

TICK-BORNE ENCEPHALITIS IN EUROPE AND BEYOND – THE EPIDEMIOLOGICAL SITUATION AS OF 2007

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This review presents an overview of the developments in the epidemiology of tick-borne encephalitis (TBE) during 2007 in Europe, the Far East and Asia, as well as some comments interpreting the various developments. The recent TBE situation in 29 European and four non-European countries is shown and discussed. The number of registered TBE cases from 1976 to 2007 in 19 European countries with endemic TBE is presented.

Although criteria for TBE reporting vary from one country to another and it is necessary to account for unreported cases, an overall increase of TBE incidence during the last 30 years can clearly be established. Besides changes in climate and weather, a number of additional factors are probably responsible for this rise: increased exposition, partly due to socio-economical and political changes, and other factors that are for the most part unknown. In addition, the immunisation coverage in the population of some of the countries is discussed.

Introduction

In this article, we provide an overview on the epidemiology of tick-borne encephalitis (TBE) in Europe, the Far East, and Asia as of 2007, and comment briefly on the situation. We refer to the extensive overview on this subject compiled in 2003 [1], which includes all available data up to 2001, and the overview of 2005 [2], which summarises the epidemiology of TBE up to 2004.

The epidemiology of TBE in Europe

Over the last 30 years, a continuous increase in TBE morbidity – 400% from 1974 to 2003 – was observed in Europe [3]. From 2004 to 2006, another considerable increase was seen in a series of TBE-endemic countries, such as the Czech Republic, Germany, Slovenia, Sweden and Switzerland. In addition to social, political, ecological, economic, and demographic factors, changing climate conditions may have created more favourable living conditions for ticks and thus led to a further spread of tick-borne diseases [4-8]. A continuous increase of the average temperatures and of the precipitations leads to increased humidity and improves the living conditions of ticks. For example in Germany there was an increase in the average temperatures of over 0.6 to 1.5°C from 1951 to 2000 (prognosis 2001 to 2055 >1.8°C) and rainfall has increased annually by 9%, = 90 mm [9]. Data show that the winter activity of ticks increases [10,11], that their life cycle accelerates [12,13], that they are found at higher and higher altitudes above sea level [14,15] and that they can be found in more northern regions [16-19, Jeskelainen pers. comm.].

TBE is a notifiable disease in 16 European countries, including 13 European Union (EU) Member States (Austria, the Czech Republic, Estonia, Finland, Germany, Greece, Hungary, Latvia, Lithuania, Poland, Slovak Republic, Slovenia, Sweden) and three non-EU Member States (Norway, Russia and Switzerland) [20].

At present, TBE is not notifiable in Belgium, France, Italy, Portugal, Spain, Denmark, and the Netherlands. In Belgium, Portugal, Spain, Denmark (cases on Bornholm only) and the Netherlands, no autochthonous TBE cases were reported; the reasons are largely unknown.

Figure 1 lists the number of TBE cases for 19 European countries in which TBE is endemic and which report reliable data from 1976 to 2007. We have tried to assess the situation as a whole, despite being aware of the fact that the registration procedure for TBE cases is different in the individual countries, that in some countries the disease is not notifiable and that different case definitions for TBE are applied. In countries without notification of TBE cases some research groups register the TBE cases. We also know that there are significant differences in the quality and quantity of the diagnostics in individual countries. In some countries, a high number of under-reporting/ under-diagnosing must be expected. In highly endemic areas where the majority of the population is vaccinated against TBE, as is the case in Austria, the number of reported cases of TBE does not adequately reflect the real risk of infection.

In these countries, between 1990 and 2007 a total of 157,584 TBE cases were documented; in Europe without Russia a total of 50,486 cases. This is an average of 8,755 cases per year in Europe within this 18-year period, or 2,805 cases in Europe excluding Russia. Between 1976 and 1989, a total of 38,572 cases in Europe and of 20,328 cases in Europe excluding Russia were registered, an average of 2,755 per year including Russia and 1,452 in Europe excluding Russia. A comparison of the two time periods shows an increase in registered TBE cases to 317.8% in Europe and to 193.2% in Europe excluding Russia. This clearly demonstrates the importance of this disease for the individual as well as for the healthcare systems of these countries and shows a significant increase in the number of registered TBE cases since 1990.

