



## 7<sup>th</sup> ISW-TBE Newsletter

June 2008

Dear colleague,

we are very proud to present to you the 7<sup>th</sup> edition of our international TBE newsletter which you will hopefully enjoy while reading. The newsletter will cover an update on the latest activities of the International Scientific Working Group on TBE (ISW-TBE).

In this edition you will find a summary on:

- 1) **ISW “TBE & EURO 2008” Activities**
- 2) **ESPID (European Society for Pediatric Infectious Diseases), Graz, Austria, 13-16 May 2008**
- 3) **NECTM (Northern European Congress on Travel Medicine), Helsinki, Finland, 21-24 May 2008**
- 4) **ECDC: New Article on TBE in Eurosurveillance: “A Survey on cases of TBE in European Countries”**
- 5) **New ISW-TBE 2008 CD Rom now available**

Please feel free and come back to us in case of comments, further suggestions and ideas for this newsletter that we will certainly try to incorporate in one of our next editions.

Best regards,

A handwritten signature in black ink that reads "Dr. Ursula Kunze". The signature is written in a cursive, flowing style.

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## 1.) ISW “TBE & EURO 2008” Activities

Each year, over 70 million people from EU member states alone travel to TBE endemic regions or countries, and the number continues to grow substantially. Austria and Switzerland are hosting the 2008 European Soccer Championship, and both countries are classified as TBE risk areas. Almost one million travelers are expected to visit EURO 2008 events. The WHO and other official bodies, as well as the International Scientific Working Group on Tick-Borne Encephalitis (ISW-TBE), recommend that everyone traveling to endemic areas should undergo vaccination, as it is the best means of protecting oneself.

In order to spread the knowledge across Europe, a campaign including a multi-stage mailing program called “tick-kick” was developed for travel professionals and certain lay public organizations upfront the EURO 2008 event.



The initiator of this program was the International Scientific Working Group on Tick-borne encephalitis (ISW-TBE). The program stages comprised two postal mails (including various information materials, e.g., poster, info flyer, immunization cards, etc.), an email and a final market survey. During all stages, a focus was placed on addressing the dialogue aspect, thus enabling mailing recipients to easily get in contact with the sender.

In March and April 2008, the Swiss and Austrian authorities posted a recommendation for TBE vaccination on their official websites:

[http://www.bmgfj.gv.at/cms/site/news\\_detail.html?channel=CH0525&doc=CMS1207311214138](http://www.bmgfj.gv.at/cms/site/news_detail.html?channel=CH0525&doc=CMS1207311214138)  
<http://www.bag.admin.ch/themen/medizin/00682/04583/index.html?lang=de>

These recommendations advise everyone who will be going outside in green areas to get vaccinated. The Union of European Football Associations (UEFA) has since adopted this recommendation for EURO 2008.

On May 17<sup>th</sup> 2008 Reuters issued a warning on the tick dangers for football fans at the occasion of the EURO 2008 event (more information under: <http://uk.reuters.com/article/topNews/idUKL0454152920080517>).

Please be aware of possible, additional TBE cases in travelers returning from EURO 2008 if you are treating patients with flu-like symptoms in the first stage or with symptoms of encephalitis in the second stage.



## **2.) ESPID (European Society for Pediatric Infectious Diseases) 2008, Graz, Austria, 13-16 May 2008**

At the Baxter satellite symposium titled: "Combating TBE & MenC: latest news & recent developments" two lectures on TBE were given, one from Prof. Uta Meyding Lamadé, Head of the Department of Neurology, Frankfurt, Krankenhaus Nordwest, Head of Neuroinfectiology, OMZ, University of Heidelberg/Germany and one from Prof. Michael Kunze, Institute of Social Medicine, Center of Public Health, Medical University of Vienna, Austria. In addition there was one interesting poster presentation by Dr. Schosser et al on the long-lasting immunological memory in subjects vaccinated against TBE.

### *TBE- symptoms changing like a chameleon*

Uta Meyding-Lamadé

Descriptions of disease compatible with tick-borne encephalitis date from the 1930's when the virus was first isolated by Russian scientists in 1937. According to WHO, "Tick borne encephalitis (TBE) is a serious acute central nervous system infection, which may result in death or long term neurological sequelae in 35-58% of patients. The fatality rate associated with clinical infection is 0.5-20%." The clinical symptoms may vary; 40 to 60% of the patients recall a tick bite 4 to 28 days prior to evolving symptoms. A couple of days with low fever, headache, fatigue and muscle pain may precede the onset of symptoms with high fever, neck stiffness and disturbances of consciousness. The meningitis subtype is characterized by photophobia, and neck stiffness.

