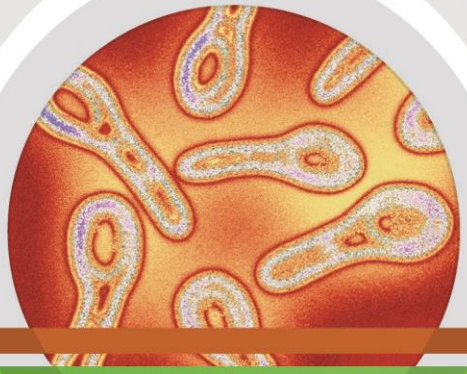


SURVEILLANCE REPORT

Annual Epidemiological Report for 2015

Diphtheria

Key facts

- In 2015, 65 cases of diphtheria caused by toxigenic *Corynebacterium* species were reported to ECDC.
- Teenagers and young adults were the most affected.
- The majority of cases were not vaccinated or the vaccination status was reported as unknown.
- Latvia reported the highest number of indigenous cases of *C. diphtheriae* infections.
- High vaccination coverage must be sustained to prevent diphtheria cases.

Methods

This report is based on data for 2015 retrieved from The European Surveillance System (TESSy) on 26 October 2016. TESSy is a system for the collection, analysis and dissemination of data on communicable diseases. EU Member States and EEA countries contribute to the system by uploading their infectious disease surveillance data at regular intervals.

For a detailed description of methods used to produce this report, please refer to the *Methods* chapter [1].

An overview of the national surveillance systems is available online [2].

Additional data on this disease are accessible from ECDC's online *Surveillance atlas of infectious diseases* [3].

ECDC has coordinated the surveillance of diphtheria at the European level since the transfer of the Diphtheria Surveillance Network (DIPNET) to ECDC in 2010.

In 2015, 29 EU/EEA Member States reported data, 11 of which reported cases of *C. diphtheriae or C. ulcerans.* Eighteen countries reported zero cases. Two countries did not report data. The majority of Member States reported data on diphtheria in accordance with the 2008 (n=13) or 2012 (n=11) EU case definition. Five countries used an alternative or unspecified case definition. Regardless of the case definition used, only cases caused by, or with a clinical syndrome consistent with toxigenic strains are reported at the EU level (Commission Implementing Decision 2012/506/EU of 8 August 2012 of the European Parliament and of the Council).

Suggested citation: European Centre for Disease Prevention and Control. Diphtheria. In: ECDC. Annual epidemiological report for 2015. Stockholm: ECDC; 2017.

Stockholm, December 2017

Clinically notified and laboratory-confirmed cases were linked and submitted to TESSy with a single record identifier. The majority of the countries reported data based on a comprehensive and compulsory case-based surveillance system.

Epidemiology

Sixty-five cases of laboratory-confirmed diphtheria were reported by eleven countries in 2015. The overall notification rate was <0.01 per 100 000 population (Table 1, Figure 1). Of the 65 cases, 40 were due to *C. diphtheriae* and 25 to *C. ulcerans* (Table 2).

Of the 40 *C. diphtheriae* cases, Latvia reported the highest number of indigenous cases and was the only EU Member State with continued indigenous transmission over several years (Table 2). From 2011 to 2015, 196 cases of diphtheria were reported in the EU/EEA, 116 of which were due to *C. diphtheriae* infections. The number of *C. diphtheriae* cases reported over the last five years has increased every year.

Table 1. Number of confirmed diphtheria cases, EU/EEA, 2011–2015

Country	2011	2012	2013	2014	2015		
	Reported cases	Reported cases	Reported cases	Reported cases	National coverage	Reported cases	Confirmed cases
	Number	Number	Number	Number		Number	
Austria	0	0	0	2	Y	0	0
Belgium	0	1	1	0	Y	3	3
Bulgaria	0	0	0	0	Y	0	0
Croatia	.	.	0	0	Y	0	0
Cyprus	0	0	0	0	Y	0	0
Czech Republic	0	0	0	0	Y	0	0
Denmark	0	0	0	0	.	.	.
Estonia	0	0	0	0	Y	0	0
Finland	0	1	0	0	Y	1	1
France	5	11	6	6	Y	14	14
Germany	4	9	4	8	Y	14	14
Greece	0	0	0	0	Y	0	0
Hungary	0	0	0	0	Y	0	0
Ireland	0	0	0	0	Y	1	1
Italy	0	0	1	1	Y	0	0
Latvia	6	8	14	13	Y	10	10
Lithuania	1	0	0	0	Y	0	0
Luxembourg	0	0	0	0	Y	0	0
Malta	0	0	0	0	Y	0	0
Netherlands	0	1	0	1	Y	5	5
Poland	0	0	0	0	Y	0	0
Portugal	0	0	0	0	Y	0	0
Romania	0	0	0	0	Y	0	0
Slovakia	0	0	0	0	Y	0	0
Slovenia	0	0	0	0	Y	0	0
Spain	0	0	0	1	Y	1	1
Sweden	2	2	2	3	Y	8	8
United Kingdom	2	1	4	1	Y	6	6
EU	**20**	**34**	**32**	**36**	**.**	**63**	**63**
Iceland	0	0	0	0	Y	0	0
Liechtenstein	.	.	.	.	.	.	.
Norway	0	0	0	2	Y	2	2
EU/EEA	**20**	**34**	**32**	**38**	**.**	**65**	**65**

