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ORIGINAL ARTICLE

Corynebacterium diphtheriae Outbreak in Migrant Populations in Europe

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ABSTRACT

BACKGROUND

A surge of cases of *Corynebacterium diphtheriae* infection was observed in reception centers for migrants in Europe beginning in the summer of 2022. Most of the cases were cutaneous, although some respiratory cases as well as one death were reported. A pan-European consortium was created to assess the clinical, epidemiologic, and microbiologic features of this outbreak.

METHODS

We assessed cases of toxigenic *C. diphtheriae* infection that were reported in 10 European countries from January through November 2022. Data regarding countries of origin and transit routes were obtained from interviews with the patients. Whole-genome sequencing and antimicrobial-susceptibility testing were performed on bacterial isolates that were obtained from the patients. The phylogenetic relationships of the isolates and their antimicrobial-resistance genes were evaluated.

RESULTS

A total of 363 toxigenic *C. diphtheriae* isolates were identified among 362 patients during the study period. Clinical data were available for 346 patients (95.6%): 268 (77.5%) had cutaneous diphtheria, 53 (15.3%) had respiratory diphtheria (11 [3.2%] had a pseudomembrane), and 9 (2.6%) had both respiratory and cutaneous symptoms. Four major genetic clusters were identified, which indicated the multiclonal nature of the outbreak. The *ermX* gene (which codes for erythromycin resistance) and the *pbp2m* and *blaOXA-2* genes (which code for beta-lactam resistance) were detected in a subgroup of isolates. Isolates that carried *ermX* were resistant to erythromycin, and isolates that carried *pbp2m* were resistant to penicillin but were susceptible to amoxicillin. On the basis of the genomic variation within the four genetic clusters, their most recent common ancestors were estimated to have existed between 2017 and 2020.

CONCLUSIONS

The distribution of each genetic cluster of *C. diphtheriae* isolates across multiple countries in Europe showed repeated cross-border spread. The large number of *C. diphtheriae* infections among migrants is a cause for concern, particularly given that antimicrobial-resistance phenotypes threaten the efficacy of first-line treatments. (Funded by the Bavarian State Ministry of Health, Care, and Prevention and others.)

Diphtheria is a potentially life-threatening and highly transmissible disease that typically causes respiratory illness but can also cause cutaneous lesions.[1] The main causative agents are toxigenic strains of the bacterium *Corynebacterium diphtheriae*, which express diphtheria toxin, a potent exotoxin that inhibits protein synthesis in eukaryotic cells.[2,3] Respiratory diphtheria is historically the most frequently detected form; patients with respiratory diphtheria present with symptoms such as sore throat with pseudomembranes and low-grade fever. Cutaneous diphtheria, characterized by skin ulcers sometimes surrounded by a greyish membrane, typically does not lead to severe complications but can play an important role in transmission. The production of diphtheria toxin can result in complications such as myocarditis, polyneuropathy, and acute kidney disease. Unvaccinated children younger than 5 years of age are particularly susceptible to diphtheria. The estimated case fatality rate among unvaccinated persons with untreated respiratory diphtheria is 29%.[4]

Between 2016 and 2021, an annual mean of 27 cases of *C. diphtheriae* infection in the European Union (EU) and the European Economic Area (EEA) were reported to the European Center for Disease Prevention and Control (ECDC). However, diphtheria remains endemic or can become epidemic in regions of the world where vaccine coverage is suboptimal.[5,6] Diagnosed cases in the EU and EEA are often observed among travelers and migrants from such regions.[7]

An unusual surge in the number of toxigenic *C. diphtheriae* infections was noted in several European countries in the summer of 2022.[8-11] The ECDC published a rapid risk-assessment document in October 2022.[12] We investigated the temporal and geographic dynamics and potential sources of the outbreak, as well as the clinical, phenotypic, and genomic characteristics of the cases and the associated *C. diphtheriae* isolates that carried the *tox* gene.

METHODS

INCLUSION CRITERIA AND CASE DEFINITION

This study assessed *C. diphtheriae* isolates that carried the *tox* gene, in accordance with the World Health Organization (WHO) recommendation for the management of diphtheria outbreaks.[13,14] Polymerase-chain-reaction testing was used to determine whether isolates carried the *tox* gene, and the findings were confirmed by means of whole-genome sequencing. Cases of diphtheria were retrospectively included on the basis of isolates obtained and cultured from January 1 to November 30, 2022. Elek's test (an immunodiffusion test) was performed on a majority of the isolates to confirm toxin production. Additional details are provided in the Supplementary Appendix, available with the full text of this article at NEJM.org.

STUDY POPULATION AND EPIDEMIOLOGIC AND CLINICAL DATA

Information was collected from interviews that had been conducted with the patients during the outbreak investigation. Data included country of origin, transit countries, and date of arrival in the reporting country. Clinical data (administration of specific antibiotic agents and diphtheria antitoxin, coinfections, clinical presentation, and inpatient admission) were obtained from patient records.

