



Retour de la diphtérie chez les migrants en Europe

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Déclaration d'intérêt de 2014 à 2025

- Intérêts financiers :
- Liens durables ou permanents :
- Interventions ponctuelles :
- Intérêts indirects :

Aucun

Diphtheria outbreak in Europe, 2022

First cases reported: June 2022



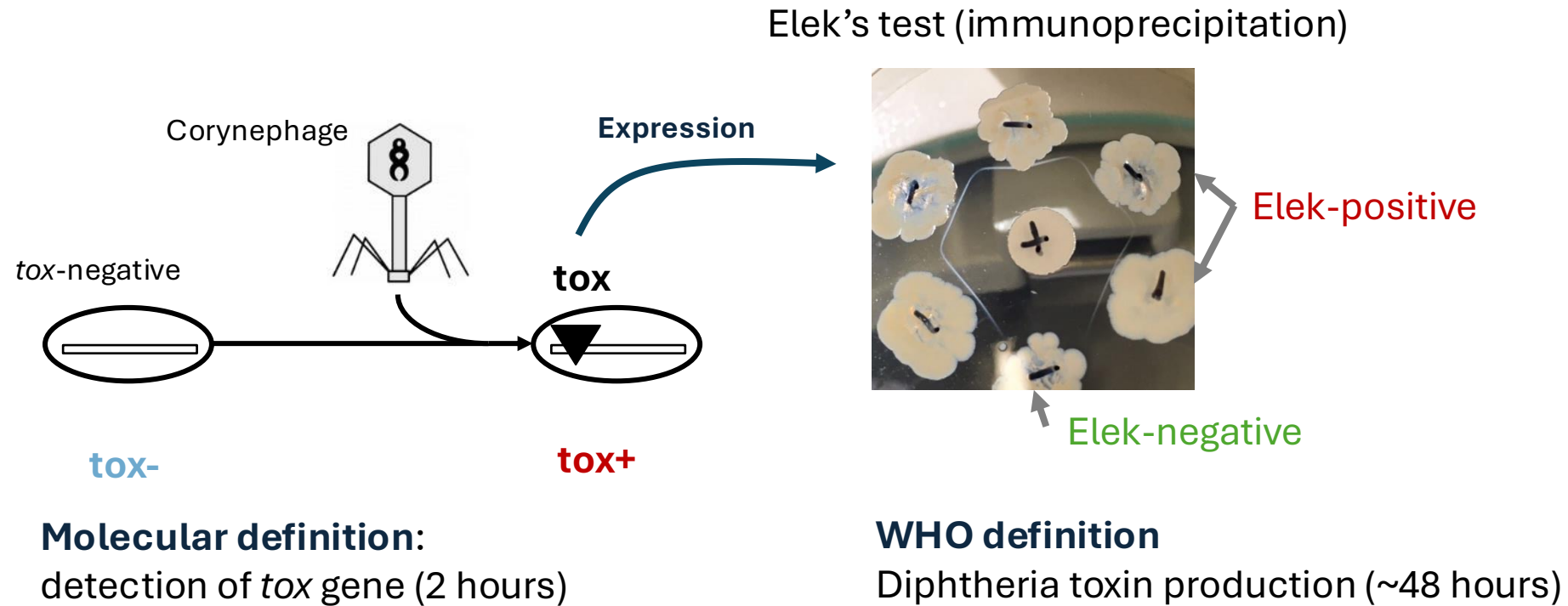
- EpiPulse data
- MLST data
- Data sharing request from ECDC
- Genome sequence comparisons

Sept. 2022: informal European working group (microbiologists, epidemiologists, clinicians)

