Medical University of Bialystok



TICK – BORNE ENCEPHALITIS

PROPHYLAXIS AND CONSEQUENCES OF ITS ”SHORTAGE” IN POLAND

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TICKS



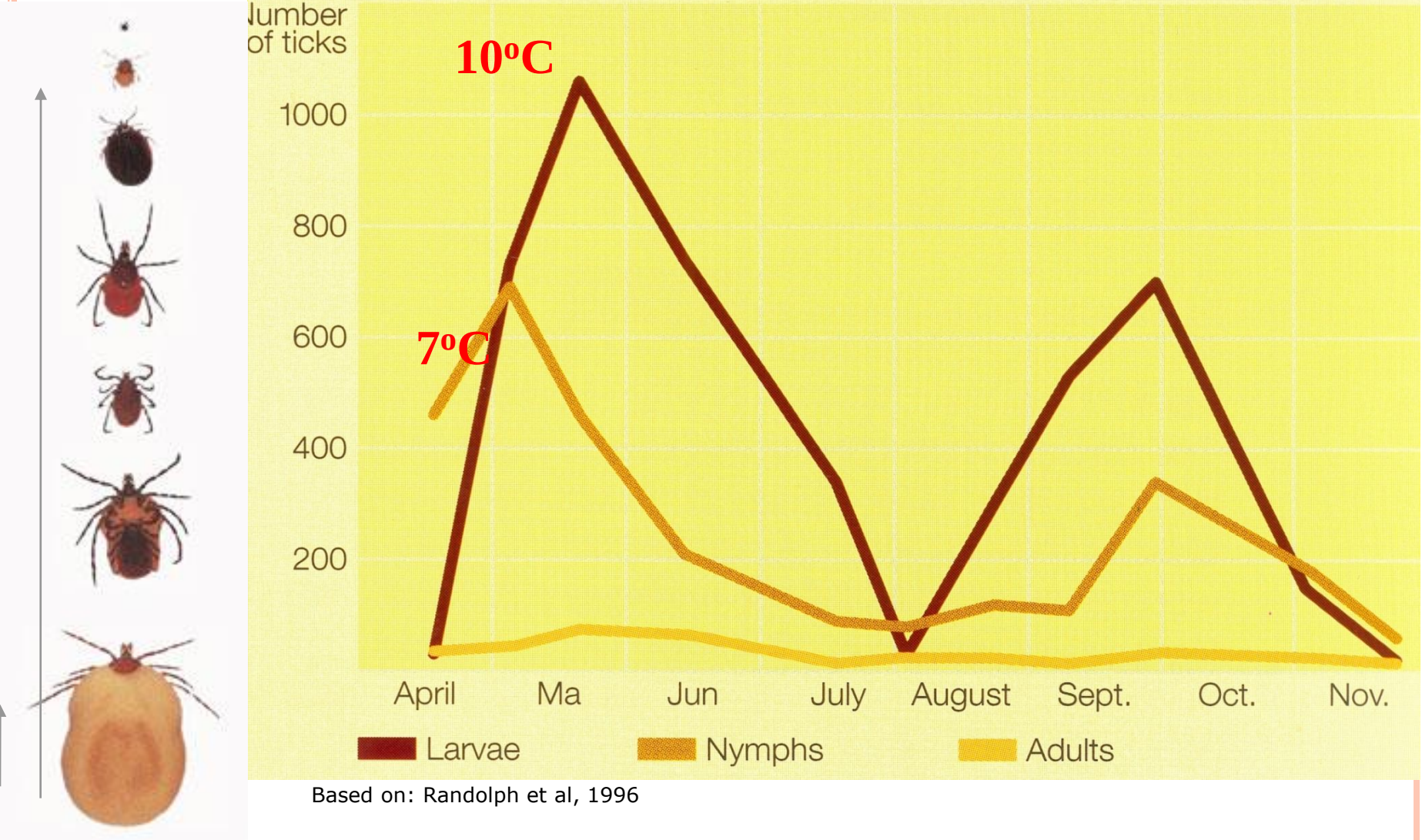
Photo by Dr M. Kondrusik, Bialystok, Poland