PHYLOGENETICS AND GENOMICS

Whole-genome sequencing was performed on all bacterial isolates. Multilocus sequence typing was performed, and the association of clinical symptoms with specific sequence types was assessed. The nucleotide sequences of 1305 shared core genes were used to generate a phylogenetic tree. Sublineages were defined as groups of core-genome multilocus sequencing typing (cgMLST) profiles with a threshold of 500 allelic mismatches. Genetic clusters were defined as groups of cgMLST profiles with a threshold of 25 allelic mismatches. To place the study isolates into a wider context, sequences belonging to sublineage (SL) 377, SL384, and SL574 were retrieved from public sequence databases and compared on the basis of cgMLST. We also performed genomewide single-nucleotide polymorphism (SNP) analysis within the four main genetic clusters, including previously published genomes from the 2022 outbreak at a refugee center in Switzerland[9] and genome data from isolates obtained in 2023. The population size history of these clusters was analyzed with the use of skygrowth.[15]

ANTIMICROBIAL RESISTANCE

Antimicrobial-susceptibility testing for penicillin and erythromycin was performed. Susceptibility testing for other antibiotics was conducted in subsets of isolates according to country-specific guidelines. Interpretation was based on European Committee on Antimicrobial Susceptibility Testing, version 13.0, clinical breakpoints.[16] Antimicrobial-resistance genes and integrons were analyzed on the basis of whole-genome sequences.

ETHICS

Owing to the public health emergency associated with the outbreak in most of the countries, no ethical approval was required. Nationwide ethical approval is available in Switzerland for outbreak investigation through the Swiss Pathogen Surveillance Platform.

RESULTS

EPIDEMIOLOGIC CHARACTERISTICS AND CHARACTERISTICS OF THE PATIENTS

From January 1 to July 31, 2022, a total of 20 cases of diphtheria were reported across six European countries. After July, there was a steep increase in case numbers, with 38 cases reported in August, 74 in September, and 115 in October, before the number plateaued at 116 cases across 10 countries in November 2022 (Fig. 1A). The number of cases of toxigenic *C. diphtheriae* infection reported in 2022 was markedly higher than in previous years (Fig. S1 in the Supplementary Appendix).

We identified 363 isolates that carried the *tox* gene among 362 patients in 10 countries: Germany (118 patients), Austria (66 patients), the United Kingdom (59 patients), Switzerland (52 patients), France (30 patients), Belgium (21 patients), Norway (8 patients), the Netherlands (5 patients), Italy (3 patients), and Spain (1 patient) (Fig. 1B). The median age of the patients was 18 years at the time of data collection; 176 patients (48.6%) were 16 to 20 years of age, and 355 (98.1%) were male. Most of the patients (348 [96.1%]) had a recent migration history, close contact with migrant populations, or a recent date of entry into the reporting country; 174 patients (48.1%) were reported to be residents in a migrant center.

Multilocus sequence typing identified 16 sequence types; 330 of 363 isolates (90.9%) belonged to one of three unrelated sequence types: sequence type (ST) 377, ST384, and ST574. These genotypes presented with similar frequencies across countries of origin, reporting countries, and over time (Fig. 1B and 1C).

CLINICAL PRESENTATIONS

Clinical data were available for 346 patients (95.6%); 268 patients (77.5%) had cutaneous diphtheria, 53 (15.3%) had respiratory diphtheria (11 [3.2%] had a pseudomembrane), and 9 (2.6%) had both respiratory and cutaneous symptoms (Fig. 2A and 2B and Figs. S7 and S8). No association of clinical symptoms with specific sequence types was observed (Fig. 1D). One patient was infected with two isolates: a cutaneous infection with ST377 and a respiratory infection with ST384. One patient with a pseudomembrane died. We identified three patients with genital involvement. Owing to the incomplete medical documentation among the patients, it was often difficult to ascertain vaccination status reliably. Four patients were reported to be vaccinated, and 10 were reported to be nonvaccinated; 290 patients were reported to have an unknown vaccination status.

Data regarding receipt of specific antibiotics were available for 75 patients. The most common agents were azithromycin (24 patients), amoxicillin (23 patients), clarithromycin (21 patients), clindamycin (11 patients), penicillin (8 patients), and doxycycline (3 patients). Specifically, patients with cutaneous diphtheria received amoxicillin (17 patients), clarithromycin (11 patients), clindamycin (8 patients), and azithromycin (7 patients). Patients with respiratory diphtheria received clarithromycin (9 patients), azithromycin (8 patients), penicillin (7 patients), and amoxicillin (5 patients). Some of the most frequently reported coinfections were with *Streptococcus pyogenes* (30 patients), methicillin-resistant *Staphylococcus aureus* (15 patients), and arcanobacteria (4 patients). Five patients also presented with scabies infestation. Coinfections were predominantly reported in cutaneous cases. Two coinfections were reported in respiratory cases: one with *Streptococcus dysgalactiae* and one with *S. pyogenes*.

