



## MEETING REPORT

# Expert consultation on tick-borne diseases with emphasis on Lyme borreliosis and tick-borne encephalitis

Stockholm, 23–24 November 2010

## Summary

Tick-borne diseases are the most common vector-borne diseases in Europe and they can cause severe or fatal illnesses. The infection rate of tick-borne diseases in Europe has been increasing since the 1980s. Even though tick-borne diseases are of concern, so far only Crimean–Congo haemorrhagic fever is a notifiable disease in the EU. The overall epidemiology and burden of tick-borne diseases in Europe remains unclear.

ECDC called an expert consultation to define a strategy at the EU level to strengthen the capacity of the EU Member States for the surveillance and prevention of tick-borne diseases, with special emphasis on Lyme borreliosis and tick-borne encephalitis. In this perspective, the objective of the meeting was to propose a way to harmonise the case definitions of tick-borne encephalitis and Lyme borreliosis in order to make a recommendation to add these to the list of notifiable diseases in the EU.

This meeting recommended adding tick-borne encephalitis to the list of mandatory notifiable diseases in the EU. For Lyme borreliosis, no consensus was reached on its notifiable status, however, the meeting expressed the need to harmonise the case definition of Lyme borreliosis in the EU.

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Stockholm, February 2011

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# 1 Background

The founding regulation<sup>i</sup> establishing the European Centre for Disease Prevention and Control (ECDC) gives ECDC a mandate to strengthen the capacity of the European Union (EU) to prevent and control infectious diseases.

Tick-borne diseases are the most common vector-borne diseases in Europe; Lyme borreliosis, tick-borne encephalitis, Crimean–Congo haemorrhagic fever and rickettsioses are endemic in certain regions of Europe. They can cause severe or fatal illnesses. About 85 000 cases of Lyme borreliosis are reported annually in Europe (estimated from available national data, 2006). However, this number is largely underestimated as case reporting is highly inconsistent across Europe and many Lyme borreliosis infections go undiagnosed. The mean number of reported tick-borne encephalitis cases in Europe is 2805 per year during the 18-year period leading up to 2007 and data indicate an increase of cases in recent years.

The incidence of tick-borne diseases in Europe has been increasing since the 1980s. Changing risk factors, including the increase in minimum temperatures, the human impact on the landscape, and the modification of human behaviour all play a significant role in the (re-)emergence of tick-borne diseases within Europe. Yet although tick-borne diseases are of concern, so far only Crimean–Congo haemorrhagic fever is a notifiable disease in the EU.

The overall epidemiology and burden of tick-borne diseases in Europe remains unclear although valuable prospective studies have been performed in some endemic regions. Several initiatives have been launched by ECDC with regard to tick-borne diseases to identify and assess the current epidemiological situation, to identify key risk areas and key risk groups for these diseases in the EU and to provide ECDC with data for input into its burden of disease study.

## 2 Objective of the consultation

The objective of this expert consultation was to define a strategy at the EU level to strengthen the capacity of the EU Member States for the surveillance and prevention of tick-borne diseases with special emphasis on Lyme borreliosis and tick-borne encephalitis.

In this perspective, the objective of the meeting was to propose a way to harmonise the case definitions of tick-borne encephalitis and Lyme borreliosis in order to make a recommendation proposing to add these diseases to the list of notifiable diseases in the EU. Thus, the meeting sought:

- to get an overview of the present situation of Lyme borreliosis and tick-borne encephalitis in the EU;
- to be informed about the different EU initiatives regarding tick-borne diseases (past and present); and
- to review the different case definitions of Lyme borreliosis and tick-borne encephalitis in the EU and to discuss the best ways for harmonisation.

## 3 Expert presentations

The morning session was dedicated to several presentations that gave a review of tick ecology and the spread of tick-borne diseases, the epidemiology, and case definitions of Lyme borreliosis, tick-borne encephalitis and Crimean–Congo haemorrhagic fever. Two countries shared their experience with tick-borne diseases. This section gives a brief overview of the different presentations.

