Western Cape Government
Health

Office of the DDG: CoO
REFERENCE: 19/5/3/4
ENQUIRIES: Ms C.A. Lawrence / Ms B. Ndlovu
TEL: 021-483-9964/3156/6878

TO:	Chief Directors	Emergency and Clinical Services Support Metro Health Services (MHS) Rural Health Services (RHS) Strategy and Health Support
	District Managers:	Metro Health Services (MHS) Substructures Rural Districts
	Directors:	Emergency Medical Services Forensic Pathology Services Professional Support Services Community Based Services - Environmental Health Communication
	Chief Executive Officers (CEOs): Managers: Heads of Health / Executive Directors:	Central, Regional and District Hospitals Private Hospitals and Private Clinics Local Authorities/Municipalities/City of Cape Town South African Military Health Services
	Managers:	National Health Laboratory Services Private Laboratories

CIRCULAR: H91/2021

DIPHTHERIA ALERT: NON-TOXIGENIC DIPHTHERIA CLUSTER IDENTIFIED IN THE WEST COAST AND CAPE WINELANDS DISTRICTS

Diphtheria is a contagious and potentially life-threatening bacterial disease. The incidence of diphtheria worldwide and in South Africa has been reduced due to increasing immunisation levels, such that only sporadic cases of disease have been identified and reported. Diphtheria is preventable by vaccination given at 6, 10, 14 weeks, with booster doses given at 18 months, 6 years and 12 years of age. Persons who are in contact with a confirmed case should receive post-exposure prophylaxis including antibiotics and vaccination to prevent spread of the bacterium, and they should have a pharyngeal swab taken.

In 2017, a cluster of four respiratory diphtheria cases were identified in the Eastern sub-district of the Cape Town Metropolitan district of the Western Cape Province. Prior to this cluster, two confirmed cases of diphtheria were identified in KwaZulu-Natal province in 2016, and an outbreak of 15 cases occurred in eThekwini, Kwa-Zulu Natal Province in 2015, affecting incompletely immunised children of primary-school-going age.

Non-toxigenic C. diphtheriae typically causes chronic skin ulceration; less common manifestations include upper respiratory tract infections, or rarely, invasive diseases (including endocarditis, mycotic aneurysms, osteomyelitis and septic arthritis). Classically, persons with underlying medical conditions (including alcoholism and IV drug users) appear to be at higher risk of developing sporadic invasive disease from non-toxigenic C. diphtheriae.

This alert serves to inform clinicians, healthcare workers or practitioners, laboratorians, district-and-sub-district public health officials in both the public and the private sector of:

- **A localised cluster/outbreak of *non-toxigenic Corynebacterium diphtheriae*** that has been detected in Citrusdal and Paarl
- **A Quick Reference Guide with adapted diphtheria case definitions for the outbreak** that has been formulated for the cluster/outbreak in the Western Cape – it includes the respiratory, cutaneous, or other clinical presentation of the disease.
- **The importance of detection of any clinical diagnosis of diphtheria, of notifying and investigating suspected cases, which includes laboratory confirmation.**
- The recommendation **to laboratories to routinely screen all oropharyngeal (OP), nasopharyngeal (NP), and abscess or cutaneous lesion swabs for C. diphtheriae** (especially from the localised outbreak area), to identify

the Corynebacterium spp. to species level if isolated from blood cultures within 2 days of incubation. Any suspect or confirmed isolates of Corynebacterium spp. must be sent to the NICD for identification/confirmation and for further characterisation (including cutaneous isolates).

