



10th ISW-TBE Newsletter

July 2009

Dear colleague,

we are very proud to present to you the 10th edition of our international TBE newsletter, which you will hopefully enjoy 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.) 10th IJSTD 2009 (International Jena Symposium on Tick- Borne Diseases, Weimar, Germany, 19-21 March 2009)**
- 2.) 11th CISTM 2009 (11th Conference of the International Society of Travel Medicine Budapest, Hungary, 24-28 May 2009)**
- 3.) ESPID 2009 (European Society of Pediatric Infectious Diseases, Brussels, Belgium, 9-13 June 2009)**
- 4.) Activities of the Austrian Self-Help Group for Tick Victims 2009**
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- 6.) Conference Announcements 2009**
 - a.) 2nd European Congress of Immunology (ECI), Berlin, Germany, 13-16 September 2009
 - b.) 5th European Meeting on Viral Zoonoses (EVZ), St. Raphaël, France, 26-29 September 2009
 - c.) 20th Annual Congress of the European Confederation of Primary Care Pediatricians (ECPCP), Berlin, Germany, 13-14 November 2009

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.) 10th IJSTD 2009 (International Jena Symposium on Tick-Borne Diseases, Weimar, Germany, 19-21 March 2009)



Some 300 scientists from 31 countries around the world gathered in Weimar, Germany, from 19-21 March 2009 to present and discuss new approaches to containing the increasing threat of tick-borne diseases, foremost among them Lyme borreliosis and tick-borne encephalitis (TBE). The focus of the 10th International Jena Symposium on Tick-Borne Diseases (IJSTD-X), jointly organized by the National Reference Laboratory for Tick-Borne Diseases of the Friedrich Loeffler Institute and the Institute for Nutritional

Sciences of Friedrich Schiller University in Jena, was on a theme perfectly fitting the occasion of the 10th anniversary of the biannual meeting: the prevention of tick-borne diseases.

“Research into the physiology of ticks and the characteristics of the pathogens they transmit is essential to allow new preventive measures to be developed,” said Professor Jochen Süss from the Friedrich Loeffler Institute, Jena, and one of the organizers of the symposium. What started out as a continued education program for a group of some 40 physicians from Austria and Germany about 19 years ago has developed into a scientific conference in its own right. The presentations given during the 3-day meeting covered a vast diversity of subjects, from the role of tick repellents, whose effectiveness has been shown to range from marginally effective to ineffective, to new technologies that chemically trap repellents in textile fibers.

Comparison of two TBE IgG antibody ELISA tests (Enzygnost[®] and Immunozy[®]) versus a neutralization assay with respect to seropositivity thresholds

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Jan Bartel, Limbach Laboratory, Heidelberg, Germany

Oskar Enzersberger, Analytical Quality Control, Baxter AG, Orth, Austria

Peter Chiba, Clinical Biochemistry Laboratories, Center for Physiology, Pathophysiology and Immunology, Institute of Medical Chemistry, Medical Univ. Vienna, Austria

Reinhard Kaiser, Neurological Clinic, Klinikum Pforzheim, Germany

Ulrich Mansmann, Department of Medical Informatics, Biometrics and Epidemiology, University of Munich, Germany

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To enable comparison of the results of studies using different ELISA test systems for the determination of anti-TBEV antibodies, knowledge of the correlation of these tests is essential. So far, there have been no data on the comparative performance of the two tests commonly used for the determination of anti-TBEV antibody levels, i.e., Enzygnost[®] Anti-FSME Virus (Dade Behring) and Immunozy[®] FSME IgG ELISA (Progen).

Schosser et al. therefore compared both test systems with the Baxter in-house neutralization assay (NT) in a post-authorization observational study. The ELISA comparison cohort included 251 study participants aged 16 years or older. Participants received a single dose of FSME-IMMUN. Because the focus of the study was on the lower range of antibody concentrations, only blood samples drawn before vaccination were used for this comparison.

