



MEETING REPORT

First annual meeting of the European Diphtheria Surveillance Network

Stockholm, 17 March 2011

Executive summary

The first annual meeting of the European Diphtheria Surveillance Network (EDSN, formerly known as DIPNET) was attended by 37 disease experts nominated for the epidemiologic and laboratory surveillance of diphtheria at the national level in the European Union Member States and Norway.

The coordination of the network's surveillance activities had been transferred to ECDC in March 2010.

EDSN covers infections caused by toxigenic *Corynebacterium diphtheriae* and *Corynebacterium ulcerans* and integrates epidemiologic and laboratory surveillance of these infections in all 27 European Union and three European Economic Area Member States. National surveillance data is transmitted from the participating countries to the European Surveillance System (TESSy) database hosted at ECDC.

Although diphtheria is relatively uncommon in the European Region, the original WHO elimination target for this disease (elimination of indigenous diphtheria from the Region by the year 2000) has still not been met. Transmission continues in several countries, notably Latvia, Ukraine, the Russian Federation and other countries of the former Soviet Union. Sporadic cases are still being reported in several European Union Member States. As a consequence, there is an ongoing risk of epidemic diphtheria returning to the European Region. High immunisation coverage must be sustained, adult booster coverage should be increased, and surveillance and laboratory capacity should be maintained in all countries.

The EDSN meeting provided a good opportunity to meet other European disease experts, learn from experiences in the Member States, and discuss how to develop and strengthen collaboration between different partners within the surveillance network.

The conclusions of the discussion are summarised on page seven. The European Centre for Disease Prevention and Control will bring forward issues that require agreement at a higher administrative level (for example the national surveillance contact points, EU Network Committee) and work towards implementing the suggested improvements.

The views expressed in this publication do not necessarily reflect the views of the European Centre for Disease Prevention and Control (ECDC).

Stockholm, August 2011

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1 Background

On 17 March 2011, public health experts nominated for the national surveillance of diphtheria by the European Union (EU) and European Economic Area (EEA) Member States gathered at the European Centre for Disease Prevention and Control (ECDC) in Stockholm for the first meeting of the European Diphtheria Surveillance Network (EDSN). The meeting, which brought together epidemiologists and laboratory surveillance experts, provided an important opportunity to share experiences and strengthen the collaboration within the network.

1.1 Objectives

The following objectives were to be attained at the meeting:

- Present the epidemiologic situation of diphtheria diseases in Europe over the last decade with a special focus on 2009.
- Develop specific surveillance objectives for diphtheria and related diseases.
- Discuss and, if necessary, revise the existing case definition to better meet the surveillance objectives.
- Discuss and, if necessary, revise the enhanced set of variables: strengths, weaknesses and improvements.
- Discuss data collection procedures as performed by ECDC's The European Surveillance System (TESSy) platform, the system's data outputs, and the reporting frequency.
- Discuss diphtheria-specific requirements for communication and how changes could be implemented using the Epidemic Intelligence Information System (EPIS) at ECDC.
- Set up a coordination group for EDSN.

1.2 Expected meeting outcomes

The following outcomes of the meeting were expected:

- Disease-specific surveillance objectives for diphtheria and related diseases developed.
- EU 2008 case definitions for diphtheria diseases revised, if necessary.
- Proposals from Member States for
 - the improvement of the system;
 - modes of collaboration with ECDC (including building new collaborations); and
 - the sustainability of collaborative efforts.
- Agreement on development of reports, outputs format and reporting frequency.
- Coordination group set-up.
- Agreement on diphtheria communication requirements.

The annual meeting was composed of plenary lectures and working groups (see Annex 1: agenda).