IXODES TICKS SEASONAL ACTIVITY



Based on: Randolph et al, 1996

WIDE RANGE OF TICKS HOSTS













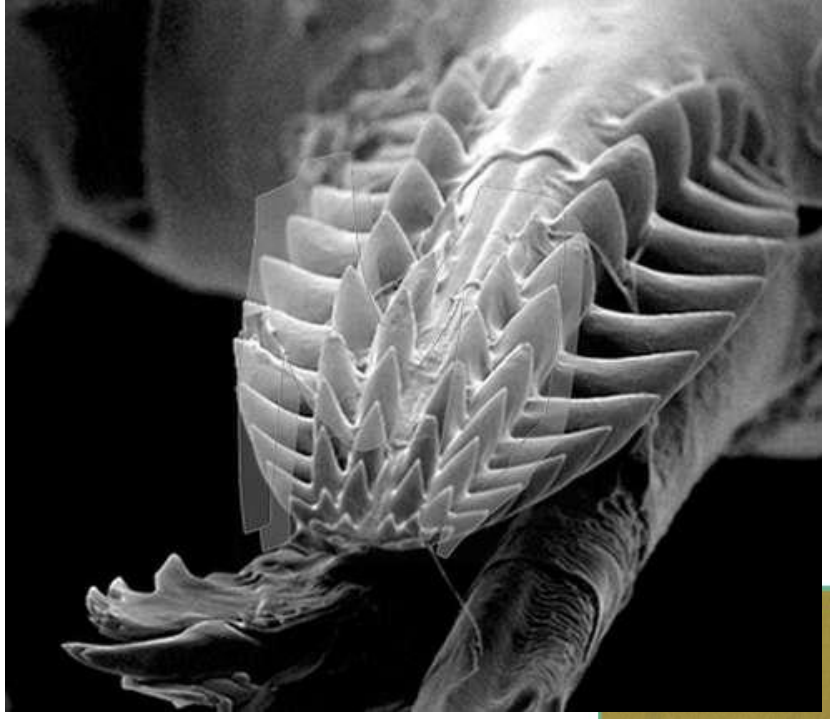
TBE virus

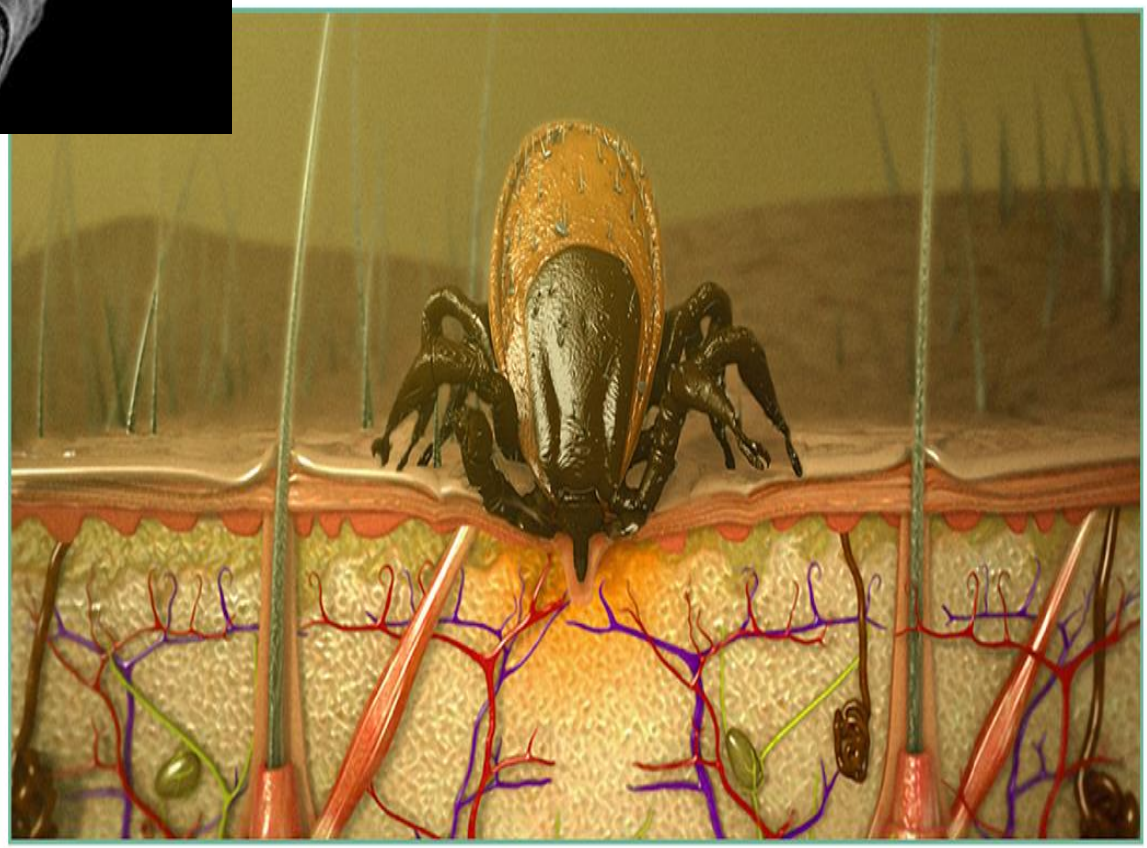
- Flaviviridae (other close relatives: Omsk hemorrhagic fever virus, Kyasanur forest disease virus, Louping ill virus, Langat virus, Yellow Fever, West Nile, Japanese Encephalitis, Dengue viruses)

- 3 subtypes:

1.Western European subtype (formerly Central European encephalitis virus, CEEV; principal tick vector: *Ixodes ricinus*)
2.Siberian subtype (formerly West Siberian virus; principal tick vector: *Ixodes persulcatus*)
3.Far Eastern subtype (formerly Russian Spring Summer encephalitis virus, RSSEV; principal tick vector: *Ixodes persulcatus*)

Mandl et al., 1997; Grard et al., 2007





Foodborne TBE

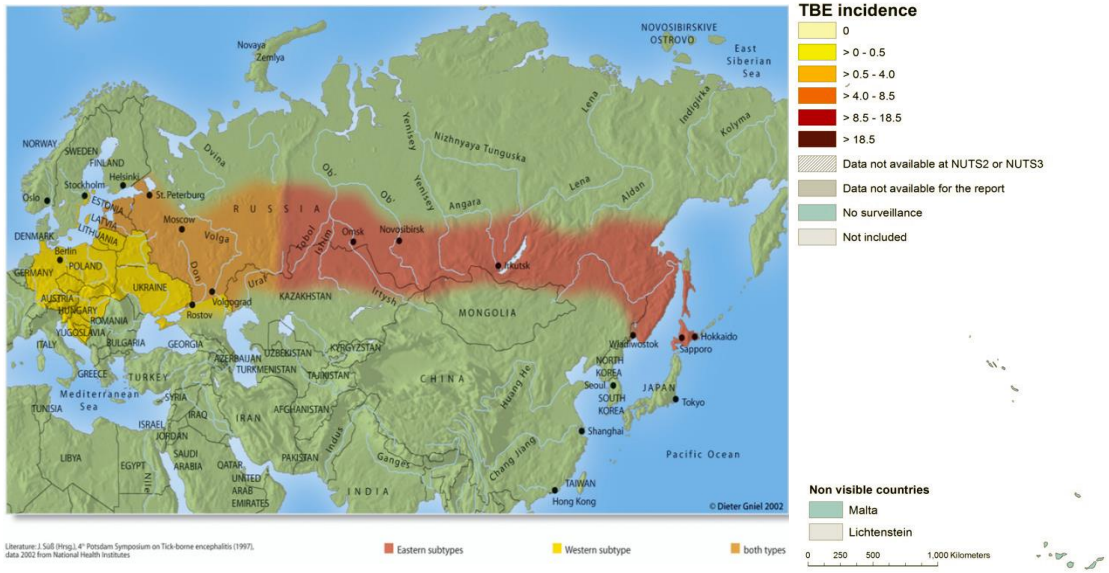


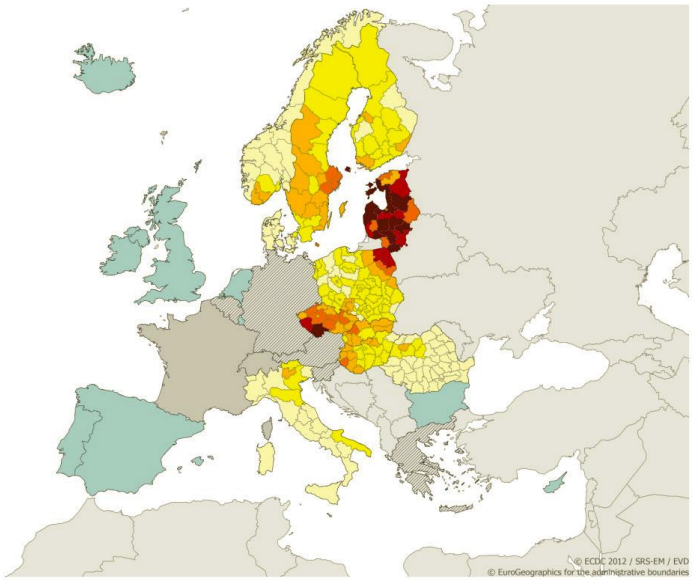
- Drinking unpasteurized milk of goat or cow
- TBE virus can be isolated from goat's milk, even after 25 days of milking
- Dairy products: yogurt, cheese, butter may be infectious

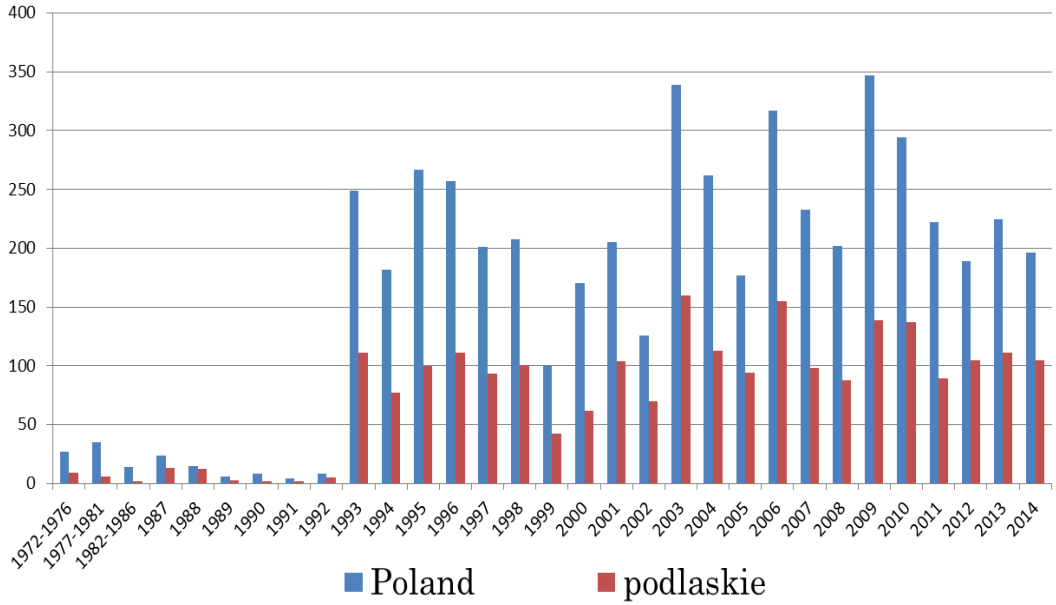
Pasteurization completely protects against infection!