The thresholds for seropositivity in the Enzygnost[®] and Immunozy[®] were ≥ 10 U/ml and >126 VIEU/ml, respectively. The Baxter in-house NT, serving as the reference for seropositivity, used a threshold of $\geq 1:10$. The positive predictive value (PPV) was used as a parameter for the suitability of seropositivity thresholds.

The PPV [95% confidence interval] of Enzygnost[®] vs Baxter NT was 99.1% [96.7%; 99.9%]. The PPV of Immunozy[®] vs Baxter NT was 98.2% [95.5%; 99.5%]. Thus, at the thresholds used, Enzygnost[®] and Immunozy[®] showed comparable performance with respect to seroconversion when compared to the Baxter NT.



Serological Response to Tick-Borne Encephalitis (TBE) Vaccination in the Elderly – a Retrospective Analysis from Clinical Practice

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V. Král, Regional Institute of Public Health (RIPH), Ústí nad Labem, Czech Republic



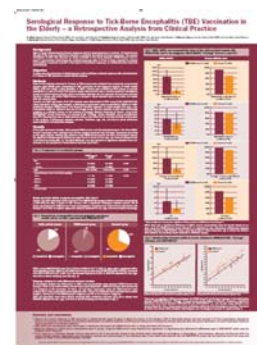
The responsiveness to vaccines is known to decrease with age. The product information of both TBE vaccines for adults (FSME-IMMUN and Encepur[®]) recommends determining the antibody response after 2 of the 3 doses required for primary immunization in persons over 60. In the event of insufficient response, an additional dose should be administered.

Jílková et al. collected data on the antibody response to 2 doses of TBE vaccine from previously unvaccinated persons aged 60-86 years presenting to the Regional Institute of Public Health (RIPH), Ústí nad Labem, Czech Republic, in 2007. All vaccinees received the first 2 doses with either FSME-IMMUN or Encepur[®]. Blood samples were to be taken 4-8 weeks after dose 2. Specific anti-TBEV IgG levels of all 245 samples were determined at RIPH using ELISA Immunozy[®] (strain Neudörfel).

During data analysis, a difference in geometric mean concentrations (GMCs) of TBEV antibodies between FSME-IMMUN and Encepur[®] became apparent. To verify whether this was a vaccine-specific effect or related to the use of a single assay, the last 80 samples were additionally analyzed, in a blinded manner, at the Institute of Virology, Medical University of Vienna, using ELISA Enzygnost[®] (strain Karlsruhe), an in-house ELISA "Virology" (strain Neudörfel), and a neutralization test (NT).

Of the 245 vaccinees included, 165 received FSME-IMMUN and 80 received Encepur[®]. 60 of the FSME-IMMUN vaccinees were excluded from further analysis because they had been vaccinated according to the rapid scheme, leaving 105 patients in the FSME-IMMUN group. No significant between-group differences were found in terms of sex, age, and interval between dose 2 and blood sampling. Also, there was no significant deviation from randomness in the sequence of administered vaccines.

Overall, 18% of vaccinated persons who had received the first 2 vaccinations required for primary immunization had antibody concentrations below the protection threshold, confirming the importance of testing the antibody response after the second vaccination and administering an additional dose in the event of insufficient response. GMC/GMTs and seropositivity rates were higher in individuals vaccinated with FSME-IMMUN than in those vaccinated with Encepur[®]. While the difference in GMCs and/or seropositivity rates in assays using the FSME-IMMUN strain Neudörfel was significant, no significance was obtained for differences seen in Enzygnost[®], which uses the Encepur[®] strain Karlsruhe. Thus, there was a difference between immune responses to the 2 vaccines with respect to the antibody levels detectable by homologous or heterologous immunoassays. Because the factor by which the results differed between heterologous and homologous vaccines was approximately 2, the difference seen in the overall data obtained with the Immunozy[®] assay may only partly be due to the assay and appears to reflect a true difference between vaccines.