In 2006, 3,914 cases were reported in Europe (7,424 if Russia is included). This was the highest value since 1995. In 2007,

the number of registered cases in Europe fell to 2,364 (5,462 if Russia is included). This is a reduction of 60.4 %. This decrease was observed in nearly all European countries (Croatia, Czech Republic, Estonia, Germany, Lithuania, Poland, Russia, Slovak Republic, Slovenia and Switzerland), with the exception of Sweden, Norway, and Hungary, where a further increase of incidence was observed, and Latvia, where the numbers stabilised at the low level of 2006. It should be noted, however, that more attention to the disease may have led to a higher number of registered cases in these countries.

Possible factors influencing the epidemiology

The reasons for the increase of TBE cases over a period of 30 years throughout Europe and their decrease in most of the countries in 2007 are unknown. However, there may be an association with the exceptional weather conditions in 2007 (in Central Europe). After the extremely warm winter 2006/07, the ticks were active very early in the year (February/early March) and had certainly lost some of their energy due to their constant activity. The urgently required search for a host for a blood meal, however, was hampered in April by the extremely warm and dry weather conditions. As a rule, the ticks had to retreat to the leaf litter as a humidity reservoir. In the summer of 2007, strong precipitations led to a reduced exposure of humans due to a reduced rate of outdoor activities. It is also supposed that the development cycle (larva-nymph) of *Ixodes ricinus* was changed in a so far unknown way by the mild winter and the weather conditions that followed [13].

These extreme fluctuations in the morbidity of TBE within two years which were observed in most European countries can neither be explained by weather phenomena only nor by the very sophisticated models published by the working group of S.E. Randolph [5-7,21]. At present, an explanation for this almost uniform trend in geographically distant countries with different climatic, microclimatic and weather conditions and with completely different political and socioeconomic structures remains to be found.

Even if we regard the epidemiology of TBE from 1976 to 2007 in general, most questions remain to be answered. Thus, the political turnaround and the resulting socioeconomic changes and changes in the behavioural pattern of the exposed population in the former Eastern Bloc at the beginning of the 1990s [5] certainly are a significant influence factor. However, this does not explain the similar development, the strong increase in the number of TBE cases since the 1990s, in Sweden, Italy, Hungary, Finland and Germany. As a result, the TBE incidence in the German risk areas shows the same trend as in the Baltic States; the political turnaround, however, only took place in the eastern part of the country, where TBE incidence is very low compared to southern Germany and the influence on the total number of registered cases consequently is very low. The strong reduction of the incidence in Russia since 1999 cannot be interpreted either.

Clinical presentation of TBE

TBE usually takes one of three clinical courses: complete recovery within two months, occurring in approximately one quarter of patients; protracted, mainly cognitive dysfunction; or persisting spinal nerve paralysis with or without other post-encephalitic symptoms. Up to 46% of patients are left with permanent sequelae at long-time follow-up, the most commonly reported residuals being

various cognitive or neuropsychiatric complaints, balance disorders, headache, dysphasia, hearing defects, and spinal paralysis [22].

Long-lasting or lifelong damage and a mortality rate of 1 to 2% in Europe [22,23] in patients whose central nervous system is affected by the virus, can be prevented by relatively simple means of vaccination. Human infection with the Far Eastern subtype (previously Russian Spring Summer Encephalitis virus, RSSEV) results in the most severe form of CNS disorder with a tendency for focal meningoencephalitis or polyencephalitis to develop, accompanied by loss of consciousness and prolonged feelings of fatigue during recovery. Case-fatality rates of 20-40% have been recorded following outbreaks of RSSEV in some years [24]. According to data collected in Western Siberia over the past 20 years, TBE becomes chronic in 1.7% of patients. In the acute period, the disease in such cases usually progresses in the form of meningoencephalitis [25]. Human infections with the Siberian subtype virus in the Western Siberian region of Russia are associated with a milder acute period and a high prevalence of the non-paralytic febrile form of encephalitis. Case fatality rates rarely exceed 6-8% [24].

Prevention through vaccination

TBE can be prevented by vaccination and the quality of the vaccines and their effectivity are excellent. New reliable statistics show that with a field effectiveness of 99% (2000 to 2006) with no statistically significant difference between age groups [26] TBE vaccines have one of the highest effectiveness rates of all inactivated vaccines. The data of Heinz et al. [26] confirm the excellent performance of TBE vaccine under field conditions and provide evidence that, in Austria, about 2,800 TBE cases were prevented by vaccination in the years 2000 to 2006. These statistics clearly show the tasks of the health care systems concerned.

