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Reliable surveillance of tick-borne encephalitis in European countries is necessary to improve the quality of vaccine recommendations

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ABSTRACT

In July–November 2009, 26 European Union (EU) Member States (MSs), Norway and Iceland, participated in a survey seeking information on national tick-borne encephalitis (TBE) vaccination recommendations. Information on TBE surveillance, methods used to ascertain endemic areas, vaccination recommendations, vaccine coverage and methods of monitoring of vaccine coverage were obtained. Sixteen countries (57%) reported presence of TBE endemic areas on their territory. Vaccination against TBE was recommended for the general population in 8 (28%) countries, for occupational risk groups – in 13 (46%) countries, and for tourists going abroad – in 22 (78%) countries. Although vaccination recommendations for country residents, and for tourists always referred to endemic areas, there was no uniform, standardized method used to define endemic areas. For this reason, clear recommendations for tourists need to be developed, and standardized surveillance directed to efficient assessment of TBE risk need to be implemented in European countries.

1. Introduction

Tick-borne encephalitis (TBE) is an acute disease of the central nervous system caused by viruses from the Flaviviridae family. Infection most commonly occurs following exposure to ticks infected with one of the 3 viruses belonging to the TBE complex [1]. Food borne transmission of TBE has also been increasingly reported following consumption of unpasteurised milk or dairy products [2,3]. The infection usually progresses biphasically. The first (viremic) phase often is asymptomatic or causes influenza like symptoms. Only about one third of cases progresses to the second phase which may present as meningitis, encephalitis, meningoencephalitis, meningoencephalomyelitis or cause other clinical syndromes. Post encephalitic sequelae (e.g. sustained paresis, ataxia, headache, hearing impairment) are reported in 35–58% of symptomatic patients [1]. Diagnosis of TBE is based on detection of specific IgM and IgG antibodies in serum or cerebro-spinal fluid using the enzyme-linked immunosorbent assays (ELISA), however cross-reactivity with other flaviviruses has been observed [4]. Neutralization testing allows confirmation of specific anti-TBE antibodies presence. There is no specific treatment for TBE. Although personal protective measures (such as covering limbs, wearing insect repellants and removing ticks), as well as avoidance of unpasteurised milk coming from endemic areas is usually encouraged, the only efficient measure of disease prevention is active immunization. In Europe two highly effective and safe vaccines are used

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for prevention of TBE infections and their chronic sequelae [5]. The two vaccines available are whole-virus inactivated products: FSME-IMMUN (Baxter AG, Vienna, Austria) and ENCEPUR (Novartis AG, Basel, Switzerland). Typically three doses are needed for primary immunization at 0, 1, 6–12 months, and booster doses every 3–5 years [5].

Despite availability of safe and effective vaccines, TBE is an increasing public health problem in Central and Northern Europe [6,7]. During the previous decade, on average 3000 clinical cases have been reported annually from European countries [6–9].

The optimal vaccination strategy is difficult to establish as TBE is a zoonotic disease, with highly focal natural distribution. Mass immunization would not affect the local circulation of the virus in enzootic cycles [10,11]. Theoretically, the best approach would be a combination of health promotion, vaccination of high risk groups, and, potentially, vector control measures. To define the best strategy for TBE control, however, good quality data are needed on TBE virus (TBEV) occurrence, as well as information on population-level and individual risk factors.

The aim of the present study was to summarize vaccine recommendations in European Union (EU) and European Economic Area (EEA) countries, in context of surveillance of human cases, and monitoring TBE endemic areas.

Box 1: Case classification used in three countries, results of VENICE survey, 2009.