### Ticks and tick-borne diseases in Europe

Understanding the distribution of *Ixodes ricinus* and *Hyalomma marginatum* is key in comprehending the ecology of the diseases they transmit. *Ixodes ricinus* is a widespread species occupying different climatic zones and ecological habitats with different strategies for adaptation. The areas of climatic suitability for the species have increased in the last 10 years around the Baltic Sea, along the Scandinavian coast and in central Europe. The infection rates of *Ixodes ricinus* with *Borrelia burgdorferi sensu lato* are spatially heterogeneous and the question of whether there is any relationship between climate traits and *Borrelia burgdorferi s.l.* prevalence rates in ticks was addressed.

<sup>i</sup> Regulation 851/2004 of the European Parliament and of the Council.

The exact distribution of Crimean–Congo haemorrhagic fever is unknown. The reason for the absence of Crimean–Congo haemorrhagic fever in the south-western part of Europe, where the vector is present, is not clear and should be the subject of further study.

## Lyme borreliosis in the EU

A good knowledge of clinical features is pivotal in diagnosing Lyme borreliosis. The clinical manifestations show that Lyme borreliosis is a complex disease. With the exception of typical erythema migrans, laboratory involvement is essential in the diagnosis and is mostly based on serology. However, serological tests do not necessarily identify active disease. Serology is particularly impaired by the lack of uniformly standardised test systems that are available and is influenced by sero-prevalence in the healthy population in endemic areas. This is particularly relevant for persons who are repeatedly exposed to tick bites (e.g. hunters). Epidemiological data from those countries of central Europe, that coined national case definitions and made Lyme borreliosis a mandatory reportable disease more than a decade ago, tell us that the number of cases of Lyme borreliosis is constantly increasing (e.g. Slovenia: from 113 per 100 000 inhabitants in 1993 to 225 per 100 000 in 2007 and over 300 per 100 000 in 2009). Concerning prevention, there is no vaccine available; the most practical and also effective preventive measure is to remove an attached tick as soon as possible – preferably on the same day.

In order to assist physicians, researchers and epidemiologists, clinical case definitions for diagnosis and management of Lyme borreliosis in Europe<sup>1</sup> were elaborated on a broad consultation which included 11 clinicians and scientists from eight EU countries. All of them belong to the advisory board of the European Concerted Action on Lyme Borreliosis (EUCALB). EUCALB was an EU-supported concerted action in the 1990s. EUCALB.com is now an information resource of the European Society for Clinical Microbiology and Infectious Diseases (ESCMID) study group and European Study Group on Lyme Borreliosis (ESGBOR). These case definitions are intended to serve practitioners and clinicians, but they are also considered to be appropriate for epidemiological purposes.

## Tick-borne encephalitis in the EU

A survey on tick-borne encephalitis in European countries was presented. A variety of human case surveillance systems and ticks carriage studies exist in different EU countries. Knowledge about tick-borne encephalitis endemic foci needs to be based on a clear case definition. Information on distribution of endemic areas needs to be regularly updated in order to identify the risk for the exposed population and to apply appropriate control measures such as vaccination. The survey concluded that:

- there is a need for a broad standard case definition in order to avoid under-ascertainment of cases and to increase the knowledge on the true incidence;
- serological and/or molecular testing should be performed using standard operation protocols and should be regularly monitored by European quality assurance programmes to guarantee the comparability of data;
- investigations on tick-transmitted diseases should be done more systematically (e.g. prevalence studies on ticks, animal reservoirs and pathogens across the EU) to improve the surveillance and to get more information on trends of tick-borne encephalitis, Lyme borreliosis, and rickettsioses and a multi-disciplinary approach including clinicians, veterinarians, biologists and laboratory experts is needed.