October 2022: rapid Risk Assessment by ECDC

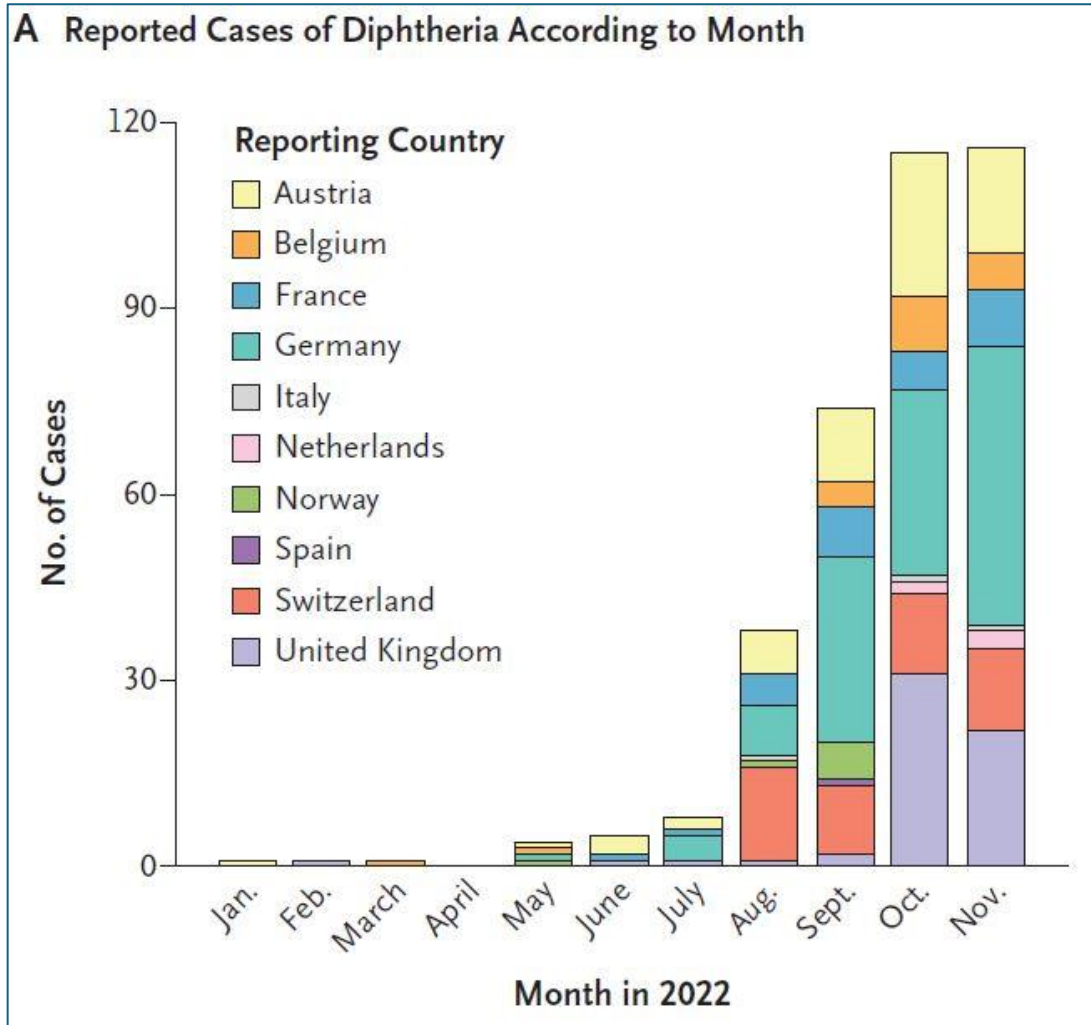


Diphtheria definitions: *tox* gene or toxigenicity



- Europe 2022 case definition: *tox* PCR-positive patients, Jan-Nov 2022
- EU/EAA and Switzerland+UK

Epidemic curve – 2022



- **Total of 363 isolates in 362 individuals**
- 96% had a recent migration history, and/or close contact with migrant populations
- 96% of cases where clinical data was available (77%), **were cutaneous**
- Germany (118), Austria (66), UK (59), Switzerland (52), France (30), Belgium (21), Norway (8), The Netherlands (5), Italy (3), and Spain (1)
- 355/362 (98%) patients were male
- Median age of 18 years

Diphtheria outbreak in Europe, 2022



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.



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Diphtheria Outbreak among Migrants in Europe

A. Hoefer and Others



Une ou plusieurs lésions pustuleuses puis ulcérées, douloureuses, à bordure érythémateuse/violacée, d'évolution récente, couvertes généralement d'une **fausse membrane grisâtre** très adhérente.

Prédominant au niveau des **membres inférieurs**

Des manifestations toxiques peuvent être présentes précocement ou apparaître secondairement.

Le prélèvement de la lésion conduit souvent à isoler d'autres bactéries que la corynébactérie (*S. aureus*, *S. pyogenes*).



- **Forme extra-respiratoire la plus fréquente**
- Patients vivant ou en provenance de pays en développement, de Mayotte, de la Réunion, de Guyane ou de Nouvelle Calédonie.
- Situation de précarité
- Voir aussi: Série par Chêne *et al.*, 2024
Emerging Microbes & Infections

Cutaneous diphtheria from 2018 to 2022: an observational, retrospective study of epidemiological, microbiological, clinical, and therapeutic characteristics in metropolitan France

Laure Chêne^a, Jean-Jacques Morand^a, Edgar Badell^{b,c}, Julie Toubiana^{b,c,d}, Frédéric Janvier^e, Hugo Marthinet^f, Jean-philippe Suppini^g, Aude Valois^a, Gaetan Texier^{f,h}, Sylvain Brisse^{b,c} and Fabien Dutastaⁱ CEDIPE Study Groupⁱ

Clinical aspects

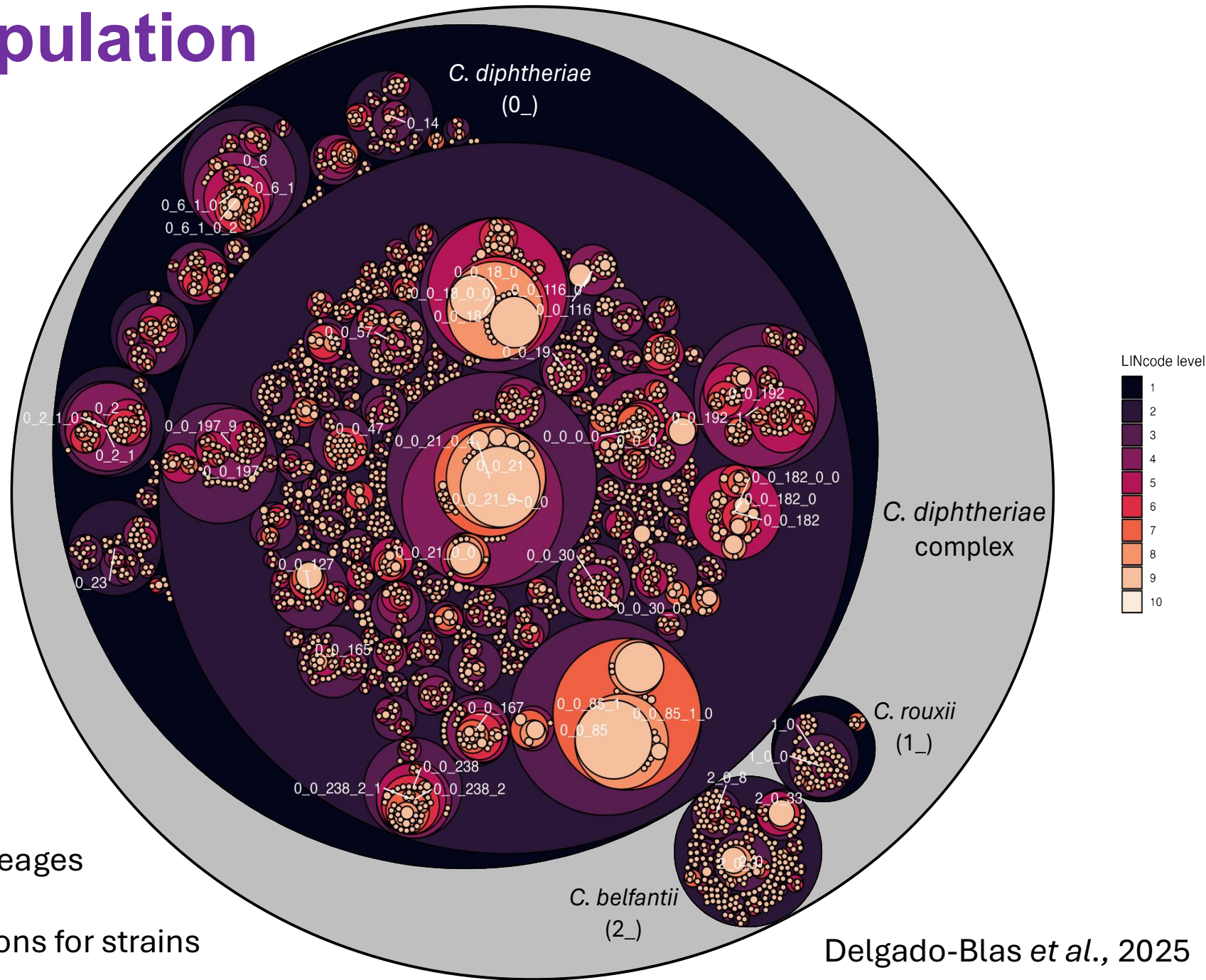
- 17 patients were admitted to a hospital: 5 cutaneous, 12 respiratory diphtheria (7 of whom had a pseudomembrane).
- All 12 patients with respiratory diphtheria were treated with diphtheria antitoxin (+ antibiotics).
- Diphtheria antitoxin doses ranged from 5000 to 100,000 IU; 8 patients: doses >60,000 IU.
- The 12 patients received treatment within a mean ($\pm$ 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).

