

Neuroinfections

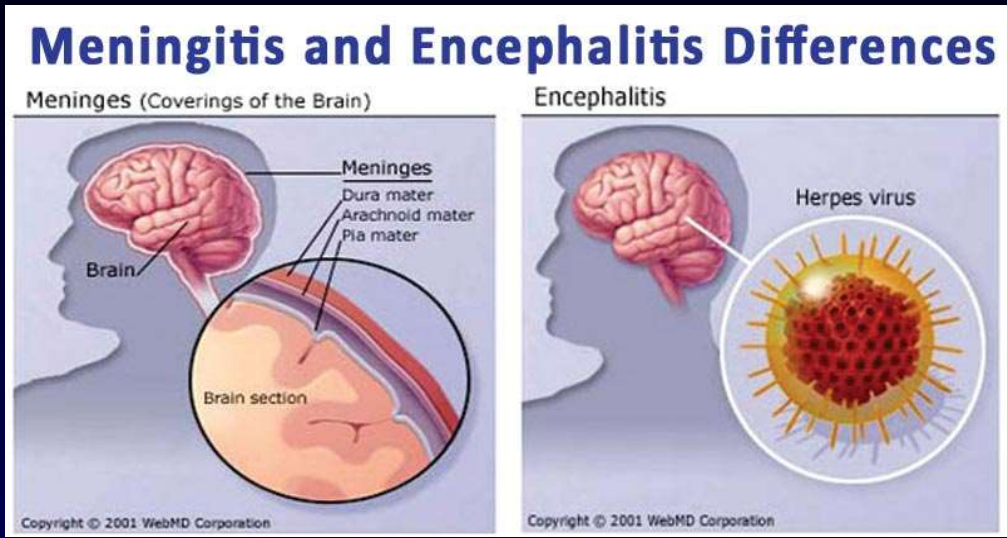


Pavel Drevinek



Meningitis or encephalitis

.. or abscess, empyema



diffuse	diffuse, but also localized
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Encephalitis	Meningitis
viruses	bacteria, viruses
clinical signs	
fever	fever
hedeache	hedeache
convulsions	meningeal symptoms
behavioral changes	

other accompanying symptoms:

- cranial nerve palsy: borreliosis
- flaccid paralysis: polio, TBE
- cerebellar ataxia: VZV
- skin manifestations: N. men, VZV, rubella
- respiratory symptoms: S. pneu, influenza

<p>WHO encephalitis*</p> <p>Person of any age, at any time of year with an acute onset of fever and either a change in mental status† (including confusion, disorientation, coma, or inability to talk) or new onset of seizures (excluding simple febrile seizures) or both.</p>	<p>WHO meningitis*</p> <p>Patient with a history of fever or documented fever (>37.5°C)‡ and one of the following signs: neck stiffness, altered consciousness,† or other meningeal signs.</p>
<p>WHO meningoenkephalitis*</p> <p>Meeting both encephalitis and meningitis criteria.</p>	