Of the 17 patients who were admitted to a hospital, 5 had cutaneous diphtheria and 12 had respiratory diphtheria (7 of whom had a pseudomembrane). All 12 patients with respiratory diphtheria were treated with diphtheria antitoxin along with antibiotics. Diphtheria antitoxin doses ranged from 5000 to 100,000 IU; 8 patients received doses higher than 60,000 IU. The 12 patients received treatment within a mean (±SD) of 2.8±1.5 days after symptom onset, with most (9 patients) receiving treatment within 3 days. Of 54 patients who were not admitted to a hospital and were treated on site, 40 had cutaneous diphtheria and 14 had respiratory diphtheria (7 of whom had a pseudomembrane).

Of the 52 patients for whom information was available on specific clinical signs and symptoms, 4 patients with cutaneous diphtheria had symptoms that were atypical, and 40 had symptoms that were typical. One case of respiratory diphtheria was reported to be atypical, and 6 were reported to be typical. The most common symptoms reported among the patients with respiratory manifestations were tonsillitis (8 patients),

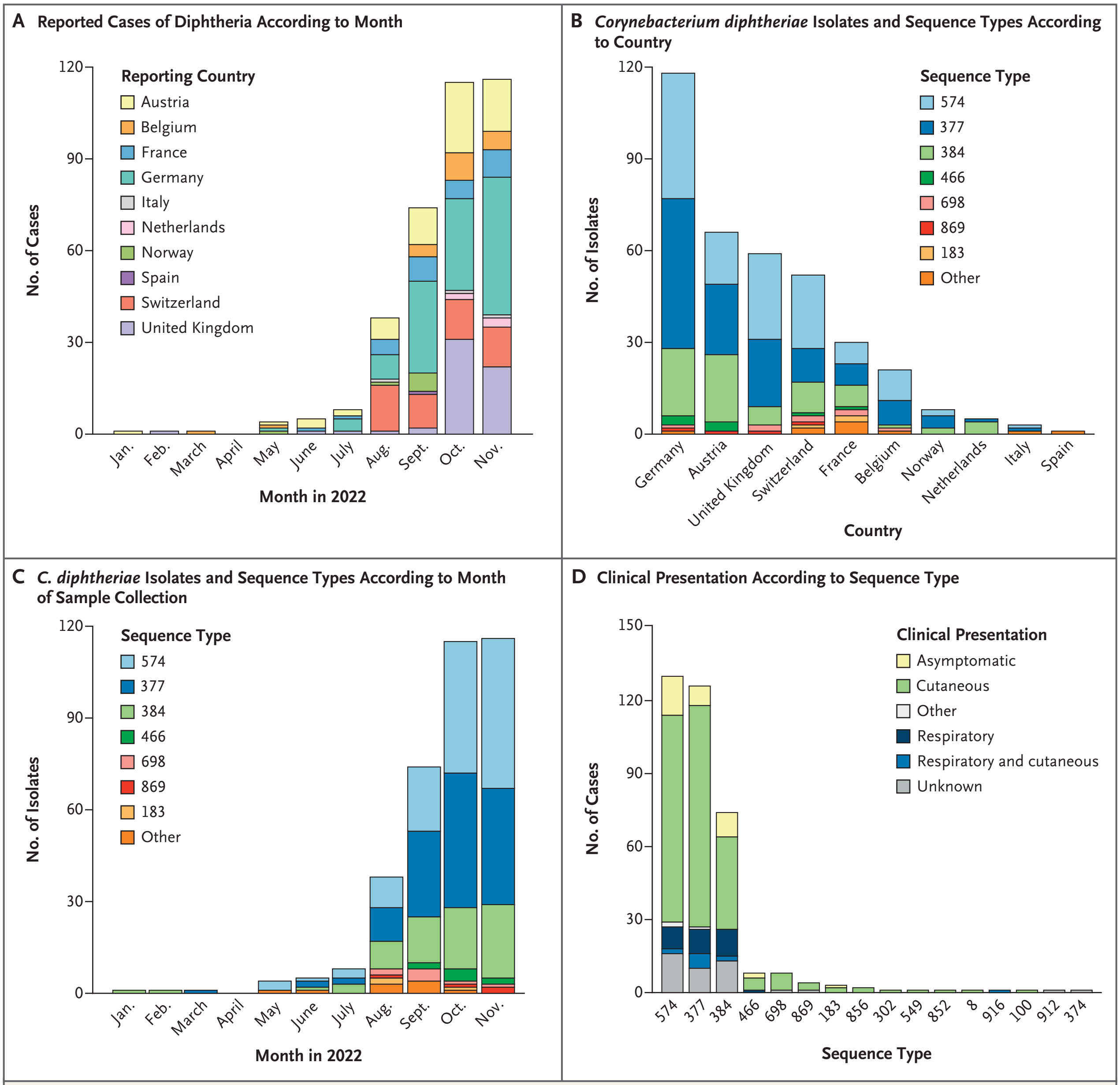


Figure 1. Diphtheria Cases, Isolates and Sequence Types, and Clinical Presentation.