- Most common symptoms, respiratory manifestations: tonsillitis (8 patients), sore throat (6 patients), and lymphadenopathy (4 patients).
- The patient with atypical respiratory diphtheria presented with a peritonsillar abscess.
- 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.

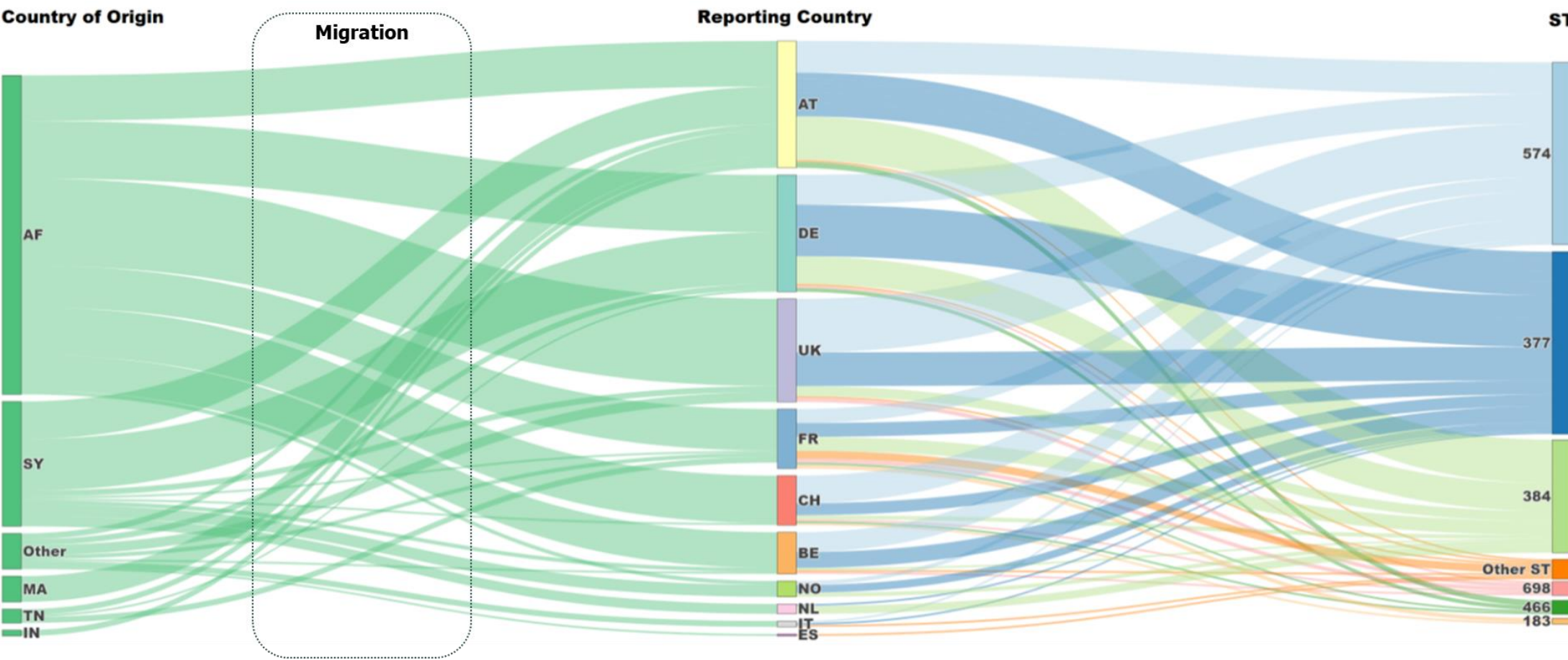
C. diphtheriae population structure

Circular packing plot based on LIN codes:

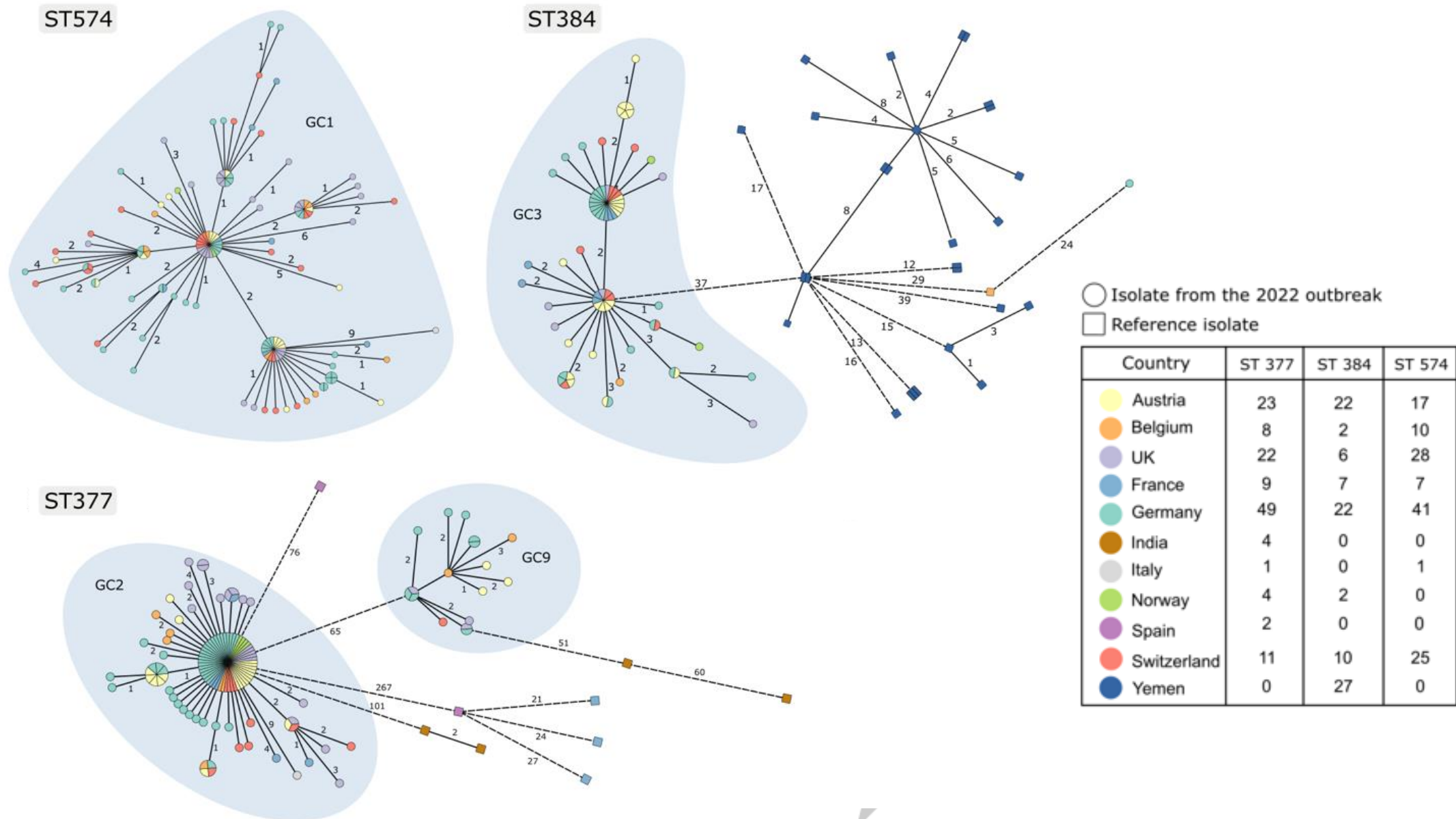
- Recapitulates diversity
- Highlights emerging (outbreak) lineages
- Provides standard genetic definitions for strains



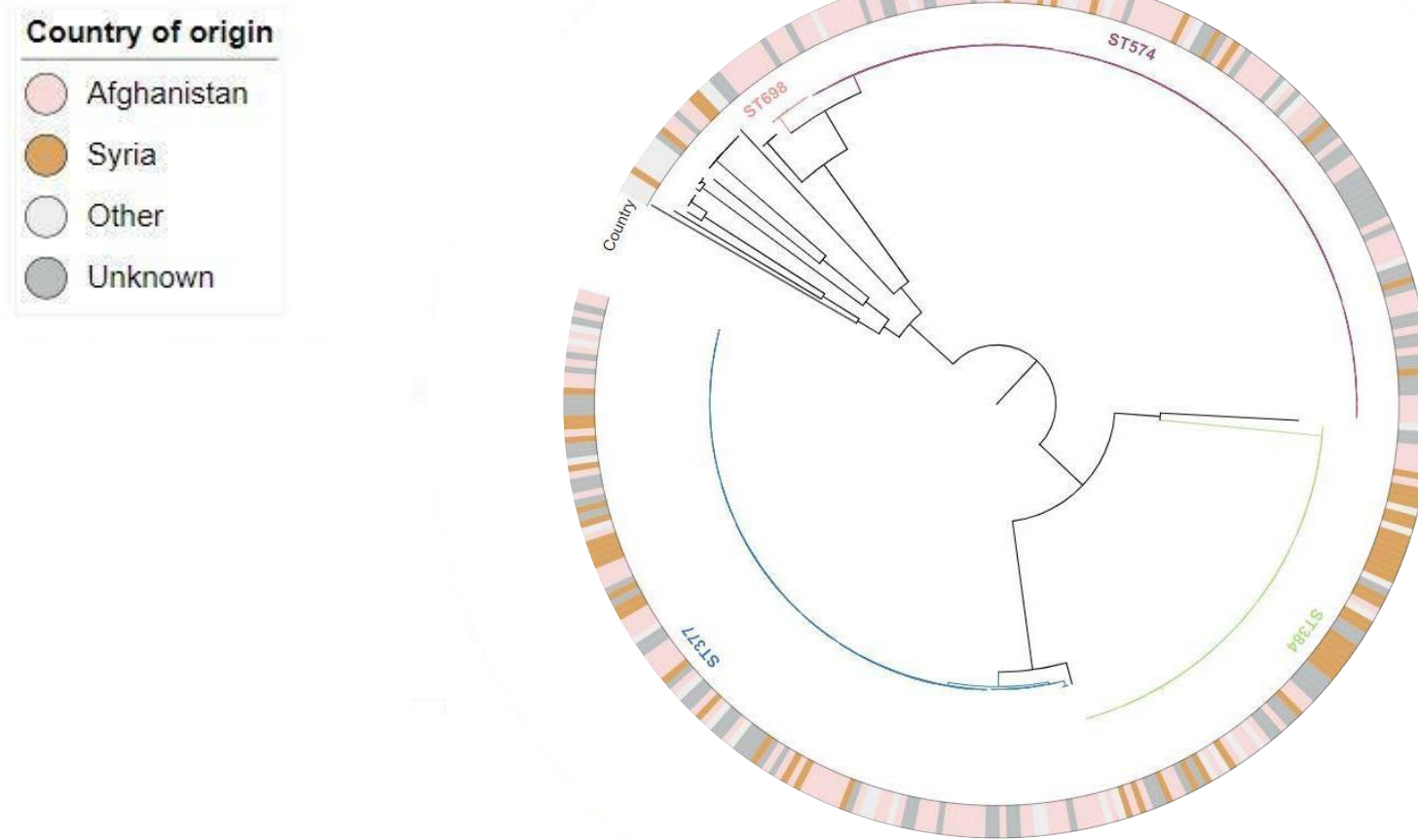
Phylogenetic diversity *versus* reporting country