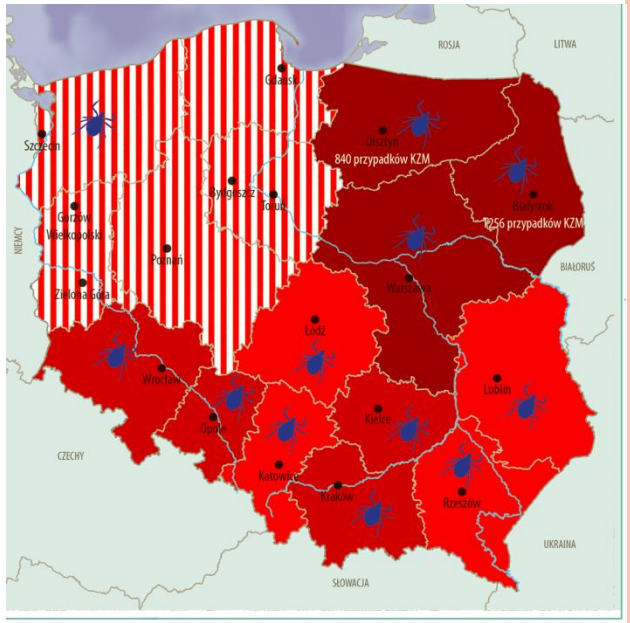


Balogh et al., 2010









>100 przypadków KZM
50 - 100 przypadków KZM
10 - 50 przypadków KZM
<10 przypadków KZM
zachorowania na KZM w 2011 roku

Mapa opracowana na podstawie meldunków Państwowego Zakładu Higieny „Choroby zakaźne i zatrucia w Polsce" w latach 2001-2011, www.pzh.gov.pl, czerwiec 2011 r.

Based on www.pzh.gov.pl; www.ecdc.europa.eu

RISK GROUPS



- Forestry workers
- National Parks employees
- Mushrooms pickers
- Berry pickers
- Hunters
- Dogs owners







Clinical presentation



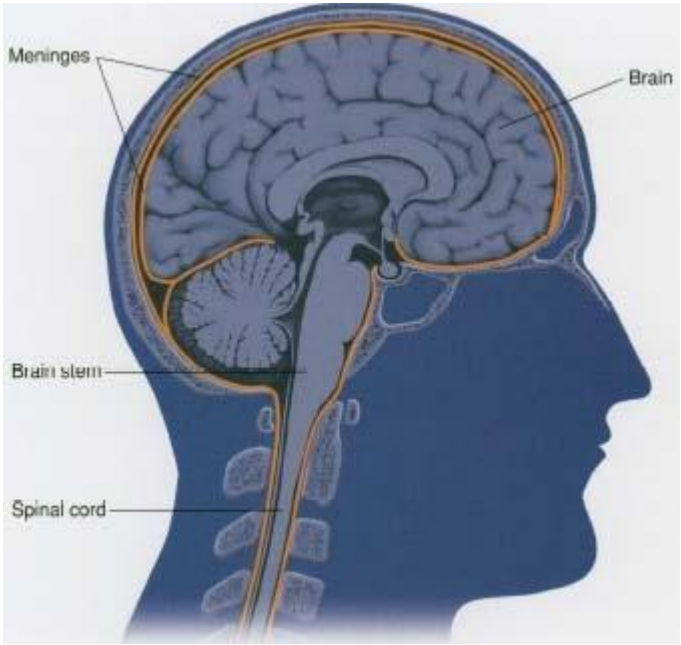
- **Depending on location of inflammatory process neurologic phase of infection may take course of:**