2 Meeting sessions

Session 1: Epidemiology of diphtheria diseases in the EU

Ida Czumbel (ECDC) gave a presentation on ECDC's mandate and its coordinating role within the EU and highlighted the close working relationships with EU and EEA Member States. She emphasised how much European communicable disease surveillance relied on the high quality services provided by national public health microbiology laboratories. She then went on to outline the general surveillance activities at ECDC, followed by a description of European vaccine-preventable disease (VPD) surveillance including diphtheria. A comprehensive overview of DIPNET activities during the last ten years was given by Joanne White (HPA, London). She described the purpose of the network, the objectives of the diphtheria work packages (WP 1-9), pointing out the main problems with the disease, for example the lack of appropriate treatment with diphtheria antitoxin, the increasing susceptibility to the disease of older people, and the importance of the resumption of seroprevalence studies. David Mercer (WHO) presented the current epidemiology of the disease and the operational targets for elimination of diphtheria from the WHO European Region.

There are currently three VPD surveillance networks operating in the EU/EEA: EU-IBD (European Invasive Bacterial Disease Surveillance Network), EDSN (European Diphtheria Surveillance Network), and EUVAC.NET (European Surveillance Community Network for Vaccine-Preventable Diseases). The key partners in each network are the nominated epidemiologists and laboratory experts from 27 EU Member States and three EEA countries. The purpose of EDSN is to establish and maintain a pool of expertise for the prevention and control of diphtheria and to strengthen and harmonise the laboratory capacity at Member State level. The network has an epidemiologic and a laboratory component. The former is coordinated by ECDC and focuses on surveillance data collection and analysis, while the latter is outsourced to the Health Protection Agency (HPA), London, focussing on external quality assurance (EQA), training, and molecular typing. Diphtheria surveillance data will be stored and analysed in TESSy. Integration of diphtheria data into TESSy required a few changes to the DIPNET variables to ensure full compatibility with the system.

Although ten years past the elimination target date, diphtheria cases still occur in the European Region, mainly in Latvia, Ukraine and the Russian Federation. But the goal of elimination is within reach. More work will be necessary to sustain this success: high vaccine coverage has to stay high, surveillance and laboratory capacity must be maintained, adult booster coverage must increase, and more research must be carried out to better understand the risk groups.

Session 2: Diphtheria diseases – outsourced laboratory activities

Androulla Efstratiou, the coordinator of the outsourced diphtheria laboratory network, gave some historic background and presented an update on the network's current and future work.

She described how the diphtheria epidemics in the former Soviet Union led to the formation of the European Laboratory Working Group on Diphtheria (ELWGD). In 1993, following an initiative of WHO, EURO.DIPNET was established with funding from the European Commission, involving all countries from the WHO European Region in the network.

The presenter then described her network's contractual obligations and achievements during the first year, including diagnostic and serology EQAs, training activities, and molecular typing.

Given the potential for re-emergence of diphtheria, it is important that the low numbers of cases do not result in complacency. Therefore the greatest challenges are retaining and developing microbiological skills as shown by recent EQA results. It is essential for EDSN to maintain links with all countries in the EURO Region and beyond. Representatives from these countries should be invited to relevant meetings. Also, biannual conferences on diphtheria and related infections should be continued.

Session 3: Developments in the reporting of diphtheria diseases to TESSy

Daniel Faensen (ECDC) presented recent enhancements of the TESSy platform. Using the new diphtheria metadata set, he demonstrated how data are entered manually, emphasising the principles and challenges of real-time reporting.

Session 4: Risk assessment and the exchange of information on current or emerging public health threats with a potential impact on the EU

In this session, Thomas Mollet (ECDC) updated the network on the most recent developments of the Epidemic Intelligence Information System (EPIS). He gave a short overview of the added value of the system, its planned structure, main functionalities, navigation, and its intended users and their training needs. According to its guiding principles, EPIS should be user friendly and easy to use, requiring only minimal training. EPIS should also be upgradable, with subsequent releases offering additional functionalities.

Thomas Mollet then presented the disease-specific EPIS modules already in place. EPIS-VPD is under development with a sub-module planned for EDSN. Users of EPIS-VPD will be offered training through an online tutorial and receive a user manual. A helpdesk will be set up at ECDC to answer questions or assist in solving user problems.