Genetic diversity of four main genomic clusters (GC)

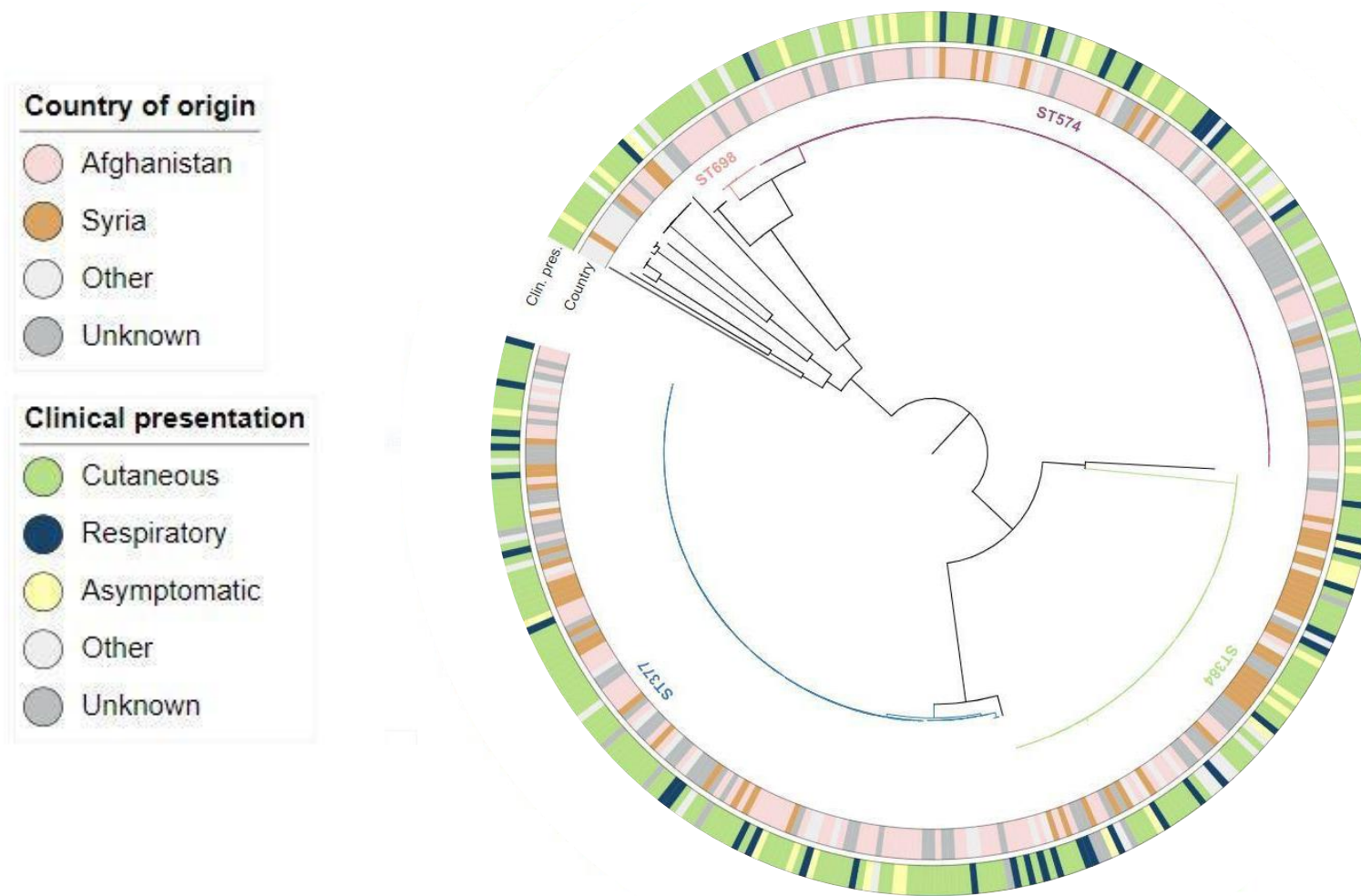


Phylogenetic diversity of the 363 *C. diphtheriae*



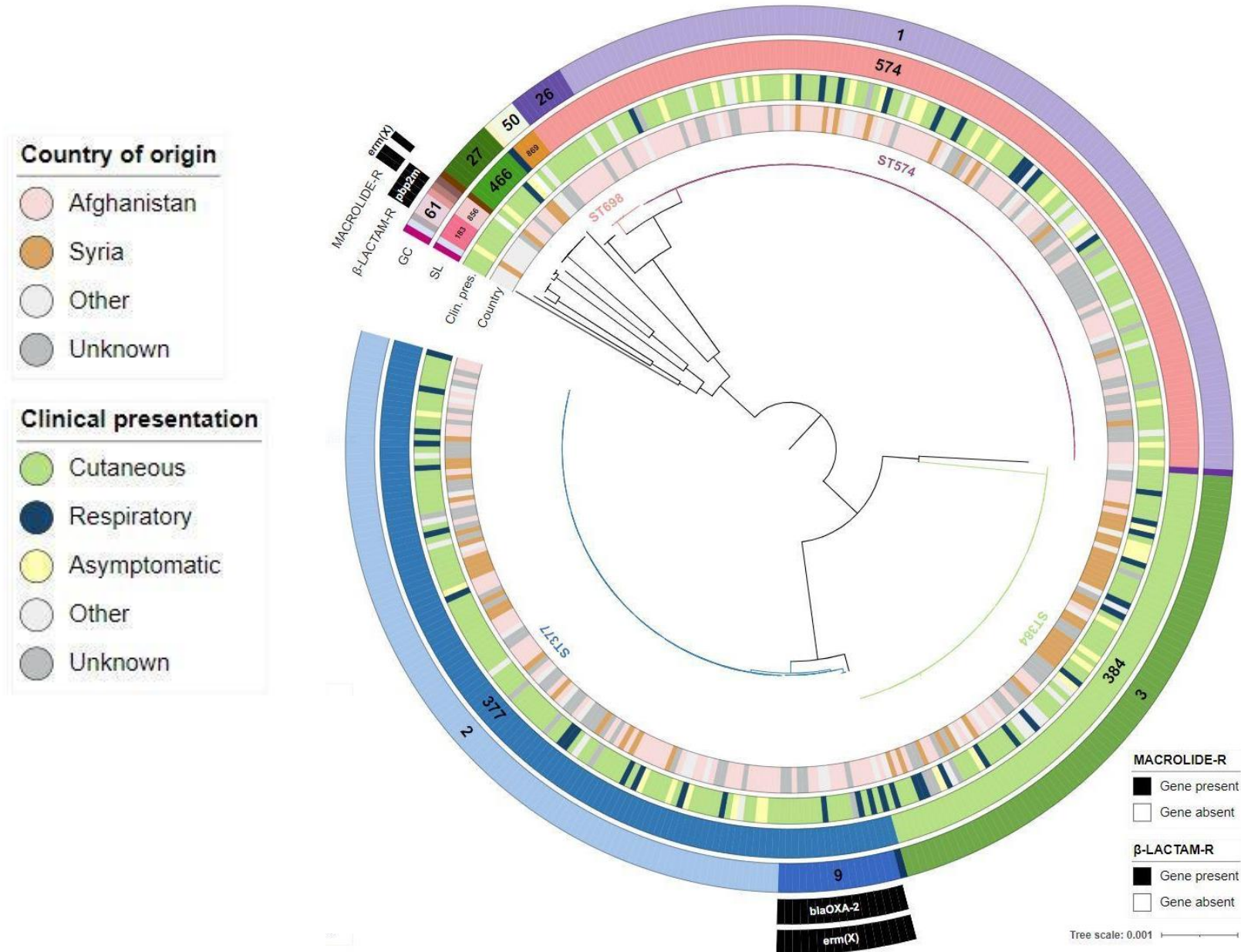
- Lack of association of ST and country of origin
- Transmission of three STs along migration routes

Phylogenetic diversity of the 363 *C. diphtheriae*