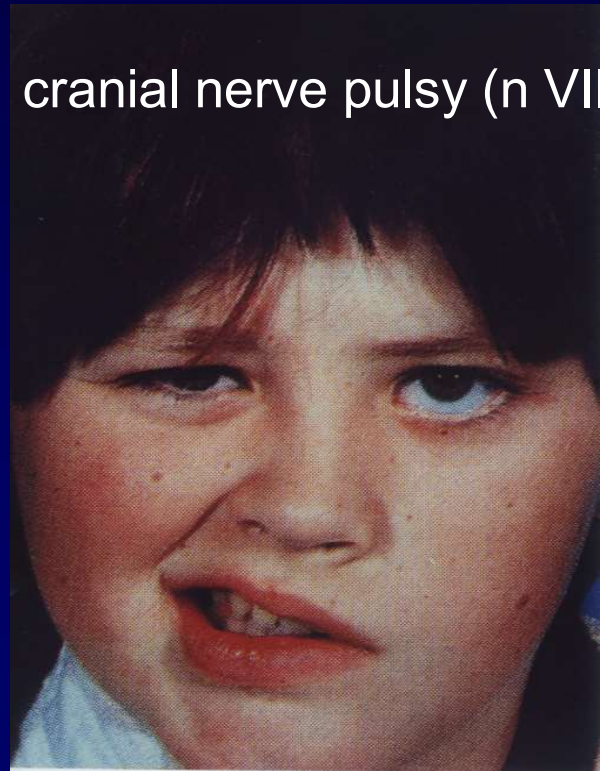


rubeola



petechial rash, *N. meningitidis*

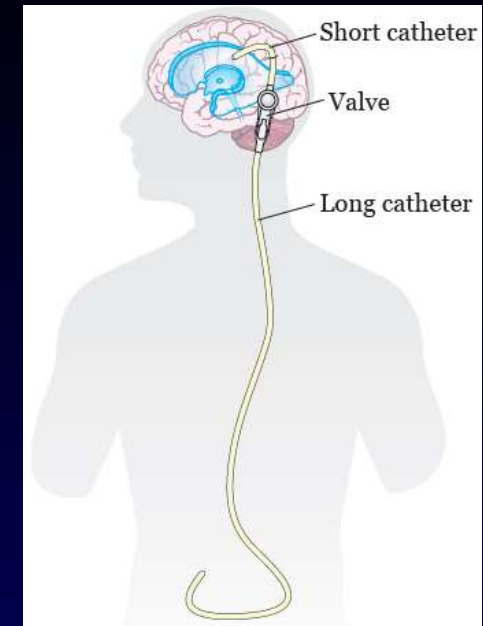
erythema migrans



cranial nerve palsy (n VII)

Routes of transmission

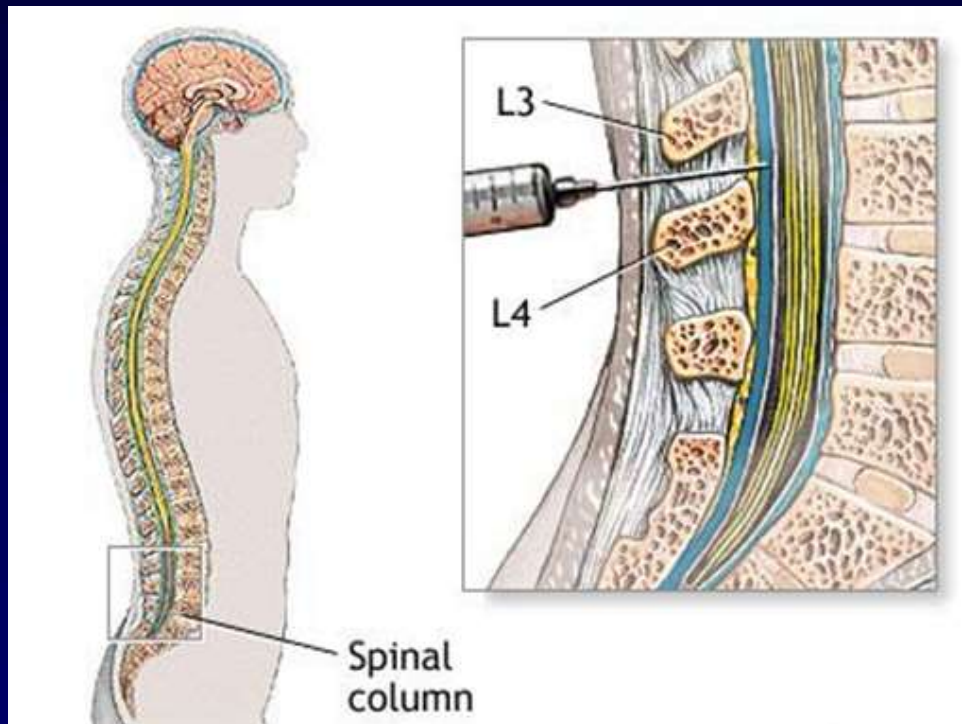
- per continuitatem
 - otitis, sinusitis (*S. pneumoniae*)
 - trauma
 - VP shunt (staphylococci)
- hematogenous spread
 - pneumonia (*S. pneumoniae*)
 - N. meningitidis*
 - polioviruses, mumps
 - > meningitis --> can result in meningoencephalitis (viruses)
- nerves (HSV, VZV, rabies)
 - > encephalitis



Clinical materials

- CSF

in this case, collection does not have to precede AB therapy
(*N. meningitidis*)