The study included *Corynebacterium diphtheriae* isolates that were obtained from January through November 2022; 362 cases of diphtheria and 363 isolates were identified. Panel A shows the numbers of cases in each reporting country according to month. Panel B shows the number of isolates and their sequence types according to the reporting country. Panel C shows the number of isolates and sequence type according to month. Panel D shows the clinical presentation of the 325 cases for which clinical presentation was reported, according to sequence type.

sore throat (6 patients), and lymphadenopathy (4 patients) (Fig. 2C). The patient with atypical respiratory diphtheria presented with a peritonsillar abscess (Fig. 2D). Aside from one death, no other severe clinical complications were reported after antibiotic treatment. The patient who died presented with purulent secretions and thick membranes that covered the entire pharyngeal wall. Diphtheria antitoxin was administered during a late stage of the disease, and this delay probably contributed to a severe course, resulting in multiorgan failure and death.[17]

MIGRATION ROUTES AND TRAVEL HISTORY

Information regarding country of origin was available for 266 patients (73.5%). A total of 19 countries of origin were reported; 222 patients (83.5%) were reported to have originated from Afghanistan or Syria. In addition, 28 transit countries were reported (Fig. 3 and Fig. S2). Although several patients migrated from Africa or through eastern Europe, most followed a migration route through the western Balkans.

PHENOTYPIC AND GENOMIC FEATURES OF THE *C. DIPHTHERIAE* ISOLATES

Among the 363 isolates, all of which carried the *tox* gene, Elek's test was performed on 306 (84.3%); all of the isolates were confirmed to produce the diphtheria toxin. Therefore, no nontoxigenic isolates bearing the *tox* gene were identified over the course of the study.[18]

Antimicrobial-susceptibility testing for penicillin was performed on 287 isolates, and susceptibility testing for erythromycin was performed on 282 isolates. A total of 286 of 287 isolates (99.7%)

Figure 2. Clinical Presentations of Cutaneous and Respiratory Diphtheria.

Panel A shows a patient with cutaneous diphtheria with inflammatory plaques with pustules, erosions, and crusts with superinfection with *Streptococcus pyogenes* (photograph obtained at the Department of Dermatology, Klinikum Klagenfurt am Wörthersee). Panel B shows a patient with cutaneous diphtheria with multiple pustules on the feet and hands; the patient had superinfection with *S. pyogenes* and methicillin-resistant *Staphylococcus aureus* (photograph obtained at the Department of Dermatology, Klinikum Klagenfurt am Wörthersee). Panel C shows a patient with respiratory diphtheria with the characteristic bull's neck appearance due to massive lymphadenopathy and swelling (photograph obtained at the Department of Infectious Diseases, Klinik Favoriten). Panel D shows a patient with respiratory diphtheria with a peritonsillar abscess and pseudomembranes on the right tonsil (photograph obtained at the Department of Infectious Diseases, Klinik Favoriten). Ethical approval was obtained for the release of images obtained in Switzerland.

were susceptible to penicillin with increased exposure, and 264 of 282 (93.6%) isolates were susceptible to erythromycin. One isolate (accession ID: f82239e6; ST183) was resistant to penicillin and meropenem but not to erythromycin. All 114 isolates that underwent phenotypic testing against amoxicillin were susceptible. A total of 18 erythromycin-resistant isolates were in most cases also resistant to ciprofloxacin, tetracycline, doxycycline, and trimethoprim–sulfamethoxazole. Concurrent phenotypic resistance to both beta-lactams and macrolides was not observed for any isolate. The tested isolates showed the highest resistance to trimethoprim–sulfamethoxazole (142 of 175 isolates [81.1%]), tetracycline (59 of 180 [32.8%]), and ciprofloxacin (57 of 255 [22.4%]) (Table S3).

The phylogenetic analysis is shown in Figure 4. A total of 12 sublineages were discerned, 3 of which were most frequent: SL377 (corresponding to ST377), SL384 (corresponding to ST384), and SL574 (corresponding to ST574 and ST698). Within these sublineages, four major genetic clusters containing more than 15 genomes were identified: genetic cluster (GC) 1 (131 isolates) within SL574, GC3 (74 isolates) within SL384, and GC2 (110 isolates) and GC9 (17 isolates) within SL377. GC2 and GC9 were distinct at 65 cgMLST loci. The genetic clusters of the study isolates were newly defined and distinct from previously sequenced isolates. Each of the dominant sequence types, sublineages, and genetic clusters were associated with multiple countries of origin and reporting countries (Figs. 4 and 5). The public sequences most closely related to SL384 were from the Yemen outbreak[20]; however, these sequences differed from the study isolates by at least 37 cgMLST alleles and therefore did not belong to the same genetic cluster (Fig. 5). Similarly, the most closely related isolates to the SL377 isolates from the European outbreak were from India, with more than 50 cgMLST allele differences. No public isolates were found to belong to SL574. Of note, the predominant genetic clusters (GC1, GC2, and GC3) comprised distinct genotypes (cgMLST profiles), many of which were found in more than one reporting country (Fig. 4).