## Crimean–Congo haemorrhagic fever, a notified disease in the EU

Crimean–Congo haemorrhagic fever is a notifiable disease in the EU and has the widest range among all tick-borne diseases (present in 30 countries in Africa, central and south-west Asia, the Middle East and south-eastern Europe). In late stages the disease manifests as a febrile haemorrhagic syndrome with an up to 50% fatality rate and the potential of causing nosocomial infections and outbreaks. The emergence or re-emergence of Crimean–Congo haemorrhagic fever in the last decade in south-east Europe and neighbouring countries (Albania, Kosovo, Turkey, Bulgaria, south-west Russia, Ukraine and Greece) might be related to anthropogenic factors (e.g. movement of animals, changes in land use) or climate change. The reason for the absence of Crimean–Congo haemorrhagic fever in western parts of the EU remains unclear. Based on models it is speculated that a possible expansion of its current distribution may be attributed to a geographic expansion of *Hyalomma* ticks due to climate changes that modify tick-related biological factors.

<sup>1</sup>Stanek G, et al. 2011. Lyme borreliosis: Clinical case definitions for diagnosis and management in Europe. *Clinical Microbiology Infection* 17:69-79

## Tick-borne encephalitis and Lyme borreliosis in the Czech Republic

Tick-borne encephalitis in the Czech Republic has been known for 60 years but in recent years an important increase has been observed. Higher numbers of cases are recorded from well known endemic areas. Re-emergence of tick-borne encephalitis has been observed in areas where the disease was present in the 1950s and 1960s. New tick-borne encephalitis foci have emerged in the southern and western parts of the country and in the mountainous areas. A shift of tick-borne encephalitis towards earlier spring and later autumn months has also been observed. This shift coincides with a similar shift of *Ixodes ricinus* activity.

The so-called TICKPRO programme was developed to predict *Ixodes ricinus* host-seeking activity as a function of meteorological data. The outcome is published as a warning system on the website of the National Institute of Public Health, Prague. A spatial tick-borne encephalitis risk map and predictive maps of *Ixodes ricinus* have been developed.

## Tick-borne encephalitis in Scandinavia

In Sweden, Norway and Finland an increase of tick-borne encephalitis has been observed and the disease has been recorded in Denmark. In Sweden this upsurge resulted in a westward spread of the disease.

## ECDC initiatives regarding tick-borne diseases: the Venice survey, the tick-borne disease toolkit and VBORNET

The *Venice survey* on tick-borne encephalitis<sup>i</sup> concluded that:

- tick-borne encephalitis vaccination can control the burden of disease but cannot reduce the virus circulation;
- implementation of an epidemiological European case definition for tick-borne encephalitis is needed for a comparable collection of epidemiological data;
- surveillance of tick-borne encephalitis should be implemented in all countries where the disease is endemic;
- vaccine coverage for tick-borne encephalitis should be monitored in the countries where vaccination is recommended;
- surveillance is the key to addressing the appropriate target groups in endemic areas;
- risk maps were seen as the appropriate support for effective vaccine recommendation to travellers.

The *ECDC toolkits* aim at providing scientifically correct information to countries and public health institutes. These toolkits can be adapted to country needs and feedback from the Member States is highly welcome.

The toolkit on tick-borne diseases (published in June 2010) was presented and suggestions were made to improve it (e.g. use of pictures, possible misinterpretation of some messages). Some concerns were raised on the number of messages that are sent to the general public and possible 'health message fatigue'. The communication to the Member States on the existence of the toolkits can be improved.

*VBORNET*<sup>ii</sup> is a network of entomologist and public health specialists dealing with vector-borne diseases. The network aims to map vector species and collate information on vector-related surveillance and public health activities and resources in the EU.

## EFSA initiatives

The Zoonoses data collection unit of EFSA has outsourced a project on 'Inventory of available data and data sources and proposal for data collection on vector-borne zoonoses in animals'. The data inventory is based on the results of a systematic literature review, as well as on questionnaires submitted to the members of the Task Force on Zoonoses data collection. Pathogens covered by this project are *Borrelia* spp., tick-borne encephalitis virus group, *Leishmania* spp., West Nile virus, Crimean–Congo haemorrhagic fever virus, Hantaviruses, *Francisella tularensis*, and *Leptospira* spp. The final report is expected by the end of June 2011.

The Zoonoses unit also reports on food-borne outbreaks at the EU level. Food-borne outbreaks caused by tick-borne encephalitis virus through unpasteurised goat milk were reported by Member States during the period 2006 to 2008.