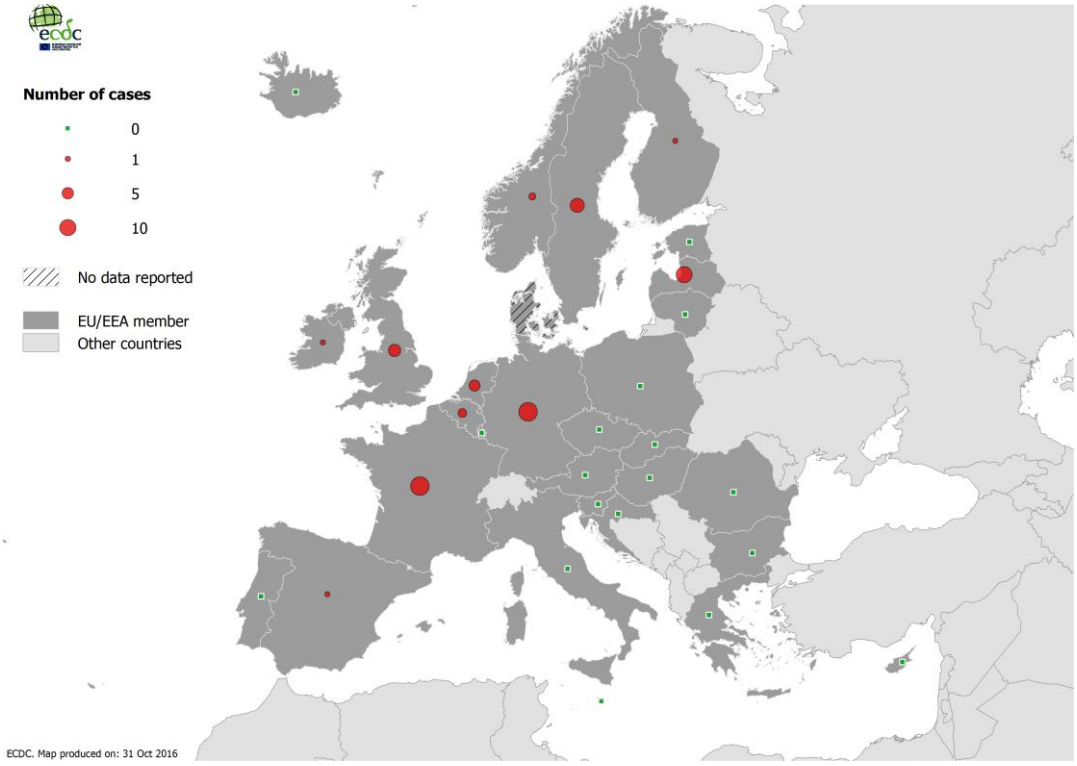
Source: Country reports. Legend: Y = yes, N = no, C = case based, A = aggregated, ASR: age-standardised rate, · = no data reported, - = no notification rate calculated

Table 2. Number of confirmed cases of diphtheria by pathogen in the EU/EEA by country, 2015

Country	*C. diphtheriae*	*C. ulcerans*
	Number of cases	Number of cases
Belgium	1	2
Finland	1	0
France	6	8
Germany	9	5
Ireland	0	1
Latvia	9	1
Netherlands	3	2
Spain	1	0
Sweden	5	3
United Kingdom	3	3
Norway	2	0
Total EU/EEA	40	25

Source: Country reports

Figure 1. Distribution of confirmed cases of diphtheria, by country, EU/EEA, 2015



Source: Country reports from Austria, Belgium, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, the United Kingdom.

