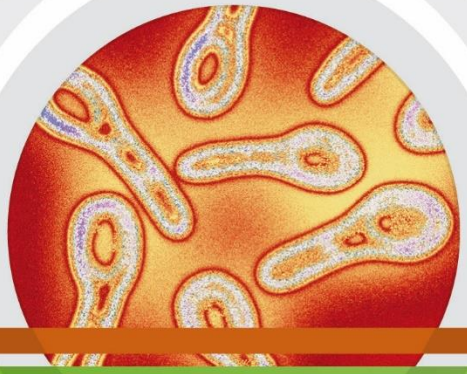


SURVEILLANCE REPORT

Annual Epidemiological Report for 2016

Diphtheria

Key facts

- In 2016, 47 cases of diphtheria due to toxigenic *C. diphtheriae* or *C. ulcerans* were reported to ECDC.
- The highest proportion of cases was among adults and the elderly.
- Among *C. diphtheriae* cases, 65% were reported as imported.
- Latvia was the only country in the EU to report continued indigenous transmission of *C. diphtheriae* cases.
- The majority of cases were not vaccinated or their vaccination status was reported as unknown.
- High vaccination coverage is crucial to prevent diphtheria cases.

Methods

This report is based on data for 2016 retrieved from The European Surveillance System (TESSy) on 7 February 2018. 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 [1].

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

A subset of the data used for this report is available through the interactive *Surveillance atlas of infectious diseases* [3].

In 2016, 29 EU/EEA Member States reported data on diphtheria and related toxigenic pathogens to TESSy. Of these, 12 countries reported cases of *C. diphtheriae or C. ulcerans.* One country did not report data.

The majority of Member States reported data on diphtheria according to the 2008 (n=11) or 2012 (n=12) EU case definition. Six 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 [15].

The majority of countries reported data from a comprehensive and compulsory case-based surveillance system [2,4].

Suggested citation: European Centre for Disease Prevention and Control. Diphtheria. In: ECDC. Annual epidemiological report for 2016. Stockholm: ECDC; 2018.

Stockholm, July 2018

Epidemiology

Forty-seven cases of laboratory-confirmed diphtheria and related toxigenic pathogens were reported in 2016 (Table 1, Figure 1). Twenty-six cases were reported as due to *C. diphtheriae*, and 21 cases were due to *C. ulcerans*. The overall notification rate was below 0.01 cases per 100 000 population.

Diphtheria caused by *C. diphtheriae* was reported by 12 countries (Table 2). Among these countries, Latvia reported the highest number of indigenous cases (n=6). Latvia is also the only EU Member State with continued indigenous transmission.

Diphtheria caused by *C. ulcerans* was reported by seven countries; more than half of all cases were reported in Belgium and Germany (Table 2).

Between 2012 and 2016, 216 cases of diphtheria were reported in the EU/EEA, 134 of which were due to *C. diphtheriae*. The number of cases due to *C. diphtheriae* reported over the last five years increased, especially the number of imported cutaneous cases.

Table 1. Number of diphtheria cases, by country and year, EU/EEA, 2012–2016

Country	2012	2013	2014	2015	2016		
	Reported cases Number	Reported cases Number	Reported cases Number	Reported cases Number	National coverage	Reported cases Number	Confirmed cases
Austria	0	0	2	0	Y	2	2
Belgium	1	1	0	3	Y	6	6
Bulgaria	0	0	0	0	Y	0	0
Croatia	.	0	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	.	.	.	.
Estonia	0	0	0	0	Y	0	0
Finland	1	0	0	1	Y	0	0
France	11	6	6	14	Y	8	8
Germany	9	4	8	14	Y	9	9
Greece	0	0	0	0	Y	0	0
Hungary	0	0	0	0	Y	0	0
Iceland	0	0	0	0	Y	0	0
Ireland	0	0	0	1	Y	1	1
Italy	0	1	1	0	Y	1	1
Latvia	8	14	13	10	Y	6	6
Lithuania	0	0	0	0	Y	0	0
Luxembourg	0	0	0	0	Y	0	0
Malta	0	0	0	0	Y	0	0
Netherlands	1	0	1	5	Y	2	2
Norway	0	0	2	2	Y	1	1
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	1	1	Y	1	1
Sweden	2	2	3	8	Y	4	4
United Kingdom	1	4	1	6	Y	6	6
EU/EEA	**34**	**32**	**38**	**65**	**.**	**47**	**47**

