Situational Report, Week 15, 2025

Toxigenic *Corynebacterium diphtheriae* disease in South Africa in 2024-2025

Date of report: 17 April 2025

Period included in the report: 1 January 2024 to 13 April 2025

Report compiled by: Centre for Respiratory Diseases and Meningitis (CRDM), National Institute for Communicable Diseases (NICD)

Highlights:

- Since the last situational report (week 14), the following updates are included in this report
  - Three new laboratory-confirmed cases of toxigenic respiratory diphtheria, one from Limpopo, one from Mpumalanga and one from the Western Cape
  - Two new asymptomatic carriers of toxigenic *C. diphtheriae*, both from Limpopo
- Appropriate public health responses have been initiated for each case

Table 1: Number of suspected, probable and confirmed cases of respiratory diphtheria, South Africa, 1 January 2024 to 13 April 2025[1]

Case definition	Number	Provincial distribution
Laboratory-confirmed toxigenic respiratory diphtheria	43	Gauteng (2/43, 5%) KwaZulu Natal (1/43, 2%) Limpopo (4/43, 9%) Mpumalanga (5/43, 12%) Western Cape (31/43, 72%)
Probable diphtheria cases	1	Limpopo (1/1, 100%)
Suspected diphtheria cases with specimens sent to exclude diphtheria and tested negative	238	Eastern Cape (3/238, 1%) Free State (3/238, 1%) Gauteng (24/238, 10%) KwaZulu Natal (5/238, 2%) Limpopo (3/238, 1%) Mpumalanga (19/238, 8%) Northern Cape (1/238, 0%) North West (4/238, 2%) Western Cape (176/238, 74%)
Asymptomatic carriers of toxigenic *C. diphtheriae* identified during contact tracing	40	Limpopo (2/40, 5%) Mpumalanga (3/40, 8%) Western Cape (35/40, 88%)
Deaths in probable and laboratory-confirmed toxigenic respiratory diphtheria cases	9	Gauteng (1/9, 11%) Limpopo (1/9, 11%) Mpumalanga (2/9, 22%) Western Cape (5/9, 55%)

[1]For case definitions please see Table 3 at the end of this report

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Public health actions instituted

For every case, a public health response has been initiated. Public health response includes the swabbing of close contacts, isolation of at-risk contacts, provision of prophylaxis and vaccination of contacts. These public health actions are instituted for contacts in all settings including household, work, healthcare facility staff and emergency medical services staff. Additional vaccination campaigns have been conducted in schools and communities in the Western Cape.

Epidemiology of respiratory diphtheria cases and asymptomatic carriers 1 January 2024- 13 April 2025

Between 1 January 2024 and 13 April 2025, 43 confirmed cases of respiratory diphtheria, 1 probable respiratory diphtheria case and 40 asymptomatic carriers of toxigenic C. *diphtheriae,* detected during contact tracing, have been identified in South Africa. The majority of confirmed cases and carriers (80%, 66/83) were from the Western Cape, comprising 31 respiratory diphtheria cases and 35 asymptomatic carriers (Figure 1, Table 1). The median age of cases of confirmed respiratory diphtheria was 28 years (range: 2–55 years), with 74% (32/43) being 18 years and older. The overall case-fatality ratio (CFR) among probable and confirmed respiratory diphtheria cases was 20% (9/44). Among children and adolescents under 18 years, the CFR was 18% (2/11), compared to 22% (7/32) among adults.

In the first half of 2024, two confirmed respiratory diphtheria cases were reported—one in **KwaZulu-Natal** and one in the **Western Cape**. Between week 31 (beginning 29 July 2024) and week 37 (beginning 9 September 2024), a cluster of three respiratory diphtheria cases and seven asymptomatic carriers was identified in a school-linked community in the Western Sub-District of Cape Town. Additionally, two sporadic confirmed respiratory diphtheria cases were reported in Cape Town during this period, unlinked to this cluster.