Clinical materials

- CSF : purulent or serous?
 - cytology (not microbiology)
 - biochemistry (not microbiology)

Type of CSF:	normal	purulent	serous
colour	clear	cloudy	clear
WBC	< 10 / 3 ul	↑↑↑↑	↑↑
dominant type	lymfocytes	neutrophils	lymfocytes
protein	150 - 450 mg/L	↑↑	↑
glucose	2.5 – 3.5 mmol/L	↓	normal
lactate	normal	↑	normal

Encephalitis	Meningitis	
viruses	bacteria, viruses	
clinical signs		
fever	fever	
hedeache	hedeache	
convulsions	meningeal symptoms	
behavioral changes		
type of inflammation		
serous	purulent:	bacteria (pyogenic)
	serous (aseptic meningitis):	viruses Borrelia Listeria (occasionally) <i>M. tuberculosis</i> (occassionally)

Clinical materials

- CSF

- Direct detection methods

- microscopy
 - (latex agglutination questionable)
 - culture (and agglutination in *N. meningitidis* upon its growth)
 - PCR (multiplex)



Meningitis

S. pneumoniae

N. meningitidis

H. influenzae

S. agalactiae

E. coli

L. monocytogenes

enteroviruses

HSV1

HSV2

VZV

CMV

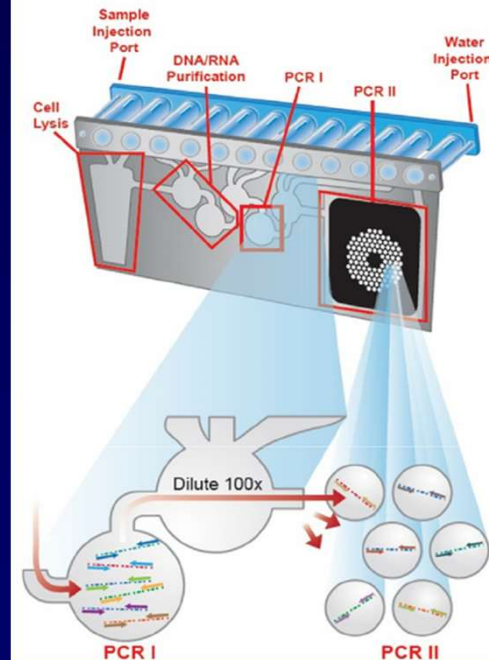
HHV6

parechovirus

Cryptococcus neoformans



The FilmArray Pouch



Clinical materials

- CSF

Indirect detection methods

- ELISA
- Western Blot

useful in Lyme disease

Clinical materials

- CSF
- Urine
 - antigen *S. pneumoniae*
- Serum
 - TBE, WNV,
- Blood culture

Key pathogens

bacteria	viruses (neurotropic)	yeasts
<p><i>S. agalactiae</i> <i>E. coli</i> <i>L. monocytogenes</i></p> <p><i>S. pneumoniae</i> <i>N. meningitidis</i> <i>H. influenzae</i></p> <p><i>M. tuberculosis</i> <i>B. burgdorferi</i> <i>M. pneumoniae</i> <i>T. pallidum</i></p>	<p>enteroviruses (and polioviruses) tick-borne encephalitis virus herpesviruses HSV, VZV, EBV, HHV6 West Nile virus rabies virus measles, rubella, mumps virus Zika virus JC virus</p>	<p><i>C. neoformans</i></p>

protozoa
<p>Toxoplasma Naegleria (améby)</p>

helminths
<p>cysticercóza <i>T. solium</i> hydatidy echinokoka</p>

cerebral malaria

Key pathogens

bacteria

S. agalactiae
E. coli
L. monocytogenes

S. pneumoniae
N. meningitidis
H. influenzae

Purulent (suppurative) meningitis

AB therapy:

- cefotaxim or ceftriaxon
- ampicilin for *L. monocytogenes*

Supportive therapy:

- brain oedema, vital functions, ...