Source: Country reports. Legend: Y = yes, · = no data reported

Table 2. Number of reported cases of diphtheria by pathogen, EU/EEA, 2016

Country	*C. diphtheriae*	*C. ulcerans*
	Number	Number
Austria	1	1
Belgium	1	5
Germany	1	8
France	6	2
Ireland	1	0
Italy	1	0
Latvia	6	0
Netherlands	1	1
Norway	1	0
Spain	1	0
Sweden	2	2
United Kingdom	4	2
EU/EEA	**26**	**21**

Figure 1. Number of reported cases of diphtheria in EU/EEA by country, 2016

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

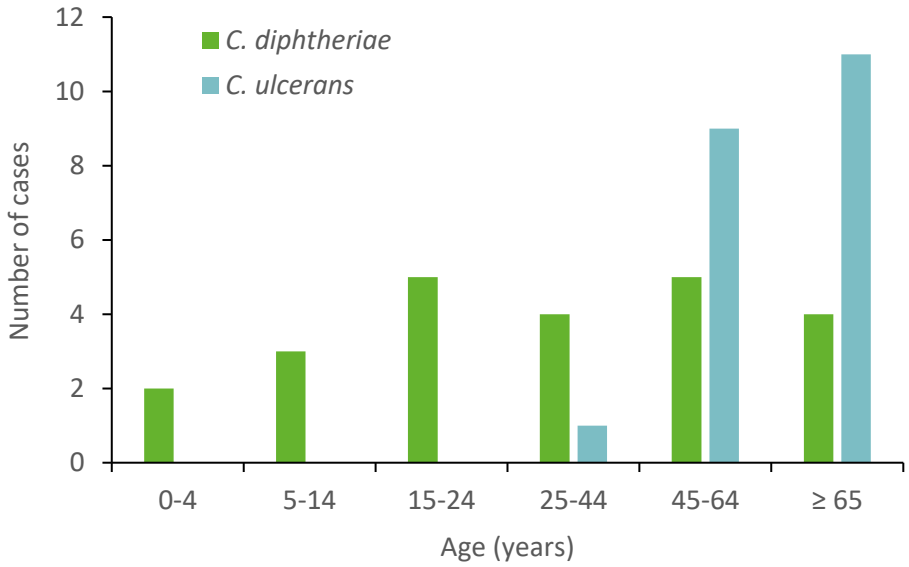
Age and gender distribution

In 2016, cases were reported among all age groups, with the majority of cases in those aged 45–64 years (32%) and those 65 years or older (34%). Twenty-eight of the 47 cases were reported in females.

Of the *C. diphtheriae* cases with known age (n=23), five were aged below 15 years, five cases were reported in teenagers and young adults between 15 and 24 years of age, and 13 cases were reported in adults aged 25 years and over. Fifteen of the 25 cases with known gender were reported in females.

C. ulcerans cases (n= 21) were reported mainly in adults over 45 years of age; 12 of the 21 cases with known gender were reported in females (Table 2).

Table 2. Age distribution of diphtheria cases in EU/EEA by species, 2016



Seasonality

The low number of cases reported does not allow for an analysis of seasonal variation. Similar to previous years, cases in 2016 were reported throughout the year, peaking in the second half.

Clinical presentation and outcome

Twenty cases due to *C. diphtheriae* were reported with known clinical presentation. Out of these 20 cases, seven confirmed cases were reported as classical respiratory diphtheria, including five indigenous cases from Latvia, one indigenous case from Belgium, and one case from Spain that was probably imported from Senegal. Twelve confirmed *C. diphtheriae* cases were reported with cutaneous infections. One case from Norway was reported with some 'other' clinical presentation.

Six cases imported from diphtheria-endemic countries were reported with unknown clinical presentation from France; these were most probably cutaneous infections.

Overall, 16 out of 25 cases due to *C. diphtheriae* were reported as imported, and the probable country of origin was known for 12 cases. They were imported from Ghana (1), Indonesia (1), Comoros (1), Madagascar (1), Philippines (1), Senegal (3), Sri Lanka (2) and Thailand (2). Eight confirmed cases due to *C. diphtheriae* were reported as indigenous cases and seven of these were due to biotype Var Gravis.