2.) 11th CISTM 2009 (11th Conference of the International Society of Travel Medicine Budapest, Hungary, 24-28 May 2009)

The 11th Conference of the International Society of Travel Medicine (CISTM11) was held in Budapest, Hungary from 24-28 May 2009. The goal of the international meeting was to share advances in the science of travel medicine presented in a spectacular European city.

Not only does Budapest have a rich and fascinating history it has also managed to maintain its and is rightly known as the “Queen of the Danube”.

Designed to meet the needs of travel media industry and manufactures of travel-health-related products, drugs and vaccines. The conference was intended for those interested in the latest scientific and educational developments, in the field of travel and migration medicine.

Combating TBE: Vaccination Rates on the Rise



PROF. DR. MICHAEL KUNZE
Institute for Social Medicine, Medical University, Vienna

TBE is endemic in regions of 27 European countries, and new risk areas are discovered every year. At least 13,000 cases of TBE are referred to hospitals each year, but due to underreporting, the true incidence of TBE is likely to not have been fully recognized. One reason for this is that TBE produces clinical features similar to those of many other types of meningitis and encephalitis.

Treatment of TBE is purely symptomatic—a causal therapy is not available. Vaccination is the only efficient protection. Austria is the country with the highest TBE vaccination rate in Europe. According to representative surveys, 87% of Austrians have had at least one TBE vaccination, and 66% are within the officially recommended vaccination schedule. Compared with vaccinations for other diseases, TBE vaccination has a protective effectiveness of about 99%. As a result, annual numbers of new TBE infections in Austria have dropped to about 10% of the levels registered in the pre-vaccination era. In the same period however, Austria’s neighboring countries have witnessed a dramatic increase in TBE infections, indicating that the virus has not become less rampant or virulent. According to recent estimates, TBE vaccination between 2000 and 2006 prevented at least 2,800 TBE cases in Austria – about 20 of them lethal. Unfortunately, because the virus does not depend on humans for survival, the high vaccination coverage has no effect on the circulation of the TBE virus in nature. Social marketing is an indispensable tool of science-oriented social medicine, striving to integrate the concept of disease prevention into public health care. The International Scientific Working Group ISW-TBE, comprised of internationally recognized scientific experts, provides the scientific background to public health recommendations on TBE. One of the main future challenges will be to change the perception of TBE vaccination being a measure only for people living in endemic regions. Especially among people traveling from non-endemic to endemic areas, there is still a lack of awareness of the disease.

From Childhood to Golden Age: Increased Mobility – Increased Risk for Contracting TBE?



DDr. MARTIN HADITSCH
Institute for Hygiene, Microbiology and Tropical Medicine, Elisabethinen Hospital, Linz, and TravelMedCenter Leonding, Austria

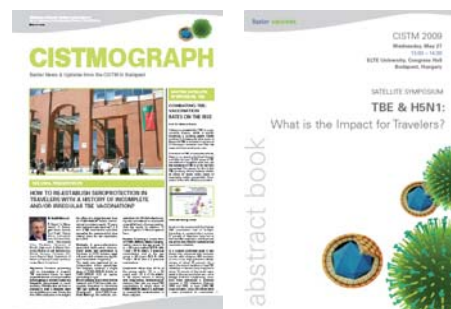
Over the past three decades, TBE has become a growing public health problem in Europe and other parts of the world, with more than 13,000 cases of TBE requiring hospitalization every year. Travel streams of non-vaccinated individuals from non-endemic to high-risk areas are also on the rise, with high-risk areas today covering much of Eastern and Central Europe and increasingly spreading to parts of Northern, Southern and Western Europe.



Based on sound statistical data the risk of contracting TBE in a highly endemic area is comparable to the risk of contracting typhoid fever in India (1:10,000 per month). Whereas vaccination against typhoid fever (a treatable disease by the way) is invariably recommended to travelers going to India, TBE is still a largely neglected risk.