However, as there have repeatedly been reports of clinical TBE in vaccinated individuals over the age of 50 years, it seems increasingly important to focus future investigations not only on long-term protection after TBE booster vaccination, particularly in older-age groups, but also on low responsiveness to vaccination and T-cell immunity [27].

In addition, the economic consequences of this disease should not remain unmentioned.

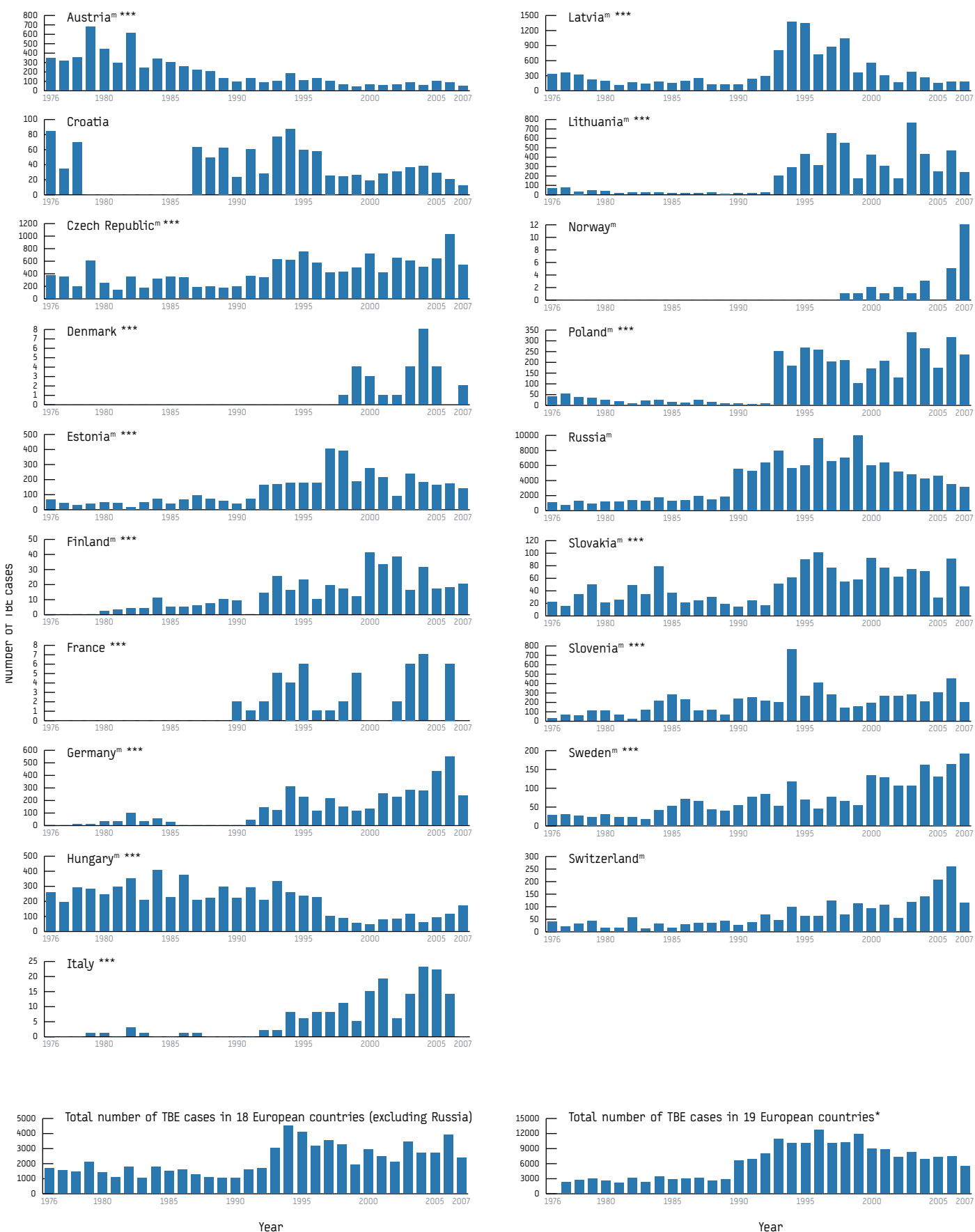
With the exception of Austria, the low TBE vaccination rate in the other countries is either not responsible at all for this lower incidence, or only marginally so. Today, 88% of Austrians have had at least one TBE vaccination, and 58% are within the officially recommended vaccination schedule [26]. With this vaccination rate, however, a massive influence on the number of cases can be seen. In the pre-vaccination era, 600 to 700 cases were registered per year, within the past 10 years the annual number has decreased to 64 [26] (Figure 1).

