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# Characterisation of *Corynebacterium diphtheriae* isolates in the Northern Territory of Australia

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## Abstract

This article summarises our review of 41 *Corynebacterium diphtheriae* wound swab isolates from the tropical Northern Territory of Australia. On polymerase chain reaction and whole genome sequencing, no isolates were toxigenic strains.

Keywords: *Corynebacterium*; diphtheria; tropical; wounds; phage; toxin

We reviewed the toxigenic potential and phylogeny of *Corynebacterium diphtheriae* from skin isolates in the Northern Territory (NT) of Australia. *C. diphtheriae* is a human-only pathogen found throughout the NT; it is a common laboratory isolate from skin swabs.<sup>1</sup> Geographically, the Top End of the Northern Territory is a region of almost 250,000 km<sup>2</sup> with a tropical climate and *C. diphtheriae* is frequently endemic in tropical regions. *C. diphtheriae* is often a component of polymicrobial wound cultures.

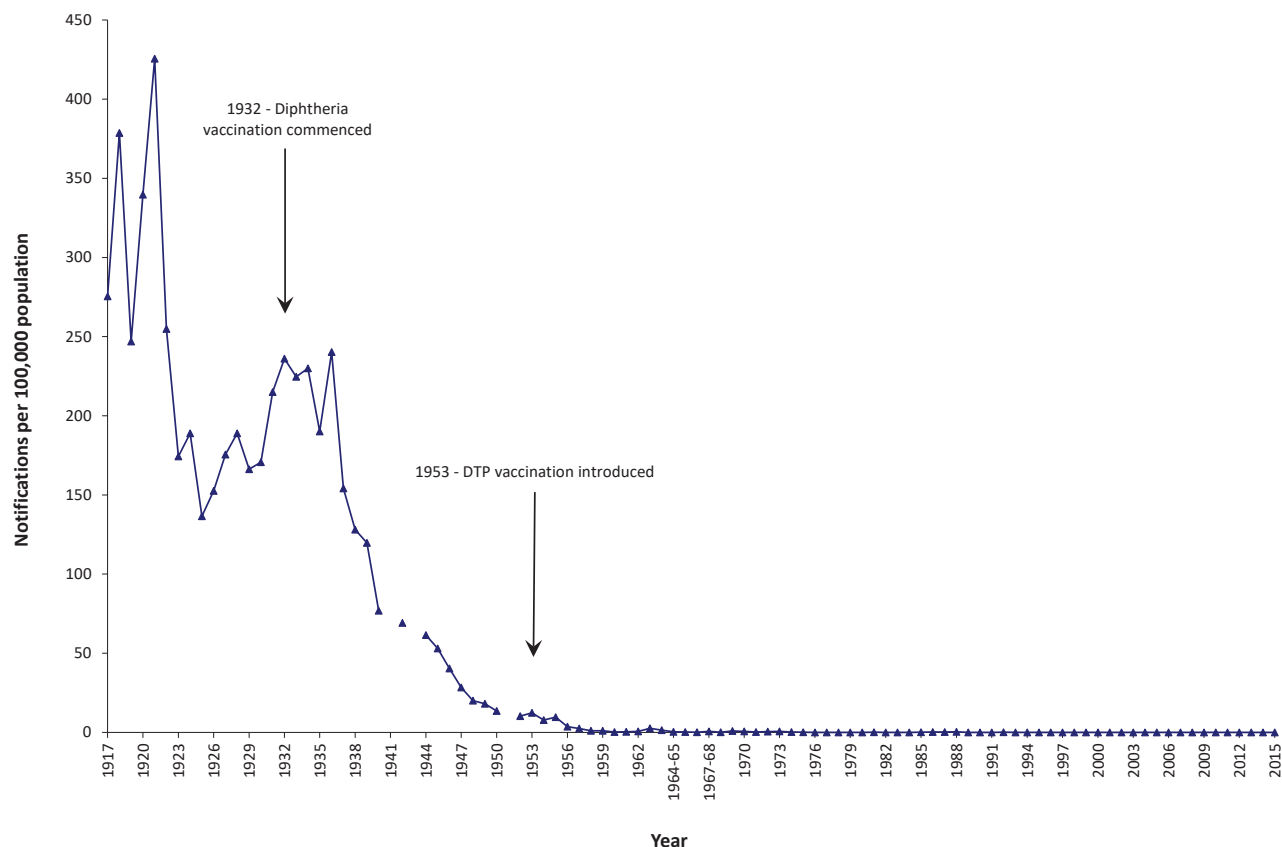
Strains of *C. diphtheriae* can be divided into those that produce toxin (toxigenic strains) and those that do not (non-toxigenic strains). Toxigenic strains of *C. diphtheriae* are the commonest causative agent of respiratory diphtheria, a potentially fatal clinical syndrome.<sup>2</sup> Toxigenic diphtheria is very rare in the NT, with only one toxigenic isolate recorded since 1992 in a worker returning from East Timor.<sup>3</sup> Notifications have significantly reduced since the early twentieth century, largely due to vaccination (introduced in 1932) as demonstrated in Figure 1.