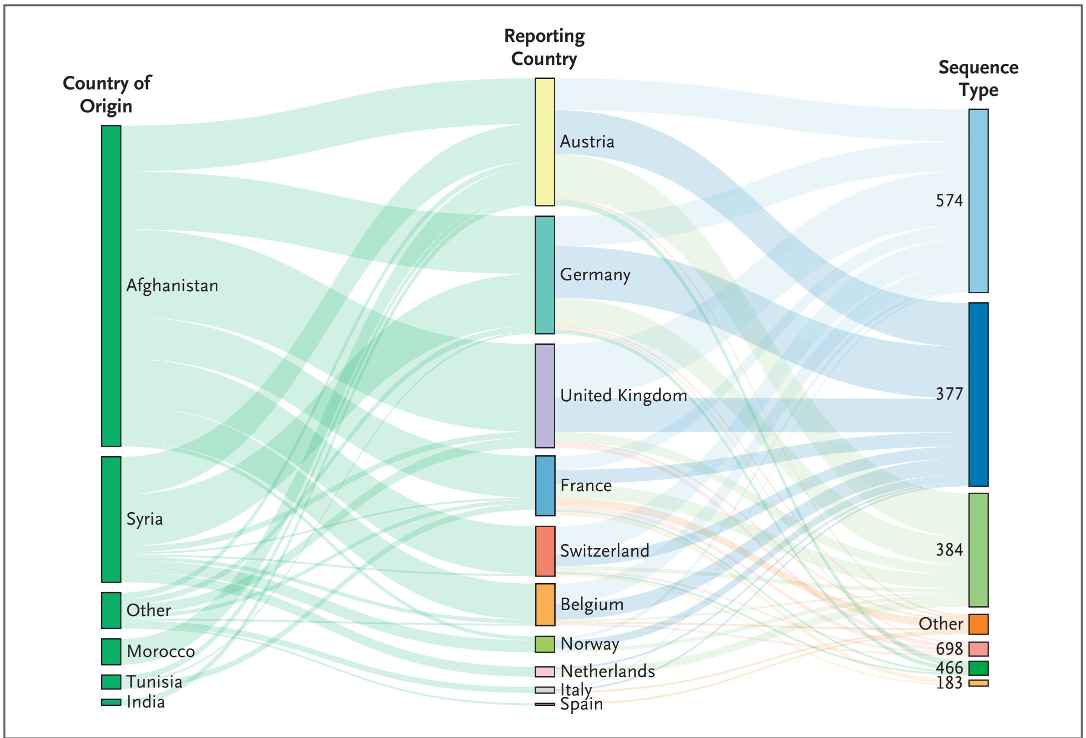


Figure 3. Association of Country of Origin, Reporting Country, and Sequence Type.

An alluvial diagram shows the frequency of migration from various countries of origin (left column) to the reporting countries (middle column) and which sequence types were identified (right column).

The genome assemblies carried several predicted resistance genes or mutations. In particular, *tet(33)* and *dfrA1*, as well as the *gyrA* mutations S89F and D93Y, were observed, and their presence was highly concordant with phenotypic data for tetracycline, trimethoprim, and ciprofloxacin, respectively (Fig. S3). In addition, *sul1* was found specifically in isolates belonging to SL698 and SL377, and these were resistant to sulfonamides. A subgroup of isolates (GC9, within SL377) carried an integron containing the *ermX* gene (which encodes for erythromycin resistance) and the *blaOXA-2* gene, as previously described (Fig. 4).[9] The distal position of *blaOXA-2* in the integron may imply that it is not expressed, because the tested isolates remained susceptible to penicillin and amoxicillin, as previously reported.[9] The *pbp2m* gene, which reduces susceptibility to penicillin,[21] and the erythromycin-resistance gene *ermX* were also found in a handful of diverse

