alkhurma hemorrhagic fever virus	AHFV	*Ornithodorus savignyi*	Saudi Arabia
Langat virus	LGTV	*Ixodes granulatus*	Malaysia, Thailand, Siberia
Karshi virus	KSIV	*Ornithodorus papillipes*	Uzbekistan
Royal Farm virus	RFV	*Argas hermanni*	Afganistan
Gadgets Gully virus	GGYV	*Ixodes uriae*	Macquarie Island (Southern Ocean)

Neurological syndrome (arboviral)

- Japanese encephalitis (sim. Nipah, bat-borne)
- TBEV
- West Nile Fever (sim. Kunjin virus)
- Rift Valley Fever
- WEE, VEE, EEE
- St Louis Encephalitis
- California, LaCrosse, James Canyon
- Oropouche
- Colorado Tick Fever
- Toscane virus (Mediterranean)

Map showing approximate global distribution of major neurotropic flaviviruses; JE=Japanese encephalitis; MVE=Murray valley encephalitis; WN=West Nile; WTBE=Western tick-borne encephalitis; FETBE=Far Eastern tick-borne encephalitis; LI=Louping III virus; SLE=St Louis



Tom Solomon et al. J Neurol Neurosurg Psychiatry 2000;68:405-415

Hemorrhagic syndrome (arboviral)

- Yellow Fever
- Dengue HF
- Rift Valley

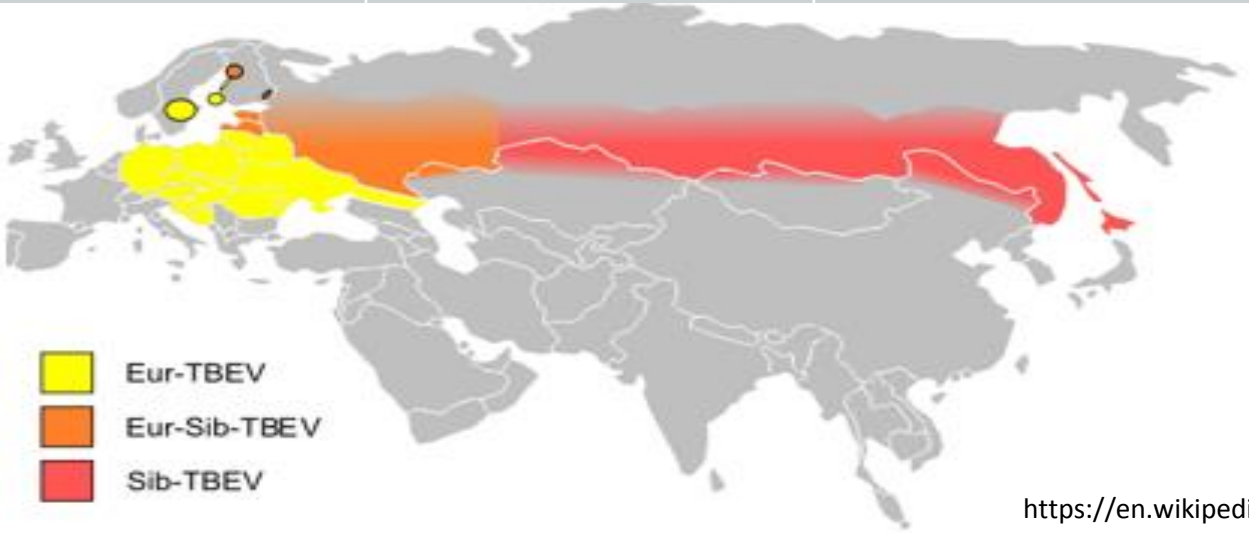
} Mosquitoes (epidemic potential)

- CCHF
- Omsk HF
- Kyasanur Forest

} Ticks (no epidemic potential)

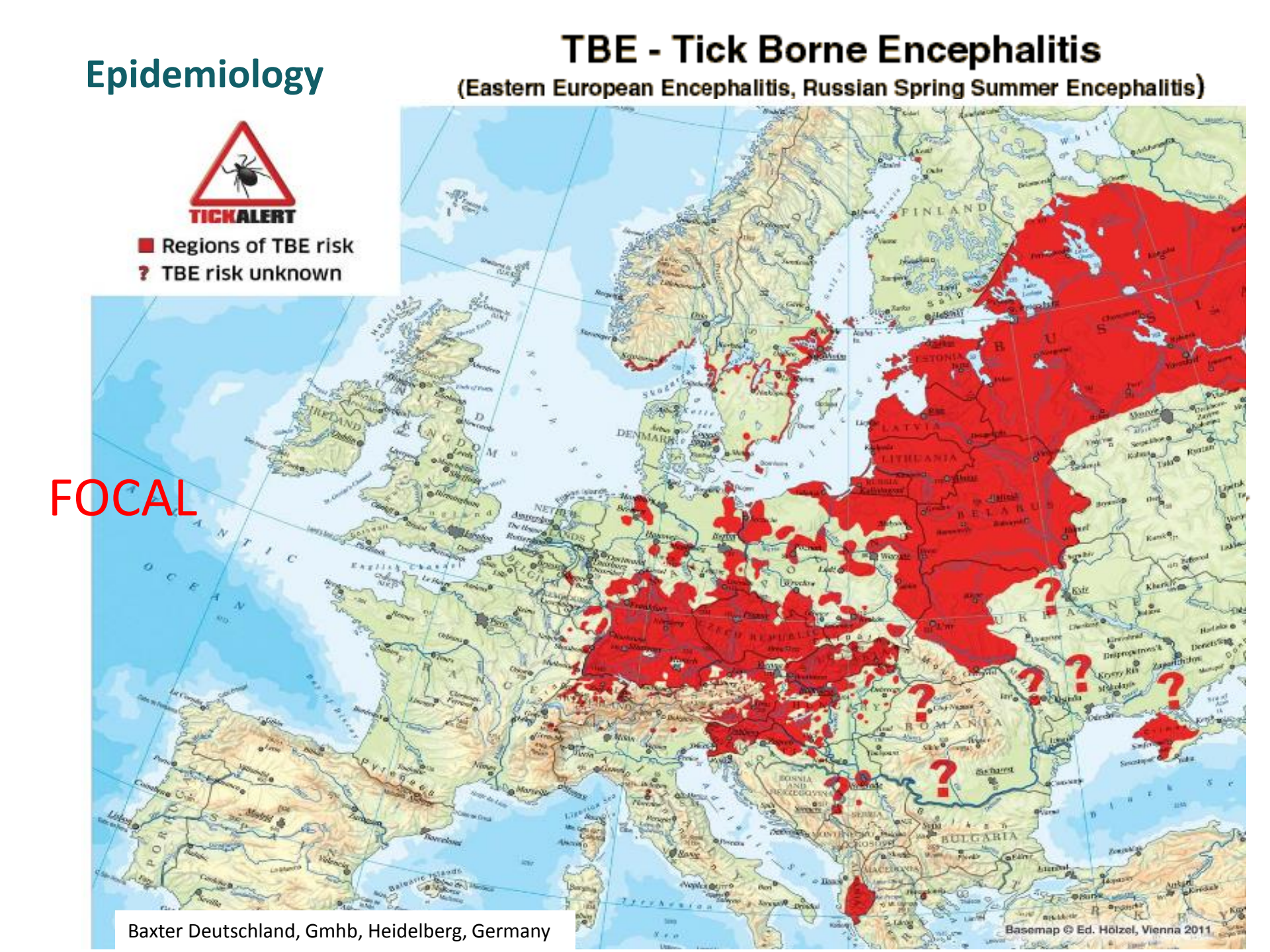
TBEV Subtypes

Subtype	European (Eu)	Siberian (Sib)	Far-Eastern (FE)
Ohter names	FSME, CEEV		RSSEV
Case fatality rate	1-2 %	1-3 %	5-40 %
Sequelae	Moderate	Frequent	Rare
Main vector	*Ixodes ricinus*	*Ixodes persulcatus*	*Ixodes persulcatus*
Distribution	Europe	Urals/Siberia & Northern Europe	Far-East (till Japan), Russia & Baltic states