TBE in children can also run a severe course and may lead to permanent sequelae with meningitis being the predominant form of the disease. Although the infection usually takes a milder course with better prognosis in children than in adults, there have been severe cases reported in young children with permanent neurological sequelae, mild or severe, such as headache, behavioural disorders, seizures and pareses.

The meningoencephalitic subtype is characterized by altered consciousness, focal neurological signs like for example epileptic seizures, hemiparesis and neck stiffness and photophobia. Very old patients, babies and immunosuppressed patients may not have any signs of meningeal irritation. A polio-like type is common in TBE patients, characterized by a progressive motor weakness – easily being misdiagnosed in one of the differential diagnosis like myelitis, like Guillain Barré syndrome. Diagnostic procedures and clinical knowledge are getting more experienced by now – nevertheless there are still missing data with respect to all rare but typical manifestations.



## Combating TBE: Vaccination Rates on the Rise

Michael Kunze

Tick-borne encephalitis (TBE) is one of the major human pathogenic flavivirus transmitted by tick bites. The most important are *Ixodes ricinus* (European subtype) and *Ixodes persulcatus* (Asian subtype).

TBE is endemic in 27 European countries as well as Kazakhstan, Mongolia, Japan, China and South Korea and every year new risk areas are detected. An increasing number of more than 10,000 new TBE patients is registered after a bite of an infected tick every year. These facts indicate that TBE is still far too little known, too rarely diagnosed, and not prevented to the degree which it would be possible to achieve. Unfortunately there is no causal treatment available for TBE affected patients. The only efficient prophylaxis is vaccination.

The Austrian vaccination experience over the last 30 years has clearly demonstrated success in significantly reducing the high number of TBE cases. Austria is the leading country with the highest TBE vaccination rate (88%) in Europe, whereas we do find rising, though lower coverage rates in the neighboring countries ranging from 6 to 38%. The success in Austria has been the result of two basic elements: a highly effective vaccine which has clearly for more than 10 years provided data not only on seroconversion but also on field effectiveness showing an equally high protection rate in children and adults of 99% (Heinz et al, Vaccine, 2007) as well as a long-term continuous social marketing program.

## *TBE-IGG-Antibody response to a single dose of FSME-IMMUN Adults\* in subjects with a history of incomplete and/or irregular TBE vaccination\*\**

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**BACKGROUND:** No data is available on the response to a single vaccine dose in subjects with a history of incomplete and/or irregular TBE vaccination. We aimed to investigate seroprotection after a single dose of *FSME-Immune Adults* administered to subjects aged  $\geq 16$  years (subset of  $\geq 6$  years) who presented for TBE vaccination but had at least one major irregularity in their TBE vaccination history (incomplete primary immunization and/or delayed time interval(s)).

**DESIGN AND METHODS:** A post-authorization open-label multi-center observational study was performed in 2.915 subjects aged  $\geq 6$  years. Inclusion criteria were: (1)

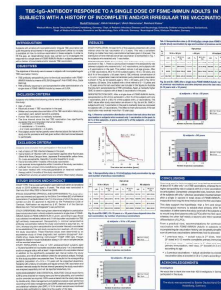


completely documented TBE vaccination history, (2) risk of tick exposure in endemic areas, and (3) informed consent. Subjects received a single dose of *FSME-Immun Adults* or *FSME-Immun 0.25 ml Junior* (according to age). Blood was collected immediately before and 21-84 days after vaccination for TBE IgG antibody measurement (*Enzygnost® Anti-FSME-Virus*, Dade Behring). Achievement of seroprotection was considered successful if the antibody concentration reached  $\geq 25$  U/ml after the study vaccination. The study was approved by an independent ethics committee. Findings for subjects  $\geq 16$  years of age ( $n = 1.251$ ) are reported here.

**RESULTS:** A single dose of *FSME-Immun Adults* achieved overall seroprotection rates as follows: 93.9 % after 1, 98.3 % after 2, 99.3 % after 3, and 98.9 % after  $\geq 4$  previous vaccinations.