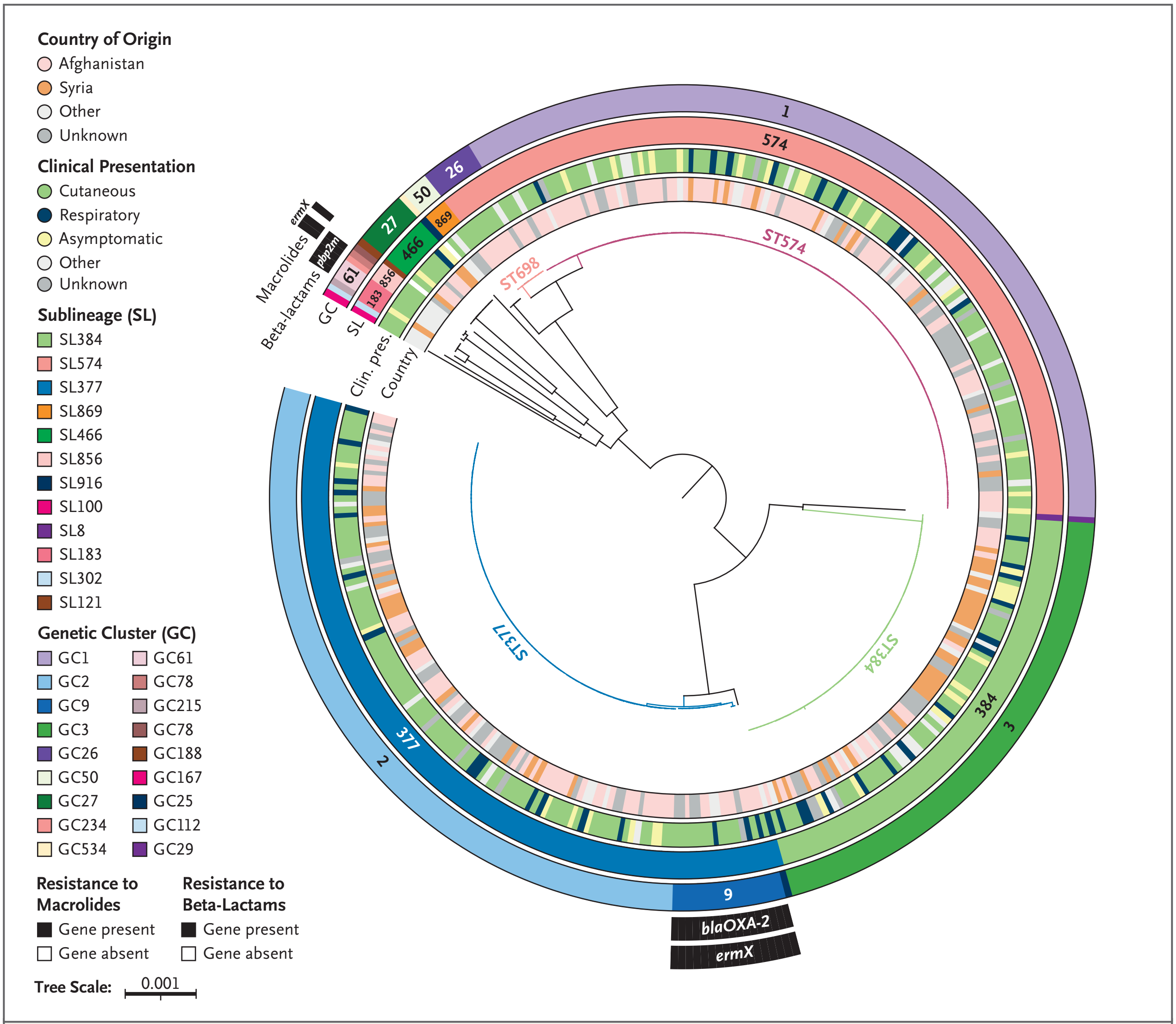


Figure 4. **Phylogenetic Diversity of the 363 *C. diphtheriae* Isolates.**

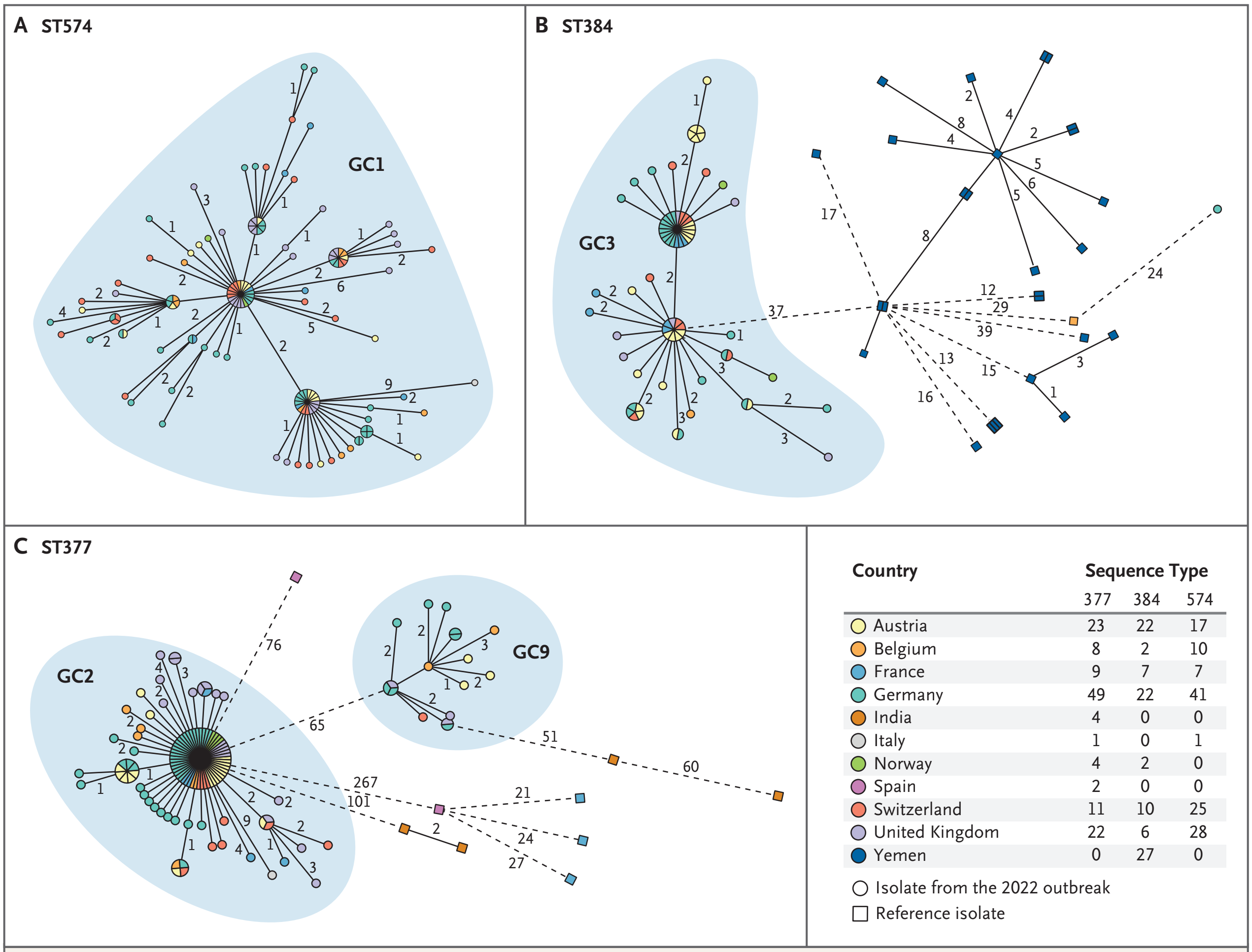
The phylogeny was obtained with the use of core gene sequences and is displayed radially. The branches corresponding to the four major sequence types (STs) are colored. The surrounding metadata circles show (from inside to outside) country of origin, clinical manifestation, sublineage (SL), genetic cluster (GC), and the presence of the following genes: *blaOXA-2* (which has no demonstrated phenotypic effect), *pbp2m* (which potentially confers resistance to penicillin and other beta-lactams), and *ermX* (which confers resistance to macrolides). The scale indicates the proportion of variable nucleotide sites.