During their holidays most tourists spend a part of their time outdoors pursuing exposure prone activities. More than one third of tourists visiting Austria in the summer come for the hiking or mountaineering experience-not knowing that TBE has already conquered regions of 1,500 m above sea level. Event tourism (sports, culture, politics, religion), more than “regular tourism“ is even more likely neglect issues other than those related to primary purpose of the trip including travel-associated health risks. Unfortunately, when it comes to leisure time activities and vaccination information on health risks is not very popular neither among travelers themselves nor among travel agencies who would play a crucial role in building awareness.

To order the CISTM TBE publications, please contact michael.leitner@publichealth.at



3.) ESPID (European Society of Pediatric Infectious Diseases , 2009 Brussels, Belgium, 9-13 June 2009)

The landmark annual meeting of the European Society for Paediatric Infectious Diseases (ESPID) was held in Brussels, Belgium, 9-13 June 2009.

The congress again included a high-quality scientific program focusing on “serious bacterial infections”. Top international experts presented new insights and initiated clinical discussions on bacteriology, epidemiology, diagnosis, prevention, and treatment of major pediatric infectious diseases.

The conference also featured *Meet the Expert* sessions, industry symposia, and a trade exhibition. At the conference, two posters on FSME-IMMUN were presented, one by Dr. Eva Maria Pöllabauer, Global Clinical and Medical Affairs , Center of Public Health, Baxter Innovation GmbH, Vienna, Austria and one by Dr. Rudolf Schosser, Medical Affairs, Baxter Germany GmbH, Heidelberg, Germany.

Seropersistence of Tick-Borne Encephalitis (TBE) Antibodies in Children and Adolescents



DR. E.M. PÖLLABAUER

Global Clinical and Medical Affairs, Baxter Innovation GmbH, Vienna, Austria

This study investigated the seropersistence of TBE antibodies and the response to a booster vaccination with FSME-IMMUN in individuals aged 3–18 years. Seropersistence was assessed at 24 and 34 months after the third vaccination with FSME IMMUN 0.25 ml administered in the context of primary immunization. The first booster was planned at 3 years after the third vaccination but was postponed for individuals who still showed high TBE antibody levels (ELISA > 1000 VIE U/ml and positive NT result). Further follow-up was done at 46 and 58 months, and a booster vaccination was offered at either 4 or 5 years after the third vaccination, depending on antibody levels. The booster response was assessed 21–35 days after vaccination.



A total of 358 individuals were enrolled in the study, and 174 received the booster 3 years after the third vaccination. Of these, 163 were still seropositive, showing ELISA levels below 1000 VIE U/ml. At 46 and 58 months 172 children were further followed for antibody persistence. At 4 years after the third vaccination a booster vaccination was administered to 29 participants – all of whom were still seropositive. At 5 years after the third vaccination, only one study participant was vaccinated. A total of 130 children did not receive the first booster vaccination during the entire study because they still had high TBE antibody levels. Overall, a very good booster response was observed in all age groups.

Can the booster interval of the adult/pediatric FSME-IMMUN TBE vaccine formulations be extended from 3 to 5 years?

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Ulrich Mansmann, Department of Medical Informatics, Biometrics and Epidemiology, University of Munich, Germany

Ulrich Heininger, Department of Pediatric Infectious Diseases and Vaccinology, University Children's Hospital Basel, Switzerland