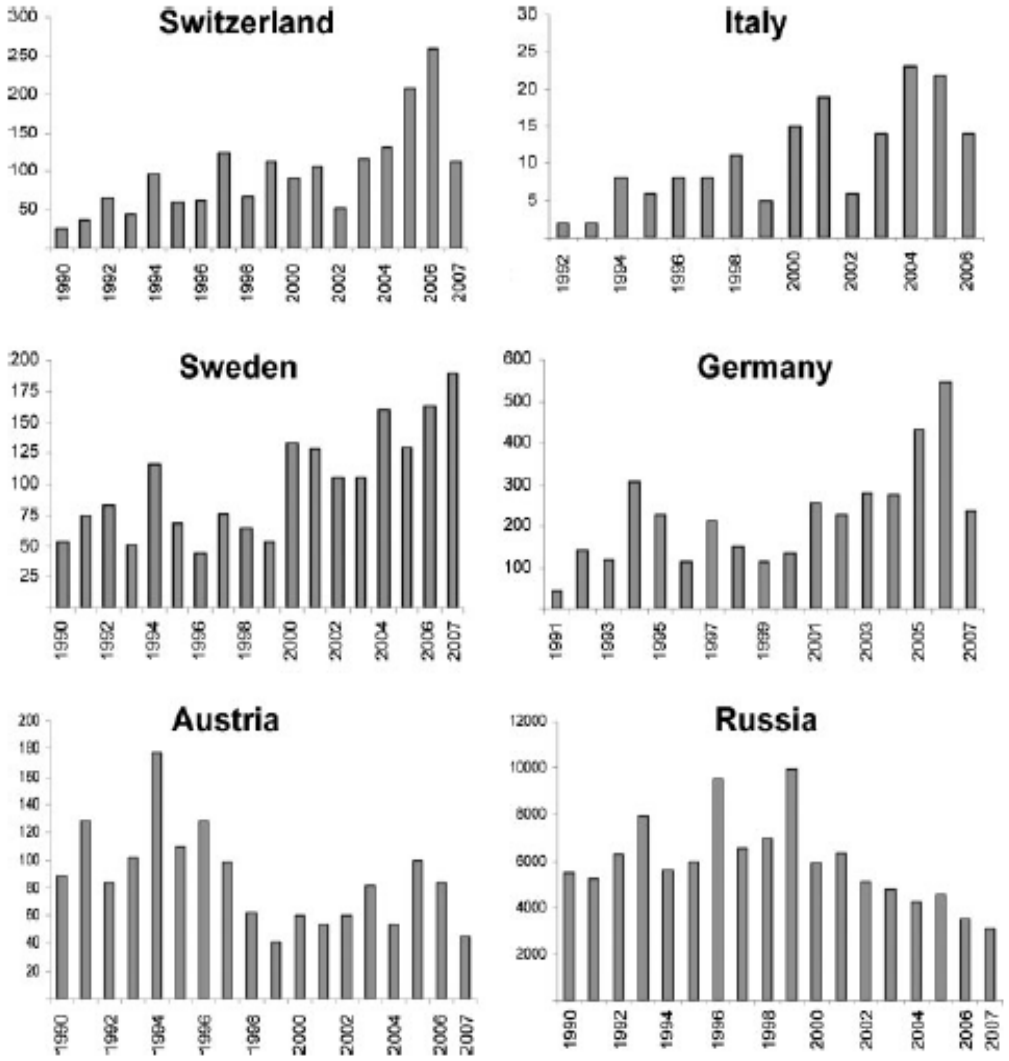


https://en.wikipedia.org/wiki/Tick-borne_encephalitis

Epidemiology



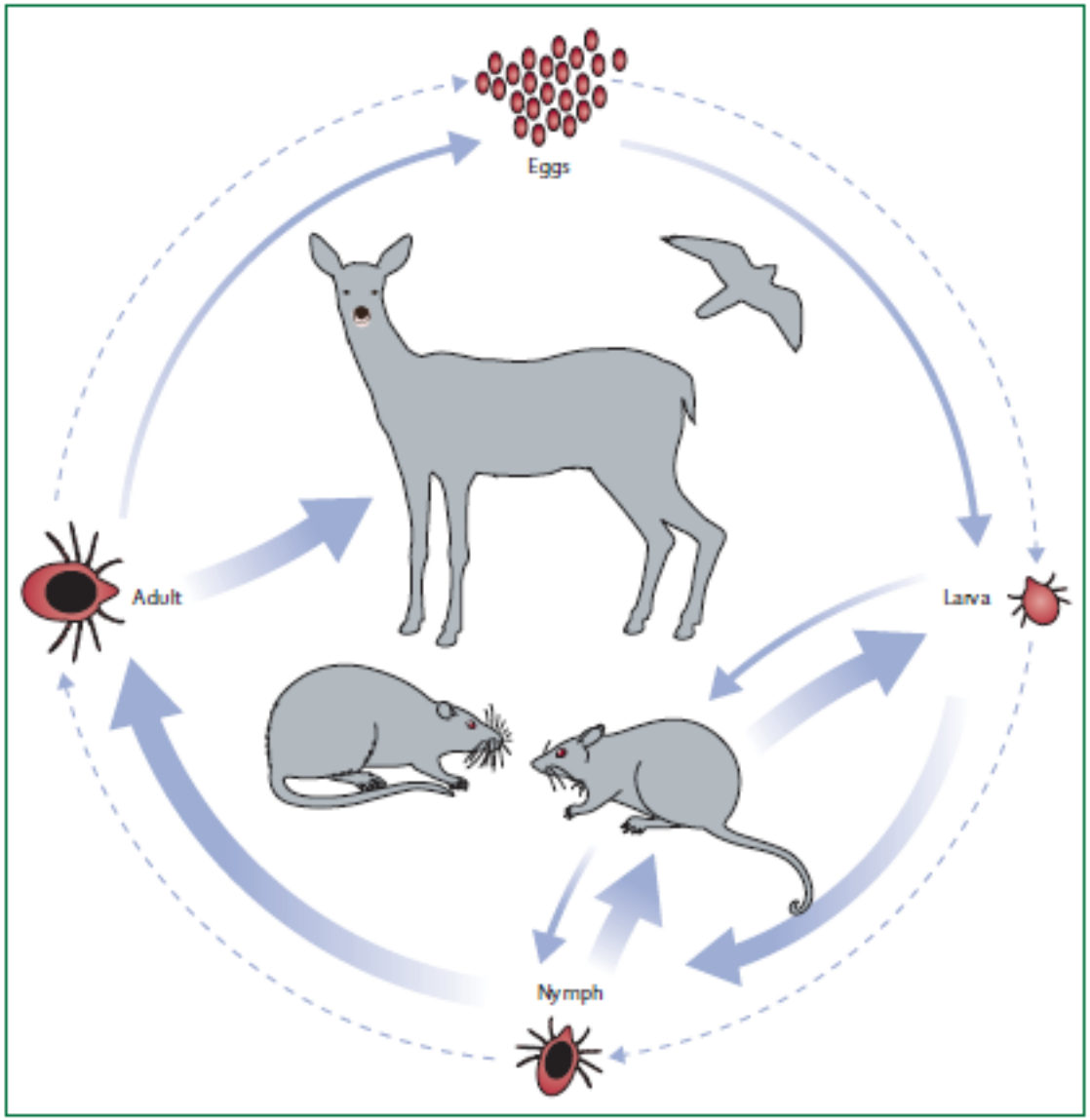
Epidemiology



- 1990 – 2009: on average 8500 cases annually
- Reported from 19 European countries
- Russia highest number (Western Siberia!)
- Incidence and severity in >50y
- Travelers!

http://www.tbe-info.com

Transmission



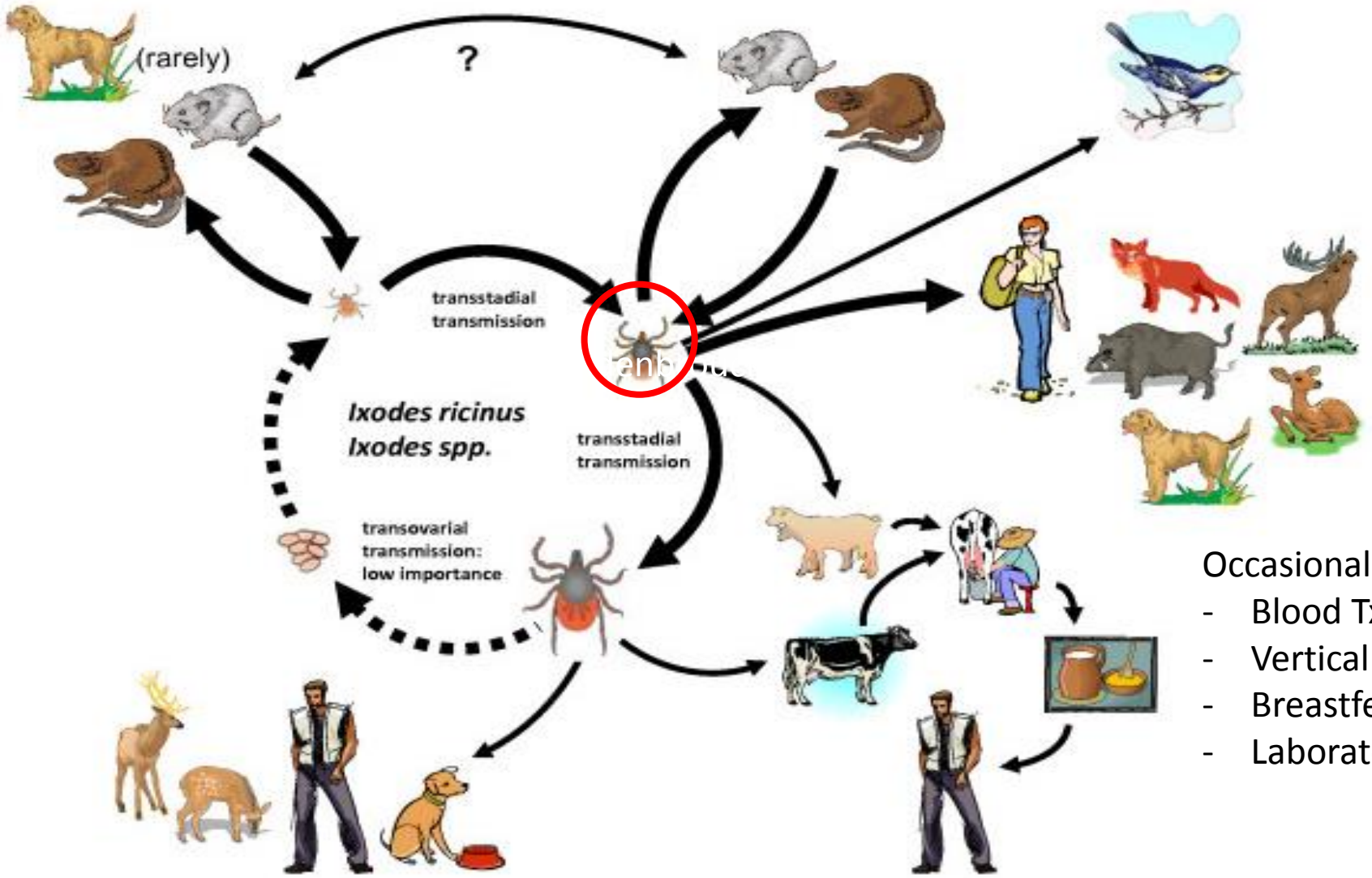
Lindquist, Vapalahti, The Lancet Vol 371 May 31, 2008