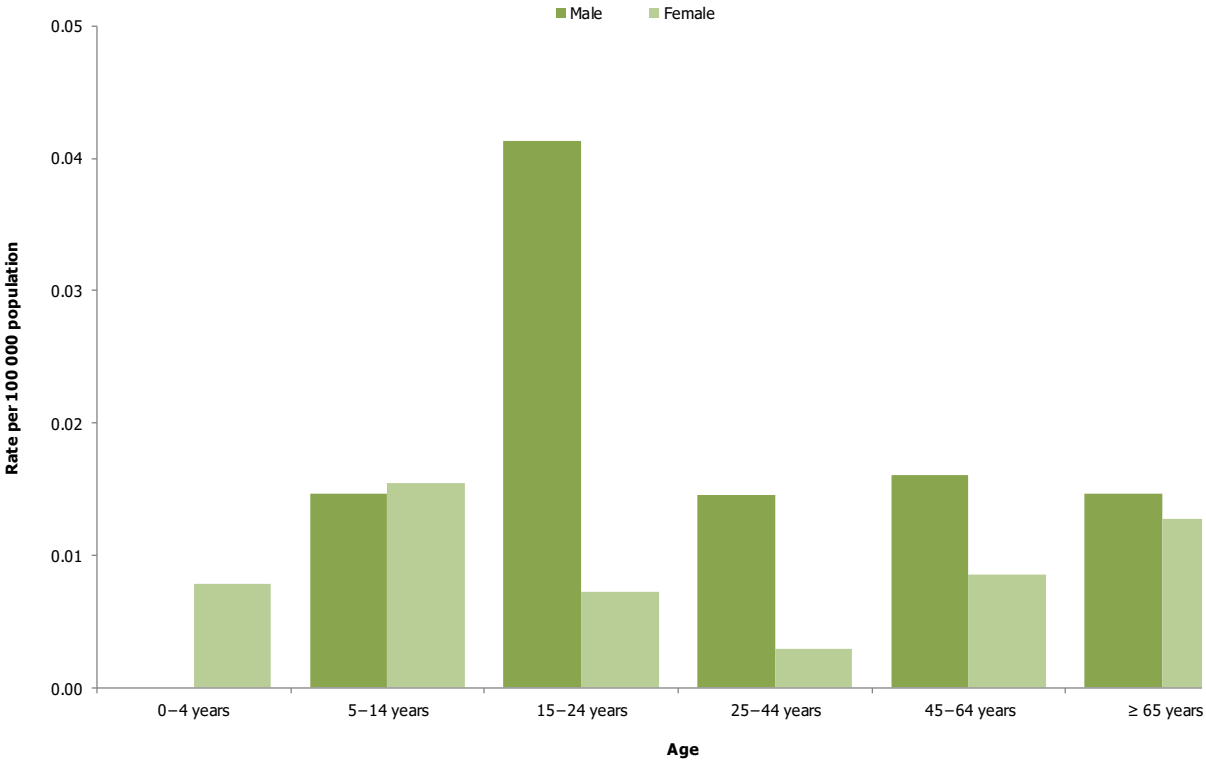
Age and gender distribution

In 2015, diphtheria cases were reported in all age groups, with a preponderance in teenagers and young adults (Figure 2). There was a single case reported in a child under five years of age, and eight cases were reported in children below 14 years of age. Fourteen cases were reported in teenagers and young adults aged 15–24 years, and 42 cases were reported in adults aged over 25 years. Forty-three of the 65 cases of laboratory-confirmed diphtheria were male.

In an analysis by pathogen, seven of the 40 *C. diphtheriae* cases were below 14 years of age, 12 were teenagers between 14 and 25, and 21 were adults over the age of 25 years. Thirty-one of the 40 cases were reported in males.

Most of the *C. ulcerans* (n=25) cases were reported in adults over 35 years of age (n= 22). The remaining three cases were seven, nine and 17 years old, respectively. In terms of gender distribution, 12 of 25 cases were male.

Figure 2. Confirmed cases of diphtheria per 100 000 population, by age and gender, EU/EEA, 2015



Source: Country reports from Austria, Belgium, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, the United Kingdom.

Seasonality

The low number of reported cases does not allow analysis of seasonal variation. In 2015, cases were reported throughout the year.