TABLE 2.1. Causative organisms of neonatal meningitis^a

Country	United Kingdom [12]	Total
Observation period	2010–2011	
<i>Streptococcus agalactiae</i>	150	565 (58%)
<i>Escherichia coli</i>	41	203 (21%)
<i>Listeria monocytogenes</i>	11	19 (2%)
<i>Streptococcus pneumoniae</i>	28	39 (4%)
Other	72	156 (16%)
Total	302	982

^aStudies were performed in different time periods, with varying vaccination st

Key pathogens

bacteria

S. agalactiae

E. coli

L. monocytogenes

S. pneumoniae

N. meningitidis

H. influenzae

TABLE 2.2. Causative organisms of **paediatric** meningitis beyond neonatal age

Country	France [20]	Denmark [21]	France [22]	Total
Observation period	2001–2007	1997–2006	1995–2004	
<i>Neisseria meningitidis</i>	1303	159	35	1805 (50%)
<i>Streptococcus pneumoniae</i>	802	195	35	1342 (37%)
<i>Haemophilus influenzae</i>	78	8	11	170 (5%)
Other	137	56	8	302 (8%)
Total	2320	418	89	3619

Key pathogens

bacteria

S. agalactiae
E. coli
L. monocytogenes

S. pneumoniae
N. meningitidis
H. influenzae

TABLE 2.3. Causative organisms of adult bacterial meningitis

Country	Denmark [25]	Turkey [26]	United Kingdom [27]	Czech Republic [28]	Netherlands [4]	Total
Observation period	1998–2012	1994–2003	1997–2002	1997–2004	2006–2012	
<i>Neisseria meningitidis</i>	42	251	550	75	171	1089 (27%)
<i>Streptococcus pneumoniae</i>	92	457	525	82	1001	2157 (53%)
<i>Haemophilus influenzae</i>	3	2	48	3	56	112 (3%)
<i>Listeria monocytogenes</i>	5	6	48	21	74	154 (4%)
Other	30	68	124	35	291	548 (13%)
Total	172	784	1295	216	1593	4060

Key pathogens

bacteria

S. agalactiae

E. coli

L. monocytogenes

S. pneumoniae

N. meningitidis

H. influenzae

M. tuberculosis

B. burgdorferi

M. pneumoniae

T. pallidum

Aseptic meningitis

less acute onset

Lyme disease



Stage		time period	characteristics	diagnostics
early	lokalized	weeks	erythema migrans	clinical
	disseminated	weeks - months	borreliolymphocytomy arthritis carditis acute neuroborreliosis - aseptic meningitis - neuritis n. facialis - polyradiculoneuritis (Bannwarth syndrome)	clinical & laboratory
late		months - years	acrodermatitis chronica atrophicans arthritis late neuroborreliosis - encephalitis	clinical & laboratory

Lyme disease

- direct detection

- PCR from joint aspirate, skin biopsy, CSF (caveat: low sensitivity)

- indirect detection

- antibodies: joint, serum, CSF (intrathecal synthesis) ELISA + WB

- auxiliary test

- chemokine CXCL13: synthesized after the onset of neuroborreliosis (caveat: low specificity)

- AB therapy

erythema migrans

- doxycycline
- amoxicilin

neuroborreliosis

- ceftriaxon or cefotaxim
- penicilin G



Key pathogens

viruses

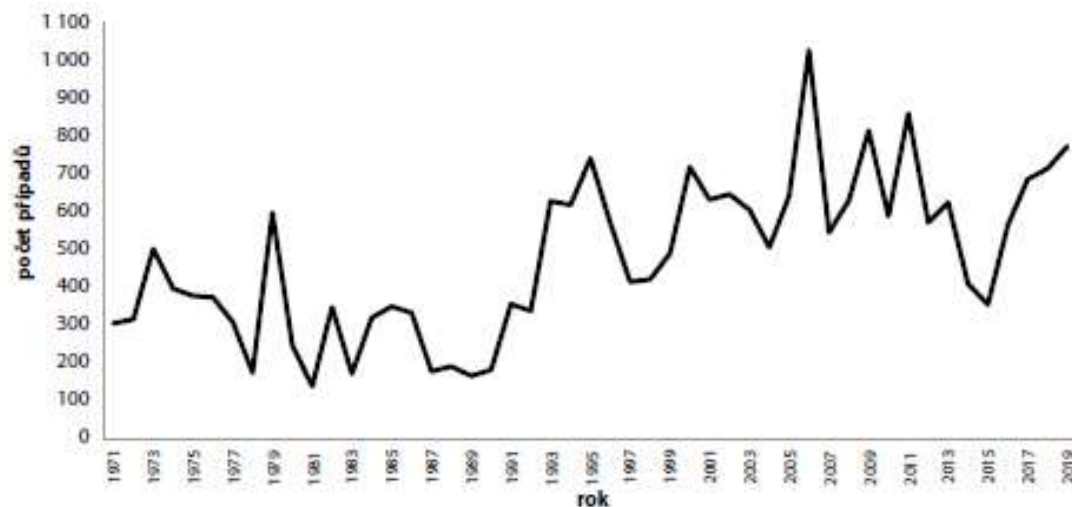
enteroviruses (and polioviruses)
tick-borne encephalitis virus
herpesviruses HSV, VZV, EBV, HHV6
West Nile virus
rabies virus
measles, rubella, mumps virus
Zika virus
JC virus