A prospective and retrospective review of *C. diphtheriae* isolates within the NT, in 2011, demonstrated no toxin-positive strains from a five-year period.<sup>1</sup> *C. diphtheriae* from wound isolates are not routinely tested for toxins due to low rates. There has been public health concern

with recent cases of diphtheria in unvaccinated children in New South Wales<sup>5</sup> and Queensland,<sup>6</sup> and a review from 2022 highlighted that 98% of diphtheria notifications in Australia between 1999 and 2019 occurred after 2011.<sup>7</sup> We therefore set out to interrogate *C. diphtheriae* in a tropical centre to ensure that we were not missing asymptomatic carriage of toxin-producing organisms. There is concern that asymptomatic carriage of toxigenic strains in wounds can disseminate to close contacts causing disease as has been previously described, particularly amongst unvaccinated individuals.<sup>8,9</sup> Twenty-two cases of toxigenic cutaneous diphtheria epidemiologically linked to a North Queensland strain have been identified between 2020 and 2022.<sup>6</sup>

Forty-one *C. diphtheriae* isolates from clinical specimens were collected prospectively during the period 1 August – 30 November 2022. The *C. diphtheriae* isolates were collected from wound and skin swabs. There were no isolates from throat swabs during this period. *C. diphtheriae* specimens then underwent in-house polymerase chain reaction (PCR) for toxin detection,<sup>10</sup> and were subjected also to whole genome sequencing for the presence of toxin-producing genes and the examination of phylogeny. No clinical data were collected and therefore no ethics application was sought.

Figure 1: Diphtheria notifications (1917–2015) for Australia<sup>a</sup>



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Of the 41 *C. diphtheriae* isolates, none were found to be toxin positive on in-house PCR. On whole genome sequencing and utilisation of toxin pipelines TAFinder,<sup>i</sup> a single specimen, S21, recorded presence of a protein associated with toxin/antitoxin (DIP0007/DIP0008). On further analysis, this has not been noted elsewhere in other toxin-producing strains and therefore is likely to be a false positive. A phylogenetic tree with a known toxin-producing strain as reference is shown in Figure 2.