Since week 46 (starting 11 November 2024), there has been a surge in diphtheria cases in the Western Cape (City of Cape Town), with 25 respiratory cases and 28 asymptomatic carriers testing positive for toxigenic *C. diphtheriae*. Five clusters were identified (Table 2), including two linked to a correctional facility (weeks 50–51 and week 7), a cluster of children who played together (weeks 1–2), a family cluster (weeks 6 and 8), and a two-person cluster (weeks 8–9). An additional 16 respiratory cases in the Western Cape had no known epidemiological links. Outside the Western Cape, one cluster was reported in **Gauteng** (week 2) consisting of two respiratory cases and another in **Mpumalanga** (weeks 9–10), involving a respiratory case and an asymptomatic carrier. Additionally, a cluster spanning **Limpopo and Mpumalanga** was reported in week 11, consisting of one probable case who resided in **Limpopo** and traveled to Mpumalanga after symptom onset, one confirmed case and two asymptomatic carriers in Mpumalanga (Table 2). Two further clusters were identified in Limpopo in weeks 14 and 15, each consisting of a case and a contact. Beyond these clusters, sporadic cases with no known epidemiological links have also been reported, including three in Mpumalanga (weeks 11, 14 and 15) and two in Limpopo—one in week 12 and two in week 15.

Notified suspected cases of diphtheria 1 January 2024 - 13 April 2025

From 1 January 2024 to 13 April 2025, 238 individuals have been reported as suspected diphtheria cases and tested negative for *C. diphtheriae*. Alternate diagnoses became available for some of the individuals with suspected diphtheria, and included *Streptococcus pyogenes*, *Corynebacterium* spp. NOT *diphtheriae,* Ludwig's angina, retrobulbar abscess or respiratory viruses including SARS-CoV-2.

Non-toxigenic diphtheria

From 1 January 2024 to 13 April 2025, 11 cases of non-toxigenic cutaneous diphtheria have been confirmed nationally including, eight cases of *C. diphtheriae*, two *C. belfantii* and one of *C. ulcerans*. In addition, 1 throat swab of a contact of a confirmed case, tested positive for non-toxigenic *C. diphtheriae*.

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Table 2. Summary of diphtheria clusters reported in South Africa from November 2024 to 13 April 2025

Cluster No.	Week (week start date)[1]	Province (City)	Details
1	50 – 51 (9 – 16 December 2024)	Western Cape (Cape Town)	1 respiratory case 12 asymptomatic carriers
2	1 – 2 (30 December 2024 – 6 January 2025)	Western Cape (Cape Town)	3 respiratory cases
3	2 (13 January 2025)	Gauteng (Tshwane)	2 respiratory cases
4	7 (10 February 2025)	Western Cape (Cape Town)	2 respiratory cases 14 asymptomatic carriers
5	6 – 8 (3 – 17 February 2025)	Western Cape (Cape Town)	1 respiratory case, 1 asymptomatic carrier
6	8 – 9 (17 – 25 February 2025)	Western Cape (Cape Town)	1 respiratory case 1 asymptomatic carrier
7	9 – 10 (25 February 2025 – 3 March 2025)	Mpumalanga (eMalahleni)	1 respiratory case 1 asymptomatic carrier
8	10 (3 March 2025)	Limpopo -Mpumalanga (Bushbuckridge)	1 probable case (travelled from Limpopo to Mpumalanga after symptom onset) 1 confirmed case 2 asymptomatic carriers in Mpumalanga
9	14 – 15 (7 – 14 April 2025)	Limpopo (Ba-Phalaborwa)	1 respiratory case, 1 asymptomatic carrier
10	14 – 15 (7 – 14 April 2025)	Limpopo (Ba-Phalaborwa)	1 respiratory case, 1 asymptomatic carrier

[1]Period between the first recorded infection and the last observed infection within each cluster, expressed in weeks. Each week starts on a Monday and is labelled by its start date, following the ISO 8601 standard. Based on the date of clinical presentation or sample collection.