- Lack of association between genotype and clinical form

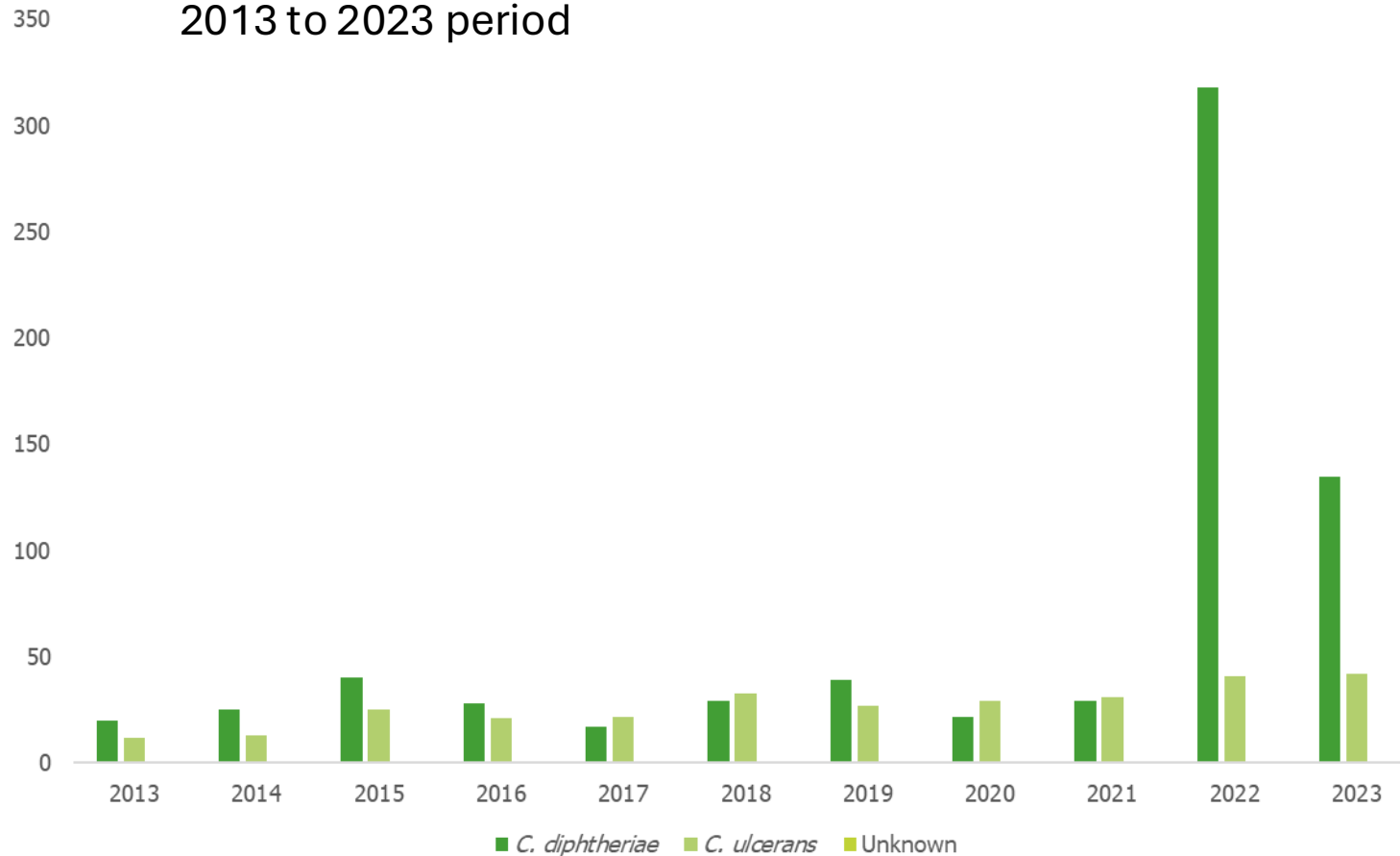
Phylogenetic diversity of the 363 *C. diphtheriae*



- Macrolide-resistance in one genetic cluster; association with *ermX* gene
- Beta-lactam resistance genes (*pbp2m*, *blaOXA-2*, but no phenotypic resistance for the latter