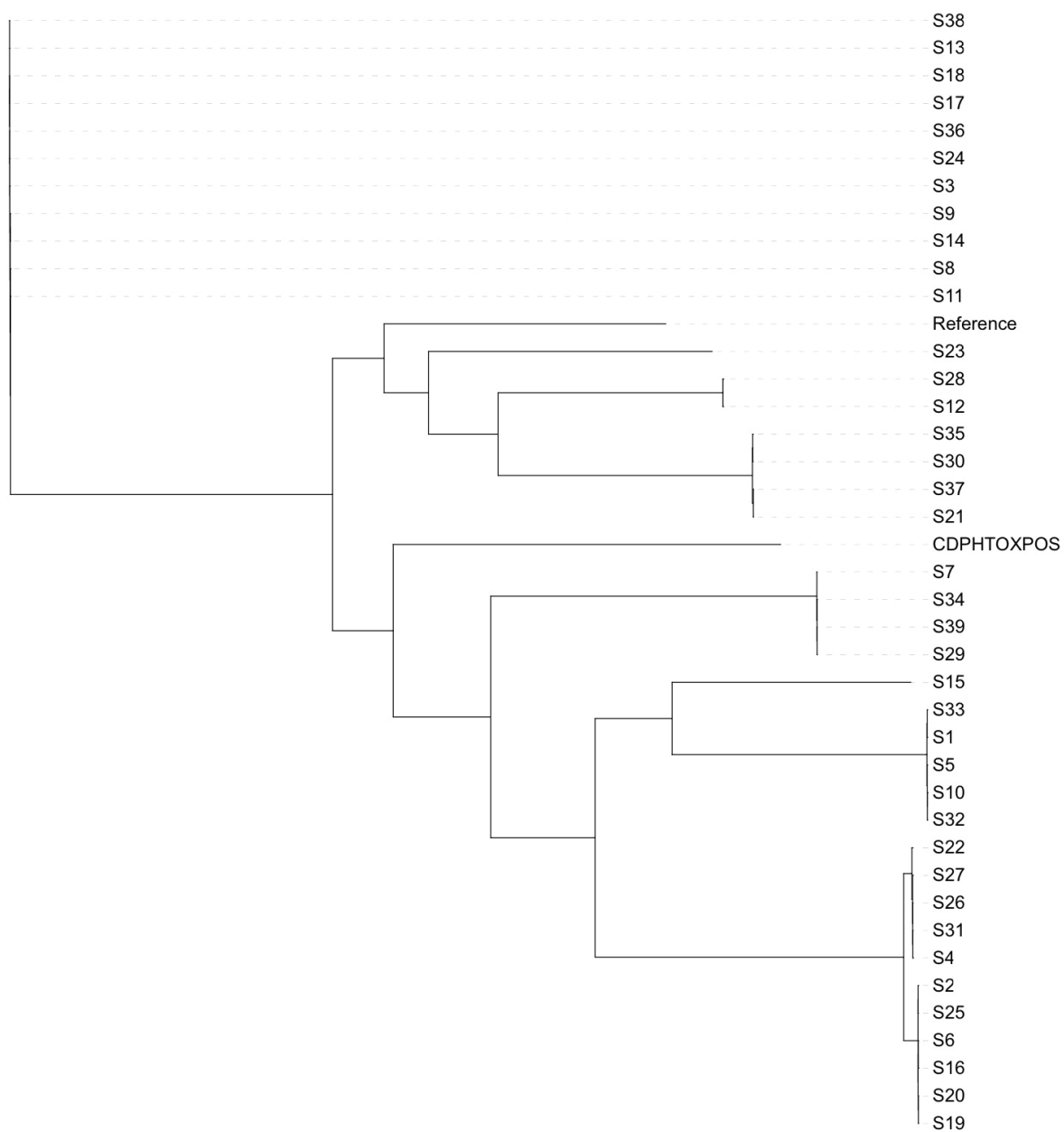
A review of all *C. diphtheriae* isolates from the start of the year revealed 148 isolates from 117 patients with not a single isolate from throat swabs. All wound swabs were polymicrobial.

This analysis highlights the frequency of *C. diphtheriae* in wound culture in a tropical setting but rarity in throat carriage. These

data provide reassurance that despite occasional cases of severe disease in Australia, our relatively high number of skin isolates do not translate into clinical diphtheria. Maintaining high rates of vaccination is essential to reduce the risk of toxigenic carriage translating into severe disease.

<sup>i</sup> <http://bioinfo-mml.sjtu.edu.cn/TADB2/>.

Figure 2: A single nucleotide pair (SNP) distance-based maximum likelihood phylogenetic tree of *C. diphtheriae* isolates<sup>a</sup>



a Tree was constructed using the FASTTREE bioinformatics tool.

## Author details

Matthew Howes,<sup>1</sup>  
Dimitrios Menouhos,<sup>1</sup>  
Stefanos Christofis,<sup>1</sup>  
Jann Hennessy,<sup>1</sup>  
Rob Baird<sup>1</sup>

1. Territory Pathology, Royal Darwin Hospital,  
Rocklands Drive TIWI NT 0810 Australia

## Corresponding author

Matthew Howes  
Territory Pathology, Royal Darwin Hospital,  
Rocklands Drive TIWI NT 0810 Australia.  
email: Mathew.Howes@nt.gov.au

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