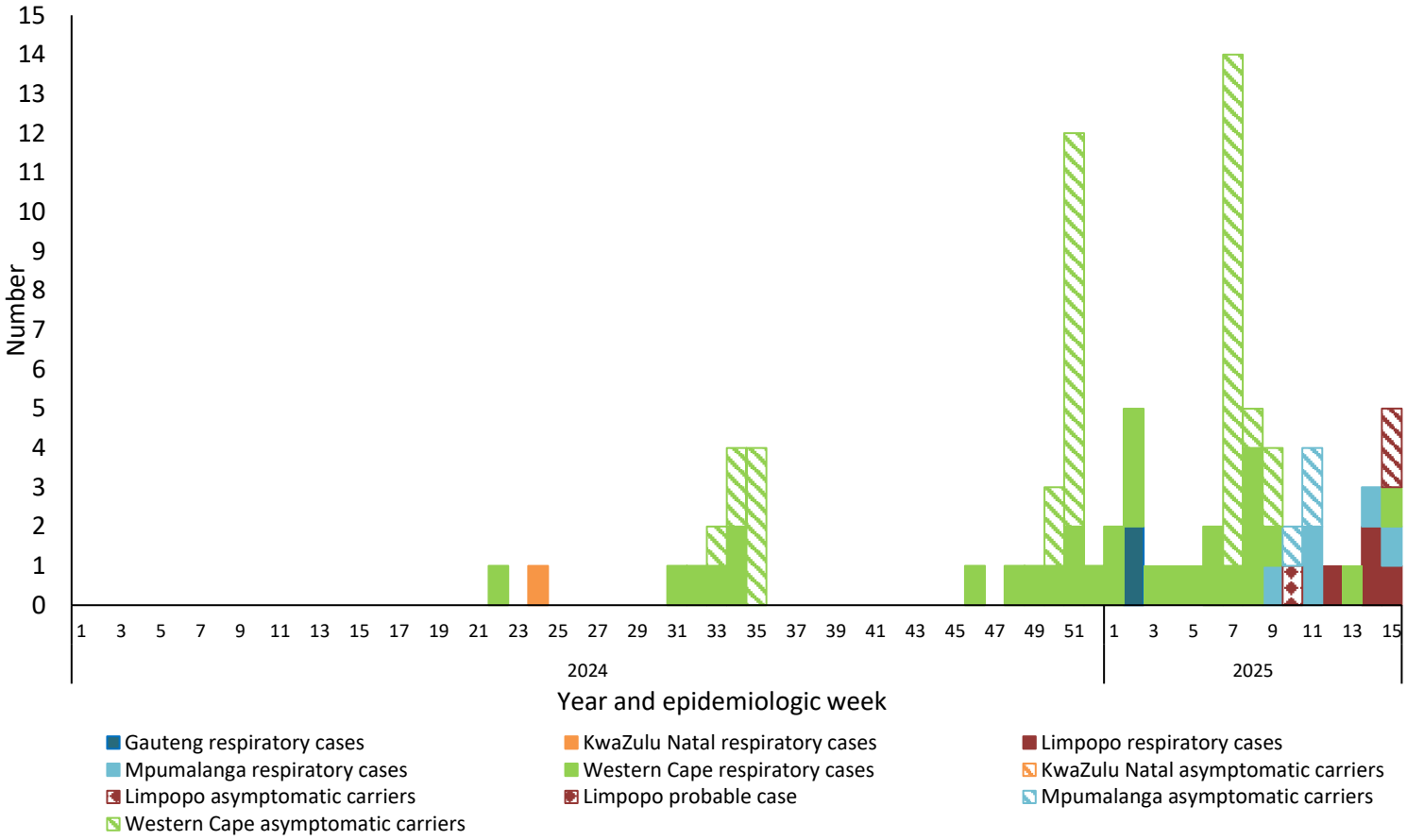

Figure 1: Number of individuals testing positive for toxigenic *C. diphtheriae* (respiratory diphtheria cases and asymptomatic carriers) and probable cases, South Africa, 1 January 2024 to 13 April 2025.Based on date of clinical presentation or sample collection (earliest date included if both available).

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Microbiology

Among the 83 toxigenic *C. diphtheriae* infections identified, 31 (37%) infections were identified on PCR only. Of the remaining culture-positive cases 44/52 (85%) had cultures available for further characterisation, the majority of the isolates were from the Western Cape and two isolates were from Mpumalanga. No cultures were available for the infections reported from KwaZulu-Natal and Gauteng.