Figure 1: Unengorged *Ixodes ricinus* ticks in different developmental stages
From top, anticlockwise, one adult female, two larvae, and one nymph.

Mansfield et al; Journal of General Virology (2009), 90, 1781–1794

Transmission

WITHIN MINUTES → early removal does NOT prevent disease!!!



Occasional:
- Blood Tx
- Vertical
- Breastfeeding
- Laboratory

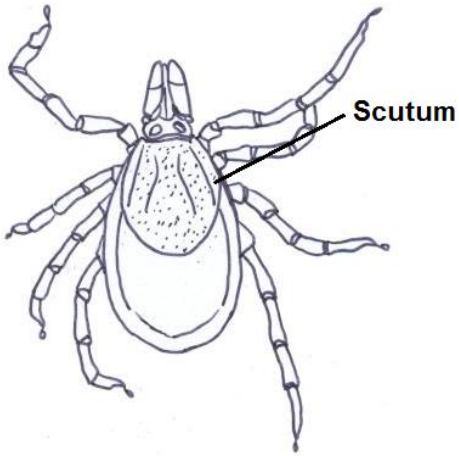
Pfeffer and Dobler *Parasites & Vectors* 2011, **4**:59
http://www.parasitesandvectors.com/content/4/1/59

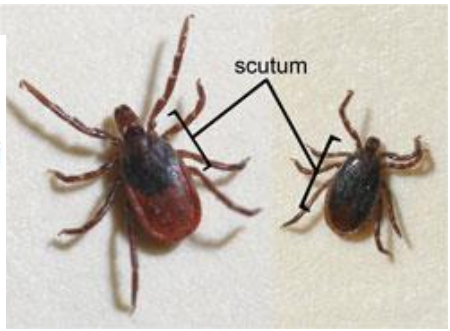
Overview of tick genera in the three families

1. Argasidae : *Argas, Ornithodoros, Otobius, Antricola, Nothoaspis*
2. Ixodidae : *Amblyomma, Aponomma, Boophilus, Cosmiomma, Dermacentor; Haemaphysalis, Hyalomma, Ixodes, Margaropus, Nosomma, Rhipicentor; Rhipicephalus*
3. Nuttalliellidae : only 1 species, rare

Soft ticks: no scutum = dorsal shield

Hard ticks: scutum



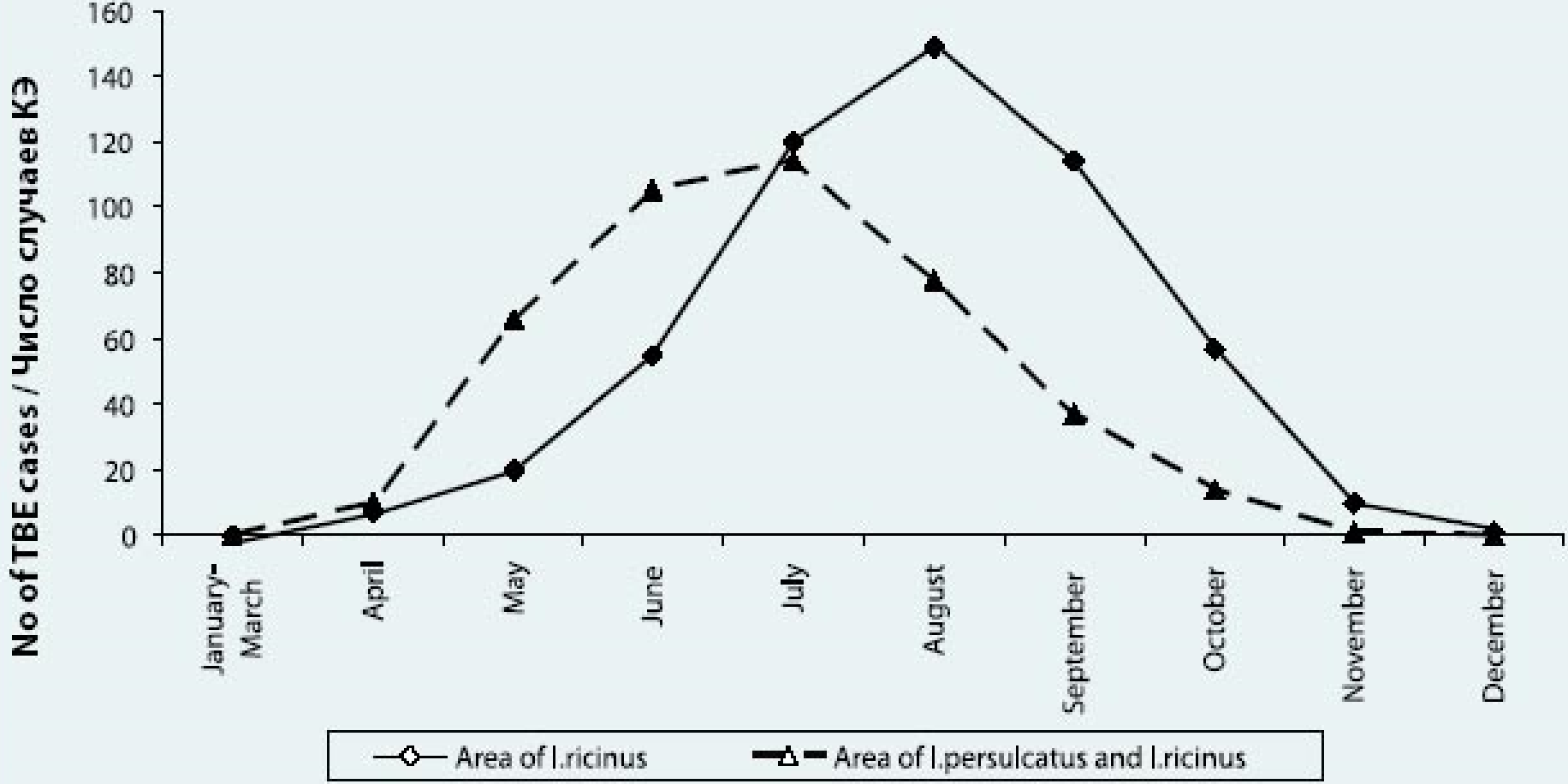


Other pathogens transmitted by ticks

- Lyme (Borrelia Burgdorferi/Afzelii, Garinii)
- Anaplasma
- Ehrlichia
- Bartonella
- Babesia
- Rickettsia: RMSF, R. conori, Japanese spotted fever,…
- Tularemia: Francisella tularensis
- Colorado Tick fever
- Hemorragic fevers: Crimean-Congo, Omsk,..
- TBRL: Tick Born Relapsing Fever (B. duttonii, hermsii,…) = soft tick