Temporal context in Europe

Diphtheria confirmed cases reported in the EU/EEA in the 2013 to 2023 period



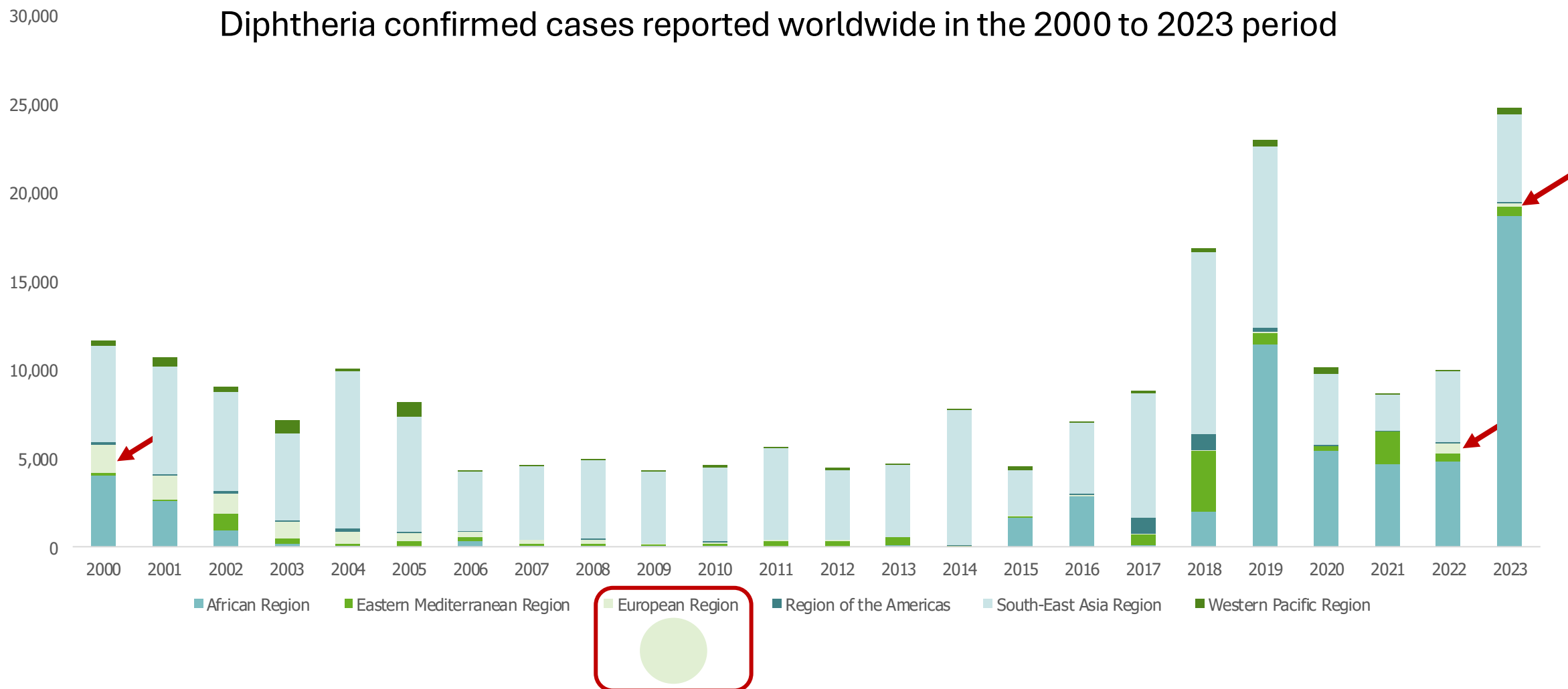
- In the period under analysis, **1,051 confirmed diphtheria cases** were reported in all the EU/EEA.
- Among these cases, **731** were attributable to ***C. diphtheriae*** (69.6% of the total)

*Data as of November 2024.

Source: The European Surveillance System (TESSy)

Cases reported in the United Kingdom included only in the 2010-2019 period.

Diphtheria resurgence: The global picture



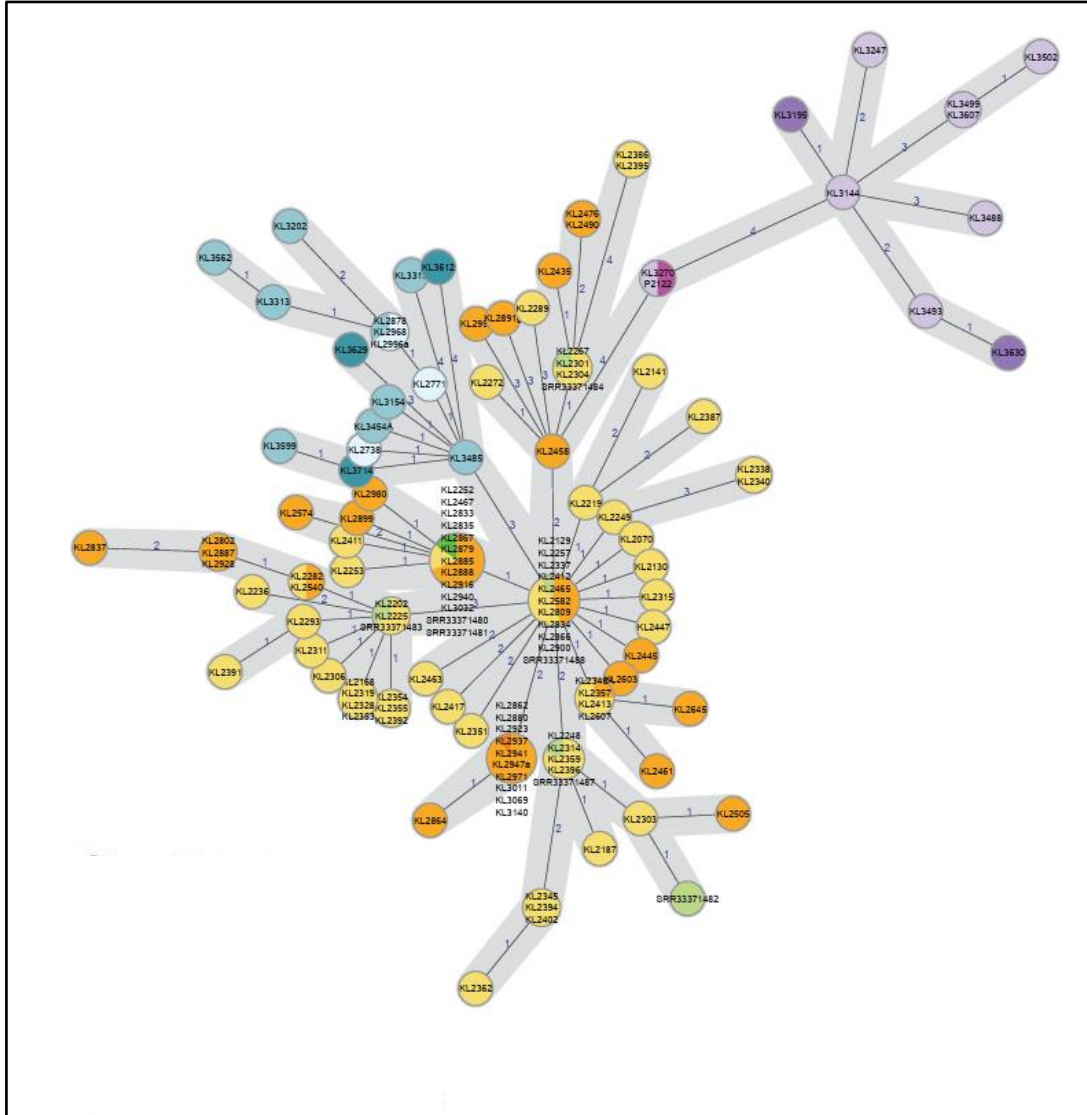
N= 216,166 confirmed diphtheria cases worldwide for the 2000-2023 period.