The phenotypic Elek test (to confirm toxin production) correlated 100% with PCR for those isolates that have had both tox gene PCR and Elek performed (n=31). Antimicrobial susceptibility testing showed that 17/52 (33%) isolates were intermediately resistant to penicillin with MICs of 0.25 µl/ml) (MIC range 0.125-0.25 µg/ml), and 40 of the tested isolates were susceptible to erythromycin (MIC range 0.016-0.125 µg/ml), using the Clinical and Laboratory Standards Institute (CLSI) guidelines for interpretation (1). Similarly, using EUCAST interpretation, the 40 isolates were susceptible to erythromycin, and 17/52 (33%) "susceptible with increased exposure" to penicillin (i.e. susceptible at higher doses) (2). All Western Cape Province isolates sequenced to date are ST906 (n=40), the same lineage that was first detected in this province in 2023 and appears to be localised in this province currently. One isolate from Mpumalanga has been sequenced and is a different lineage (ST824), not previously documented in South Africa. So far, we have not identified any isolates that are toxin gene bearing but not producing the toxin phenotypically - this is determined through correlation of Elek results with PCR results as non-toxigenic toxin-gene bearing (NTTB) isolates would be Elek negative but PCR positive for the toxin gene.

Vaccination status among respiratory diphtheria cases

Of the 43 respiratory diphtheria cases, 10 cases were among children 12 years of age and under. Vaccine history is available for 3 of these. One symptomatic case (aged 9 years) had only received three infant doses of vaccine but no booster doses and the other two were reported as unvaccinated**.**

Historical epidemiology of diphtheria in South Africa 2015-2023

Between 2015 and 2023, the National Institute for Communicable Diseases (NICD) confirmed 42 toxigenic *C. diphtheriae* infections, comprising 26 respiratory diphtheria cases, 14 asymptomatic carriers detected through contact tracing, and 2 cases of cutaneous diphtheria. All respiratory cases were reported from the Western Cape (n=9) or KwaZulu-Natal (n=17). The highest annual totals occurred in 2015 (n=11) and 2023 (n=6), while other years reported between 0 and 4 cases.

<u>Information for clinicians</u>

Clinical presentation of respiratory diphtheria

Respiratory diphtheria is a vaccine-preventable illness caused by toxigenic *C. diphtheriae* (and more rarely *C. ulcerans* or *C. pseudotuberculosis*), and can occur in persons of all ages.

The clinical presentation includes the following signs and symptoms:

- sore throat
- low-grade fever
- <u>AND</u> an adherent membrane of the nose, pharynx, tonsils, or larynx (Figure 2) - the membrane is greyish-white and firmly adherent to the tissue
- <u>AND/OR</u> enlarged glands in the neck (bull neck)
- toxin-mediated systemic signs including myocarditis, polyneuropathy and renal damage

Figure 2: Example of the adherent membrane of diphtheria

Patient management

Treatment includes antibiotics (azithromycin or penicillin) to clear the organism from the throat and prevent onward transmission, and diphtheria anti-toxin (DAT) to neutralise unbound toxin. The dosage of DAT is determined by the duration and severity of illness. **Treatment, contact tracing and chemoprophylaxis should be started prior to laboratory confirmation**. Early administration of DAT may be life-saving and should not be delayed in cases with a high index of suspicion. Supportive care is primarily aimed at airway management and includes providing oxygen, monitoring with electrocardiogram and intubation or performance of a tracheostomy if necessary.

DAT is available in South Africa through provincial pharmacies although stocks are limited. Clinicians and pharmacist are advised to secure a source of DAT and set up emergency supply lines. Clinicians may refer to "Guidelines for diagnosis, testing, and treatment of diphtheria" https://www.nicd.ac.za/diseases-a-z-index/diphtheria/. Advice is available from the NICD doctor-on-call on 080 021 2552. The NICD doctor on call is able to link clinicians to infectious disease experts to discuss individual cases if needed. Additional resources include https://iris.who.int/bitstream/handle/10665/375887/WHO-DIPH-Clinical2024.1-eng.pdf

Laboratory confirmation of *C. diphtheriae*

Most commonly a throat swab should be collected, from below the membrane if possible, using a Dacron, Rayon or nylon-flocked swab. Respiratory lesions may be pharyngeal, tonsillar, laryngeal or nasal – swabs need to be taken from relevant lesions. Ideally, the swab should be placed in Amies or modified Stuart's transport medium (this can be obtained from your local National Health Laboratory Service (NHLS) or private laboratory). However, it is possible to send a dry swab if transport medium is unavailable. The specimen should immediately be transported to the nearest diagnostic laboratory for primary culture on blood agar and ideally on selective and differential media like Hoyle's agar. All isolates and/or clinical specimens (including other *Corynebacterium* spp. e.g., *C. ulcerans* and *C. pseudotuberculosis*) should be sent to the National Institute for Communicable Disease (NICD) to confirm identification and toxin production. Please alert NICD prior to sending and label specimens clearly: "suspected diphtheria". Laboratory managers may use the NICD recommendations for diagnosis, testing, and treatment of diphtheria on https://www.nicd.ac.za/diseases-a-z-index/diphtheria/, for additional information.