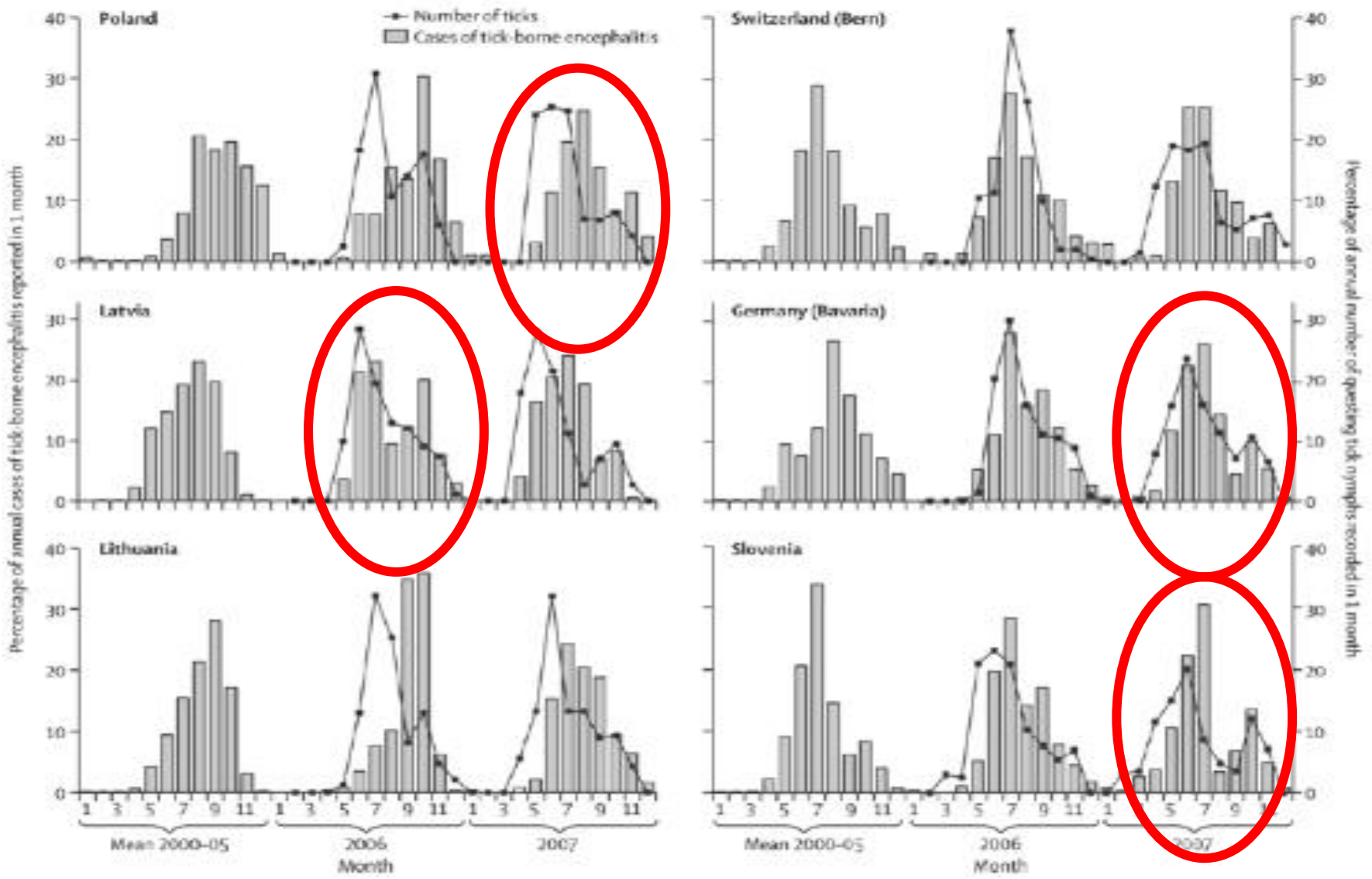
A tularemia lesion on the dorsal skin of the right hand

TBE, seasonality



Veera Vasilenko, Kuulo Kutsar, Irina Golovljova, http://www.epinorth.org/, Nat Inst for Health Development, Tallinn, Estonia

TBE, seasonality



Global Health Impacts of Vector-Borne Diseases: Workshop Summary (2016), Drivers, Dynamics, and Control of Emerging Vector-Borne Zoonotic Diseases - A. Marm Kilpatrick and Sarah E. Randolph

TBE, closer to home

RAPID COMMUNICATIONS

First human case of tick-borne encephalitis virus infection acquired in the Netherlands, July 2016

JA de Graaf [1], JHJ Reimerink [2], GP Voorn [3 4], EA bij de Vaate [5], A de Vries [2], B Rockx [2], A Schuitemaker [1], V Hira [4]

Eurosurveillance
Europe's journal on infectious disease epidemiology, prevention and control since 1996
Publisher: European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden

Euro Surveill. 2017 Mar 16; 22(11): 30482.
doi: 10.2807/1560-7917.ES.2017.22.11.30482
PMCID: PMC5356422

Increasing evidence of tick-borne encephalitis (TBE) virus transmission, the Netherlands, June 2016

Adriaan CG Weststrate, [1] Daan Knapen, [1] Gozewijn D Laverman, [1] Bart Schot, [1] Jan JW Prick, [2] Silke A Spit, [3] Johan Reimerink, [4] Barry Rockx, [4] and Felix Geeraedts [5]

3078 Derde patiënt met autochtone TBE in Nederland

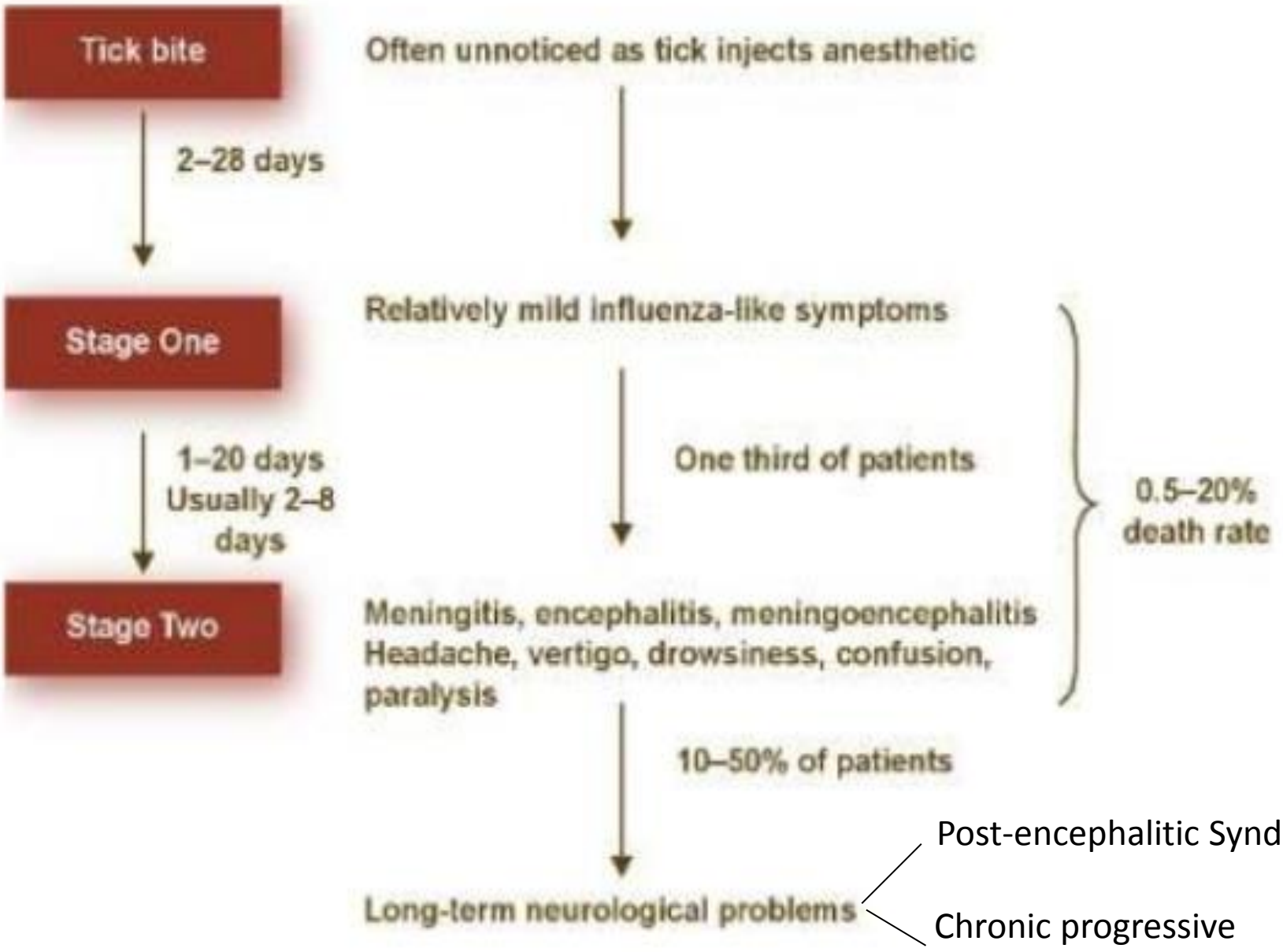
Bij een Nederlandse vrouw is infectie met het tekenencefalitisvirus (TBEV) vastgesteld. Het betreft een 51-jarige vrouw met initieel klachten van misselijkheid, myalgie, hepatitis en leukopenie. Twee weken later ontwikkelde zij neurologische klachten waaronder hoofdpijn, spraakproblemen en fotofobie. De patiënt was niet recent in het buitenland geweest, wel komt zij regelmatig op de Sallandse Heuvelrug. In juni 2017 had zij 2 maal een tekenbeet opgelopen. Ze was niet gevaccineerd tegen flavivirussen.