Meningitis

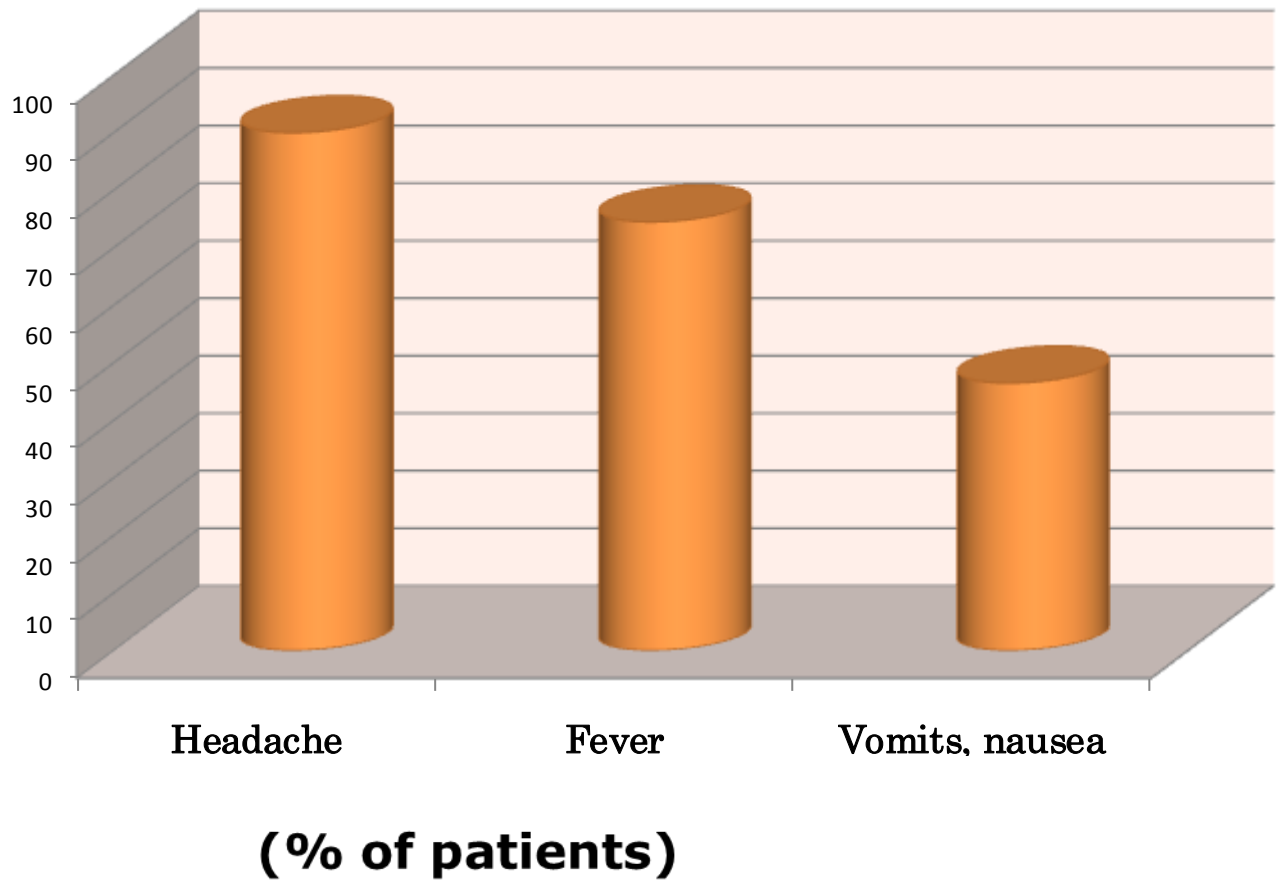
Meningoencephalitis

Meningoencephalomyelitis



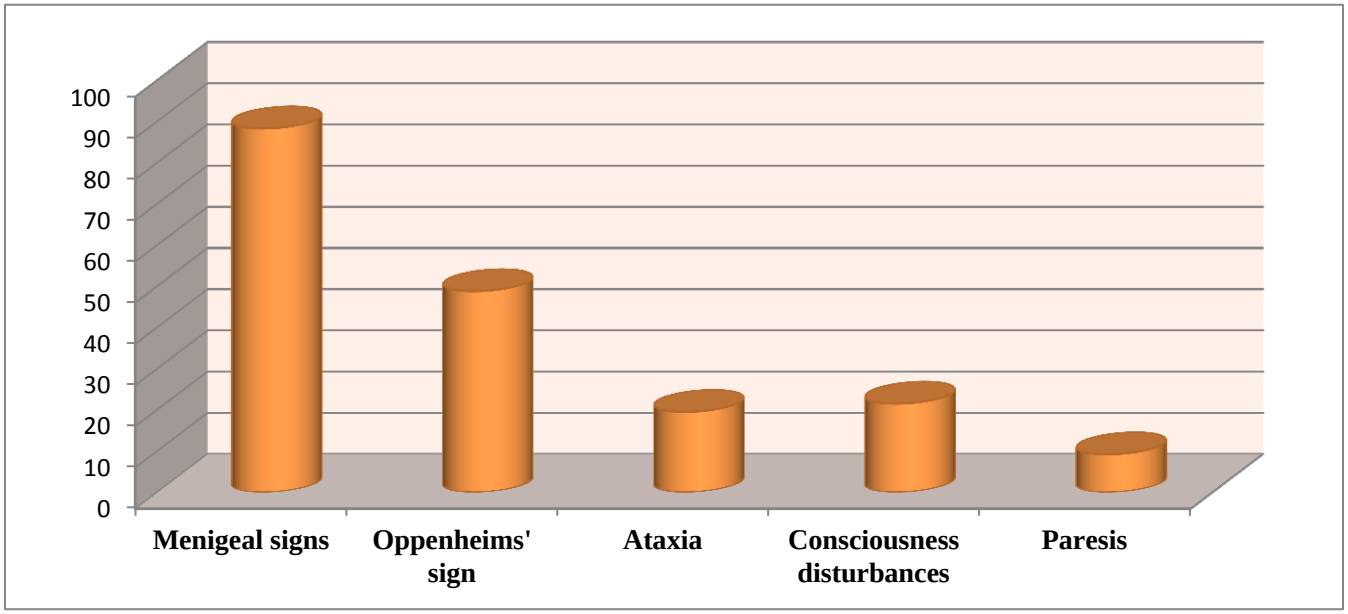
Maximova et al., 2009
www.humanillnesses.com

TBE - COMPLAINTS



Czupryna et al., 2011

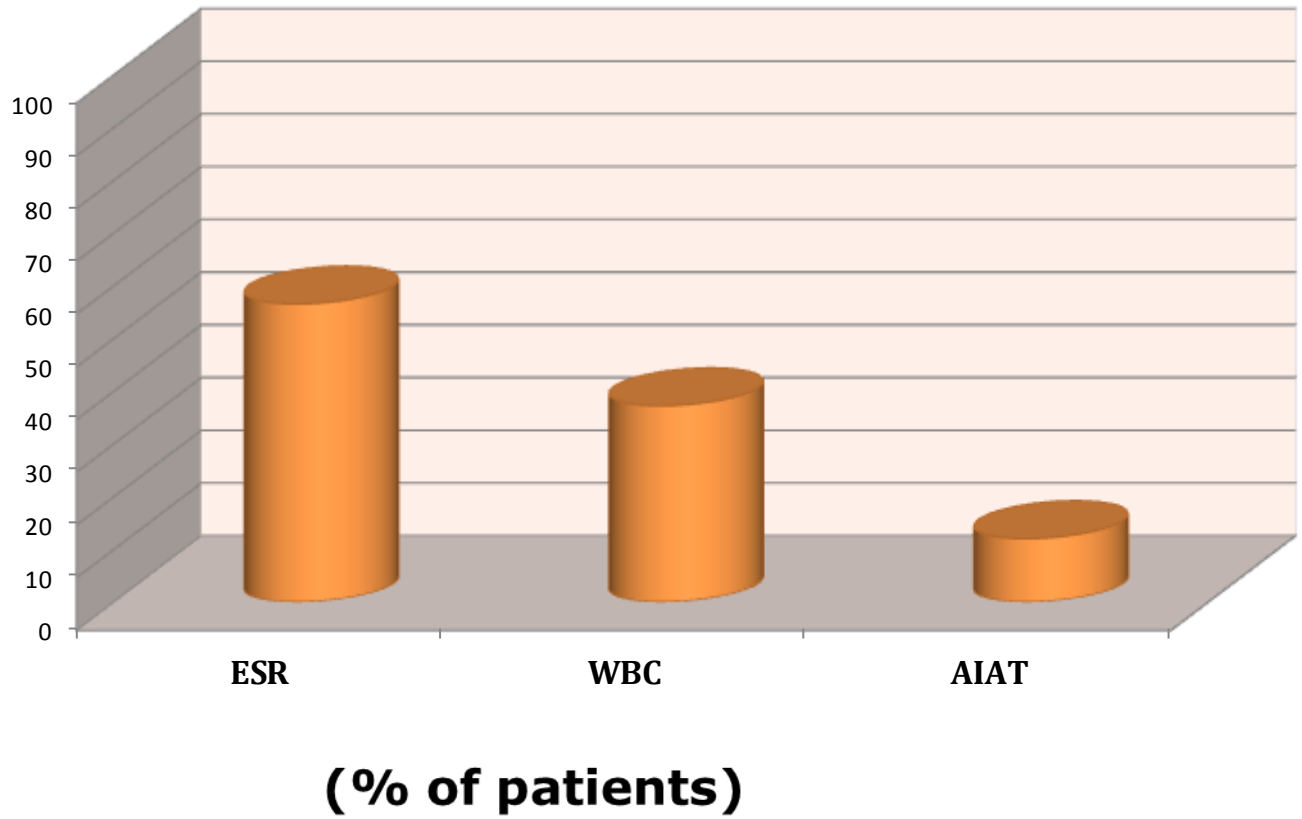
TBE – PHYSICAL EXAMINATION



(% of patients)