Vaccination coverage in the other TBE-endemic countries is low, but statistics show an increase in the number of vaccinees over the past few years.

The average vaccination rate is 38% in Latvia; between 1997 and 2006 the annual number of third-primary vaccinations (complete vaccination course) was ca. 30,000 [6]. The rate is 14% in Estonia with around 15,000 third-primary vaccinations annually between 1997 and 2006, in Lithuania 6% (around 7,500 fully

FIGURE 1

Tick-borne Encephalitis (TBE) cases in Europe 1976 – 2007, 19 TBE endemic countries* and total number of TBE cases in Europe**



* Austria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Hungary, Italy, Latvia, Lithuania, Norway, Poland, Russia, Slovakia, Slovenia, Sweden, Switzerland

** The numbers represent reported individual cases of TBE and not incidence, as in most countries the risk for TBE is restricted to some areas or regions and therefore a calculation of the incidence for the entire country might lead to false interpretations.

*** European Union Member State

m= mandatory notification

protected vaccinees annually) [6]. In Slovenia, the annual number of vaccinees who received ≥ 1 vaccine dose between 1997 and 2006 was around 15,000 [6]. The vaccination rate in Switzerland was 17% in 2007 (13% 2006), in the Czech Republic 16 % in 2007 and in Sweden 12% in 2006 and 2007 [28,29]. In Germany, 24% of the population in risk areas, not of the whole population of the country, are vaccinated [28, 29]. It should be pointed out, that in Latvia, Estonia, Lithuania, Slovenia and the Czech Republic, more or less the whole country is characterized as a risk area. These vaccine coverage data are highly preliminary and have been collected under different conditions.

These vaccination rates provide a safe protection for the vaccinated individuals, however, they hardly have any influence on the incidence. In addition, the virus circulation in the risk habitats cannot be influenced.

Recently, the knowledge on TBE in Asia has increased considerably. This is shown by reports from China, Mongolia, Japan and Korea.

The TBE situation in individual European countries

Austria

Before the annual TBE vaccination campaign was introduced in 1981, Austria had the highest recorded morbidity of TBE in Europe, with up to 700 hospitalized cases annually. The increase in vaccination coverage since 1981 has led to a steady decline in TBE. In 2007, 88% of Austrians have had at least one TBE vaccination, and 58% are within the officially recommended vaccination schedule. In the 5-year period between 2003 and 2007, an annual average of 73 cases were reported, equaling an incidence rate of 0.82 per 100,000 inhabitants. According to recent statistics, 2,800 TBE cases were prevented in Austria by vaccination between 2000 and 2006 [26]. In 2003, new endemic areas were described in the region around Mattsee, Wallersee, and Thalgau north of the city of Salzburg.

New risk areas have recently been identified upstream the valleys of Inn and Isel during 2005-2006 [30] and in Ziller valley and Voralberg, e.g. near Feldkirch.

For an unvaccinated tourist staying in a highly endemic province of southern Austria, such as Styria, the risk of acquiring TBE has been estimated at 1 to 10,000 person-months of exposure. Based on the number of tourist overnight stays in Austria during the summer, around 60 travel-associated cases of clinical TBE can be expected to occur among visitors of Austria.

Croatia

Only one natural focus in the northern part of the country is described, i.e. between the rivers Sava and Drava. Between 1998 and 2007, the annual number of cases ranged from 12 to 38. In the five-year period between 2003 and 2007, a mean of 27 cases were reported annually.