Aseptic meningitis
and encephalitis

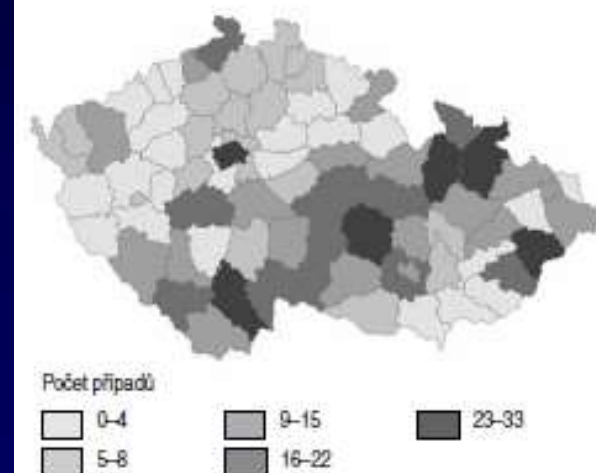
Tick-borne encephalitis (MEK, TBE)



Graf 1: Klišťová encefalitida, ČR, roky 1971–2019, počet případů



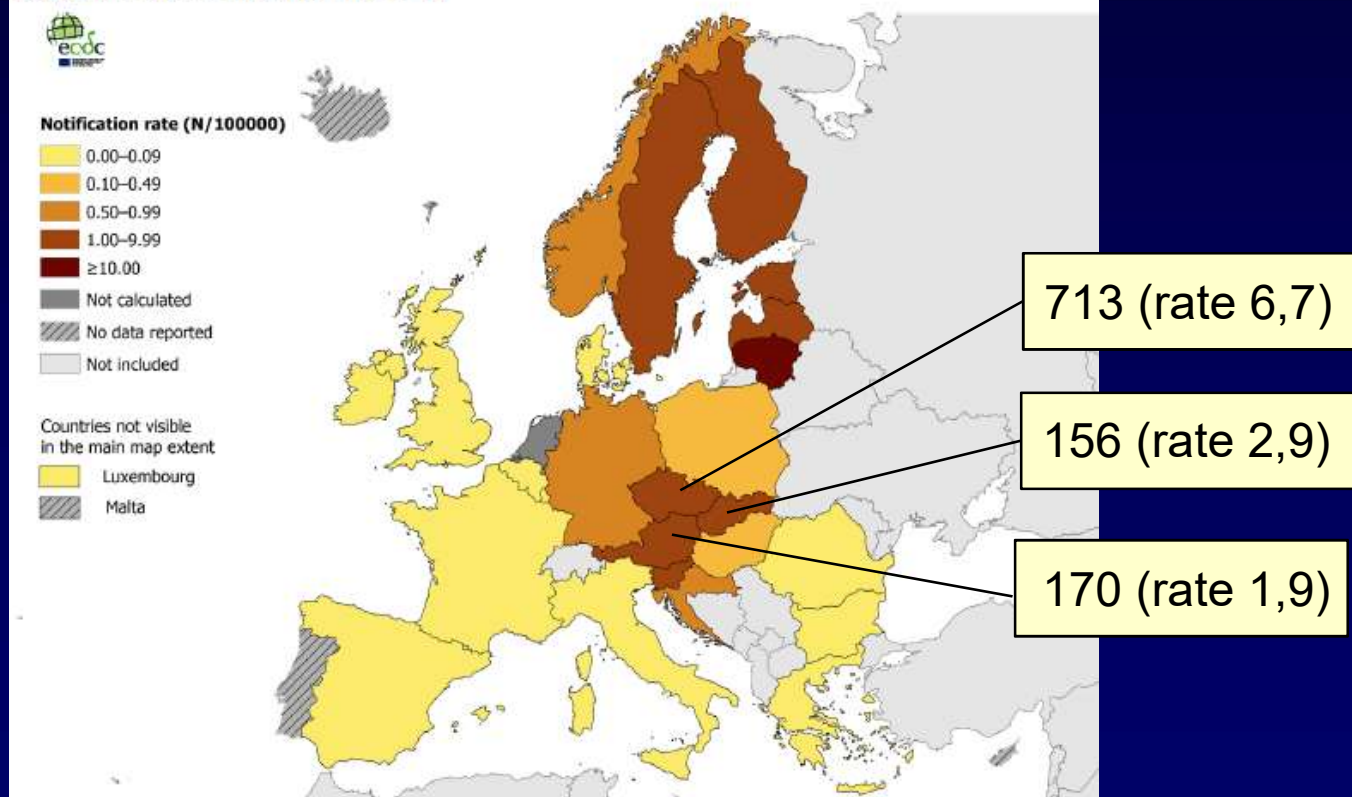
Graf 4: Klišťová encefalitida v ČR v roce 2019 – podle okresu pravděpodobné nákazy