sporadic genomes (Fig. 4). A second integron was also observed, which carried genes for resistance to trimethoprim and aminoglycosides. Most of the SL377 isolates carried this second integron, which suggests that it was acquired before the split that defines the smaller SL377 cluster GC9. This second integron flanks a genomic region where additional genes for chloramphenicol and aminoglycoside resistance are found and represents an important antimicrobial-resistance genomic region acquired horizontally in SL377.

On the basis of genomewide SNP analysis, smaller phylogenetic subdivisions of GC1, GC2, GC3, and GC9 were restricted within unique reporting countries, which indicates local chains of transmission (Figs. S4, S5, and S6). The maximal root-to-tip distance within each genetic cluster was 17 SNPs, a finding that underlines the very recent diversification of the four genetic clusters from their respective ancestors.

ANALYSIS OF DATA FROM 2023

In 2023, the countries included in the study reported 178 cases of *C. diphtheriae* infection with isolates that carried the *tox* gene: 112 in Germany, 17 in the Netherlands, 16 in France, 13 in the United Kingdom, 9 in Belgium, 8 in Switzerland, and 3 in Austria, with three deaths reported (all in migrants). Although fewer cases were reported than in 2022, the total number of cases



Country	Sequence Type		
	377	384	574
● Austria	23	22	17
● Belgium	8	2	10
● France	9	7	7
● Germany	49	22	41
● India	4	0	0
● Italy	1	0	1
● Norway	4	2	0
● Spain	2	0	0
● Switzerland	11	10	25
● United Kingdom	22	6	28
● Yemen	0	27	0

○ Isolate from the 2022 outbreak
☐ Reference isolate

Figure 5. The Genetic Diversity of the Four Main Genetic Clusters.

Shown are minimum spanning trees of *C. diphtheriae* isolates of ST574 (panel A), ST384 (panel B), and ST377 (panel C), on the basis of core-genome multilocus sequence typing.[19] Each tree includes the isolates of the outbreak described in this article (circles) as well as previous publicly available genome sequences retrieved from BIGSdb-Pasteur (squares). The blue shaded areas highlight the isolates included in this study that belong to four main genetic clusters.

reported in 2023 was substantially higher than that in previous years. Genomic data showed circulation in 2023 of each of the four main genetic clusters identified in 2022, which indicates sustained transmission (Fig. S9).

Recombination-adjusted SNP analysis estimated the ancestors of each genetic cluster to have existed between 2016 and 2019, and the population size history of these clusters showed exponential growth only since 2022, a finding consistent with the clusters not having been detected previously. Of note, among the 178 cases reported in 2023, isolates from 2 cases belonged to ST377 and isolates from 5 cases belonged to ST574; these cases were reported among unhoused persons and intravenous drug users who were not staying in a migrant center.

DISCUSSION

This outbreak represents the largest rise in diphtheria cases seen in western Europe in the past 70 years. It occurred primarily among displaced populations entering the region. No secondary infections were documented among the resident populations in 2022, and only eight such infections were detected in 2023.