The Czech Republic

TBE is present in all parts of the country. Between 2003 and 2007, an average of 666 TBE cases were reported annually. In 2006, there was an exceptionally sudden increase, with 1,029 registered TBE cases, i.e., the national incidence was 10/100,000, the highest level recorded so far. It is documented that this situation was significantly influenced by exceptional weather in 2006 [31]. It is remarkable that almost 500 cases were acquired during the last third of 2006. Thus, the Czech Republic is second only to Russia

in terms of TBE incidence in Europe. The incidence is higher in regions south of Prague near the city of Ceske Budejovice. The incidence has constantly been high near the town of Pilsen in the western part of the country. Recently [2004, 32], TBE foci have been identified in the northern part of the province of Bohemia. In the eastern part of the country, there has been a high incidence near Olomouc.

The number of TBE cases in 2007 dropped to 542, i.e. 52.7% of the number registered in 2006.

I. ricinus and TBE virus were detected in the Bohemian Mountains at an altitude of over 1,100 metres above sea level [14]. Warm winters have led to an increased number of cases during the last third of the year.

Denmark

In Denmark only the island of Bornholm has since long been considered a risk area for TBE. Between 2003 and 2007, 18 cases of TBE were reported on Bornholm. Four cases were notified in 2003, and eight in 2005. The minimum level of prevalence of TBEV in ticks on Bornholm is similar to that found in other European countries where TBEV is endemic.

Estonia

Between 2003 and 2007, 179 cases were reported in Estonia on average annually. The highest TBE distribution rates are seen in western Estonia (Pärnumaa, Läänemaa), eastern Estonia (Ida-Virumaa), on Saaremaa (island in the west), and in south-eastern Estonia (Polvamaa, Tartumaa). Between 2004 and 2007, the TBE incidence ranged between 10.4 (2007) and 13.5 (2004).

Finland

Between 2003 and 2007, an average of 20 cases were reported annually in Finland, with a record number of 41 cases in 2000. The known endemic areas are situated mainly on the Åland archipelago (66% of 125 cases reported between 1987 to 1997, 80 per 100,000 inhabitants in 2000), the archipelago of Turku (10%), and in the Kokkola (6%) and Lappeenranta regions (5%). In 2001 [33], nine cases were identified on an island close to the city of Helsinki. Finland has the northernmost occurrence of the TBE virus.

France

Single cases have been reported from the Alsace region, and from the region Nancy, Lorraine. In 2002, cases were reported from Faverges and Grenoble.

Germany

The map of TBE risk areas is updated periodically by the Robert Koch Institute (Epi. Bull.). Since 1992, between 100 and 300 autochthonous clinical TBE cases were recorded annually. An all-time high was reached in 2005, when 431 cases were reported – an increase by 58% compared to 2004. This was overshadowed by an additional increase in 2006, with 546 cases. These occurred mainly in southern Germany, i.e., in the federal states of Baden-Wuerttemberg and Bavaria, but also in Thuringia and Hesse. In 2007, only 236 TBE cases were reported.

There are risk areas in Bavaria and Baden-Wuerttemberg and newly identified risk areas in Hesse and Thuringia. One small risk area is located in Rhineland-Palatinate. Between 1994 and 2007, more than 55 single cases were reported from areas previously not defined as risk areas, i.e. in Saxony, Lower Saxony, Mecklenburg-Western Pomerania, Saxony-Anhalt, and Brandenburg. In such a

“non-risk area” a TBE case with lethal end was reported in 2007 (unpublished).

Whereas the incidence of TBE in Bavaria and Baden-Wuerttemberg has remained stable on a high level for years, increasing incidences have been reported in other areas of Germany. 132 of the 440 German counties are currently classified as TBE risk areas. In 2006, 35.6% of the cases occurred in Bavaria, 52.6% in Baden-Wuerttemberg, 10.8% in Hesse, 0.4% in Thuringia, 0.6% in Rhineland-Palatinate, 0.6% in Brandenburg, 0.2% in Mecklenburg-Western Pomerania, and 0.6% in Saxony. In 2007, the Robert Koch Institute modified the definition of risk areas (Epi. Bull. 15/2007).

Greece

For several years, there have been publications indicating a very low incidence of TBE virus in northern Greece in the province Thessaloniki. However, no cases of TBE have been registered for many years.

A new study by Pavlidou et al. [34] provides seroprevalence data in healthy blood donors from northern Greece (ELISA, IgG). According to this study, in the provinces Chalkidiki 5.8%, Evros 3.6%, Imathia 2.7%, Kastoria 2.4%, Kavala 1.6%, Pella 5.4% and Xanthi 2.9% of the test persons were TBEV-IgG-positive. Results from neutralisation tests are not available, which would exclude IgG-antibody cross-reactivity due to other flavivirus contacts (e.g. vaccination against yellow fever or Japanese encephalitis or infection with dengue viruses).