1. SITUATIONAL UPDATE (28 June 2021

- A total of 6 cases (5 laboratory-confirmed cases, and 1 probable case) of *Corynebacterium diphtheriae* have been identified, 5 from Citrusdal (West Coast), and one from Paarl (Cape Winelands) in the Western Cape. All cases presented with a diagnosis of infective endocarditis, ages ranging from 13 – 38 years, three of the cases were scholars As at 28 June 2021, 4 of the 6 cases had demised and two cases are currently being treated at a provincial hospital.
- There are currently no clear epidemiological links amongst the cases within Citrusdal (besides the fact that 3 cases attend schools in the area), as well as the link to the case from Paarl.
- On the 13th of June 2021, the Provincial CDC unit was informed about a 25-year-old patient, whose blood culture, collected on 08/06/2021, yielded a *Corynebacterium diphtheriae*. This patient however did not present with the typical respiratory diphtheria symptoms and was admitted to a provincial hospital with infective endocarditis.
- On the 15th of June 2021, the laboratory alerted the department of a possible *Corynebacterium diphtheriae* outbreak; a cluster of 4 patients, all diagnosed with infective endocarditis, none that was clinically suggestive of the typical (toxic) diphtheria.
    - Furthermore, 3 of the cases (including the case that was 1st confirmed) resides in Citrusdal, and one from Paarl.
    - At this stage, 3 of the cases all required laboratory confirmation as only Corynebacterium species were identified) and one of the 4 suspected cases, a 13- year old had already demised on the 18th of May 2021.
- The 1st confirmed case subsequently demised on the 15th of June, and the NICD confirmed non-toxigenic strain of *Corynebacterium diphtheriae* on the 17th of June 2021. A 24-year old patient admitted on the 13th of June, demised on the 20th of June 2021.
- Further investigations identified a "probable index case" – that demised on the 23rd of April 2021. Diphtheria was not suspected at the time, and no laboratory investigations were undertaken.
- A 13-year-old suspected case was subsequently admitted to the provincial hospital on the 17th of June 2021. Five of 6 cases were confirmed non-toxigenic diphtheria by the NICD.
- District health services has identified and listed close and "at-risk" contacts of the cases, that includes close household members, classmates/learners, and health care workers who provided care, to identify and prevent additional cases. The appropriate antibiotic therapy and vaccination (dependant on vaccination status and if toxigenic C. diphtheriae is detected or suspected) was provided to the close contacts and eligible at-risk contacts.
- All close and at-risk contacts are being investigated and monitored, and results of laboratory tests are awaited.
- Detailed investigations are currently still underway to determine a possible source of the outbreak.
- Further public health responses, measures and interventions will be communicated once more information regarding contact laboratory results becomes available, and whether any epidemiological links can be established.

2. RECOMMENDATIONS FOR THE MANAGEMENT AND PUBLIC HEALTH RESPONSE TO A LOCALISED CLUSTER / OUTBREAK OF NON-TOXIGENIC DIPHTHERIA IN CITRUSDAL AND PAARL

Clinicians and other healthcare workers, district and sub-district and public health officials must be vigilant and report any clinical diagnosis of diphtheria, notify suspected cases, investigate and ensure laboratory confirmation for all cases meeting the case definition of both the classical respiratory diphtheria presentation, and the updated case definitions for the outbreak specific areas - i.e. Citrusdal in the Cederberg sub-district in the West Coast District; and Paarl in the Drakenstein sub-district of the Cape Winelands District.

2.1 Diphtheria Guidelines

Attached, please find the following resource documents

- Annexure 1: Quick Reference Guide for a localised Non-toxigenic Corynebacterium diphtheria cluster / outbreak, in the Western Cape Province, 28 June 2021
- Diphtheria: NICD Recommendations for Diagnosis, Management and Public Health Response, Version 3.0 (28 May 2018), https://www.nicd.ac.za/wp-content/uploads/2017/03/NICD-guidelines_diphtheria_v3_28-May-2018.pdf
- Diphtheria Case Investigation Form, a slightly updated CIF was compiled for the outbreak situation
- Diphtheria Contact Line List, https://www.nicd.ac.za/wp-content/uploads/2017/08/SA_Diptheria_Contact_Line-List_2017.pdf
- **The Diphtheria Alert communication, Circular H113/2017** – this document is valid for use. Please note, however that the 2016 guideline referred to in the circular, was updated and the revised NICD National Diphtheria guideline dated 28 of May 2018 is currently in use.