Of the reported *C. ulcerans* cases, 15 had cutaneous infection and two cases additionally had respiratory manifestations (Belgium and the United Kingdom). For four cases, the clinical presentation was reported as 'other' (Austria and Belgium) or 'unknown' (France).

Information on outcome was available for 39 cases. One death due to *C. diphtheriae* – in a three-year-old girl in Belgium – was reported.

Vaccination status

For seven cases, the number of vaccination doses was known: six cases were due to *C. diphtheriae* and one case was due to *C. ulcerans.* Overall, fourteen cases were reported as vaccinated with an unknown number of doses. Vaccination status was uncertain for 21 cases: of these, 19 had an unknown vaccination status, and vaccination status was not reported for two cases. Five cases were reported as not vaccinated.

One case of *C. ulcerans* was reported as vaccinated and had received four doses.

Discussion

Corynebacterium diphtheriae is transmitted via droplets during close contact [7]. 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 myocarditis, neuropathies, renal failure and eventually death. Other corynebacteria, *C. ulcerans*, and very rarely *C. pseudotuberculosis*, may produce diphtheria toxin, although the toxigenic strains appear to belong to distinct species and have different routes of transmission [16,17].

This report includes cases due to *C. diphtheriae* and *C. ulcerans*. While most Member States had surveillance in place for diphtheria (n=30), only few countries reported cases to ECDC during 2012–2016. It is likely that countries that have reported cases of all diphtheria species in consecutive years have a higher awareness of these pathogens [8].

Diphtheria case detection is strongly influenced by the availability of laboratory resources, expertise and surveillance systems [10]. This varies across Europe, and very few countries perform toxigenicity testing [9,10].

As a consequence, under-ascertainment and underreporting are highly likely.

Latvia is the only country in Europe that has been reporting cases with continued indigenous transmission since 2012. This could be explained as an epidemic tail following a regional epidemic in the 1990s.

The majority of diphtheria cases with known clinical presentation were reported as cutaneous and imported from endemic geographical areas. An increasing number of susceptible travellers likely contributed to these cases [10]. European travellers may become infected and develop cutaneous diphtheria while travelling or working in endemic countries [11]. ECDC data show that most cutaneous cases were unvaccinated or had an uncertain vaccination status. Unvaccinated travellers exposed to overcrowding and poor hygienic conditions are at risk for acquiring diphtheria and, if infected, could transmit the infection upon their return [8,11,12]. Therefore, the vaccination status of travellers to diphtheria-endemic areas should be checked before travelling; missing doses should be delivered in accordance with national immunisation schedules [12,13].

Reported diphtheria vaccination coverage is high in Europe, and widespread outbreaks in Europe are therefore very unlikely. As the reported data show, sporadic cases may continue to occur in unvaccinated and partially vaccinated individuals, especially in travellers to and from endemic countries. The few cases reported in vaccinated adults and the elderly are most probably due to waning immunity [8,12,14].

Communication with the Member States experiencing diphtheria cases suggests that a significant effort is required for the clinical and public health management of cases of this disease rarely seen in Europe [8,10,12]. Member States should consider closely monitoring their diphtheria antitoxin (DAT) stock and take appropriate and timely actions to replace it. This is particularly important given the increasing number of outbreaks due to *C. diphtheriae* in diphtheria-endemic geographical areas (Indonesia, Bangladesh, Yemen and Venezuela) among people facing humanitarian crises in combination with disrupted immunisation programmes.

Public health conclusions

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. Achieving and sustaining a high vaccination coverage in the population is critical for preventing toxigenic diphtheria from causing serious or fatal illness. In addition, special attention should be given to travellers, healthcare workers, and social workers [6].

If cases occur, prompt clinical recognition, laboratory confirmation and treatment are essential, including rapid investigation and management of close contacts. If there is a strong suspicion of toxigenic *C. diphtheria* disease, regardless of clinical manifestation, early administration of DAT is essential for survival. Thus, timely mobilisation of available stock should be considered. This might sometimes require support from other countries if domestic DAT stocks are depleted.

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