Clinical presentation and origin of infection

Ten confirmed *C. diphtheriae cases* were reported as respiratory diphtheria; one of these ten cases – a 16-year-old male – was reported by Sweden as an imported case from Afghanistan. Germany reported one case with unknown importation status in a 44-year-old male. The remaining respiratory cases were reported as indigenous cases from Latvia (n=7) and Spain (n=1). Furthermore, one case from Latvia was reported with double clinical manifestation (respiratory and cutaneous).

Twenty confirmed *C. diphtheriae* cases were reported as cutaneous infection. The majority of cases were males (n=15). These 20 cases were reported by Belgium, Germany, Latvia, the Netherlands, Sweden and the United Kingdom. The probable countries of origin of imported cutaneous cases were Syria (2) Saudi Arabia (1), Afghanistan (1), Pakistan (1), Indonesia (2), Philippines (1), Sri Lanka (2), Eritrea (3), Ethiopia (1), Libya (2) and Somalia (2). The probable country of origin was not reported for two imported cases.

The clinical manifestation was unknown (n=8) or not reported (n=1) for nine *C. diphtheriae* cases. Among cases with unknown clinical manifestations, four were reported as imported from Comoros, Madagascar, Gambia and Germany.

Among the *C. ulcerans* cases, 13 were cutaneous, and three cases were respiratory diphtheria (two with membranes, one without). One case in a nine-year-old boy from the UK was reported as having 'other' clinical manifestations. Clinical manifestation was not known for eight *C. ulcerans* cases.

Laboratory investigation

All *C. diphtheriae* cases reported by Latvia were identified as biovar gravis strains. The case reported by Spain was identified as biovar mitis, as were three confirmed cases reported by the United Kingdom and one confirmed case reported by Belgium. Sweden reported one case as 'other' biotype. For the remainder of the reported cases, information on biotype was not reported.

Outcome

Information on outcome was available for 60 cases. Two deaths were reported due to *C. diphtheriae*, one in a five-year-old boy in Spain and one in a 67-year-old male in Latvia. There was one death reported due to *C. ulcerans* in an 84-year-old woman in Belgium. For five cases the outcome was not reported.

Vaccination status

Vaccination status was reported for 39 confirmed *C. diphtheriae* cases. Eight cases were reported as not vaccinated, eight as vaccinated with an unknown number of doses, and five as vaccinated with known number of doses. Eighteen cases were reported with unknown vaccination status.

Among those reported as vaccinated with a known number of doses, one adult (27 years of age) was reported as fully vaccinated with seven doses. Four other cases were reported as incompletely vaccinated: two cases (31 and 58 years) were reported as vaccinated with four doses, one 11-year-old child was reported as vaccinated with three doses, and one adult (41 years) was reported as vaccinated with a single dose.

By clinical presentation, among respiratory *C. diphtheriae* cases, eight were unvaccinated or had unknown vaccination status, one case was reported as incompletely vaccinated (three doses), and one case was reported as fully vaccinated with seven doses. Among cutaneous *C. diphtheriae* cases, all cases either had an unknown vaccination status or were incompletely vaccinated: one case was reported as vaccinated with one dose, one case was vaccinated with four doses, and one case was vaccinated with an unknown number of doses.

Information on vaccination status was available for 9 out of 25 cases of *C. ulcerans*. Of these, two were vaccinated with five doses, one was vaccinated with two doses, and six were vaccinated with an unknown number of doses.

Discussion

Diphtheria is a transmissible bacterial disease primarily infecting the pharynx, larynx, tonsils and nose. Occasionally, the bacteria affect skin or mucous membranes including conjunctivae and vagina. *Corynebacterium diphtheriae* is transmitted via direct contact with respiratory secretions or with exudate from infected cutaneous lesions. The bacterium produces a toxin that can cause severe complications. Systemic toxicity occurs in 8.1% of all diphtheria patients, which may lead to severe complications such as myocarditis, neuropathies, renal failure and eventually death. Other corynebacteria, *C. ulcerans* and very rarely *C. pseudotuberculosis*, may produce diphtheria toxin, although the strains appear to belong to distinct species and have different routes of transmission [4,8,10].

Diphtheria case detection is strongly influenced by the availability of laboratory resources (techniques and supplies), expertise and surveillance systems. As ECDC surveillance data and EQA reports have shown, the availability of these resources seems to be highly unevenly distributed across Europe, and very few countries perform toxigenicity testing [5]. Literature on analysing the underestimation of reported cases of diphtheria in a European context is scarce and therefore we do not have a clear understanding on how to interpret the zero cases reported by several countries. However, the lack of first-hand clinical experience of diphtheria and insufficient laboratory capacity to confirm toxigenic infections suggest that under-ascertainment is likely.