Source: WHO/UNICEF Joint Reporting Form on Immunization (JRF)

2022 European diphtheria Outbreak: conclusions

- High genomic conservation of cases suggested epidemiological link **not** independent introductions
- Likely sustained foci of infection on migrant route(s) to EU/EEA
- Secondary cases occurring in migrant centres in EU/EEA only (in 2022)
- Concerning antimicrobial resistance (AMR) profile identified
- Need to stay vigilant and to further support international management of diphtheria
- Genomic epidemiology has the capacity to rapidly and effectively inform public health action

Secondary cases of ST-574 detected in vulnerable populations and general public (2023-2025)



-  Germany, sub-cluster 1, 2023
-  Germany, sub-cluster 1, 2024
-  Germany, sub-cluster 1, 2025
-  Germany, sub-cluster 2, 2024
-  Germany, sub-cluster 2, 2025
-  Poland, sub-cluster 2, 2024
-  Germany, migration-associated, 2022
-  Germany, migration-associated, 2023
-  Germany, migration-associated, 2024
-  Switzerland (Urwyler et al.)^a, low risk patients, 2023
-  Switzerland (Urwyler et al.)^a, migration-associated, 2022

- Homeless and injectable drug users
- Unidentified transmissions

Overview of ST574 cases 2023-2025

- ***C. diphtheriae* ST574 continued to circulate after 2022 in at least five EU/EEA countries and in Switzerland**
 - **Between 2023 and 2025, EU/EEA countries reported 82 cases caused by *C. diphtheriae* ST574 to ECDC**
 - **Cases include cutaneous and respiratory forms; respiratory cases linked to severe outcomes and deaths (~5 confirmed)**
 - **Increasing genetic diversity and appearance of NTTB Isolates**
-
- **At least one other ST circulates too, including in France**
 - **True case numbers are likely underestimated**, given surveillance limitations in vulnerable populations
 - **Impact on vulnerable populations remains unclear**, especially where diagnostic capacity is limited
 - **Risk for undervaccinated populations**

Main options for response to these events

- Check vaccination status of newly arrived migrants and provide vaccinations
- Ensure vaccination status of all personnel working in reception centres
- Alert clinicians
- Include diphtheria into the differential diagnosis in skin ulcers.
- Timely laboratory confirmation.
- Identify close contacts.
- Provide antibiotic treatment to close contacts.
- Ensure timely reporting to competent authorities.
- Perform enhanced surveillance, molecular typing and whole genome sequencing

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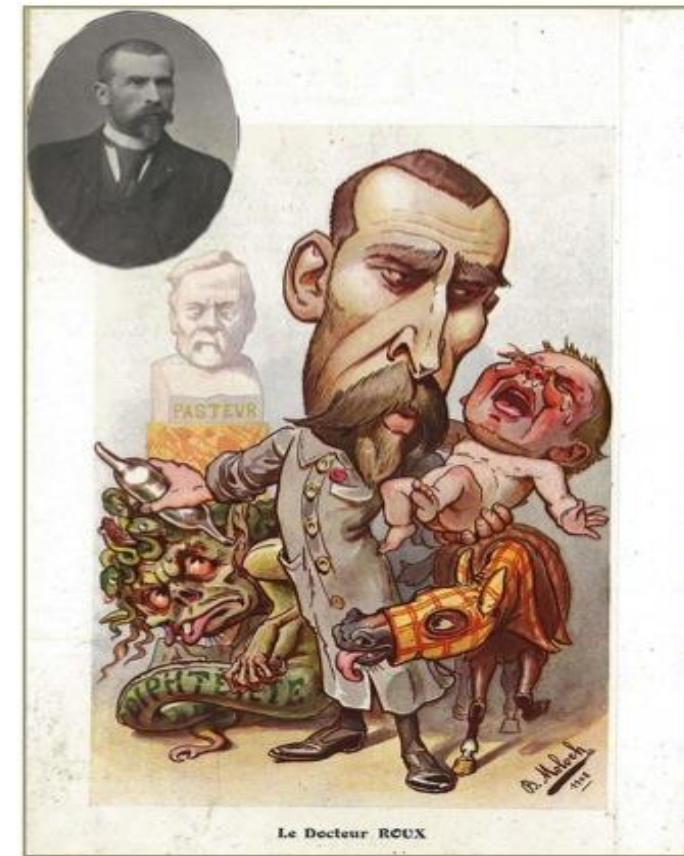
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