**CONCLUSION:** One TBE vaccination established a long-lasting immunological memory in 93.9 %, and  $\geq 2$  vaccinations in  $> 98$  % of the study subjects. Recommendations for continuation of vaccination after incomplete/irregular vaccination schemes should be revised.

- \*) Complete results as full publication will become available in the near future
- \*\*\*) FSME-IMMUN adult is licensed under the trade name FSME-IMMUN 0.5ML in most European countries

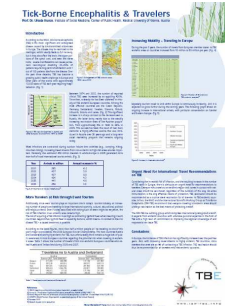


>>> *If you are interested in the symposium CD Rom and the poster from Dr. Schosser et al, please send an email to: [info@publichealth.at](mailto:info@publichealth.at)*



### 3.) NECTM (Northern European Congress on Travel Medicine) 2008, Helsinki, Finland, 21-24 May 2008

At the NECTM conference in Helsinki two posters from the International Scientific Working Group were presented, one by Prof. Ursula Kunze, Institute of Social Medicine, Center of Public Health, Medical University of Vienna, Austria and one by DDr. Martin Haditsch, Elisabethinen Hospital Linz and TravelMedCenter Leonding.



## TICK-BORNE ENCEPHALITIS & THE TRAVELERS

Ursula Kunze

According to the WHO, tick borne encephalitis (TBE) is the most important and widespread disease caused by tick transmitted arboviruses in Europe. The disease may be restricted to the meninges which usually leads to full recovery but may also involve the brain, the upper portions of the spinal cord, and even the nerve roots; these severe manifestations can cause permanent neurological disability. 20–30% of patients require long-term rehabilitation, 1 out of 100 patients dies from the disease. Over the past three decades, TBE has become a growing public health challenge in Europe and other parts of the world, with a minimum of about 13,000 cases of TBE requiring hospitalization every year. Between 1974 and 2003, the number of reported clinical TBE cases increased by an appalling 400%. Since then, a steady rise has been observed in virtually all TBE endemic European countries. Among the most affected are the Czech Republic, Germany, Switzerland, Sweden, Slovenia, Poland, Lithuania, Estonia, and Latvia. These significant increases are in sharp contrast to the decrease seen in Austria, which is mainly due to the steadily increasing vaccination rates of the Austrian population from approximately 6% in 1980 to 88% in 2006.

Most infections are contracted during outdoor leisure time activities (i.e., camping, hiking, mountain biking). Increasing travel streams from non-endemic to high-risk areas are also important. Generally, the estimated 458 mio travelers in whole Europe in 2006, generate more than half of total international tourist arrivals.

Year	Arrivals in Mio.	Annual increase in %
2001	395	- 0,2
2002	407	3,0
2003	407	0,0
2004	424	4,3
2005	441	4,0
2006	458	3,9

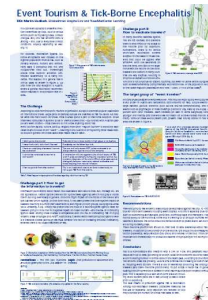


With regard to TBE, the number of travels from European member states to TBE endemic areas or countries, increased during the past 3 years from 60 millions to 70 million travels per year. Especially tourism to and within Europe is continuously increasing and expected to grow further during the next years. The latest data of a new travel stream analysis will be presented more detailed in Helsinki.

Presently no clear recommendations for travelers exist. Therefore tourists are not aware of the risk, especially when traveling in “safe” Europe. As active immunization is the only effective way of protection, TBE vaccination should be recommended as routine travel vaccination for all travelers going to TBE endemic countries.

## *EVENT TOURISM & TICK-BORNE ENCEPHALITIS*

Martin Haditsch



TBE (Tick-Borne Encephalitis) is a viral disease transmitted by ticks that attacks the nervous system and can cause both mild and severe illnesses. According to the WHO it may result in death or long-term neurological sequelae in 35–58% of patients and has a CFR of 0.5 – 2.0%.

Over the past three decades, TBE has become a growing public health problem with more than 13,000 cases requiring hospitalization every year. In addition tourism data show an increasing number of non-vaccinated persons traveling from non-endemic to high-risk areas. By now TBE is endemic in 27 European countries and parts of Asia. During the last years, Europe has become the main tourist destination: with estimated 458 mio. travelers in 2006, Europe actually generates more than half of all international tourist arrivals and the market is expected to grow further. By the EU definition of “travel” (one or more nights abroad) the number of travels within Europe to TBE endemic areas increased from 60 millions to 70 million travels per year during the past 3 years.