It is also likely that countries that reported cases of all diphtheria species in consecutive years (Austria, Belgium, France, Germany, Ireland, Latvia, Lithuania, the Netherlands, Norway, Spain, Sweden and the United Kingdom) have acquired stronger expertise and laboratory capacity for detecting and confirming diphtheria cases than other countries that did not detect and report cases. Furthermore, the epidemiology of diphtheria in EU/EEA countries may reflect different travel patterns, e.g. to subtropical regions where high rates of endemic diphtheria have been observed. However, we do not have sufficient information to confirm this hypothesis.

C. ulcerans cases were reported by Belgium, Germany, France, Ireland, Latvia, the Netherlands, Sweden and the United Kingdom, perhaps suggesting a higher level of awareness of this pathogen in these countries [6].

While in 2010 ECDC received only three reports of *C. diphtheriae* infections (one respiratory case and two imported cutaneous cases in two countries), ECDC received information on 40 confirmed cases from eleven countries in 2015. Latvia reported the highest number of respiratory cases and is the only EU Member State with continued indigenous transmission, probably due to decreasing adult vaccine booster coverage. In addition, for the first time Spain reported a single indigenous case.

Though the clinical presentation was not always reported, a notable number of *C. diphtheriae* cases were reported as imported cutaneous cases, mainly among adult male travellers. Since the majority of cases with unknown clinical presentation were reported as imported, it is likely that these cases were also cutaneous infections. It is likely that the increasing number of diphtheria cases is due to imported cutaneous cases that originated in geographical areas where the disease is endemic. Unvaccinated travellers may become infected and develop cutaneous diphtheria while travelling or working in endemic countries [13, 14]. ECDC data show that most cutaneous cases were incompletely vaccinated or had unknown vaccination status. Therefore, the observed increase could be further explained by the increased number of susceptible adult travellers to diphtheria endemic areas. Unvaccinated travellers exposed to overcrowding and poor hygiene are at risk for acquiring diphtheria and of transmitting the infection when they return [10,13,14]. Therefore, the vaccination status of travellers to diphtheria-endemic areas should be checked before travelling. Missing doses should be administered in accordance with the national immunisation schedule [9,10].

The reported vaccination coverage for diphtheria is high in Europe, and widespread outbreaks are unlikely. However, sporadic cases may continue to occur especially in unvaccinated and partially vaccinated individuals. The few cases reported in vaccinated adults and the elderly are most probably due to a waning immunity in this age group. Therefore, a booster dose in the adult population should be considered, in line with national recommendations [8,10,13]. In light of increased worldwide displacement, sporadic cases or clusters could occur and would require a rigorous public health framework for management. Communication with the Member States experiencing diphtheria cases suggests that a significant public health effort is required for the public health management of a disease that is rarely seen in Europe.

Public health implications

The diphtheria toxoid vaccine effectively protects against the effects of the exotoxin produced by *C. diphtheriae*, and immunisation is the only effective method of preventing the toxin-mediated disease.

Maintaining high vaccination coverage in the population is essential to prevent the re-emergence of *C. diphtheriae*, a disease that can cause serious illness and be fatal. This supports the WHO recommendation of achieving vaccination coverage above 90% for children and at least 75% for the adult population to eliminate the disease [15]. In addition, booster vaccine doses should be offered to travellers to endemic areas, healthcare workers, and social workers. Measures should be taken to improve the vaccination coverage in specific risk groups, e.g. the homeless, drug users, sex workers, and individuals with underlying medical conditions such as infective endocarditis, venous insufficiency, recurrent ulcers, HIV, hepatitis B and C infections [13]. Enhanced diphtheria surveillance with high data completeness should be assured.

Due to increased travel activity, dermatologists should be aware of the possibility of cutaneous diphtheria among returning travellers.

If a case of diphtheria is suspected, a prompt medical diagnosis (clinical recognition and laboratory confirmation) should be pursued. Clinical treatment guidelines [15] point out that if there is a strong suspicion for toxigenic *C. diphtheriae* disease, the rapid administration of diphtheria antitoxin is essential to increase the chances of survival and should be initiated as soon as possible, without waiting for the laboratory results. Thus, timely mobilisation of available stocks in individual countries is essential. The lack of availability of diphtheria anti-toxin in many EU countries together with the lack of information on where to get it in case of a diphtheria case, remains a pending issue in the EU.

A case of diphtheria will also prompt a rapid epidemiological investigation and management of close contacts.

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