Hungary

The average yearly incidence rate between 1977 and 1996 was 2.5 per 100,000 inhabitants (range 1.3 to 3.8), with the highest incidences between 1981 and 1990. From 1997 to 2000, a significant decrease in the number of registered TBE cases was observed, with an incidence rate of 0.5 per 100,000 in 2000. Since 2001, the incidence has increased again. Between 2003 and 2007, an average of 106 cases were reported annually. Extended areas of high risk are located in western Hungary and along the Danube river, i.e., the counties of Zala, Somogy, and Vas (western Hungary), Nógrád (northern Hungary), and around Lake Balaton.

Unconfirmed reports indicate that the reduction of the TBE incidence at the end of the 1990s was due to reduced diagnostic efforts.

Italy

A few clinical cases have been recorded in Northern Italy in the area of Florence, Trento, and Belluno. In 2006, first cases were reported in Friuli Venezia Giulia. Anti-TBEV antibodies were found in about 1% of potential risk persons, such as foresters, hunters, woodcutters, and gamekeepers. Since the early 1990s, between 2 and 19 cases were reported annually, 23 cases in 2004. In 2006, 14 cases were registered, one reported TBE case took a lethal course.

Kazakhstan [Pavel N. Deryabin, pers. comm., 29]

As supposed, there are endemic areas for TBE in Kazakhstan. These are located (among others?) in the east of the country and in the Almaty region. In the east, 34 cases were reported in 2004, 28 in 2005 and 18 in 2006; in the Almaty region, 10 cases were reported in 2004, 9 in 2005 and 6 in 2006. However, the real incidence is expected to be much higher. In Almaty itself, 6 cases were registered in 2004, 12 in 2005 and 8 in 2006. In Kazakhstan, a Russian vaccine is used (e.g. 60,630 doses in 2006). A kind of

mandatory passive immunisation with immunoglobulin is applied nationwide up to 3 days after a tick bite.

Latvia

The TBE risk areas are spread over the entire country, although there are differences in the virus load.

Latvia was considered the country with the highest TBE incidence rates in the world between 1990 and 2000, since then the number of cases has decreased considerably. Between 1990 and 1994, an average of 558 cases were reported per year, between 2003 and 2007, the average number of cases was 220 per year. TBE cases were even reported in and around the city park of Riga. Ticks in Latvia carry a higher TBEV load than those in other risk countries. Food-borne outbreaks (caused by dairy products, mainly goat milk) accounted for up to 5% of the total number of cases per year.

Between 2004 and 2007, the TBE incidence ranged from 6.2 (2005) to 10.8 (2004).

Lithuania

TBE is present in all districts of Lithuania. In 2003, the epidemiology of TBE in Lithuania was very unusual. The incidence rate (763 cases, 22 per 100,000 inhabitants) was twice the average incidence over the last ten years, and the highest annual rate recorded since notification was observed at the end of the 1960s. This rate was also the highest of all Baltic countries in 2003. Four lethal cases of TBE were notified in 2003. Between 2003 and 2007, 425 hospitalized cases were reported annually. Even though normally transmitted through a tick bite, 22 cases of TBE in 2003 (four clusters) were acquired by the consumption of unpasteurized goat milk – a well-known transmission route. The highest annual incidences of TBE, about 80% of all notified cases, are recorded in the northern and central parts of the country, i.e., mainly in the counties Kaunas, Panevezys, and Siauliai. In 2003, the incidence rates in these areas remained unchanged. However, they were much higher in many other counties. Eight of 44 districts reported an incidence rate two to five times higher than the average incidence in Lithuania. The highest incidence rate was recorded in Panevezys, with about 100 per 100,000 inhabitants.

Between 2004 and 2007, the TBE incidence ranged from 6.9 (2007) to 13.5 (2006).

Norway

Norway is an example for the occurrence of new TBE risk areas. TBE was first reported in 1997. All 28 cases between 1997 and 2007 were acquired within a limited area along the southern coast and in the municipality of Tromøy [35]. The TBE virus RNA was detected in the serum of TBE patients in Norway [36].