Sallandse Heuvelrug

TBE virus in ticks

RIVM has examined deer for the presence of antibodies against the TBE virus. Few deer tested positive, in particular in Sallandse Heuvelrug National Park. Subsequently, ticks were caught in that area, and TBE virus was found in a number of them. Recently, an infected tick was discovered after a walk in Utrechtse Heuvelrug National Park. RIVM investigates, in collaboration with other organisations, the spread of the TBE virus in the Netherlands and the risk of infection.

Clinical presentation



Neurological Symptoms

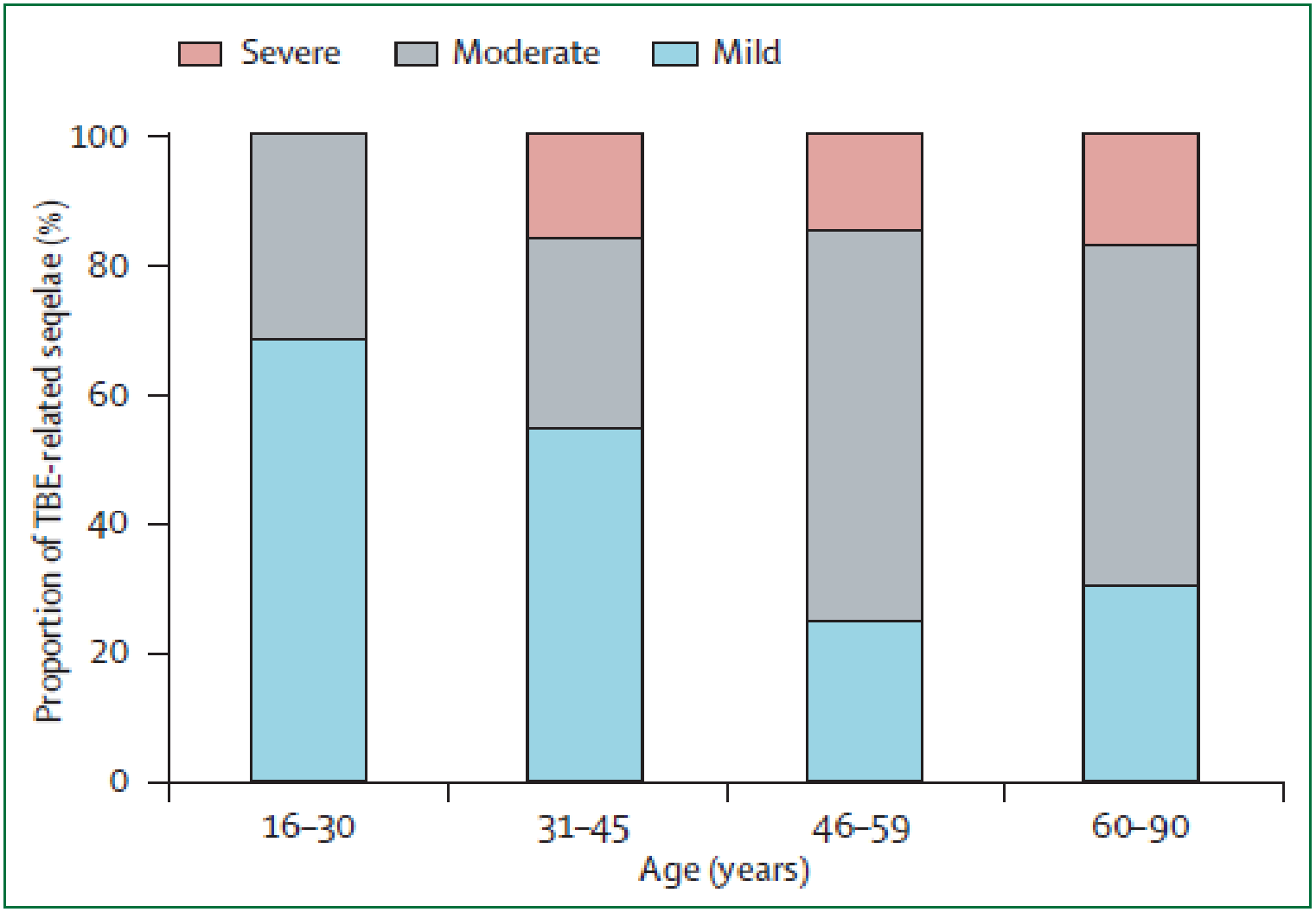
	Duniewicz et al[68]	Falisevac et al[69]	Radsel-Medvescek et al[70]	Krech et al[71]	Jezyna et al[72]	Kaiser[36]	Grygorczuk et al[73]	Mickiene et al[38]	Wahlberg et al[74]
Number of patients	589	1218	315	234	215	656	152	133	301
Headache	67%	..	100%	74%	100%		84%	95·5%	81·7%
Altered consciousness	..	..	13·7%	29%	35·5%	31%	24%	18·8%	12%
Sensory impairment	..	..	..	9%	..	2·9%	2%	..	..
Seizures	0·3%	..	..	2%	3·3%	1·7%	..	..	..
Ataxia	30%	..	..	..	..	18%	24%	26·3%	0·3%
Hemiparesis	..	0·3%	..	..	..		1·9%	2·6%	0·3%
Tremor	75%	..	78%	..	31·6%	4·3%	7%	21·8%	..
Dysphasia	..	..	..	..	..	2·5%	0·7%	3·8%	..
Spinal nerve paralysis	12·8%	2·7%	6·3%	10%	8·8%	15%	7·2%	3·8%	4·3%
Cranial nerve paralysis	..	..	3·5%	..	..	11%	3·3%	5·3%	..

..= data not given.

Table 2: **Summary of neurological symptoms in the acute stage of tick-borne encephalitis in studies including a minimum of 100 patients**

Lindquist, Vapalahti, The Lancet Vol 371 May 31, 2008

Symptoms related to Age



Mickiene, *Clin Infect Dis* 2002; 35**:** 650–58
Lindquist, Vapalahti, The Lancet Vol 371 May 31, 2008

Postencephalitic Syndrome: neurological sequelae

	Günther et al[44]	Tomazic et al[42]	Mickiene et al[38]
Study details			
Number of patients	85	492	133
Year of patient enrolment	1991–93	1994	1998–99
Number of patients lost at follow-up (%)	2 (2·3%)	6 (1·2%)	15 (11·4%)
Follow-up	12 months	6 months	12 months
Control group	Other viral meningoencephalitis	No	Healthy controls (neuropsychiatric questionnaire)
Reported sequelae at end of follow-up			
Total with incomplete recovery	39·8 %	26·1%	46·2%
Headache	10·8%	22·6%	20·5%
Concentration difficulties	8·4%	15·2%	15·4%
Memory impairment	10·8%	--	19·7%
Emotional instability	--	--	18·8%
Fatigue	--	21·7%	--
Light and sound irritability	1·2%	--	--
Mental disturbance	--	1·4%	--
Consciousness disturbances	--	0·2%	--
Sweating	--	5·5%	--
Sensory disturbance with pains and dysaesthesia	2·4%	11·2%	--
Ataxia and tremor	9·6%	10·2%	14·5%
Dysphasia	6·0%	--	--
Hearing loss	2·4%	--	--
Spinal nerve paralysis	6·0%	2·2%	6·0%
Case-fatality rate	0%	0·2%	0·8%