Czupryna et al., 2011

TBE – DIAGNOSIS-LABORATORY TESTS



Czupryna et al., 2011

TBE – LABORATORY TESTS

Cerebrospinal fluid examinations

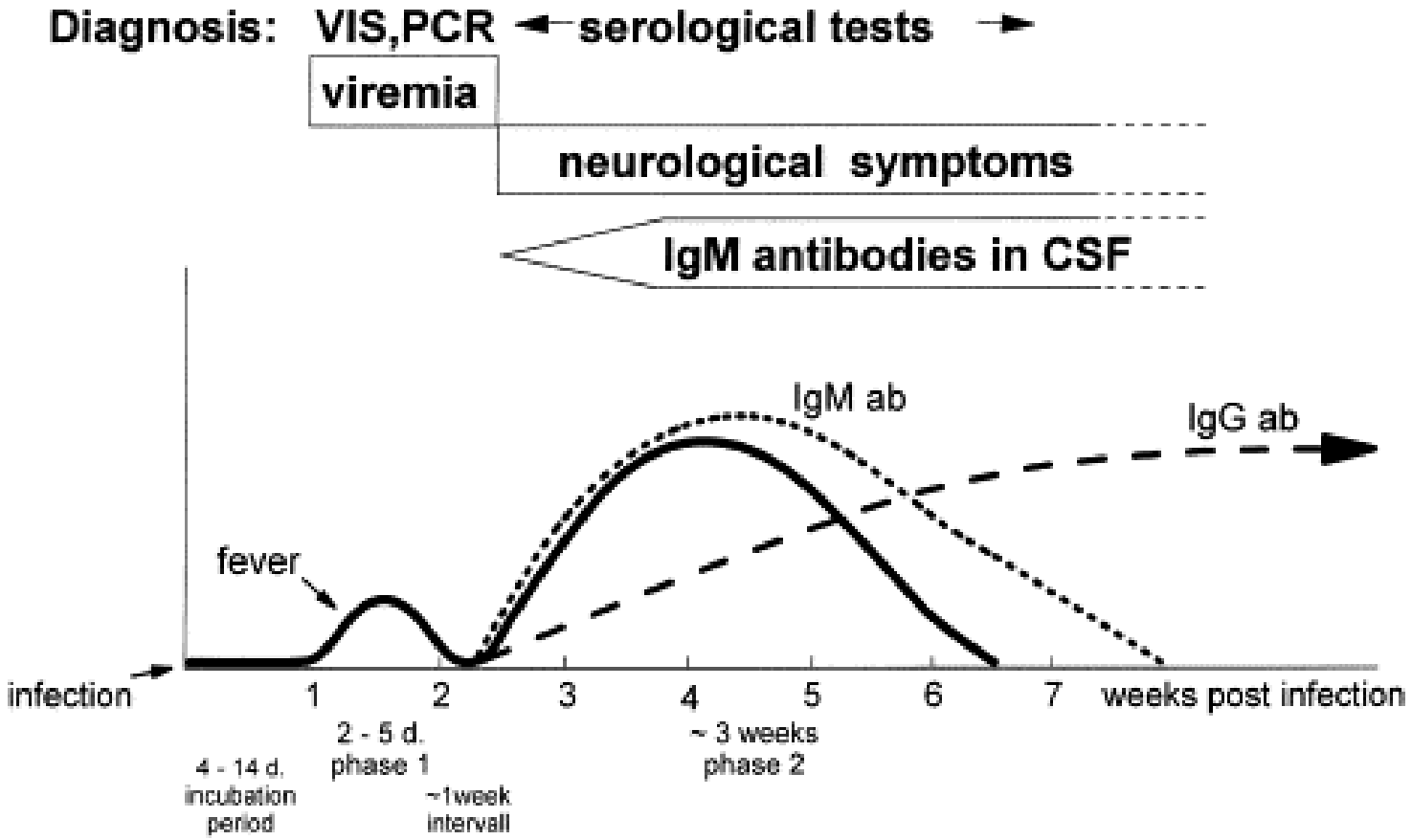
Pleocytosis – 5 – 1000 cells/μl

Lymphocytes predominate

Protein concentration – normal or elevated (>50 mg/ml)

Glucose concentration - normal

TBE – DIAGNOSIS- SEROLOGY - ELISA



Holzmann et al., 2003

TBE – TREATMENT

a) no possibility of causative treatment

b) antioedematous drugs (mannitol, diuretics)

c) pain-killers

d) antinflammatory drugs (NSAID)

e) steroids (exceptional cases)

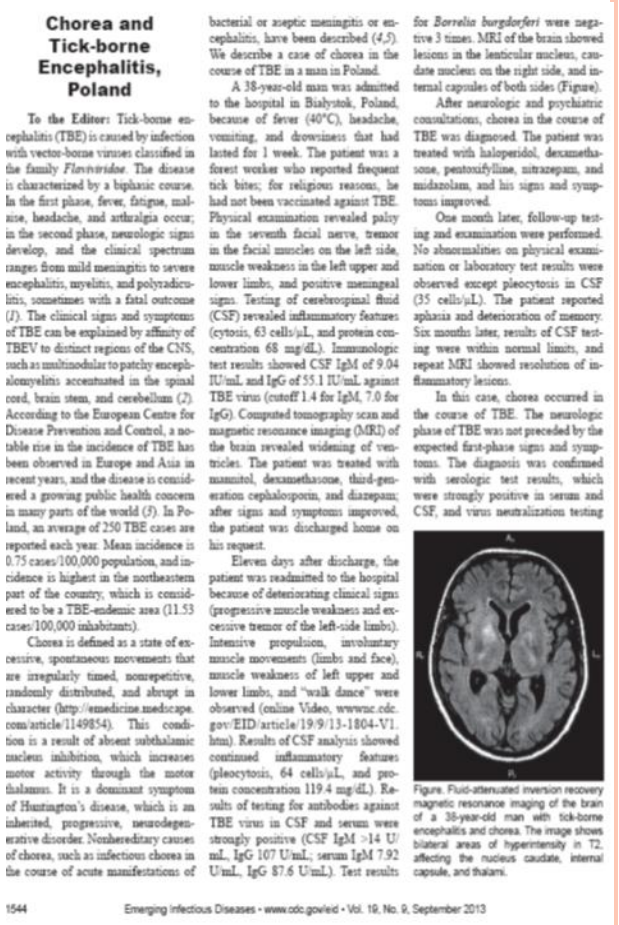
SERIOUS SEQUELAE

Neurological sequelae - 144 (23.2%):

- spinal nerve paralysis (23.7%)
- ataxia (23.7%)
- disorders of sensibility (13.2%)

All patients with neurological sequelae required rehabilitation.

Czupryna et al., 2011



Chorea and Tick-borne Encephalitis, Poland

To the Editor: Tick-borne encephalitis (TBE) is caused by infection with vector-borne viruses classified in the family *Flaviviridae*. The disease is characterized by a biphasic course. In the first phase, fever, fatigue, malaise, headache, and arthralgia occur; in the second phase, neurologic signs develop, and the clinical spectrum ranges from mild meningitis to severe encephalitis, myelitis, and polyradiculitis, sometimes with a fatal outcome (*1*). The clinical signs and symptoms of TBE can be explained by affinity of TBEV to distinct regions of the CNS, such as multinodular to patchy encephalomyelitis accentuated in the spinal cord, brain stem, and cerebellum (*2*). According to the European Centre for Disease Prevention and Control, a notable rise in the incidence of TBE has been observed in Europe and Asia in recent years, and the disease is considered a growing public health concern in many parts of the world (*3*). In Poland, an average of 250 TBE cases are reported each year. Mean incidence is 0.75 cases/100,000 population, and incidence is highest in the northeastern part of the country, which is considered to be a TBE-endemic area (11.53 cases/100,000 inhabitants).

