**b Diphtheria**

An 8-year-old boy was referred from a secondary hospital to Inkosi Albert Luthuli Central Hospital in Durban (KwaZulu-Natal Province) on 15 March 2015 for urgent assessment. There was a three-day history of fever and sore throat with progressive difficulty in swallowing and breathing, and a one-day history of swelling of the neck. Clinically, the child was severely ill; he had a massively swollen anterior neck (‘bull neck’) with marked drooling and respiratory distress. On oropharyngeal examination, massive swelling of the tonsils and a whitish membrane covering the uvula was noted. An emergency tracheostomy was performed, following which the child was transferred to the intensive care unit for further management. A sample of the pseudomembrane and a tonsillar swab were collected and submitted to the bacteriology laboratory for routine microscopy and culture, as well as culture on selective media for *Corynebacterium diphtheriae*. Penicillin, gentamycin, and metronidazole were administered to the patient.

Given the highly suggestive clinical presentation, the case was notified to provincial and city health authorities as a suspected diphtheria, and specific patient management and appropriate public health response were initiated.

The child’s mother confirmed that he had received diphtheria-containing vaccine at 6, 10 and 14 weeks of age and a booster at 18 months of age, but he had not received a booster dose at 6 years of age; through the EPI programme, diphtheria immunisation is offered at 6, 10 and 14 weeks of age with boosters at 18 months as well as 6 and 12 years of age.

The NHLS bacteriology laboratory at Inkosi Albert Luthuli Central Hospital isolated *C. diphtheriae* from the clinical samples. The *C. diphtheriae* isolate was then sent to NHLS Green Point Complex media laboratory for toxigenicity testing using the Elek test. A positive Elek test result showed that the isolate produced toxin, and confirmed the clinical diagnosis of diphtheria.

Diphtheria antitoxin (DAT) therapy was not warranted in this case, given the duration and stage of illness. Despite an initial improvement and subsequent step-down from the intensive care unit, the child developed unexpected complications and died on 22 March 2015.

**Focus on respiratory diphtheria**

Respiratory diphtheria is caused by toxin-producing strains of *C. diphtheriae*, and rarely by toxigenic strains of other *Corynebacterium* species (*C. ulcerans*, *C. hemolyticum* or *C. pseudotuberculosis*). It is infrequently reported in South Africa; a case of suspected respiratory diphtheria was reported in the September 2013 Communiqué, and the last laboratory-confirmed case of respiratory diphtheria in South Africa occurred in February 2010 (reported in the February 2010 Communiqué). Although uncommon in South Africa, there is concern that this potentially lethal disease may resurge, as it has in other regions of the world over the past decade - most notably Eastern Europe, Southeast Asia, South America and the Indian subcontinent.

It is important that clinicians are aware of the range of clinical presentations and appropriate diagnostic investigations in order to detect cases timeously and limit mortality. A presumptive diagnosis of respiratory diphtheria may be based on a number of clinical clues, including: mildly painful tonsillitis/pharyngitis associated with an exudate/membrane; adenopathy and cervical swelling; hoarseness and stridor; palatal paralysis; serosanguinous nasal discharge with associated mucosal membrane (‘pseudomembrane’), and low-grade fever. The pseudomembrane is typically grey, thick, fibrinous and firmly adherent. Mild cases of disease mimic streptococcal pharyngitis, and the pharyngeal pseudomembrane may not develop, particularly in vaccinated people. The classic presentation of toxic diphtheria is associated with extensive pseudomembranous pharyngitis, massive swelling of the tonsils, uvula, cervical lymph nodes, submandibular region, and anterior neck (‘bull neck’). Laryngeal diphtheria presents as gradually worsening hoarseness and stridor, usually as an extension of pharyngeal involvement in children. Nasal diphtheria is characteristically a mild, chronic illness with serous/serosanguinous nasal discharge.

Absorption of diphtheria toxin from the site of infection can cause systemic complications, including cardiac toxicity (myocarditis, acute congestive failure), neurotoxicity (paralysis of soft palate, cranial neuropathies and peripheral neuritis) and renal toxicity (renal failure). Confirmation of the diagnosis relies on the isolation of toxigenic *C. diphtheriae* from appropriate specimens; specimens should be taken from the nose and throat, and from beneath the membrane, if present. Multiple site sampling should always be considered in a suspected case as this may increase the organism recovery rate. The specimens must be...
sent to the laboratory immediately since rapid inoculation of selective culture media is extremely important for organism recovery; if the transportation is likely to be delayed, the specimens must be submitted in a suitable transport medium (e.g. Amies). The laboratory must be contacted beforehand to ensure that the selective media is available and that the specimen is processed immediately on arrival. Following isolation of *C. diphtheriae*, the isolate/s is subjected to testing for toxigenicity since non-toxigenic *C. diphtheriae* may be isolated, but do not cause clinical diphtheria.

The mainstay of treatment of a suspected diphtheria case is prompt administration of DAT; this should be given without waiting for laboratory confirmation of a diagnosis. DAT only neutralises toxin before its entry into cells so it is critical that DAT be administered as a matter of urgency. The recommended dosage and route of administration depend on the extent and duration of disease. Antibiotics should also be given, in order to eradicate carriage of the organism, limit transmission, and stop further production of diphtheria toxin. The current recommendations for antibiotic therapy of diphtheria include erythromycin or penicillin.

Unfortunately, there are currently few manufacturers of DAT globally and supplies are limited to few facilities/institutions worldwide. South Africa does not stock any supplies of DAT, and it must be sourced from overseas suppliers on a case-by-case basis through an emergency MCC Section 21 application.

Diphtheria is a notifiable disease in South Africa and all suspected cases must be reported to the Department of Health authorities. Management of contacts should include screening for possible respiratory diphtheria, obtaining nasopharyngeal cultures for *C. diphtheriae*, administering chemoprophylaxis, and assessing diphtheria vaccination status.

Source: Division of Public Health Surveillance and Response, NICD-NHLS; Microbiology Laboratory, NHLS KwaZulu-Natal Academic Complex; Diagnostic Media Production Laboratory, NHLS Green Point Complex; Clinicians at Inkosi Albert Luthuli Central Hospital, KwaZulu-Natal Province; KwaZulu-Natal Province Department of Health