Available data on transit routes showed that most of the patients had migrated through the western Balkan region. Travel restrictions related to the coronavirus disease 2019 pandemic in many European countries further increased population densities in migrant centers and camps,[22] which contributed to additional strain on hygiene systems and medical services. Cutaneous diphtheria is generally considered to be a milder form of the disease that is less likely to lead to systemic infection, and it is less often diagnosed (it requires microbiologic analysis), perhaps explaining in part why this outbreak went unnoticed in western Balkan transit countries. The lower incidence of respiratory cases (15% in this study) than that in previous outbreaks (in which cutaneous cases may have been under-reported) could be the result of frequent and poorly managed skin injuries and close contact with infected persons, in combination with poor hygienic conditions during migration.

The prevalence of cases among male migrants could potentially be explained by differences between women and men in health care–seeking behavior. However, countries that screen all incoming migrants did not identify higher proportions among women. Another explanation could be behavioral differences between male and female migrants — namely, that male migrants may circulate more among the population than female migrants, who operate in smaller social circles. In addition, women may have more contact with health care providers because of pregnancies, through which they could be vaccinated against diphtheria.

The macrolide resistance observed in GC9 poses a substantial threat to treatment outcomes, increases the likelihood of systemic complications warranting diphtheria antitoxin treatment, and may favor transmission. Although most cases were managed with antibiotics only, some patients with respiratory cases received diphtheria antitoxin treatment.[17] In some countries (e.g., Switzerland), a booster vaccine was supplied in the refugee camps.

Timely generation and sharing of genomic data are recommended as an integral part of outbreak responses.[23,24] During the 2022 European outbreak, regular discussion within the 2022 European Diphtheria Consortium and the sharing of sequencing data among reporting countries allowed the identification of four main genetic clusters. These data allowed us to define their commonalities in antimicrobial susceptibility and contributed to public health actions and response options, such as the identification of and screening for erythromycin resistance.

Our study builds on earlier observations in local outbreaks[8,9,11,25] and has enabled an analysis of the event at a continental scale. The multiclonal nature of the outbreak that was revealed is consistent with previous diphtheria outbreaks[20,26,27] and supports an origin from several distinct emergence events of previously unreported strains, whose transmission was enabled among unidentified sustained foci of infection en route to Europe. The timing of the common ancestors of the main genetic clusters, estimated to have been between 2017 and 2020, suggests that transmission at low levels might have gone unnoticed for some time and might have existed even earlier in the origin countries of migrants, perhaps enabled by low vaccination levels and limited health care infrastructure for diagnosis and surveillance of diphtheria.

In the months after the end of the study period, a reduction in the number of cases was observed in all reporting countries. We suspect that this can in part be attributed to several countermeasures, including interview-based contact tracing and screening to identify secondary cases. Several countries have initiated chemoprophylaxis of contacts of persons with diphtheria, whereas others have opted for chemoprophylaxis or vaccination campaigns in the wider population within and around migrant centers.[28,29] Interventions were launched immediately after this outbreak was identified and continued, in some cases, until the spring of 2023. However, owing to very limited active collection of isolates in 2023 as compared with 2022, it is difficult to make inferences regarding drivers of the reduction in cases. Because migrant populations are difficult to study, we suspect the number of cases might have been substantially higher. Genetic clusters from the original outbreak were also identified in 2023, which suggests sustained foci of infection. Secondary cases in vulnerable populations, such as persons experiencing homelessness and intravenous drug users, were also identified. The secondary cases highlight the need for heightened public health measures and clinical awareness.[30]

The rise in the number of *C. diphtheriae* infections observed among migrants in western Europe in the second half of 2022 was seemingly halted by response measures, but some forward transmission in the reporting countries was observed in 2023. The distal origin of these events remains to be determined, even though it might be linked to low vaccination coverage in countries with political unrest and disturbed public health systems that favor local reemergence and motivate migrations to Europe. These data suggest a number of actions that are needed in Europe to reduce the risk of such outbreaks in the future, including improvement in awareness among migrants, their physicians, and relevant personnel with whom migrants are in contact; thorough vaccination protocols for migrants, local populations, and medical and social care personnel; clinical monitoring of persons who are at risk; rapid diagnosis in symptomatic persons and screening of contacts, with laboratory confirmation of cases; antimicrobial-susceptibility testing to define appropriate antimicrobial treatment and prophylaxis; and whole-genome sequencing of toxigenic strains and sharing of sequencing data to inform local and regional dissemination. Strengthening the implementation of immunization programs and seeking to achieve high vaccination coverage (both for primary series and booster doses) remains the key intervention for protection against diphtheria at the population level. Although childhood vaccination coverage in Europe remains stable, waning immunity and lower levels of protection in older persons may create vulnerability. An additional booster dose later in life to ensure lifelong protection has not yet been recommended by the WHO,[31] but studies have shown a decline in seroprotection among older adults.[32,33] Increasing the global production of diphtheria antitoxin and maintaining a stable, communal stockpile that can be rapidly deployed in outbreak situations should also be an international public health priority.

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