Belgium	
Possible case:	Clinical criteria AND epidemiological link (travel to endemic area)
Probable case:	Clinical criteria AND epidemiological link (travel to endemic area) AND laboratory criterion (IgM in serum)
Confirmed case:	Clinical criteria AND laboratory criteria (seroconversion, fourfold antibody rise, PCR)
Germany	
Possible case:	NA
Probable case:	NA
Confirmed case:	Clinical criteria (biphasic course or CNS infection symptoms) AND laboratory criteria (IgM and IgG detection in serum, in CSF, or marked increase in antibody titre)
Poland	
Possible case:	Clinical criteria AND visit to endemic area during April-November
Probable case:	Clinical criteria AND epidemiological link (consumption of raw diary products) OR laboratory criterion (IgM in serum)
Confirmed case:	Clinical criteria AND laboratory criteria (IgM and IgG detection in serum, in CSF, and confirmation by neutralization test)

2. Materials and methods

A cross-sectional survey was undertaken as a collaborative study between the European Centre for Disease Control and Prevention (ECDC), the Vaccine European New Integrated Collaboration Effort (VENICE) project and EU/EEA Member States. The respondents of the survey were identified using a network of VENICE contact points among experts working with national vaccination programmes and TBE surveillance. Currently the VENICE collaboration involves representatives of 27 EU and two EEA (Norway and Iceland) countries.

A standardized questionnaire was developed in June–July 2009 using mostly close-ended questions. The questionnaire covered the following topics: surveillance of TBE, ascertainment of endemic areas, vaccination recommendations, vaccination coverage, payment and administration costs for the vaccine. The web-based platform was developed by CINECA (Consortium of University, Bologna, Italy), and the survey was made available on the platform for all participating countries. Respondents of the survey entered data directly on-line.

The questionnaire was pilot tested and its corrected version was published online in July 2009. Reminders were sent during the following three months in order to improve compliance. The collection of data was completed in November 2009. We have also asked national contact points to validate the preliminary report, and inconsistencies were further verified.

Collected data were analyzed using EpiInfo software and descriptive statistics were produced. Selected surveillance indicators and vaccination recommendations were compared. The present paper describes only selected indicators. The detailed survey report was published on the VENICE website for Members area, which will be made public by the end of 2010 (http://venice.cineca.org).

3. Results

We obtained filled questionnaires from 28 out of 29 countries (response rate 96%). We did not receive output from Luxembourg. The report was further validated by 71% (20/28) national contact persons. Among the 28 participating countries, eighteen (64%) reported evidence of TBE risk within their territory. Table 1 summarizes availability of surveillance data on TBE, and classification of TBE risk based on surveillance figures.

3.1. TBE surveillance

Surveillance for TBE was implemented in 17 (61%) countries. However, only in three countries (Belgium, Germany and Poland), a standardized case definition was used to classify cases reported to surveillance (Box 1). In four countries (Austria, Czech Republic, Finland, Greece) there was no standardized surveillance definition which was published and disseminated, but the surveillance system accepted only laboratory confirmed cases. All countries with TBE surveillance used ELISA tests to confirm cases, the majority of countries used also the polymerase-chain reaction (PCR) and immunofluorescence tests (Table 1).

Endemic areas existed in 16 countries (57%), including 14 countries where surveillance was set up, and two countries (Denmark and France), where no TBE surveillance existed. Only one country had an official definition of "endemic area". In Germany, an endemic area was defined by average recorded 5-year incidence of locally acquired cases in a district or region consisting of the district and adjoining districts significantly exceeding 1 case per 100,000 inhabitants. Based on this definition, experts from Robert Koch Institut prepared and disseminated maps of Germany presenting endemic areas, which were updated annually [12].

Amongst 16 countries with identified endemic areas, 10 (63%) used the number of TBE cases in administrative regions to ascertain their endemic areas, and 8 (50%) used reported incidence. Although many countries indicated diverse methods of confirmation of endemic areas presence (detection of virus in ticks, screening of sentinel animals), there was no indication that these methods were applied routinely, and repeatedly, in order to monitor eventual fluctuations in endemic areas extent. Fifteen countries (94%) disseminated information on TBE endemic areas to the public. The most common modality for dissemination was risk maps in printed materials or published on websites. Information on endemic areas was disseminated most commonly by the National Institutes of Public Health (81%), local public health authorities (75%), and vaccination centres (63%).