Session 5: Country presentation

The presenter from Turkey sent her apologies.

Session 6: Working groups (parallel session)

The parallel working groups dealt with diphtheria surveillance objectives, the diphtheria case definition, and laboratory activities, respectively. The two working groups in charge of discussing the first two topics were merged because of the low number of participants who had signed up for these two topics. The participants were assigned to one of the two groups according to their expertise and interest. All participants had received a number of background documents intended to clarify the context and stimulate discussion.

The working groups on diphtheria surveillance objectives and the diphtheria case definition were expected to discuss the disease-specific surveillance objectives taking into account the existing vaccine-preventable disease surveillance objectives and to review, and if necessary revise, the current case definition for diphtheria, established through Decision No 426/2008/EU of the European Parliament and of the Council.

The working group's proposal on diphtheria objectives included the following:

- Estimate the incidence of the diphtheria diseases in Europe by Member State, age and gender.
- Monitor and assess diphtheria disease trends (*C. diphtheriae*, *C. ulcerans*, *C. pseudotuberculosis*) and strain distribution over time in Europe.
- Monitor case-fatality ratio.
- Monitor the population susceptibility by vaccination status of cases.
- Improve the quality, timeliness and comparability of available data.
- Promote early detection and control.
- Support specialised studies, including screening in specific population groups (e.g. occupational health).
- Promote and maintain knowledge, expertise and capacity at the Member State level.
- Encourage integration of laboratory and epidemiology activities.
- Promote the improvement of a laboratory network for disease, including quality assurance and molecular typing.
- Promote standardisation and quality assurance of laboratory methods, including molecular epidemiological typing and serological studies.
- Promote serological studies conducted in collaboration between epidemiologists and microbiologists.
- Support training for microbiologists and public health experts in disease surveillance methods.

The working group members expressed their concern regarding real-time reporting. The option of monthly reporting was favoured.

The working group revised the current EU case definition for diphtheria diseases. The revised case definition would read as follows:

Clinical criteria

Any person with at least one of the following clinical forms:

- Classic respiratory diphtheria
 - An upper respiratory tract illness with laryngitis or nasopharyngitis or tonsillitis plus an adherent membrane/pseudomembrane
- Mild respiratory diphtheria
 - An upper respiratory tract illness with laryngitis or nasopharyngitis or tonsillitis, without an adherent membrane/pseudomembrane.
- Cutaneous
 - Skin lesion
- Diphtheria of other sites
 - Lesion of conjunctiva or mucous membranes

Laboratory criteria

Isolation of toxin-producing *C. diphtheriae*, *C. ulcerans* or *C. pseudotuberculosis* from a clinical specimen (respiratory or cutaneous).

Epidemiological criteria

An epidemiological link to a confirmed case (human or animal).

Case classification

Possible case: any person meeting the clinical criteria for diphtheria (classic respiratory diphtheria , mild respiratory diphtheria, cutaneous).

Probable case: any person meeting the clinical criteria for diphtheria (classic respiratory diphtheria, mild respiratory diphtheria, cutaneous) with an epidemiological link to a confirmed case (human or animal).

Confirmed case: any person meeting the laboratory criteria and at least one of the clinical forms.

Note: Non-toxigenic *C. diphtheriae*, *C. ulcerans* or *C. pseudotuberculosis* should not be reported.

The working group on specific laboratory activities dealt with laboratory capabilities and the availability of specialised media, toxin testing, rapid assays, molecular typing capabilities, serology, screening practices, EQA and training needs.

While the majority of countries use classic laboratory tests for case confirmation, there are difficulties in procurement of specialised media: Elek basal medium, antitoxin strips/discs, and newborn bovine serum; more recently Tinsdale medium. For toxin testing, the majority of the laboratories use the classic or modified Elek test. However, in some centres, PCR is also used to detect the toxin gene.

About 50% of the centres are able to carry out molecular typing (MLST and VNTR) and almost all of them were interested in novel typing developments based on whole genome target. The existing ribotype database hosted by HPA London needs to be transferred to ECDC.