<sup>i</sup> Stefanoff P, et al. 2011. Reliable surveillance of tick-borne encephalitis in European countries is necessary to improve the quality of vaccine recommendations. *Vaccine*. 29; 1283-1288.

<sup>ii</sup> <http://ecdc.europa.eu/en/activities/diseaseprogrammes/Pages/VBORNET.aspx>

The Animal health and welfare (AHAW) unit developed two scientific opinions on ticks and tick-borne diseases in 2010:

- Role of ticks in the epidemiology of Crimean–Congo haemorrhagic fever and African swine fever<sup>i</sup>;
- Geographic distribution of ticks and their associated pathogens in Europe and in the Mediterranean basin<sup>ii</sup>.

Mapping ticks and tick-borne pathogens in these scientific opinions was based on a systematic literature review. The data extracted generated a database of about 16 000 entries on tick distribution. This database was made available to ECDC as a complement to the VBORNET tick database.

Future projects of AHAW Unit of EFSA are: launching a call for mapping sandflies and sandfly-borne pathogens by means of a systematic literature review, and to obtain a technical external report on 'Definition of epidemiological data requirements for risk assessment of vector-borne zoonoses in animals'.

## WHO EURO activities

WHO collects information on the number of cases and incidence data of Crimean–Congo haemorrhagic fever, tick-borne encephalitis and Lyme borreliosis (plus a number of other vector-borne diseases) of member states of the WHO European Region in the centralized information system for infectious diseases (CISID, <http://data.euro.who.int/cisid/>).

In addition to basic surveillance, WHO EURO responded to Crimean–Congo haemorrhagic fever outbreaks (evaluation team, training of physicians) and developed guidelines for environmental surveillance and food safety.

WHO EURO is involved in the Circum-polar infectious disease group. This group covers a range of diseases including tick-borne diseases.

## 4 Working groups on harmonisation of case definitions

ECDC is financing two projects related to tick-borne diseases. One project is working on Lyme borreliosis, the other on tick-borne encephalitis, rickettsioses, and Q fever. The objectives of these projects are to:

- characterise the different reporting systems for Lyme borreliosis, tick-borne encephalitis and rickettsial diseases in the EU;
- identify and assess the current and epidemiological situation for Lyme borreliosis, tick-borne encephalitis and rickettsial diseases in the EU;
- identify key risk areas of Lyme borreliosis, tick-borne encephalitis and rickettsial diseases in the EU;
- identify key risk groups for Lyme borreliosis, tick-borne encephalitis and rickettsial diseases;
- provide ECDC with data for input into its burden of disease study (Lyme borreliosis, tick-borne encephalitis, Q fever).

The coordinators of both projects chaired the working groups on harmonisation of case definitions.

### Working group on Lyme borreliosis

This section summarises the discussion and conclusion of the two working groups on the harmonisation of the case definition of Lyme borreliosis.

The response to the question of the necessity of making Lyme borreliosis notifiable at the Member State or the EU level was mixed, with strong opinions in each direction. In one of the working groups it was suggested that mandatory notification should be limited to erythema migrans or neuroborreliosis. In the general discussion after the working groups no consensus was reached on this topic.

<sup>i</sup>EFSA Panel on Animal and Welfare (AHAW). 2010. Scientific Opinion on the Role of Tick Vectors in the Epidemiology of Crimean-Congo Hemorrhagic Fever and African Swine Fever in Eurasia. EFSA Journal 8:1703. <http://www.efsa.europa.eu/en/scdocs/scdoc/1703.htm>

<sup>ii</sup>EFSA Panel on Animal Health and Welfare (AHAW). 2010. Scientific Opinion on Geographic Distribution of Tick-borne Infections and their Vectors in Europe and the other Regions of the Mediterranean Basin. EFSA Journal 8:1723. <http://www.efsa.europa.eu/en/scdocs/scdoc/1723.htm>

The need for harmonisation of the case definition was agreed. The difference between a case definition for clinical use and for public health use was recognised. The case definition should be as simple and practical as possible and be applicable to the majority of countries.