Poland

Since 1993, the number of reported cases at country level has ranged from 100 to 350 cases per year. In 2003, the number of reported cases was 339 (0.89 per 100,000). In 2006, 316 cases were reported. Between 2003 and 2007, 265 cases annually were reported. The north-east of the country around Białystok is the main area of endemicity. 80% of cases occurred in the two north-eastern provinces adjacent to Lithuania and Belarus. Another important focus of the disease is in the south-western part of Poland, in districts adjacent to the Czech Republic. A present serosurveillance study (human and goat samples) indicates the possible existence of endemic foci in north-western provinces of Poland, in which barely any cases were reported during 1070 – 2005 [37].

Romania

Risk of tick-borne encephalitis is reported for the Tulcea district and in Transylvania at the base of the Carpathian Mountains and the Transylvanian Alps. However, details about the annual numbers of TBE cases have not been published.

Russia

Russia is the country with by far the highest number of registered TBE cases.

Approx. 58 million people who are potentially at risk of acquiring TBE live in a broad TBE corridor ranging from St. Petersburg over Chelyabinsk, Kazan, Tyumen, Novosibirsk, Irkutsk to the Far East as far as Khabarovsk and Vladivostok.

In Russia, a total of 54,526 cases of TBE were registered over the past 10 years (1998 to 2007), in addition the real incidence is expected to be much higher. 8,725 of these cases were reported in children < 14 years.

Western Siberia is the region with the highest known incidence of TBE in the world, with 40 to >80 cases/100,000 population [38]. In this region the Aina strain of the Siberian virus subtype could be isolated.

The highest numbers were registered in 1996 (10,298 cases) and 1999 (9,955 cases). Since then, the numbers have decreased continually and have reached the lowest level in 2007 with 3,098 cases. The strongest decrease in morbidity was registered in the Ural Mountains and in Western Siberia. However, the majority of TBE infections is acquired in Siberia (e.g. 2003–2007: 11,440) and in the Ural Mountains (e.g. 2003–2007: 4,181). These are 56.7% and 20.7% of the total morbidity in Russia (20,164 cases from 2003 to 2007).

The reasons for this reduction are unclear, an influence of the vaccination rate can be excluded.

As there are records on the incidence of TBE in Russia since 1950, a certain dynamic of the frequency can be observed. Thus, the total incidence reached a peak of approx. 4/100,000 inhabitants between 1955 and 1965 and, after a period with a lower incidence (between 1–2/100,000 inhabitants) between 1993 and 1998, a further peak occurred with approx. 6–7/100,000 inhabitants, followed by a reduction up to the year 2007 [39].

Serbia

A few cases have been reported in the area near Belgrade, including food-borne outbreaks near the coastal regions of the Adria, but there is no published information available on these cases.

Slovakia

Between 1998 and 2007, the average annual number of reported cases was 67, ranging from 46 to 92. In 2006, 91 cases of TBE were reported compared to 46 in 2007. Between 2003 and 2007, 66 cases annually were reported. Some of the reported cases were caused by the consumption of homemade raw goat and sheep milk. New foci have recently been identified in areas of eastern Slovakia traditionally thought to be free of the virus.

Slovenia

Endemic foci of TBE are spread all over the country. Between 2001 and 2005, the 5-year average was 261 cases. The highest number of TBE cases had been reported in 1994, with a total of 492 cases. In 2006, 445 cases were reported. Between 2003 and 2007, 283 cases annually were reported.

Sweden

In the five-year period between 2003 and 2007, the average was 150 annual cases. Occurrence has been highest in 2007, with 190 reported cases. Except for Hungary, this makes Sweden the only country, where no significant reduction in the number of cases is observed from 2006 to 2007. Most of the infections were acquired in the counties of Stockholm (62%), Södermanland (13%), and Uppsala (8%). In the county of Västra Götaland, south of Lake Vänern, 5 to 10 cases are notified annually. Sporadic cases occur in the rest of Sweden every year.

A recent study of Brinkley et al. [40] (virus prevalence data in ticks, sequence data) show a distinct migration of the virus (Western subtype) to the western parts (Västra Götaland).

Also, data of Eisen [19] provided tantalizing hints that climate warming allowed *I. ricinus* to expand its distribution toward the north and become more abundant in Central Sweden from the early 1980s to the early 1990s.