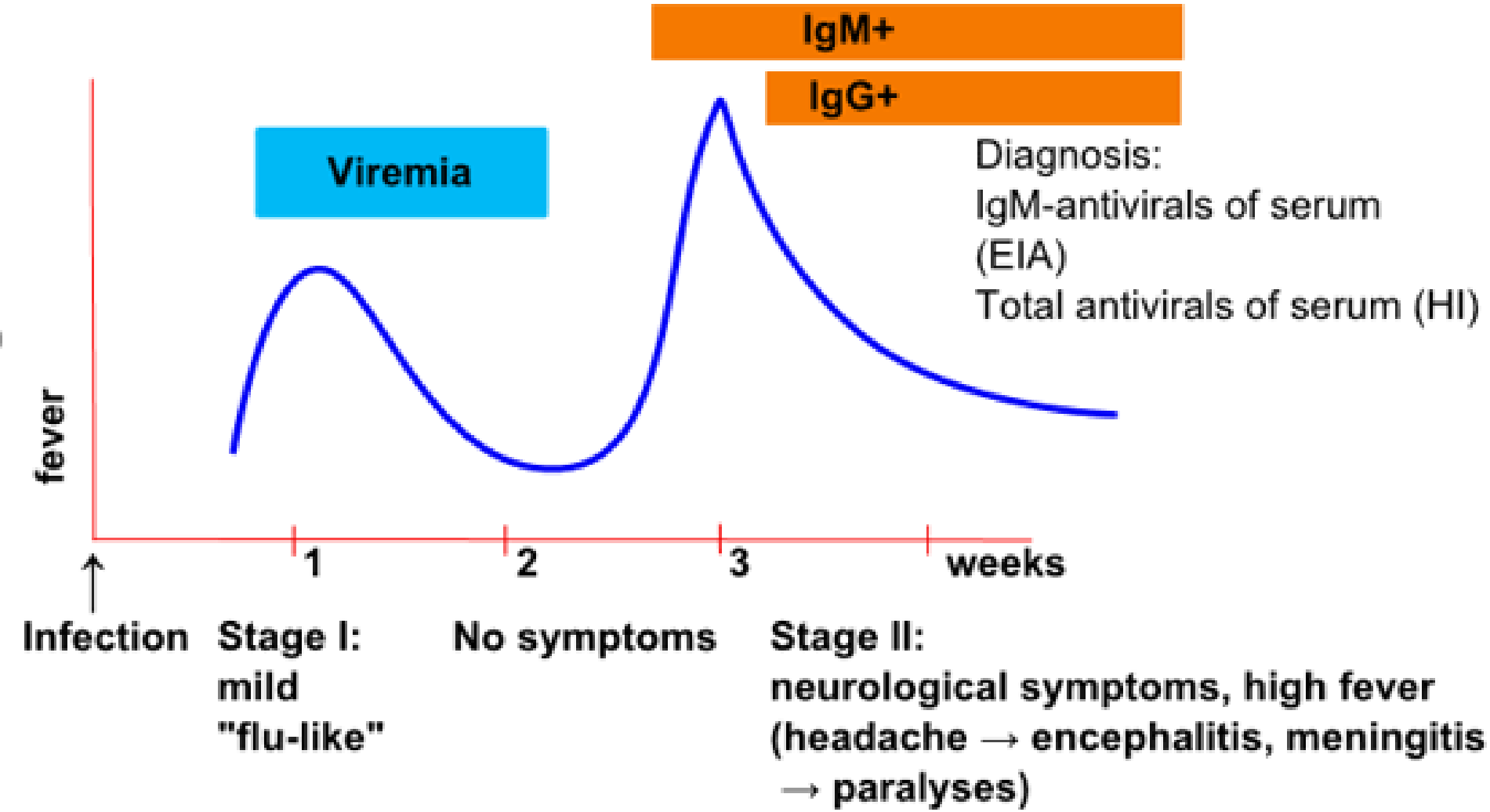
-- = data not given.

Table 3: Neurological sequelae at follow-up in prospective studies on patients with tick-borne encephalitis

Cavé: no control groups

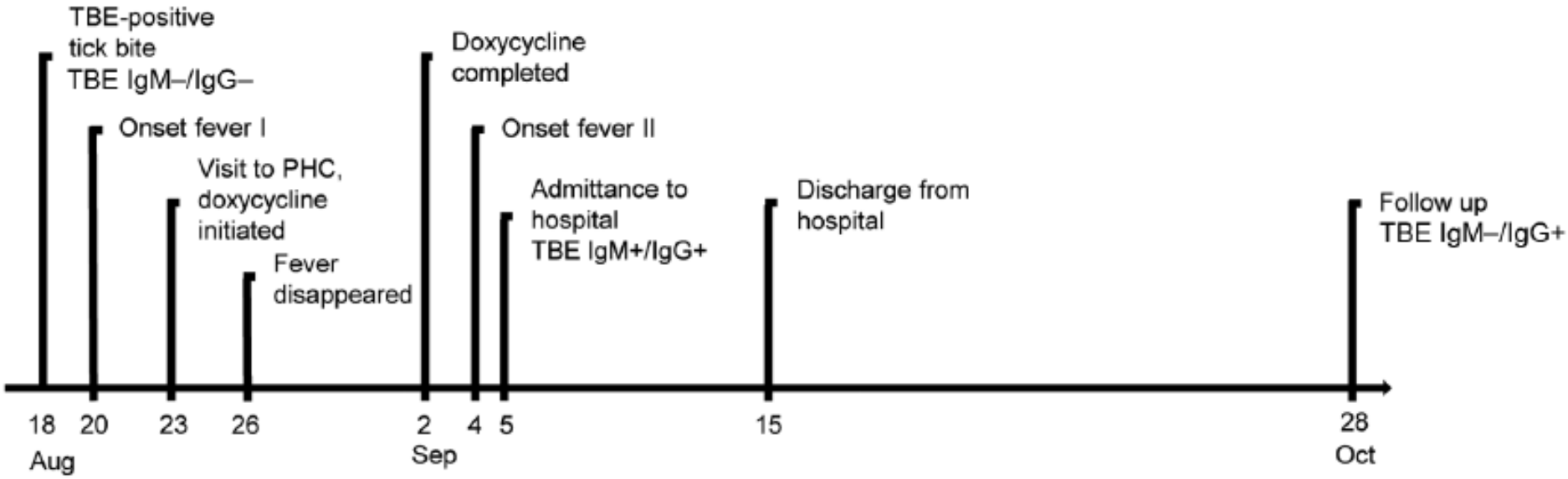
Lindquist, Vapalahti, The Lancet Vol 371 May 31, 2008

Diagnosis



https://en.wikipedia.org/wiki/Tick-borne_encephalitis

A case from Sweden



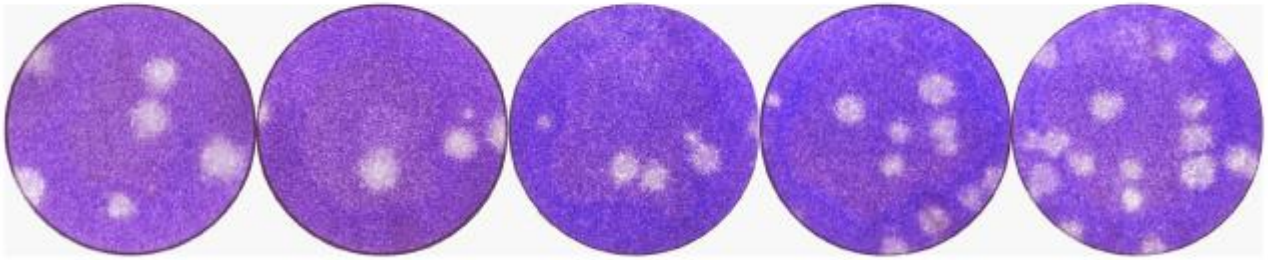
Henningsson, Emerging Infectious Diseases, Vol. 22, No. 8, August 2016

Diagnostic pitfalls

- Vaccination status? And JE, YF vaccination?
- IgM present after 1° and 2° vaccination
- Cross reaction with other flaviviruses
  - IgM > 500 AU
  - VNT
- CSF not always IgM/G present
- CSF: early-on neutrophiles may predominate
- IgM detectable up to ≥ 10 months, IgG persist for life

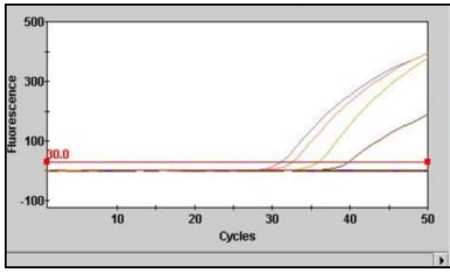
Virus Neutralisation Test

Virus Control	Negative Serum Control	Mock Control	Positive Serum Control	Fab 1 80 µg/ml

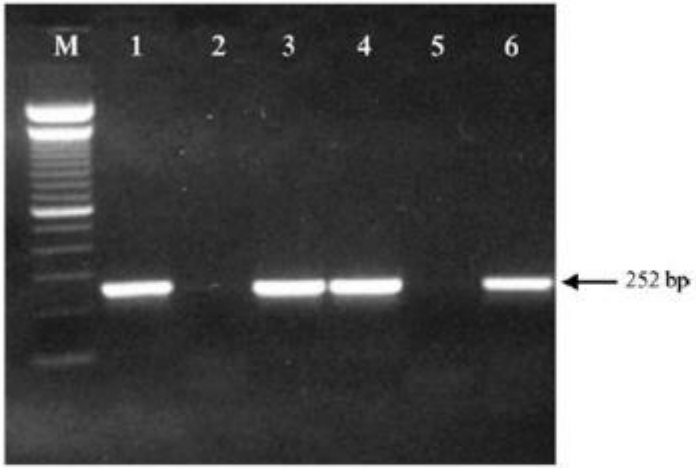


Fab 13 320 µg/ml	Fab 25 160 µg/ml	Fab 1 40 µg/ml	Fab 1 10 µg/ml	Fab 1 2.5 µg/ml

www.omisconline.org



PCR-method for early differential diagnosis of tick-borne encephalitis



- 252-bp long portion of highly conserved NS5 region of TBEV genome
- AMV reverse transcriptase

URINE!?