Case definitions were discussed and it was concluded that the EUCALB case definition can be used as a common basis, but needs to be adapted at the EU level from a public health perspective and to the classification defined by Commission Decision 2008/426/EC<sup>i</sup> laying down case definitions for reporting communicable diseases in the EU. Exposure to risk of tick bite was proposed as epidemiological criterion without the need for a documented tick bite.

The discussion revealed the need for more insight into the value and limitations of laboratory tests for *Borrelia burgdorferi* infections. This area requires detailed expert input to provide epidemiologists and public health experts with a view on which to base policy decisions. The input should also include a detailed assessment of the laboratory facilities and methods available in European countries.

## Working group on tick-borne encephalitis

This section summarises the discussion and conclusion of the two working groups on the harmonisation of the case definition of tick-borne encephalitis.

The meeting recommended adding tick-borne encephalitis (i.e. tick-borne central nervous system infection) to the list of mandatory notifiable diseases in the EU.

The following case definition and classification was proposed as a common basis for further harmonisation:

Case definitions:

- Clinical criteria:
  - Meningitis or encephalitis
- Epidemiological criteria:

[The epidemiological criteria need further discussion as the meeting did not agree on them]

- Laboratory criteria for probable case:
  - IgM positive in unique serum sample ascertained with test different from neutralisation (\*)

[This needs further discussion as different views were presented during the meeting.]

- Laboratory criteria for confirmed case:
  - Sero-conversion or fourfold increase in antibody titre in convalescent serum sample
  - Confirmation of anti-tick-borne encephalitis antibodies by neutralisation
  - Detection of virus nucleic acid in sera or cerebrospinal fluid or tissue or other body fluid by PCR or virus isolation
  - Detection of specific IgM in central nervous system (to be verified with evidence)

(\*) Laboratory results need to be interpreted according to the vaccination status.

Case classification:

- Possible case
  - Not relevant for notification at EU level
- Probable case

[Further discussion is needed on the use of the epidemiological criteria and the laboratory criteria in the classification of a probable case ]

- Confirmed case
  - Clinical criteria and one of the laboratory criteria for confirmed case

The value and the limitation of the different laboratory tests for tick-borne encephalitis should be further assessed.

More data are needed on probable and confirmed cases that can serve as basis for harmonisation of case definition.

A geographic risk assessment map should be produced by ECDC and made available on the internet.

<sup>i</sup> 2008/426/EC: Commission Decision of 28 April 2008 amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council. OJ L 159, 18.6.2008, p. 46–90.

## 5 Recommendations and next steps

It was recommended that ECDC proposes a case definition for Lyme borreliosis based on the EUCLB definition including the feedback from the meeting groups and also proposes a case classification to conform to the system applied with notifiable diseases. This will be shared with the expert group for comments and be the basis for harmonisation.

The value and the limitations of the different laboratory tests used for Lyme borreliosis and for tick-borne encephalitis should be further assessed and quality standards should be defined.

The meeting recommended that tick-borne encephalitis be added to the list of mandatory notifiable diseases in the EU.

It was recommended that ECDC assess the geographic risk of tick-borne encephalitis represented on a map available on internet.