It was considered essential to have EQA panels for laboratory diagnostics every two years, and 12 countries strongly expressed the wish to participate in the training workshop later this year. Three host sites were offered: Greece, Romania and Latvia.

21 countries will participate in the serology EQA. With regard to screening practices, most countries only investigate throat swabs or other samples when clinically indicated.

Final remarks

The ECDC terms of reference for the EDSN coordination group had been shared with the network members prior to the meeting and a call for applications had been sent out in March with a deadline for the end of March. Ida Czumbel added some clarifications regarding the membership, tasks of the group, and selection procedures.

The participants agreed on the revised objectives, however the possibility for further comments on the case definition was offered. Before closing the meeting, Ida Czumbel thanked all participants for their attendance and contributions.

3 Conclusions

The EDSN meeting succeeded in bringing together a wide range of partners working in the field of diphtheria surveillance for the first time to discuss a variety of topics related to the surveillance of diphtheria in EU and EEA countries. These partners included country-nominated epidemiological and laboratory experts, members of the European diphtheria laboratory network, and colleagues working in different fields at ECDC (general surveillance, preparedness and response, scientific advice).

The main challenges in terms of diphtheria remain:

- Declining immunity with age, coupled with a proportion of unvaccinated adults can lead to a susceptible population in older age groups, as shown in ESEN projects conducted in the 1990s.
- Currently, there are no known seroepidemiological activities in the Member States.
- Routine screening activities at the Member State level were suspended.
- Prompt recognition and reporting of diphtheria is important to ensure early and appropriate treatment with diphtheria antitoxin (DAT), contact tracing, and treatment.
- Apparently, there is only one source of antitoxin in Europe (Institute of Immunology in Croatia).

Overall, the participants felt the meeting was a success, with many lessons learned and useful and concrete suggestions which will enable improvements to diphtheria surveillance in the EU/EEA. The following proposals were made, taking into account the challenges and the current status of disease elimination:

- Diphtheria-related activities should continue at EU level.
- The ribotype database needs to be transferred to ECDC.
- Availability of therapeutic antitoxin was again raised; there is a need for an inventory of availability at ECDC.
- Additional support and capacity-building is needed for several EU countries.
- More networking is required.
- Country surveillance activities and national surveillance protocols should be revised.
- Need to have longer discussions on specific topics and more time dedicated to working groups.
- More practical training and more training on diagnostics is required.
- Additional time for social activities after the meeting would have been appreciated.

The following eight members were accepted to serve a two-year term on the EDSN coordination group:

- Androulla Efstratiou, HPA London
- Aleksandra Zasada, Narodowy Instytut Zdrowia Publicznego, Poland
- Andreas Sing, Konsiliarlaboratorium für Diphtherie; Bayerisches Landesamt für Gesundheit und Lebensmittelsicherheit, Germany
- Emmanuel Belchior, Institut de Veille Sanitaire, France
- Georgina Tzanakaki, National School of Public Health, Greece
- Irina Lucenko, State Agency 'Infectology Center of Latvia'
- Joanna White, HPA London
- Maria Damian, National Institute for Research and Development for Microbiology and Immunology, Romania

Annex 1: Meeting programme

First Annual Meeting of the
European Diphtheria Surveillance Network
ECDC, Stockholm, Sweden
17 March 2011

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8:30 Bus from the Hotel to ECDC
8:30-9:00 Registrations at ECDC
9:00-9:15 Welcome and opening of the meeting, *Andrew Amato-Gauci, Deputy Head of Surveillance Unit (ECDC)*

SESSION 1: Epidemiology of diphtheria in the EU, an overview

Chairperson: *David Mercer (WHO), Androulla Efstratiou (HPA, London)*

9:15-9:35 ECDC's vaccine preventable diseases activities including diphtheria, *Ida Czumbel (ECDC)*
9:35-10:00 Epidemiology of diphtheria in EU, 2009, *Joanne White (HPA, London)*
10:00-10:25 Epidemiology of diphtheria in WHO European Region
David Mercer (WHO, Copenhagen)
10:20-10:30 Discussions
10:30-10:45 Coffee break