Tick-borne encephalitis (MEK, TBE)



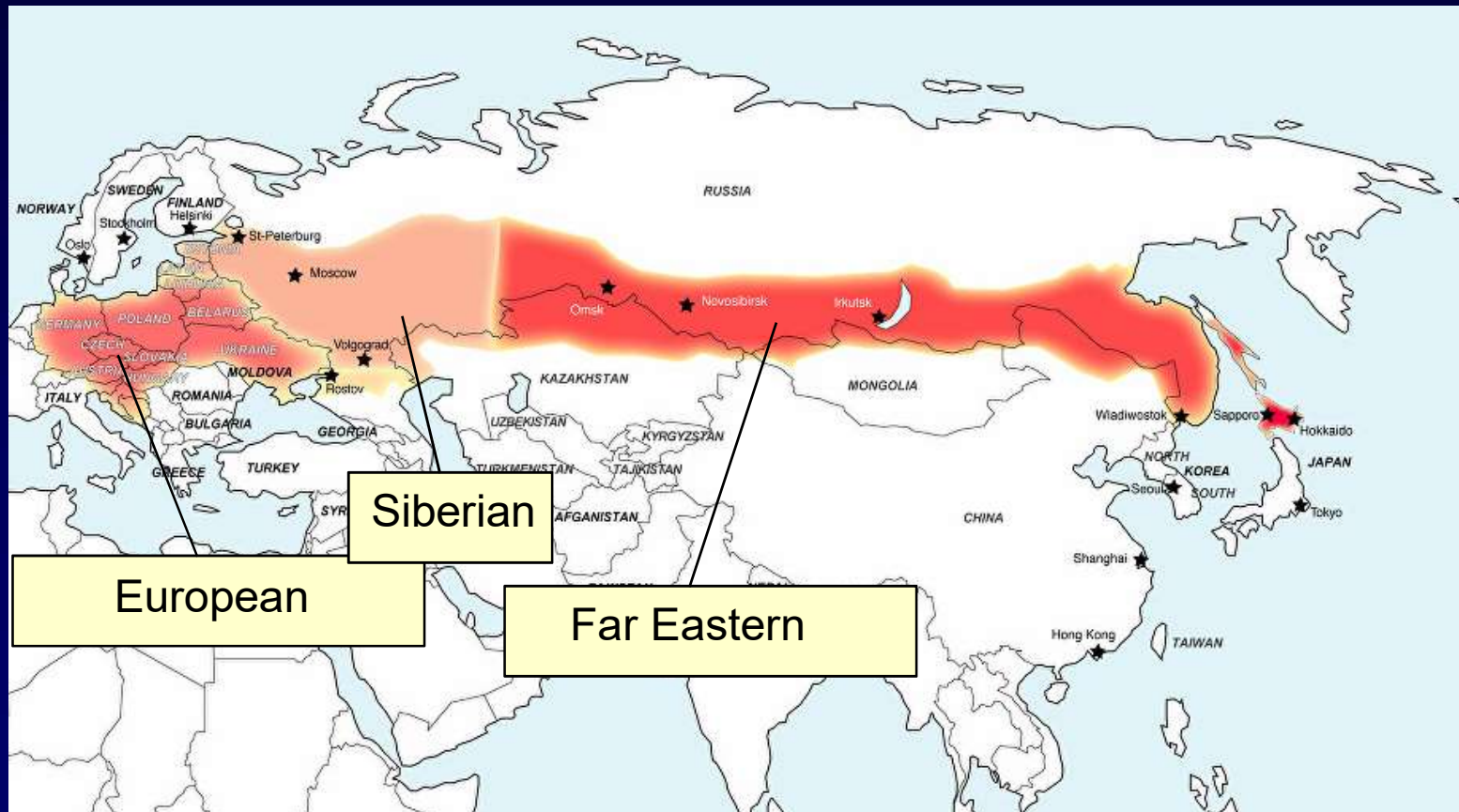
Figure 1. Distribution of confirmed tick-borne encephalitis case notification rate per 100 000 population by country, EU/EEA, 2018



