



Sudden increase of diphtheria with *Corynebacterium diphtheriae* among migrants arriving in Germany, 2022: statistical outlier – or detection of an outbreak?

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Background

In early August 2022, Germany's national public health institute for disease prevention and control, the Robert Koch Institute (RKI), noticed an upsurge in diphtheria cases: 26 cases were notified in that year, 8 of which were migrants, mainly from Afghanistan and Syria. However, the annual average is 22 cases, including 3 migrants.

Here, we describe the outbreak *detection*, and evaluate how routine surveillance contributed. The outbreak *description* with quantitative epidemiological data is published elsewhere [1].

Results

Comparison of cases from 2022 with cases from previous years

Table 1: Expected vs. observed diphtheria cases in Germany in 2022

Population	2019–2021 Annual average	January–July 2022			July 2022		
		Expected	Observed	Difference	Expected	Observed	Difference
Local residents	13.8	8.1	17	+111%	1.2	1	–13%
Arriving migrants	2.8	1.6	8	+390%	0.2	7	+3329%

Check that there were no alternative explanations

- In July 2022, fewer Afghans and fewer Syrians (–19% each) applied for asylum in Germany for the first time, compared to July 2021.
 - More cases were observed than expected, based on the number of new asylum seekers in Germany in 2022.
- Afghanistan reported 61 cases in 2021 to the WHO, after several years with zero or single-digit case counts, or no reporting. No details are known. Syria reported zero cases again in 2021.
 - There was no indication that the incidence of diphtheria in the main countries of origin might have changed.
- Several diphtheria cases were detected after mpox had been initially suspected but ruled out.
 - Detection bias due to more frequent diagnostics of skin lesions in spring 2022 might have helped to detect early outbreak cases.

Discussion

Upsurge, statistical outlier or outbreak?

Conclusion within six weeks of the event's beginning: Unprecedented number of diphtheria cases in Germany represents an outbreak which is, moreover, part of an international outbreak in Europe.

Reasons for relatively quick outbreak detection

- Reports from abroad and exchange with ECDC boosted vigilance.
- RKI conducted timely case controls for each diphtheria case.
- RKI probed that there were no other reasons but an outbreak.
- RKI, NCLD and ECDC voluntarily exchanged data.

References

- [1] Badenschier F et al. Outbreak of imported diphtheria with *Corynebacterium diphtheriae* among migrants arriving in Germany, 2022. Euro Surveill. 2022;27(46):pii=2200849.
- [2] Robert Koch Institute. Häufung von Fällen mit Hautdiphtherie in Deutschland und Europa. [Upsurge of cases of cutaneous diphtheria in Germany and Europe]. Epidemiol Bull. 2022; (36):27-8.

Methods

RKI initiated investigations to confirm an outbreak. First tasks were:

- Analyse cases reported in 2022 and compare with previous years, based on the annual average of the previous three calendar years;
- Assess possible alternative explanations;
- Compile epidemiological data from routine surveillance and microbiological data from Germany's National Consiliary Laboratory for Diphtheria (NCLD).

Simultaneously, RKI exchanged additional information with federal and local health authorities as well as with ECDC and WHO/Europe.

Figure 1: Diphtheria cases in Germany by notification week, pathogen, and acquisition, 01/01/2019–19/03/2023

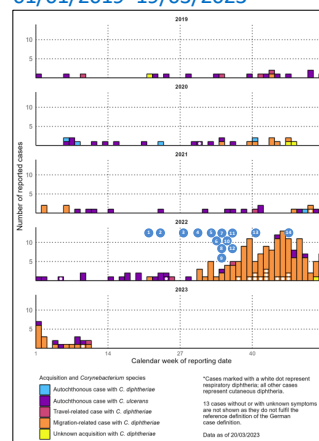


Table 2: Chronology of key events in the outbreak detection

- 24/05/2022: NCLD reports to RKI laboratory confirmation of toxigenic *Corynebacterium (C.) diphtheriae* in a male migrant, the first such case in 2022.
- 03/06/2022: Austria informs about a migrant originally from Afghanistan who had died of respiratory diphtheria, using the Early Warning and Response System of the European Union (ECDC EWRS).
- RKI assesses that currently there seems no risk for spread to Germany and that there is no epidemiological change in Germany. Therefore, RKI decides to not inform expert audience.
- 07/07/2022 & 04/08/2022: Austria informs on ECDC EWRS about further cases of cutaneous diphtheria among migrants.
- RKI increases awareness and double-checks recently notified and reported cases.
- 09/08/2022: During the weekly epidemiological teleconference with national and federal health authorities ("EpiTag"), RKI informs about several cases of cutaneous and respiratory diphtheria among migrants arriving in Austria, Italy, and Switzerland, reminds of notification obligation and diagnostics free of costs at NCLD, provides contact details for questions.
- 17/08/2022: Single case controls and assessments at RKI reveal: Within 7.5 months, diphtheria cases reported reaches the annual number of previous years – and more cases among migrants than the all-time high for one year (Table 1).
- 22/08/2022: Austria creates an item at EpiPulse, the European surveillance portal for infectious diseases.
- 23/08/2022: During the "EpiTag", Baden-Württemberg informs about five migrants with cutaneous diphtheria due to *C. diphtheriae*.
- RKI advises on case and contact person management and investigations.
- 25/08/2022: First official telephone conference of RKI and NCLD to discuss the situation and next steps.
- 29/08/2022 & 01/09/2022: RKI informs on EpiPulse about current situation: 33 cases of diphtheria reported for 2022, incl. 12 among migrants (11 from Afghanistan, 1 from Syria; all male; all toxigenic *C. diphtheriae*); whole genome sequencing at NCLD pending.
- 09/09/2022: RKI publishes detected signal in Epidemiological Bulletin [2].
- End of 08/2022 & early 09/2022: NCLD contacts colleagues in Austria and Switzerland to discuss diagnostic methods and to offer technical support.
- 06/10/2022: ECDC publishes Rapid Risk Assessment to which RKI and NCLD have contributed. In 7 European countries (AT, BE, CH, DE, FR, NO, UK) 50 cases.
- 17/11/2022: Outbreak description as Rapid Communication in EuroSurveillance [1].

Compilation of epidemiological and microbiological data

- Whole genome sequencing and phylogenetic analysis at NCLD and migration route analysis at RKI suggested: Migrants had acquired toxigenic *Corynebacterium diphtheriae* neither in their home country nor in Germany, but in between – along the Balkan route.

Where to go from here

- Outbreak detection in general:** Is an iterative process that requires a thoroughly conducted outbreak confirmation.
- Ongoing outbreak:** 169 outbreak-related diphtheria cases among migrants in Germany by 19/03/2023. Epicentres not identified.
- Of utmost public health relevance:** Active case finding and outbreak detection in supposedly unaffected countries along the Balkan route and in Europe.
- Needed:** Increased awareness among clinicians, microbiologists, and institutions working with migrants; intensified sample collection from wounds with subsequent laboratory diagnostics.