Switzerland and Liechtenstein

In the five-year period between 2003 and 2007, a mean of 165 cases were reported annually. In 2006, 259 cases were reported, the highest number in recorded history in Switzerland. There are two high-risk regions, the larger one covering the midland, with the exception of the far-western part, and the smaller one located in the upper Rhine valley, including the principality of Liechtenstein. A focus of ticks infected with the TBE virus (TBEV) is located on a much-used forest path near Vaduz, the capital of the principality. The canton Zürich has become the most dangerous region for TBE in Switzerland, followed by Thurgau, St. Gallen, Aargau, and Bern. The TBE risk areas in the northeast of Switzerland remain stable, however, new risk areas in the western part of the country (Neuchâtel) have been identified.

Turkey

TBEV has not been detected in Turkey, there are no safely confirmed cases of disease. The serosurveillance data published by Esen et al. [41] (ELISA, 7 TBEV-IgG-Ab positive sera, 1 TBEV-IgM-Ab) have not been confirmed by neutralisation tests and presumably are due to cross-reactivity. It is known that the presumably false-positive sera were collected in areas endemic for Crimean Congo Haemorrhagic Fever, in addition other flaviviruses not belonging to the TBEV complex persist in Turkey.

Belarus, Bosnia, Moldavia, and Albania

Belarus, Bosnia, Moldavia, and Albania are believed to be countries with risk areas and a high TBEV prevalence in ticks, information on clinical cases is scarce.

The TBE situation outside Europe

Outside Europe, only data from China, Japan, Mongolia, and more recently from South Korea have become available, which indicate that there are TBE risk areas in these countries:

First data from China [Guo-Dong Liang, pers. comm., 29,42]:

TBE is endemic in China, but the disease is not notifiable so data are only sporadic. The disease is mainly reported in the northeastern forest areas of Changbai Mountains in Jilin Province, Daxingán Mountain in Inner Mongolia Province, and Xiaoxingán Mountain in Hei Longjiang Province. Moreover, TBE is intermittently reported in the forest regions in the northern slope of Tianshan Mountain and the southern slope of the Altai Mountains in Xinjiang Uygur Autonomous Region (north-western China). There are also some

reports related to TBEV in Yunnan (south-western China) as well as in Tibet (western China).

The main endemic areas are located in the province Heilongjiang in the far northeast of the peoples' republic. In this area, 2,202 cases were reported between 1980 and 1998, although a much higher number must be expected, as the disease is not notifiable. Between 1995 and 1998, 420 cases were diagnosed, most cases were reported in May (44 cases) and June (210 cases). The first case was registered in 1943, in 1953 TBE virus was first isolated from a patient and from ticks. The main vector is *I. persulcatus*.

Japan [Ikuo Takashima, pers. com., 29]

The unusual TBE situation in Japan remains unchanged. The autochthonous case of a 37-year-old woman from the city of Kamiiso on Hokkaido described in 1993 has remained unique. However, the virus has been isolated several times from sentinel dogs and ticks (*I. ovatus*) and a serosurvey of sera from domestic animals suggested the presence of TBE foci in Hokkaido [43,44]. The Oshima 5-10 virus is a far eastern strain. Animal studies have shown that the vaccine produced based on the central European prototype completely covers this Oshima strain as well as other far eastern and Siberian strains. The Japanese have become more interested in protective vaccination since a Japanese tourist acquired the infection in Salzburg and died after his return to Japan.

Mongolia

In 2004, some endemic areas were described close to the Russian border in the north of the country (provinces of Selenga and Bulgan) and around the capital city Ulan-Bataar [45].

South Korea – new among TBE-endemic countries

TBEV was isolated recently from ticks (*Haemaphysalis longicornis*; *Ixodes nipponensis*) and mice (*Apodemus agrarius*) [46]. Surprisingly, the virus belonged to the western European subtype. Virus isolation was successful in the regions Dongducheon, Geyonggi-do; Jeongseon, Gangwon-do; Hapcheon, Gyeongsangnam-do; and Gurye, Jeonrabuk-do. TBE cases have not been registered yet, but a series of diseases of unknown origin affecting the central nervous system recently [46] have been reported. Further investigations have been initiated.

Note:

The author invites more detailed and additional information regarding the epidemiology of TBE in individual countries. Please email jochen.suess@fl.bund.de.

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