Tick-borne encephalitis (MEK, TBE)

subtypes transmitted with *Ixodes ricinus*,
or *Ixodes persulcatus* and
unpasteurized products

Other than TBE transmitted by ticks:
Borrelia burgdorferi,
Francisella tularensis,
Coxiella burnetii,
Anaplasma, *Rickettsia helvetica*



Tick-borne encephalitis (MEK, TBE)

all age groups

highest incidence: 45 - 70 years of age

course of infection: ID 3 - 30 days

- asymptomatic
- abortive
- biphasic with meningitis
- biphasic with meningoencephalitis (most commonly diagnosed)
- biphasic with encephalomyelitis (flaccid paralysis, one upper limb)

mortality below 1%

- indirect detection

antibodies in serum (IgM + IgG positivity, low avidity IgG)

Herpetic encephalitis

HSV 1, 2

haemorrhagic, necrotizing
usually localized in temporal lobe
(not necessarily primo-infection)



Direct detection

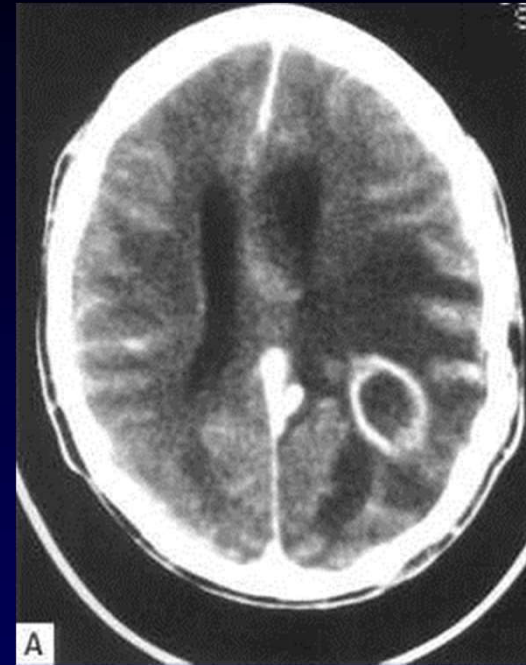
PCR in CSF (cytology negative)

Therapy

aciclovir 3 weeks

Brain abscesses

- Toxoplasma gondii*
 - Nocardia asteroides*
 - Listeria monocytogenes* (also meningitis)
 - Staphylococcus aureus*
 - Streptococcus intermedius*
 - Oral streptococci
 - anaerobes
-
- Cryptococcus neoformans* (also meningitis)
 - Aspergillus*
 - Zygomycetes*



When to consider neuroinfection

Clinical picture

(nuchal rigidity, neurological deficit)

Epidemiology

(traveller, vaccination, season - ticks)

Past history

(immunosuppression or immunodeficiency, shunt, lesions in mouth)