Chorea is defined as a state of excessive, spontaneous movements that are irregularly timed, nonrepetitive, randomly distributed, and abrupt in character (http://emedicine.medscape.com/article/1149854). This condition is a result of absent subthalamic nucleus inhibition, which increases motor activity through the motor thalamus. It is a dominant symptom of Huntington's disease, which is an inherited, progressive, neurodegenerative disorder. Nonhereditary causes of chorea, such as infectious chorea in the course of acute manifestations of bacterial or aseptic meningitis or encephalitis, have been described (*4*,*5*). We describe a case of chorea in the course of TBE in a man in Poland.

A 38-year-old man was admitted to the hospital in Bialystok, Poland, because of fever (40°C), headache, vomiting, and drowsiness that had lasted for 1 week. The patient was a forest worker who reported frequent tick bites; for religious reasons, he had not been vaccinated against TBE. Physical examination revealed palsy in the seventh facial nerve, tremor in the facial muscles on the left side, muscle weakness in the left upper and lower limbs, and positive meningeal signs. Testing of cerebrospinal fluid (CSF) revealed inflammatory features (cytosis, 63 cells/μL, and protein concentration 68 mg/dL). Immunologic test results showed CSF IgM of 9.04 IU/mL and IgG of 55.1 IU/mL against TBE virus (cutoff 1.4 for IgM, 7.0 for IgG). Computed tomography scan and magnetic resonance imaging (MRI) of the brain revealed widening of ventricles. The patient was treated with mannitol, dexamethasone, third-generation cephalosporin, and diazepam; after signs and symptoms improved, the patient was discharged home on his request.

Eleven days after discharge, the patient was readmitted to the hospital because of deteriorating clinical signs (progressive muscle weakness and excessive tremor of the left-side limbs). Intensive propulsion, involuntary muscle movements (limbs and face), muscle weakness of left upper and lower limbs, and "walk dance" were observed (online Video, wwwnc.cdc.gov/EID/article/19/9/13-1804-V1.htm). Results of CSF analysis showed continued inflammatory features (pleocytosis, 64 cells/μL, and protein concentration 119.4 mg/dL). Results of testing for antibodies against TBE virus in CSF and serum were strongly positive (CSF IgM >14 U/mL, IgG 107 U/mL; serum IgM 7.92 U/mL, IgG 87.6 U/mL). Test results for *Borrelia burgdorferi* were negative 3 times. MRI of the brain showed lesions in the lenticular nucleus, caudate nucleus on the right side, and internal capsules of both sides (Figure).

After neurologic and psychiatric consultations, chorea in the course of TBE was diagnosed. The patient was treated with haloperidol, dexamethasone, pentoxifylline, nitrazepam, and midazolam, and his signs and symptoms improved.

One month later, follow-up testing and examination were performed. No abnormalities on physical examination or laboratory test results were observed except pleocytosis in CSF (35 cells/μL). The patient reported aphasia and deterioration of memory. Six months later, results of CSF testing were within normal limits, and repeat MRI showed resolution of inflammatory lesions.

In this case, chorea occurred in the course of TBE. The neurologic phase of TBE was not preceded by the expected first-phase signs and symptoms. The diagnosis was confirmed with serologic test results, which were strongly positive in serum and CSF, and virus neutralization testing

Figure. Fluid-attenuated inversion recovery magnetic resonance imaging of the brain of a 38-year-old man with tick-borne encephalitis and chorea. The image shows bilateral areas of hyperintensity in T2, affecting the nucleus caudate, internal capsule, and thalami.