Event tourism plays an important role in nowadays’ tourism industry: an increasing number of people are traveling to big international sporting, cultural, educational, political and religious events. Even in short-term travels to endemic areas there is still a risk of TBE infection. Almost half a million people will be traveling to one of this year’s major sports events, the European Soccer Championship. The host countries Austria and Switzerland are endemic for TBE. Unfortunately, there is still a big lack of awareness concerning this risk.

The WHO, the CDC and other official bodies as the International Scientific Working Group on Tick-Borne Encephalitis (ISW-TBE) recommend that everybody traveling to endemic areas should undergo vaccination – the best way of protection. To support the spreading of the information about the disease and preventive measures the ISW-TBE has created a range of information material such as TBE info flyers, posters, endemic pocket maps, immunization cards and a CD ROM containing relevant information for download. In addition, the ISW-TBE started a comprehensive multi-stage mailing initiative to figure out to which extent the topic “event tourism &



TBE” might be interesting for target groups including lay public organizations (like youth groups, sport & leisure clubs, embassies) as well as for travel experts (first results are thought to be presented at this conference).

>>> If you are interested in the original posters, please send an email to:  
[info@publichealth.at](mailto:info@publichealth.at)

#### 4.) ECDC: New Article on TBE in Eurosurveillance: “A Survey on cases of TBE in European Countries”

The European Network for Diagnostics of “Imported” Viral Diseases (ENIVD) is finalizing a project to improve the diagnostic and monitoring of encephalitis viruses in Europe. Part of this study was to analyze the present surveillance situation for tick-borne encephalitis (TBE). A questionnaire was mailed to contact points in all Member States of the EU and three non-EU countries (Norway, Russia and Switzerland) to summarize their TBE surveillance and prevention activities. Information was requested on case definition, type of laboratory tests for TBE diagnostics, investigations regarding tick-transmitted diseases, mapping of endemic foci, vaccination programs, and recommendations for travelers. The survey gives an overview of the existing epidemiological and laboratory sources of information and the number of TBE cases from 2004 until 2007, but also showed that, in particular, case definitions, diagnostic assays for confirmation, and methods/indicators for mapping risk areas differ widely across the participating countries.

The full article is available under:

<http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=18848>

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Surveillance and outbreak reports

A SURVEY ON CASES OF TICK-BORNE ENCEPHALITIS IN EUROPEAN COUNTRIES

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 Date of submission: 05 December 2007

The European Network for Diagnostics of “Imported” Viral Diseases (ENIVD) is finalizing a project to improve the diagnostic and monitoring of encephalitis viruses in Europe. Part of this study was to analyse the present surveillance situation for tick-borne encephalitis (TBE), which is the most important flavivirus infection of the central nervous system in the European Union (EU) and Russia. A questionnaire was mailed to contact points in all Member States of the EU and three non-EU countries (Norway, Russia and Switzerland) to summarise their TBE surveillance and prevention activities. Information was requested on case definition, type of laboratory tests for TBE diagnostics, investigations regarding tick-transmitted diseases, mapping of endemic foci, vaccination programmes, and recommendations for travellers. The survey gives an overview of the existing epidemiological and laboratory sources of information and the number of TBE cases from 2004 until 2007, but also showed that, in particular, case definitions, diagnostic assays for confirmation, and methods/indicators for mapping risk areas differ widely across the participating countries. The data will help to develop recommendations for the standardisation and quality control of TBE surveillance and diagnostics.

Introduction

Tick-borne encephalitis (TBE) is the most important flavivirus infection of the central nervous system (CNS) in Europe and Russia. The total annual number of cases is estimated to be up to 10,000 in Russia and about 3,000 in European countries [1-4]. According to the International Committee for Taxonomy of Viruses, TBE virus is classified as one species with three subtypes, namely the European subtype (which comprises almost all known isolates from Europe), the Siberian subtype (mainly isolates from Ural, Siberia and far-eastern Russia) and the Far Eastern subtype (mainly isolates from far-eastern Russia, China and Japan).

The three TBE virus subtypes are associated with varying degrees of disease severity [2-4]. Human infections with Far Eastern subtype viruses are usually severe, frequently with encephalitic symptoms (focal meningoencephalitis or polyencephalitis), with an associated fatality rate between 5 and 35%.