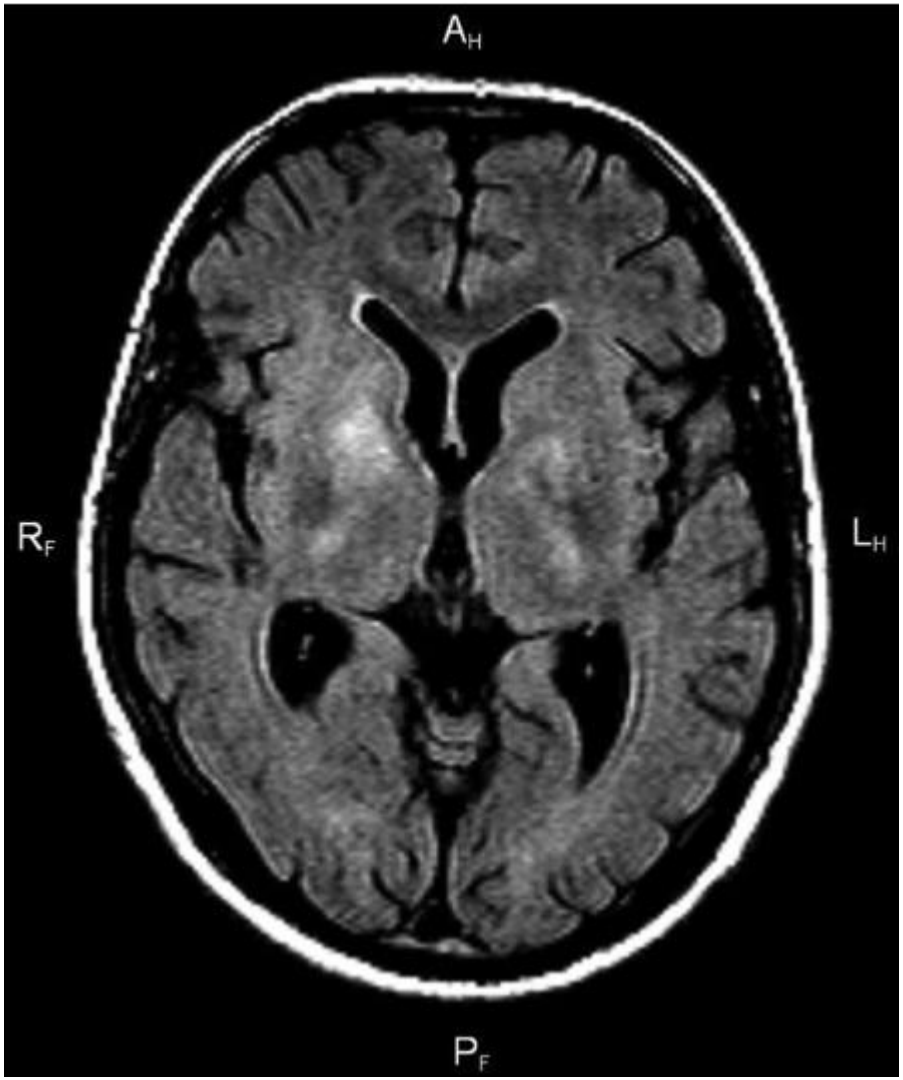
Fig. 1. Agarose gel analysis after TBEV RT-PCR. Lanes 1–4: results obtained from serum samples of patients with TBE; lane 5: negative control; lane 6: positive control; lane M: GeneRuler™ 100 bp DNA Ladder (Fermentas GmbH, Germany).

(Saksida et al., 2005)

The number of samples that tested positive for TBEV RNA in comparison to serum antibody status

	Serum	Whole blood	CSF	Brain tissue
IgG−/IgM−	30/30 (100%)	19/19 (100%)	1/10 (10%)	/
IgG−/IgM+	3/13 (23.1%)	3/5 (60%)	0/2 (0%)	/
IgG+/IgM+	1/34 (2.9%)	1/6 (16.7%)	0/19 (0%)	1/1 (100%)

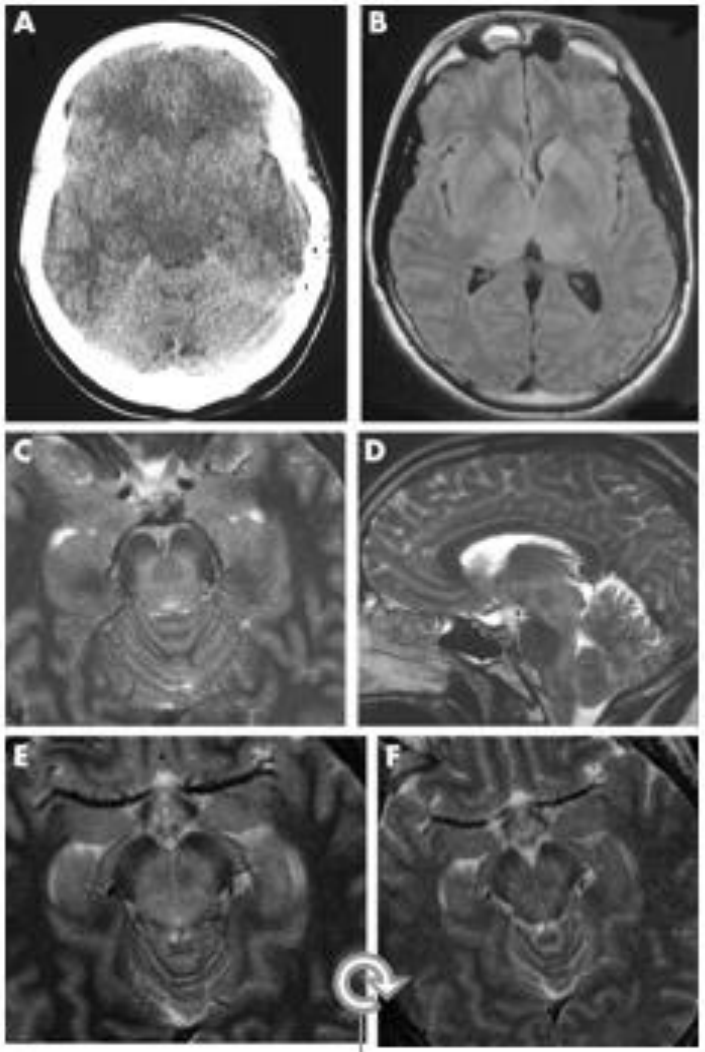
MRI



- 38y old main
- TBEV Encephalitis and Chorea
- Hyperintensity T2 in:
  - Nucleus caudatus
  - Capsula interna
  - Thalamus bilateral
- MRI abnormal: 15-20%