Zajkowska et al., 2013

Right lower limb paresis
Atrophy of right lower limb

2 years after TBE, intensive physiotherapy



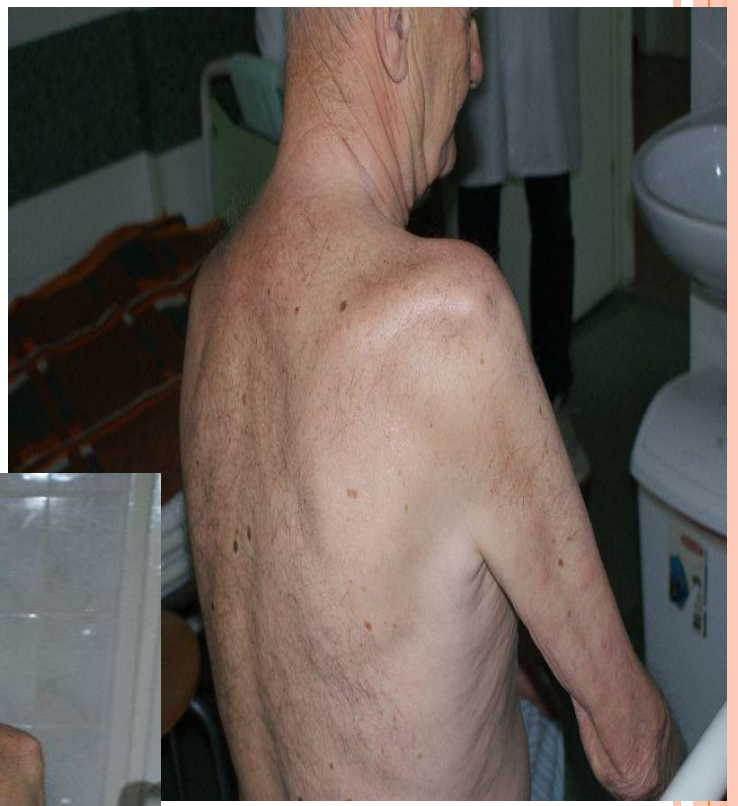






Photo by Prof. J. Zajkowska, Bialystok, Poland







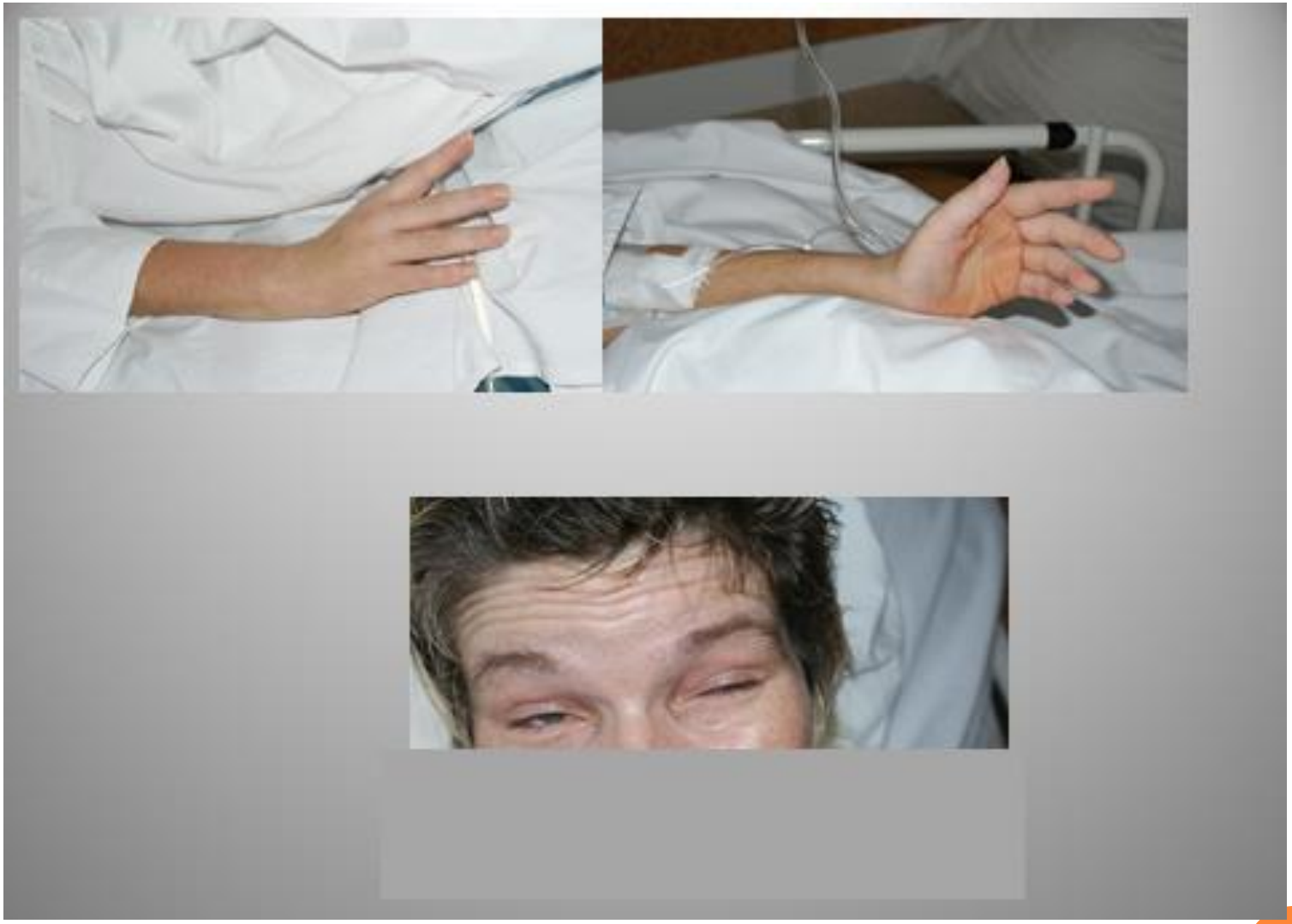
Right brachial plexus paresis

Photo by Prof. J. Zajkowska, Bialystok, Poland



Bilateral brachial plexus paresis

Photo by Prof. J. Zajkowska, Bialystok, Poland



Tetraparesis; cranial nerves paresis

Photo by Prof. J. Zajkowska, Bialystok, Poland

IN THE COURSE OF TBE



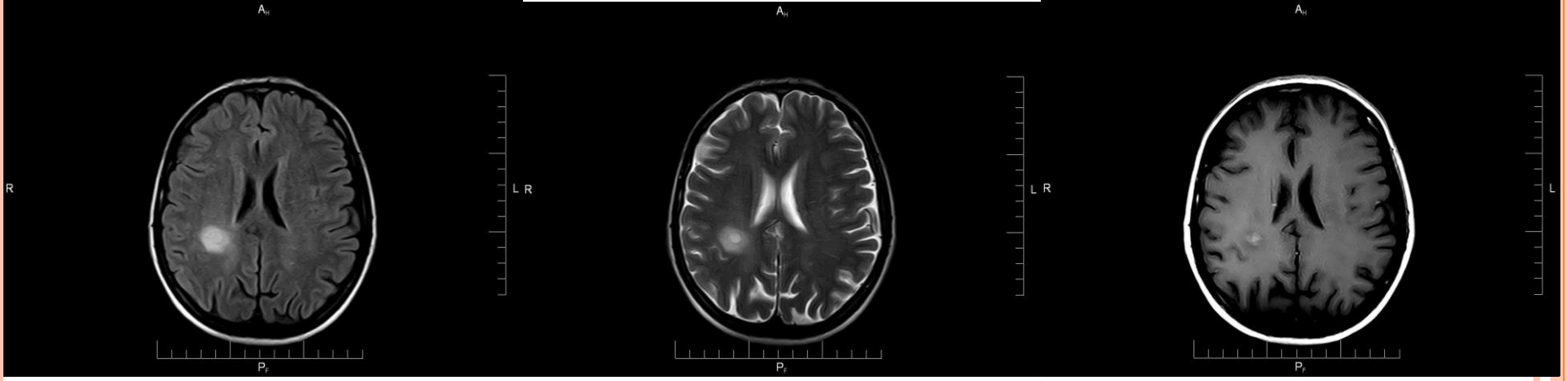
Horizontal nystagmus

Eye lids falling, dilated eye pupils not reacting to light (brainstem affected)

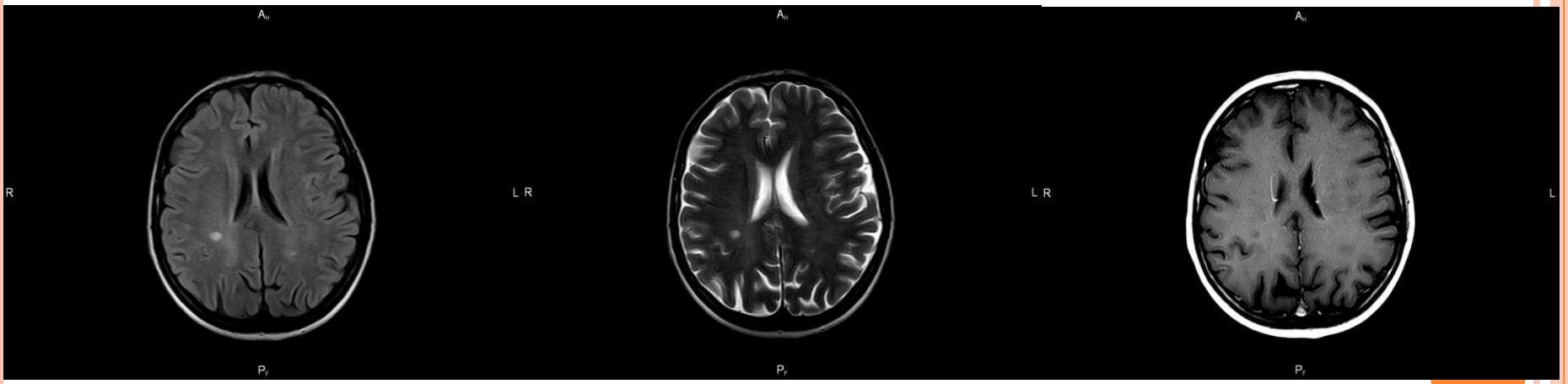
Paresis of cranial nerves: VII dx, XI

Weakness of shoulders muscules

Photo by Prof. J. Zajkowska, Bialystok, Poland



1-3 months after the TBE meningitis ; persistent headaches



1 year after the TBE meningitis; resolving lesions

Photo by Prof. J. Zajkowska, Bialystok, Poland

TBE – Sequelae

Daefness
Vision impairment
Vegetative (over 50% of patients): hyperactivity
irritability
mood changes
sweats
Intelectual problems: concentration (64%)
memory disorder (79%)