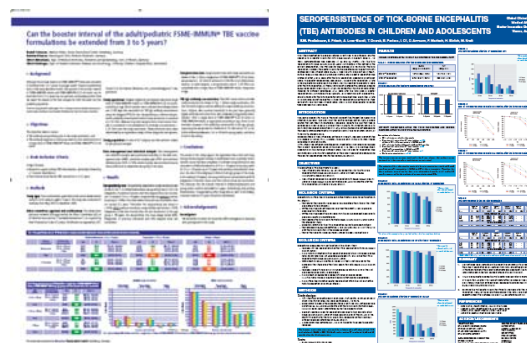


There is an absence of data on whether the booster interval of FSME-IMMUN Adults and FSME-IMMUN 0.25 ml Junior can be extended from 3 to 5 years. Therefore a post-authorization open-label multicenter observational study was performed in 2915 individuals aged ≥ 6 years. Study participants had to have received at least one TBE vaccination and had to have exceeded the recommended interval until the next vaccination by $\geq 20\%$. Depending on their age, participants received a single dose of FSME-IMMUN Adults or FSME-IMMUN 0.25 ml Junior. Blood was collected immediately before and 21-84 days after vaccination for TBE IgG antibody measurement using (Enzygnost[®]). Seropositivity was assumed at ≥ 10 U/ml and seroprotection at ≥ 25 U/ml. Cohort reported here: $n=1,204$; regular primary immunization with (B+) or without (B-) booster; time since last vaccination ≥ 4.5 to <5.5 (T1), ≥ 5.5 to <8 (T2), and ≥ 8 yrs (T3). Age stratification: children <16 , young adults ≥ 16 to <50 , and elderly ≥ 50 years.

Seropositivity rates before the study vaccination (T1/T2/T3) were as follows: children (B-) 100.0/93.5/96.0%, (B+) 100.0/100.0/100.0%; young adults (B-) 100.0/87.9/84.8%, (B+) 97.7/99.0/97.8%; elderly (B-) 83.3/60.0/54.4%, (B+) 88.9/83.7/79.6%. Seroprotection after the study vaccination was $\geq 96.5\%$ irrespective of age and booster status.

Overall, study participants aged <50 years had a sufficient seropositivity rate up to 5.5 years after primary immunization, supporting extension of the booster interval to 5 years if backed by data from clinical studies. In persons aged ≥ 50 years the seropositivity rate was consistently $<90\%$ indicating that, in this age group a booster interval of 3 years should be maintained.

To order the ESPID poster presentations, please contact michael.leitner@publichealth.at





4.) Activities of the Austrian Self-help Group for Tick Victims 2009

It's Tick Time: Information Campaign in Austrian Hospitals



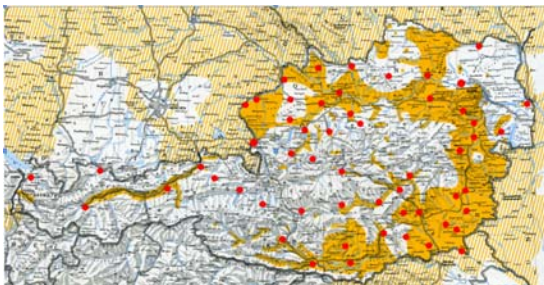
MRS. CHRISTINE FREUND,
TBE-Victim Self-Help Group,
Vienna "Advice and Help for Tick Victims".

It's already 10 years that the "Tick-Victim" Self-Help Group (SHG) first started its activities with a rather unconventional information campaign: Equipped with educational brochures on TBE and borreliosis, we set up a small information booth in the lobbies of hospitals located in regions endemic for TBE to make visitors aware of the potential dangers of a tick bite. We soon realized that we needed to extend our activities to hospitals located outside high-risk areas. Many visitors and physicians initially viewed our action with some skepticism, particularly in Austria's western federal provinces where, at that time, the risk of TBE and borreliosis was comparatively low.

Since then, however, our original idea has developed into a treasured tradition, which is also reflected in our annual information campaign having become a cooperative effort between the hospital administrations and the SHG.

Moreover, the "Tick-Victim" SHG is regularly invited by the nursing schools run by the respective hospitals to give lectures on TBE (viral infection) and borreliosis (bacterial infection), covering two training units of the "Infection and Hygiene" training module.

Our initiative, taking place in no less than 65 hospitals, rehab centers, pharmacies, and insurance companies throughout Austria, takes place from April to June.



The red points show the places, where the TBE-Victim Self Help Group organized their Information days in the hospitals, drug stores and rehab hospitals in the last 10 years.