This type does not cause chronic disease. In contrast, TBE virus infections of the Siberian subtype cause a less severe disease (fatality rate between 1 and 3%), with a tendency for patients to develop chronic or extremely prolonged infections accompanied by diverse neurological and/or neuropsychiatric symptoms. In contrast to these two forms, infections caused by European strains

typically take a biphasic course [5]: after a short incubation period (usually 7-14 days, with extremes of 4-28 days), the first (viraemic) phase presents as an uncharacteristic influenza-like illness lasting 2-4 days (range 1-8 days) with fever, malaise, headache, myalgia, gastrointestinal symptoms, leukocytopenia, thrombocytopenia and elevated liver enzymes, often followed by a symptom-free interval of about one week (range 1-33 days). The second phase of TBE occurs in 20-30% of infected patients and is marked by four clinical features of different severity (meningitis, meningoencephalitis, meningoencephalomyelitis or meningoencephalo-radiculitis) and the appearance of specific antibodies in the serum and cerebrospinal fluid (CSF). This is usually the time when patients with high fever and severe headache seek medical advice. The fatality rate in adult patients is less than 2%. However, severe courses of TBE infection with higher mortality and long-lasting sequelae often affecting the patient's quality of life have been correlated with increased age [6-8]. More detailed information on the clinical picture, case definition and other issues of interest are available in a TBE fact sheet on the ENIVD website (<http://www.enivd.org>).

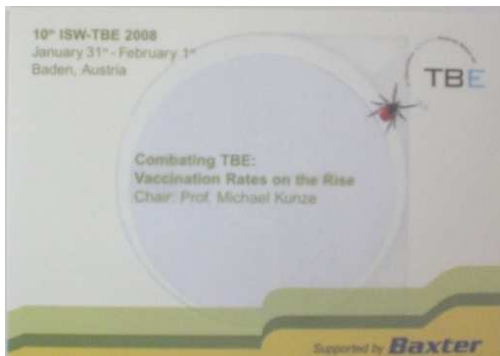
The epidemiology of TBE is closely related to the ecology and biology of ticks [2,3,9,10]. In nature, TBE virus is propagated in a cycle involving permanently infected ticks and wild vertebrate hosts. Virus transmission occurs horizontally between tick vectors and vertebrates, especially between spring and autumn, with small mammals (mainly rodents) serving as virus reservoirs. In addition, trans-stadial and trans-ovarial transmission of the virus, as well as co-feeding of infected and non-infected ticks on the same host play a major role in virus transmission [11]. In contrast to other tick-transmitted diseases, such as Lyme borreliosis, TBE is distributed in an endemic pattern of so-called natural foci over a wide geographical area focussed on central Europe, the Baltic states and Russia. The distribution of TBE is determined by the occurrence of the respective tick vectors in certain regions [3,10]. While *Ixodes ricinus* is the prevalent hard tick species across Europe and therefore the most important transmitter of the European TBE virus subtype, *Ixodes persulcatus* occurs in forest regions of the Ural, Siberia and far-eastern Russia and is the main vector of the other subtypes. Co-circulation of two or all three subtypes could be shown for Finland and the Baltic states where the distribution areas of the two main tick species overlap [12,13].

However, the virus prevalence in ticks as well as the prevalence of infected ticks within the risk areas can vary [4,9,14,15]. Countries with high-risk areas are Russia, Latvia, Lithuania and Estonia. TBE is also a significant issue in Germany, the Czech Republic, Poland, Switzerland, Sweden, Finland, Slovakia, Hungary and Slovenia. Even in Austria, the only country with progressively decreasing



## 5.) New ISW-TBE 2008 CD-ROM now available

The new ISW-TBE CDROM from the latest meeting in January 2008 in Baden, near Vienna is now available containing all new aspects on epidemiology, vaccination coverage, new clinical trials and publications.



>>> *If you are interested in the latest ISW-TBE information package including the CDROM, please contact: [info@publichealth.at](mailto:info@publichealth.at)*

### **Additional information:**

>>> *On the TBE prevention website ([www.TBE-prevention.info](http://www.TBE-prevention.info)) a listing of TBE vaccination centres has been introduced. In case you would like to your vaccination center to be a part of this list, please contact Michael Leitner at: [info@publichealth.at](mailto:info@publichealth.at)*