SESSION 2: Diphtheria: Outsourced laboratory activities

Chairperson: *Jaana Voupio (THL), Dora Navarro (ECDC)*

10:45-11:10 ECDC outsourced laboratory activities, *Androulla Efstratiou (HPA, London)*
11:10-11:25 Discussion

SESSION 3: Diphtheria data reporting to TESSy

Chairperson: *Edward van Straten (ECDC), Gaetan Guyodo (ECDC)*

11:25-11:45 Presentation of enhanced set of diphtheria variables, *Daniel Faensen (ECDC)*
11:45-12:00 Discussion

SESSION 4: Risk assessment entities to exchange information regarding current or emerging public health threats with a potential impact in the EU

Chairperson: *Daniel Faensen (ECDC), Tarik Derrouh (ECDC)*

12:00-12:20 Alert mechanism for cases and clusters- Epidemic Intelligence Information System (EPIS), *Thomas Mollet (ECDC)*
12:20-12:30 Discussions
12:30-13:30 Lunch

SESSION 5: Country Presentation

Chairperson: *Pierluigi Lopalco (ECDC), Ida Czumbel (ECDC)*

13:30-13:45 *Epidemiology of Diphtheria in Turkey, Aslihan Coskun (PHI, Turkey)*

SESSION 6: Working group sessions (WG) parallel sessions – participants will split into groups

Chairperson: *Joanne White (HPA, London), Irina Lucenko (PHI, Latvia)*

13:45-15:45 WG 1. Diphtheria surveillance objectives and proposal for diphtheria variables
WG 2. Diphtheria case definition
WG 3. Specific laboratory activities/EQA and typing/databases
15:45-16:15 Coffee break
16:15-16:45 Summary reports from the WGs
16:45-17:00 Discussions
17:00 Closing remarks

Annex 2: Participants

#	Country	Family name	First name
1	BE	Wybo	Ingrid
2	BG	Detcheva	Antoaneta
3	CZ	Zavadilova	Jana
4	CZ	Fabianova	Katerina
5	DE	Sing	Andreas
6	DE	Reiter	Sabine
7	DK	Andersen	Peter Henrik
8	EE	Peetso	Rita
9	EE	Dontsenko	Irina
10	ES	Masa Calle	Josefa
11	FI	Vuopio	Jaana
12	FR	Edgar	Badell-Ocando
13	FR	Belchior	Emmanuel
14	GR	Pangalis	Anastasia
15	GR	Tzanakaki	Georgina
16	HU	Tirczka	Tamás
17	IT	Monaco	Monica
18	LT	Liachaviciute	Aurelija
19	LT	Savickiene	Egle
20	LV	Paberza	Ruta
21	LV	Lucenko	Irina
22	NO	Steinbakk	Martin
23	PL	Zasada	Aleksandra
24	PL	Paradowska-Stankiewicz	Iwona
25	PT	Bajanca Lavado	Maria Paula
26	RO	Stanescu	Aurora Violeta
27	RO	Damian	Maria
28	SE	Morfeldt	Eva
29	SE	Lepp	Tiia
30	SI	Mioc	Verica
31	SK	Belyová	Anna
32	SK	Lengyelová	Viera
33	UK	Efstratiou	Androulla
34	UK	White	Joanne
35	*	Mercer	David
36	ECDC	Amato	Andrew
37	ECDC	Navarro	Adoracion
38	ECDC	Derrough	Tarik
39	ECDC	van Straten	Edward
40	ECDC	Hruba	Frantiska
41	ECDC	Faensen	Daniel
42	ECDC	Johansen	Kari
43	ECDC	Carrillo-Santistev	Paloma
44	ECDC	Kreidl	Peter
45	ECDC	Zucs	Phillip
46	ECDC	Mollet	Thomas
47	ECDC	Guyodo	Gaetan

* Invited speaker (WHO)