5.) Vaccination Reminder on www.tbe-prevention.info

Vaccination reminder

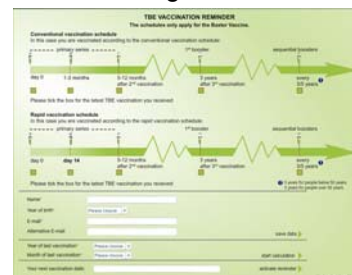
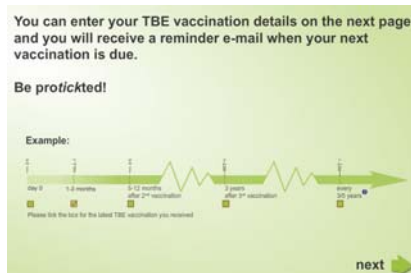
The vaccination reminder was implemented on the www.tbe-prevention.info website in a matter of only a few weeks (planning: Q1.2009; pilot phase: Q2.2009).

The purpose of the project was to allow visitors to the site to sign up for being reminded by email when their next vaccination is due. The need for this service had become evident through market research showing that a sizeable proportion of the population keeps forgetting when their next booster vaccination is due. The aim was to keep the system simple and straightforward to reach people of all age groups. This was also the reason why both the standard and the rapid immunization scheme are presented.



To guarantee ease of use for all age groups, the system is based mainly on check and dropdown boxes. In a first step, users are asked to select the type of TBE vaccination they last received. They are then asked to enter their name, year of birth, email address, and the year and month of their most recent TBE vaccination. From these data, the system calculates the date the next vaccination is due.

The TBE Prevention website is an ideal platform for implementing the vaccination reminder. After a detailed planning phase, the reminder was introduced and promoted at various international congresses. Folders distributed carried stickers with the reminder logo, and at the congresses in Budapest (CISTM) and Brussels (ESPID), buttons with the reminder logo were distributed at the Baxter booth and drew much attention.



6.) Conference Announcements:

a.) 2nd European Congress of Immunology (ECI), Berlin, Germany, 13-16 September 2009



The Scientific Program Committee has worked out an outstanding scientific program in four tracks covering the most recent developments in basic and clinical immunology. In addition, this meeting has a pan-European educational objective in exposing young European scientists to an international rather than a national audience. Their aim is to present an overview of fundamental and applied aspects of immunology.

For more information, please go to: <http://www.eci-berlin2009.com/>

b.) 5th European Meeting on Viral Zoonoses (EVZ), St. Raphaël, France, 26-29 September 2009



As a continuation to the successful European meetings on viral zoonoses in St. Raphaël in 2001, 2003, 2005, and in St. Andrews in 2007, the fifth meeting similarly covers research on ecology, epidemiology, virology and prevention of zoonotic viral diseases.

For more information, please go to: <http://www.euroviralzoon.com/index.html>

c.) 20th Annual Congress of the European Confederation of Primary Care Pediatricians (ECPCP), Berlin, Germany, 13-14 November 2009



The congress will take place in the Ludwig-Ehrhard-Haus with its interesting architecture, providing a good meeting place and atmosphere for stimulating lectures. The lectures will concentrate on the emergent problems of socially disadvantaged and migrant children, on early language development and the importance of good intercultural communication. Furthermore, you will learn about the impact of climate change on new infectious diseases, the development of antibiotic resistance in Europe and traveling with children in the tropics.

For more information, please go to: <http://www.pza-berlin2009.de/index>.

This email is intended merely to highlight issues and not to be comprehensive, nor to provide medical advice. Should you have any questions on issues reported here, please contact Prof. Ursula Kunze (ursula.kunze@meduniwien.ac.at). We hold your email address, which we use to send you this electronic news update on TBE and on the activities of the ISW -TBE group. We use your details for our own internal purposes only. If any of your details are incorrect or if you no longer wish to receive emails from us, please let us know by emailing us at ursula.kunze@meduniwien.ac.at.