2.2 Updated Diphtheria case definitions specific for the cluster or outbreak:

- Diphtheria is a notifiable medical condition in South Africa. Complete the NMC form (available at http://www.nicd.ac.za/index.php/nmc/notifiable-medical-conditions-list/)
- **Adapted diphtheria case definitions for the outbreak has been compiled that includes the respiratory, cutaneous, or other clinical presentation of the disease. (Table 1)**
- Obtain detailed demographic, clinical and risk factor information. A case-investigation form (CIF) is available. Submit both forms (CIF and NMC) to the provincial and the district CDC focal person as well as emailing to NMCSurveillanceReport@nicd.ac.za and outbreak@nicd.ac.za
- Compile a case and contact line list and apply case definitions

Table 1: Case Definitions for the non-toxigenic diphtheria cluster/outbreak in Citrusdal/Paarl, June 2021	
Suspected case of diphtheria	Individual of any age resident in Citrusdal/Paarl with ANY of the following: • an upper-respiratory tract illness characterised by sore throat, low-grade fever or an adherent membrane of the nose, pharynx, tonsils, or larynx **OR** • a chronic skin lesion (may include scaling rash or ulcers with clearly demarcated edges) **OR** • fever or infection without a clear source **OR** • symptoms or signs of infective endocarditis **OR** • symptoms or signs of septic arthritis/osteomyelitis **OR** • a history of drug use **AND** presenting with non-specific symptoms or symptoms or signs consistent with an infection with no clear source
Confirmed case of diphtheria	Individual of any age resident in Citrusdal/Paarl with clinical presentation compatible with illness (as described above) AND with laboratory-confirmed C. diphtheriae (culture and/or PCR)
For case definitions of probable cases, and asymptomatic carriers, see Annexure 1: Quick Reference Guide for Diphtheria Outbreak, Western Cape Province, 28 June 2021	

- All public and private healthcare workers, laboratorians, and public health officials at district and sub-district levels are remined to report any cases meeting the case definition as stated below for respiratory diphtheria.

Table 2: Case Definitions for Respiratory Diphtheria	
Suspected case	A person who presents with an upper-respiratory tract illness characterised by sore throat, low-grade fever AND ***an adherent (pseudo-) membrane of the nose, pharynx, tonsils, or larynx.***
Confirmed case	A person who presents with an upper respiratory tract illness characterised by sore throat, low-grade fever and/or an adherent (pseudo-)membrane of the nose, pharynx, tonsils or larynx **AND** culture of *C. diphtheriae*, *C. pseudotuberculosis* or *C. ulcerans* which is confirmed to be toxin producing by ELEK or *tox* gene positive by PCR
For case definitions of probable & possible cases, and asymptomatic carriers, see page 11 in attached guideline.	

2.3 Public Health Response – Key Points

- These measures listed below must be implemented by both **public and private healthcare providers, health practitioners, sub-district, and district health offices.**

Table 3 Measures for implementation to ensure early detection and public health response to diphtheria cases

	Objective	**Action**
1.	**Intensify surveillance, notification, report and investigation of suspected diphtheria cases**	✓ **All suspected/probable/confirmed cases should be reported IMMEDIATELY to:** o the Infection Prevention and Control (IPC) Practitioners at health care facilities where applicable, as well as o District and Provincial Communicable Disease Control Coordinators / focal persons, urgently. ✓ Contact the Communicable Disease Control (CDC) sub-directorate: Ms Charlene A. Lawrence/Ms Babongile Ndlovu/Ms Washiefa Isaacs at 021-4839964/3156/6878/3737 (tel.), 086-6111-092 / 021-483-2682 (fax), 072-356-5146, 082-327-0394 (cell), if a suspected case is detected at your facility or diphtheria (toxigenic or non-toxigenic *Corynebacterium diphtheriae*) is identified at the laboratory.