Zajkowska, EID Volume 19, Number 9—September 2013

MRI

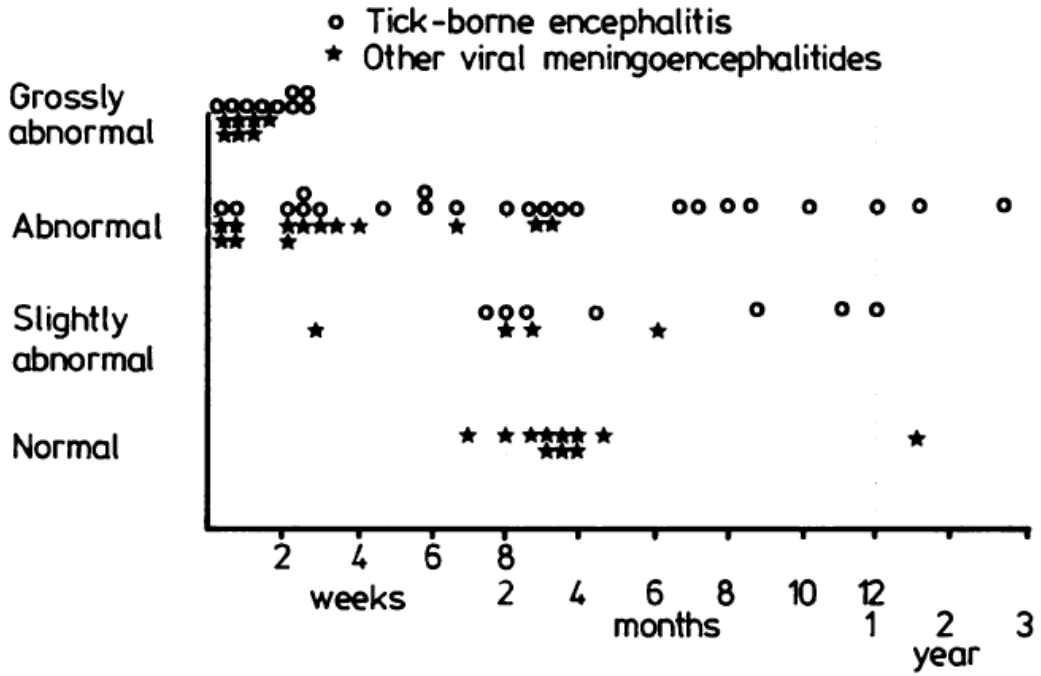


A Bender et al. J Neurol Neurosurg Psychiatry 2005;76:135-137

A Bender et al. J Neurol Neurosurg Psychiatry 2005;76:135-137

EEG

- 77% abnormal



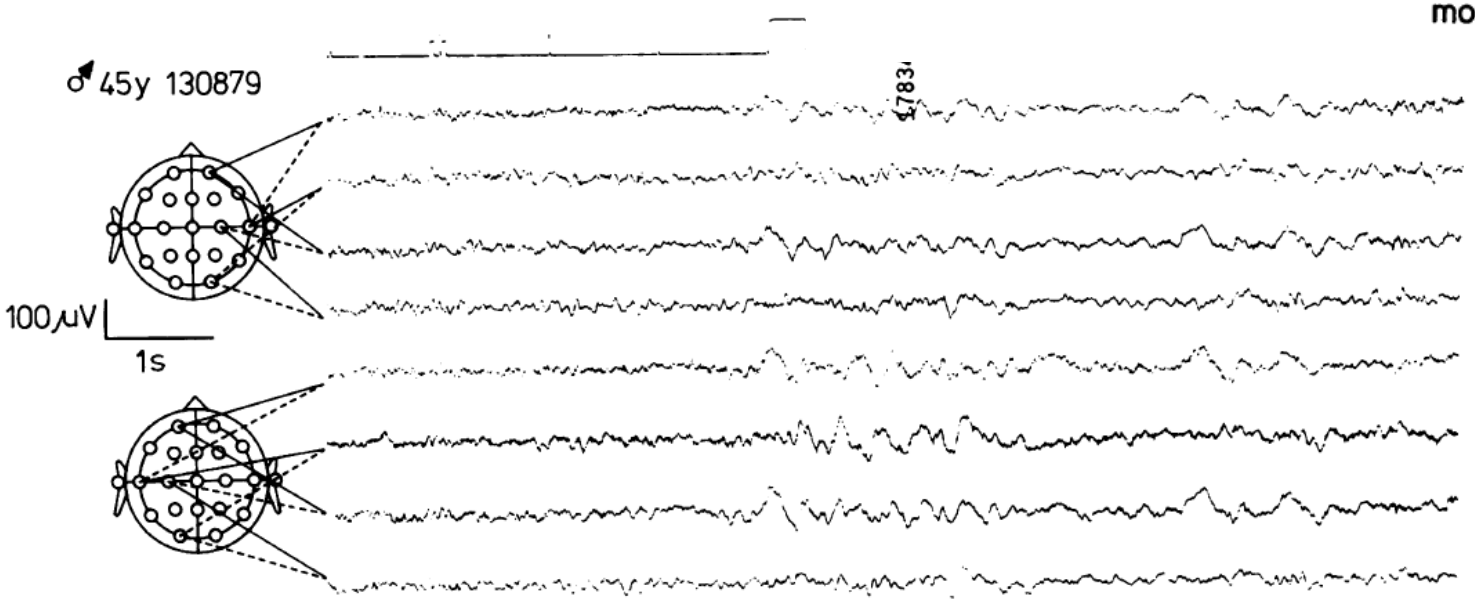
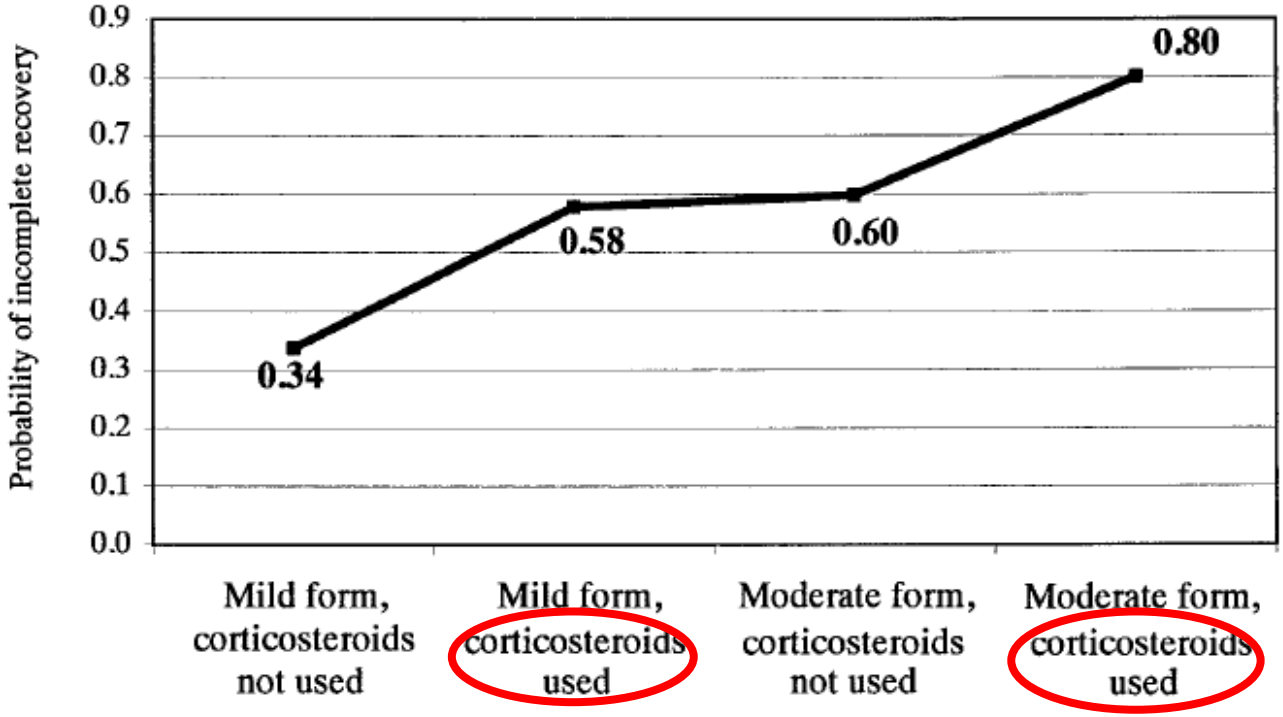


Fig 3 *Typical EEG recording of tick-borne encephalitis in the acute phase of the disease (5 days after the onset of the symptoms). General disturbance and frontal intermittent rhythmic delta activity (FIRDA) are prominent.*

Treatment

- No specific antiviral treatment
- Supportive care: 12% ICU, 5% intubation
- Corticoids
  - Hospit longer?
- Hyperimmune IgG



Mickiene, *Clin Infect Dis* 2002; 35: 650–58

Prevention


Protect Yourself Against Lyme Disease in Spring, Summer, and Fall
1 Walk in the middle of trails, away from tall grass and bushes.
2 Wear a long-sleeved shirt.
3 Wear white or light-colored clothing to make it easier to see ticks.
4 Wear a hat.
5 Spray tick repellent on clothes and shoes before entering woods.
6 Wear long pants tucked into high socks.
7 Wear shoes—no bare feet or sandals.


care PLUS
DEET
ANTI-INSECT
lotion 50%
care PLUS
DEET
ANTI-INSECT
lotion 50%


RAW MILK
Whole unpasteurized milk
DEAN FARMS
Raw Milk

Vaccination

- Interchangeable
- Accelerated schemes
- No herd immunity
- Cave: Breakthrough

Table 3-19. Tickborne encephalitis (TBE) vaccines licensed in Europe and Russia[1]

TRADE NAME (MANUFACTURER, LOCATION)	AGE (Y)	DOSE	ROUTE	PRIMARY SERIES	FIRST BOOSTER (Y)	SUBSEQUENT BOOSTERS (Y)
FSME-IMMUN (Baxter, Austria)	≥16	0.5 mL	IM	3 doses (0, 1–3 mo, 6–15 mo)[2]	3	5[3]
FSME-IMMUN Junior (Baxter, Austria)	1–15	0.25 mL	IM	3 doses (0, 1–3 mo, 6–15 mo)[2]	3	5
Encepur-Adults (Novartis, Germany)	≥17	0.5 mL	IM	3 doses (0, 1–3 mo, 9–12 mo)[4]	3	5[3]
Encepur-Children (Novartis, Germany)	1–11	0.25 mL	IM	3 doses (0, 1–3 mo, 9–12 mo)[4]	3	5
EnceVir (Microgen, Russia)	≥3	0.5 mL	IM	2 doses (0, 5–7 mo)[5]	1	3
TBE-Moscow (Chumakov Institute, Russia)	≥3	0.5 mL	IM	2 doses (0, 1–7 mo)	1	3

THANKS!

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