Notification of cases and public health response.

Respiratory diphtheria is a **highly contagious vaccine-preventable illness** caused by the toxin-producing strains of *C. diphtheriae* and occasionally *C. ulcerans* and *C. pseudotuberculosis.* **Primary prevention is through vaccination**, including the infant vaccine course (6, 10 and 14 weeks) with boosters at 18 months, 6 years and 12 years of age. Individuals of all ages can seek assistance at public health care clinics (or private facilities) to review their vaccine status

and receive booster dose/s as indicated. Health-care workers are reminded to review vaccination records/status of individuals of all ages and recommend vaccine as indicated.

Respiratory and cutaneous diphtheria is a category 1 notifiable condition and should be notified within 24 hours. All suspected cases should be notified urgently to district or provincial communicable disease coordinators (CDCCs) as per notifiable medical condition notification procedures. Contact tracing, including the taking of throat swabs, administration of prophylaxis (azithromycin) with or without catch-up vaccination should start prior to laboratory confirmation. Vaccine campaigns and reassessment of vaccine status should be considered for all patients presenting to primary health care (regardless of symptoms). Additional school and community-based vaccine campaigns should also be considered. https://www.nicd.ac.za/nmc-overview/notification-process/

Table 3: Case definitions for respiratory and cutaneous diphtheria, South African notifiable medical conditions' flipchart

Suspected case	A person meeting the **clinical criteria** for **classic respiratory diphtheria**
Probable case*	Any person meeting the **clinical criteria** for **classic respiratory diphtheria** **AND** with an **epidemiological link** to a confirmed case but **no diphtheria testing** was performed **OR** Any person meeting the **clinical criteria** for **classic respiratory diphtheria** **AND** **laboratory confirmation of the organism** but **toxin production has not been confirmed**.
Confirmed case	Any person meeting the clinical criteria for at least **one of the clinical forms of diphtheria** **AND** **laboratory confirmation of the organism and toxin production**
Asymptomatic carrier	A person with **no symptoms** **AND** **laboratory confirmation of the organism and toxin production**
Clinical criteria Any person with at least one of the following clinical forms: **Classic respiratory diphtheria**: An upper-respiratory tract illness characterised by sore throat, low-grade fever AND a typical adherent membrane of the nose, pharynx, tonsils, or larynx **Mild respiratory diphtheria**: An upper respiratory tract illness with laryngitis or nasopharyngitis or tonsillitis WITHOUT an adherent membrane/pseudomembrane. **Cutaneous diphtheria:** Skin lesion consistent with diphtheria **Diphtheria of other sites:** Lesion of conjunctiva or mucous membranes consistent with diphtheria **Laboratory criteria** **Laboratory confirmation of the organism**: *C. diphtheriae* or *C. ulcerans* or *C. pseudotuberculosis* isolated from a clinical specimen or detected by polymerase chain reaction (PCR) **Laboratory confirmation of toxin production**: laboratory confirmation of diphtheria (as above) and also confirmed to be *tox* gene positive by PCR, and toxin producing by Elek testing (if an isolate is available).	
Additional notes Clinicians who suspect diphtheria should contact the NICD 24-hour hotline **(0800-212-552)** for assistance with specimen collection and diagnosis. It is essential to: 1) collect a throat swab from suspected cases using the correct procedures, and 2) to complete a case investigation to provide authorities with information to identify contacts and implement prevention measures. See resources below.	
Additional resources A case-investigation form (CIF), frequently asked questions document (FAQ), Guidelines for the management and public health response to diphtheria (2018), and specimen collection guidelines are available at http://www.nicd.ac.za/diseases-a-z-index/diphtheria/	

References

1. Clinical and Laboratory Standards Institute. Methods for Antimicrobial dilution and disk susceptibility testing of infrequently isolated or fastidious bacteria, M45 3rd Edition. 2015.
2. EUCAST. Antimicrobial susceptibility testing: EUCAST disk diffusion method. Version 11.0. 2023. http://www.eucast.org/ast_of_bacteria/ disk_diffusion_methodology/