# Annex 1: Meeting programme

## 23 November 2010

09:00-09:15	<b>Welcome and introduction</b> Johan Giesecke & Herve Zeller
09:15-09:45	<b>Ticks and TBDs in Europe: ecology, distribution, climate suitability and the implications for pathogen transmission and human health</b> Agustin Estrada-Peña
09:45-10:15	<b>Lyme borreliosis in the EU: epidemiology, clinics, and prevention</b> Gerold Stanek
10:15-10:45	<b>Tick-borne encephalitis in the EU: epidemiology, clinics, and prevention</b> Martin Pfeiffer
11:15-11:35	<b>Crimean–Congo haemorrhagic fever a notified disease in the EU: epidemiology, case definition and areas of uncertainty</b> Helena Maltezou
11:35-11:50	<b>Tick-borne encephalitis and Lyme borreliosis in the Czech Republic</b> Bohumir Kriz
11:55-12:10	<b>Tick-borne encephalitis in Scandinavia</b> Göran Günther
12:15-13:00	<b>ECDC initiatives regarding TBD: Venice survey, Toolkit TBD, VBORNET</b> Perliugi Lopalco, Niklas Danielsson, Wim Van Bortel
14:00-14:20	<b>ECDC initiative on Lyme borreliosis</b> Robert Smith
14:20-15:30	<b>WG on LB case definition and harmonisation:</b> Chaired by Robert Smith, Susan O'Connell, Paul McKeown, and Sofia Nuncio
15:45-17:00	<b>WG on LB case definition and harmonisation, continue</b>
17:00-17:30	<b>Feed-back from the working groups and conclusions of day 1</b>

## 24 November 2010

09:00-09:15	<b>Summary of day 1 and introduction of day 2</b> Herve Zeller
09:15-09:30	<b>EFSA and WHO perspectives on Tick-Borne Diseases</b> Jordi Tarres, David Mercer
09:30-9:50	<b>ECDC initiative on TBE</b> Pawel Stefanoff
10:10-12:20	<b>Working group on TBE case definition and harmonisation</b> Chaired by Pawel Stefanoff and Fortunato Paolo D'Ancona
13:20-13:50	<b>Feedback from the working groups</b>
13:50-14:50	<b>General discussion, next steps and conclusions</b>
14:50-15:00	<b>Closure of the meeting</b>

## Annex 2: Participants

Name	Organisation	Country
Agustín Estrada-Peña	University of Zaragoza	Spain
Anders Fomsgaard	Statens Serum Institute	Denmark
Ana Paula Brito	Directorate-General of Health	Portugal
Anna Reye	Institute of Immunology	Luxembourg
Auksė Mickienė	Institute of Hygiene	Lithuania
Bohumir Kriz	National Institute of Public Health	Czech Republic
Claude Muller	Institute of Immunology	Luxembourg
David Mercer	World Health Organization	
Fortunato Paolo D'Ancona	National Centre for Epidemiology, Surveillance and Health Promotion	Italy
Gerold Stanek	Medical University of Vienna	Austria
Göran Günther	Uppsala University Hospital	Sweden
Helena Maltezos	Hellenic Centre for Disease Control and Prevention	Greece
Inger Andersson von Rosen	National Board of Health and Welfare	Sweden
Irina Lucenko	State Agency 'Latvian Infectology Centre'	Latvia
Iva Christova	National Centre of Infectious and Parasitic Diseases	Bulgaria
Jordi Tarres	EFSA - European Food Safety Authority	Italy
Katalin Krisztalovics	National Centre for Epidemiology	Hungary
Maria Grazia Ciufolini	Istituto Superiore di Sanita	Italy
Marika Hjerqvist	Swedish Institute for Infectious Disease Control	Sweden
Marta Vitek	National Institute of Public Health	Slovenia
Martin Pfeffer	University of Leipzig	Germany
Michael Kunze	Medical University of Vienna	Austria
Paul McKeown	Health Protection Surveillance Centre (HPSC)	Ireland
Pawel Stefanoff	National Institute of Public Health National Institute of Hygiene	Poland
Preben Ottesen	Norwegian Institute of Public Health	Norway
René Bødker	National Veterinary Institute Technical University of Denmark International EpiLab	Denmark
Robert Smith	Public Health Wales - Health Protection	United Kingdom
Steven Van Gucht	Scientific Institute of Public Health	Belgium
Sofia Nuncio	National Insitute of Health Dr. Ricardo Jorge	Portugal
Susan O'Connell	Health Protection Agency	United Kingdom
Valerie Choumet	CNR des Borrelia - Institut Pasteur	France
Véronique Vaillant	InVS - Institut de Veille Sanitaire	France
Volker Fingerle	Bayerisches Landesamt für Gesundheit und Lebensmittelsicherheit	Germany
Wilfrid Van Pelt	National Institute for public Health and the Environment	The Netherlands

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