		✓ Email: charlene.lawrence@westerncape.gov.za and babongile.ndlovu@westerncape.gov.za ✓ Infection prevention and control measures and supportive care must be initiated. ✓ The attached Diphtheria Case Investigation Form (CIF) found at: https://www.nicd.ac.za/wp-content/uploads/2017/08/Suspected-Diphtheria-Case-Investigation-Form.pdf and Diphtheria Contact Line List at can be used. ✓ Obtain detailed demographic, clinical and risk factor information. Submit both NMC (paper-based or electronic) form found on the following website: https://www.nicd.ac.za/nmc-overview/notification-forms/ , to the provincial and the district CDC focal person as well as emailing to NMCSurveillanceReport@nicd.ac.za and outbreak@nicd.ac.za
2.	**Adequate clinical management of cases**	✓ Isolation and treatment of the index case - administration of diphtheria antitoxin (DAT), antibiotics and immunisation (booster dose for confirmed and probable cases once clinically stable, with vaccine appropriate for age and immunisation history) ✓ See the attached guideline: Diphtheria: NICD Recommendations for Diagnosis, Management and Public Health Response, Version 3.0 (28 May 2018)
3.	**Public Health Response to a case or outbreak to diphtheria**	1. Conduct a detailed case investigation (demographic, clinical and risk factor information: case investigation form, case line list, case-contact line list 2. Identify close and at-risk contacts 3. Conduct laboratory investigation of close contacts and eligible at-risk contacts o Isolation of C. *diphtheriae* on culture and toxigenicity testing (Elek test) 4. Administer chemoprophylaxis to close contacts and at-risk contacts 5. Monitor close and eligible at-risk contacts (prophylactic antibiotics, booster vaccination appropriate for age, throat swabs for diphtheria diagnosis) 6. Exclude close and eligible at-risk contacts in high-risk occupations 7. Vaccinate close and eligible at-risk contacts 8. Alert other healthcare facilities in the area 9. Conduct health promotion activities and health education 10. Selective vaccination campaigns targeting at-risk groups in response to an outbreak may be required. 11. District and sub-district health authorities must put measures in place to improve the routine vaccination coverage in the primary series, and especially at 6 and 12 years of age.

Kindly bring the content of this alert/circular to the attention of all healthcare workers at your facility, institution, sub-district, and district.

We trust on your continued support in the early detection, report, investigation, and control of communicable diseases in the Western Cape Province.

DR SAADIQ KARIEM

DDG: CHIEF OF OPERATIONS

DATE: 30 June 2021

Annexure 1: Quick Reference Guide for a localised Non-toxigenic Corynebacterium diphtheria cluster / outbreak, in the Western Cape Province, 28 June 2021

Diphtheria infection is caused by the organism, Corynebacterium diphtheriae. Infection can be either toxigenic or non-toxigenic. Infection with toxigenic strains characteristically manifests with pharyngeal involvement. Non-toxigenic strains can cause skin infections and invasive disease, such as infective endocarditis and septic arthritis.

Treatment of a diphtheria case

1. Prevent transmission of *Corynebacterium diphtheriae* by practising contact and droplet precautions
2. Provide supportive care
3. Treat with antibiotics (any *C. diphtheriae*)
4. If clinical signs of toxigenic diphtheria and/or toxin production demonstrated, provide diphtheria antitoxin according to severity of illness and mass of patient (for toxigenic *C. diphtheriae* only)

Notification of cases:

- **Diphtheria is a category 1 notifiable medical condition and immediate reporting should be done electronically/paper-based within 24 hours of diagnosing a case**
- Please complete the NMC form and case investigation form and submit to provincial & district CDC coordinators and to the NICD: NMCSurveillanceReport@nicd.ac.za and outbreak@nicd.ac.za

Adapted diphtheria case definitions for Western Cape cluster (June 2021) includes respiratory, cutaneous or other clinical presentation:

1. Suspected case of diphtheria:
Individual of any age resident in Citrusdal/Paarl with **ANY** of the following:

- an upper-respiratory tract illness characterised by sore throat, low-grade fever or an adherent membrane of the nose, pharynx, tonsils, or larynx OR
- a chronic skin lesion (may include scaling rash or ulcers with clearly demarcated edges) OR
- fever or infection without a clear source OR
- symptoms or signs of infective endocarditis OR
- symptoms or signs of septic arthritis/osteomyelitis OR
- a history of drug use AND presenting with non-specific symptoms or symptoms or signs consistent with an infection with no clear source

2. Probable case of diphtheria:
Individual of any age resident in Citrusdal/Paarl with **ANY** of the following symptoms **WITHOUT** laboratory confirmation of *C. diphtheriae*:

- an upper-respiratory tract illness characterised by sore throat, low-grade fever AND an adherent membrane of the nose, pharynx, tonsils, or larynx OR
- a chronic skin lesion (may include scaling rash or ulcers with clearly demarcated edges) OR
- fever or infection without a clear source OR
- symptoms or signs of infective endocarditis OR
- symptoms or signs of septic arthritis/osteomyelitis OR
- A history of drug use AND presenting with non-specific symptoms or symptoms or signs consistent with an infection with no clear source

AND
with an epidemiological link to a confirmed case

3. Confirmed case of diphtheria:
Individual of any age resident in Citrusdal/Paarl with clinical presentation compatible with illness (as described above)
AND
with laboratory-confirmed *C. diphtheriae* (culture and/or PCR)

4. Asymptomatic carrier
Individual of any age resident in Citrusdal/Paarl, who is asymptomatic (with or without an epidemiologic link to a confirmed case) **AND** with laboratory-confirmed *C. diphtheriae* (culture and/or PCR)

*Please be aware that SARS-CoV-2 is circulating, and these symptoms may overlap. Ensure that suspected cases meeting case definitions for both pathogens are investigated appropriately and relevant guidelines are followed.

Sample collection from individuals with suspected diphtheria:

1. Collect samples from specific sites where infection is suspected e.g., tissue, pus swab from abscess or cutaneous lesion/non-healing ulcer
2. If suspected bacteraemia, collect at least 2 blood specimens at different times for blood culture
3. Collect an oropharyngeal swab (ideally in Amies transport medium)

Laboratory identification of *C. diphtheriae*:

1. Plate swab/tissue for single colonies on
   a) Blood agar (incubate at 37°C in CO_2 for 24 hours) and
   b) Hoyle's agar (incubate at 37°C in O_2 for 48 hours)
2. *C. diphtheriae* form black colonies on Hoyle's. Other organisms (e.g., enterococci and certain staphylococci) grow as black colonies on Hoyle's
3. *C. diphtheriae* are catalase-positive, Gram-positive bacilli - confirm identification using API Coryne, VITEK or MALDI-TOF
4. Submit culture and any clinical specimens to NICD for confirmation, ELEK and PCR. Please include specimen submission form clearly indicating suspected diphtheria

Management of close contacts:

1. Identify 'close' and 'at-risk' contacts
2. Identify if any respiratory and/or chronic skin lesions (may include scaling rash or ulcers with clearly demarcated edges) are present
3. Collect an oropharyngeal swab and/or skin swab from contacts and complete contact line list
4. Administer chemoprophylaxis after swab collection
5. Vaccinate contacts appropriately (depending on vaccination status and if toxigenic *C. diphtheriae* is detected or suspected in the case)
6. Monitor contacts for 10 days for symptoms or development of skin lesions
7. Collect follow-up swabs (from contacts that were culture or PCR positive for *C. diphtheriae*) after completion of chemoprophylaxis
8. Repeat chemoprophylaxis if contacts are still *C. diphtheriae* positive

Recommendation for laboratories:

1. Please routinely screen all oropharyngeal (OP), nasopharyngeal (NP), and abscess or cutaneous lesion swabs for *C. diphtheriae*
2. Please identify *Corynebacterium* spp. to species level if isolated from blood cultures within 2 days of incubation
3. Please send any suspect or confirmed isolates of *Corynebacterium* spp. to the NICD for identification/confirmation and for further characterisation (including cutaneous isolates)
4. Please include the original specimen (NP/OP or abscess/cutaneous lesion swab, pseudomembrane tissue, blood or blood culture fluid) for PCR testing
5. Please also send culture-negative swabs/specimens to NICD for PCR testing

NICD Contact details: NICD Hotline: 082 883 9920

- Clinical queries: Dr Anne von Gottberg (011-555-0316, annev@nicd.ac.za, Dr Sibongile Walaza (011-386-6321, sibongilew@nicd.ac.za)
- Microbiology Laboratory Manager: Mrs Linda de Gouveia (011-555-0327, lindad@nicd.ac.za)
  Molecular laboratory: Dr Mignon du Plessis (011-555-0387, mignond@nicd.ac.za), Dr Nicole Wolter (011-555-0352, nicolew@nicd.ac.za