Psychiatric syndromes: neurasthenia (5.17%)
depression (15.1%)
psychoorganic (17.24%)

Pancewicz et al., 2006

Psychiatric sequelae - 272 patients (43.8%):

- cognitive disorders (42.1%)
- depression (28.9%)
- sleep disorders (13.2%)
- anxiety (10.5%)

Czupryna et al., 2011

TBE – LETHAL CASES

Mortality rate: 1-4%

68-years old female, coinfection with *Listeria monocytogenes*

71-years old female for 20 years treated with steroids – RA

66- years old kidney transplant recipent

64-years old female, two years after renal transplant (on immunosupression)

Own data

September 5, 2012 the European Commission published an official decision on the addition of TBE to the list of notifiable diseases in the European Union

September 18, 2012 the ECDC published raport about:

- Implementation of the standard case definition of TBE infection
- Collecting standardized, comparable data at EU level
- The need to develop recommendations for immunization of EU citizens as well as for those traveling to areas endemic of this disease!

- **Travel medicine!!!!!**



1. Official Journal of the European Union, 5.9.2012, L 239/3, http://eurlex.europe.eu
2. Epidemiological situation of tick-borne encephalitis in the European Union and European Free Trade Association countries, Technical Report, The European Centre for Disease Prevention and Control (ECDC), http://www.ecdc.europa.eu/en/publications/Publications/TBE-in- -EU-EFTA.pdf
3. World Health Organisation (WHO) Background Document on Vaccines and Vaccination against Tick-borne Encephalitis (TBE), 2011, http://www.who.int/immunization/sage/6_TBE_backgr_18_Mar_net_apr_2011.pdf



TBE – PROPHYLAXIS



Non specific- avoiding tick bites, proper clothes in nature, use of repelents

Specific- vaccination

TBE – Vaccination - Recommendation

persons residing in areas with increased risk of the disease:

- ✓ foresters
- ✓ soldiers
- ✓ firemen
- ✓ border guards
- ✓ farmers
- ✓ trainees in forest areas
- ✓ tourists, participants of colonies and camps

it is recommended when travelling to countries where the disease is endemic, especially if there is a risk of a tick bite

Austria
Albania
Belarus
Bosnia
Croatia
Czech Republic
Denmark
Estonia
Finland
France
Greece
Hungary
Italy
Lithuania
Latvia
Moldova
Germany
Norway
Poland
Romania
Russia
Serbia
Slovakia
Slovenia
Sweden
Switzerland
Ukraine

Kollaritsch et al., 2010; WHO, 2010

TBE – PROPHYLAXIS

- 1st Vaccine – 1970 - (Immuno AG Austri
- In Europe
  - FSME – IMMUN Baxter AG - Pfi
  - Encepur - Novartis - GSK





- Both vaccines – highly immunogenic
- Antibodies, produced after vaccination, have cross-neutralizing response against various strains of the virus of TBE in Europe and Asia (including Siberian and Far Eastern subtype)

Kunz et al., 1976; Heinz et al., 2007; Kunz, 2003

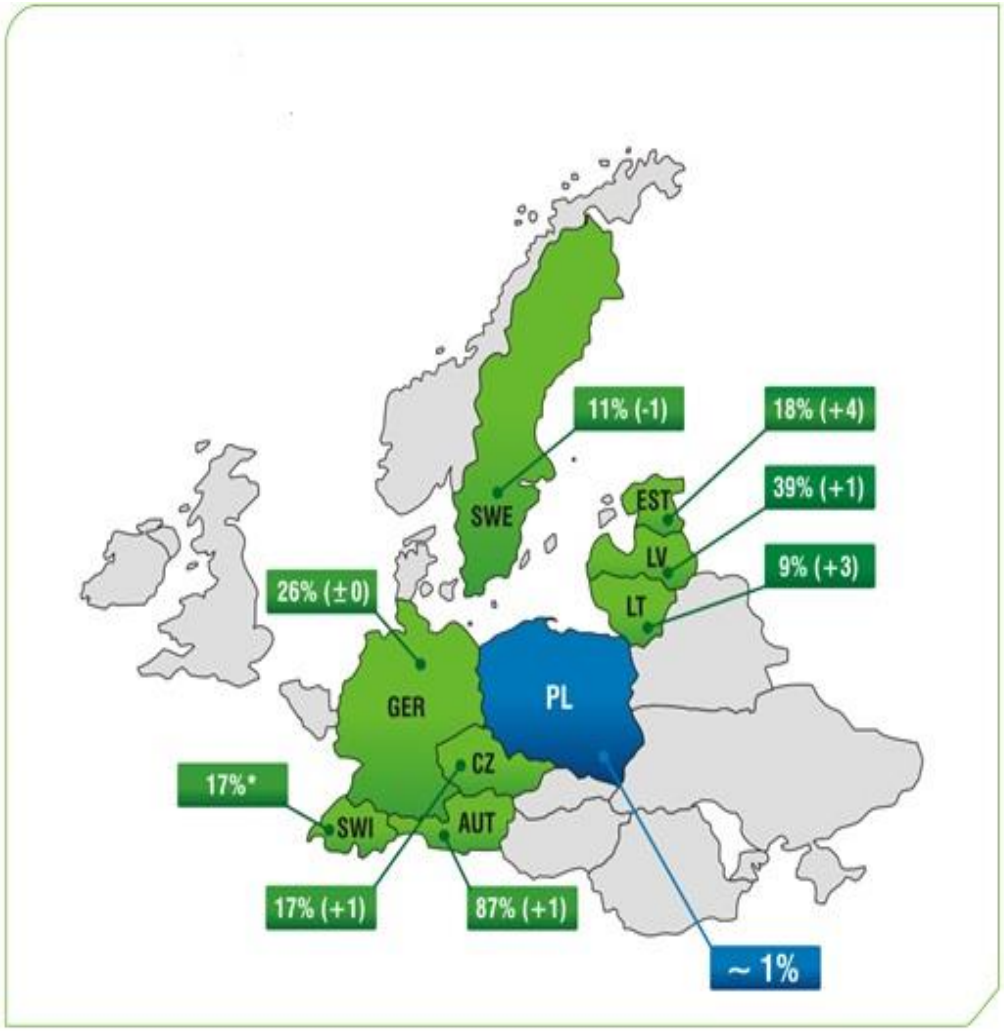
TBE – Vaccination - Schedule

- Administrated in 3-steps scheme - 0, 1-3 and 9-12 months; booster every 3- 5 years
- If the need for rapid immunization (simlilar response):

1. For Encepur® a rapid immunization schedule is licenced with 3 vaccinations on days 0-7-21 and a first booster after 12-18 months
2. For FSME-Immun® the rapid immunization ("modified or accelerated conventional schedule") consists of vaccinations on day 0 and 14 and an (early) third vaccination after 5-12 months (for the adult formulation) and a booster after 12-18 months

Zent et al.,2005; Wittermann et al., 2009b; Schondorf et al., 2007

TBE – VACCINATION - RATE



Reasons:

- Vaccination cost (refunded only for foresters)
- Lack of the awareness of the disease and vaccination


Thank
You for
attention