

TITLE: ISOLATION OF *Corynebacterium diphtheriae* AND *Corynebacterium ulcerans* FROM CLINICAL SPECIMENS IN BRAZIL: AN ALERT TO BRAZILIAN PUBLIC HEALTH

AUTHORS: ARAÚJO, M.R.B.¹; SANT'ANNA, L.O.²; SANTANA, G.S.²; CUCINELLI, A.E.S.²; MATTOS-GUARALDI, A. L.²; SANTOS, L.S.²

INSTITUTIONS: ¹INSTITUTO HERMES PARDINI (AV. DAS NAÇÕES, 2448, CEP 33200-000, VESPASIANO - MG, BRASIL);²UNIVERSIDADE DO ESTADO DO RIO DE JANEIRO, RIO DE JANEIRO, RJ (AV. 28 DE SETEMBRO, 87, 3º ANDAR, CEP 20551-030, RIO DE JANEIRO - RJ, BRASIL).

ABSTRACT:

Diphtheria toxin (DT), the main factor associated with diphtheria severity, is produced by *Corynebacterium diphtheriae* and other related species that harbor the *tox* gene. Among them, *Corynebacterium ulcerans*, a zoonotic pathogen, emerged as the main causative agent of diphtheria in some countries. Non-DT-producing strains of *C. diphtheriae* and *C. ulcerans* are a matter of concern worldwide since they are also able to cause severe infections in humans. Furthermore, these strains can acquire the *tox* gene and thus contribute to the emergence of diphtheria cases, especially in susceptible populations. In the last years, mainly during the COVID-19 pandemic, the coverage of the diphtheria vaccine declined in many countries, including Brazil. Moreover, the vaccination with booster doses among young and adults remained very low. In this context, the isolation of *C. diphtheriae* and *C. ulcerans* strains, even non-DT producing, needs to be considered. Thus, the present work aimed to report the isolation of diphtheria bacilli strains from clinical specimens during 2020 and 2021 in Brazil. The strains were identified by MALDI-TOF mass spectrometry and the antimicrobial susceptibility profiles were determined by the disk diffusion method. The presence of the *tox* gene was investigated by Polymerase Chain Reaction assays. Among the 12 isolated strains, 6 were identified as *C. diphtheriae* and the others as *C. ulcerans*. The *tox* gene was not detected in any of them. Half of *C. diphtheriae* strains (n=3) was isolated from humans, 1 from an elderly, all from male patients, and mainly from lower limb lesions (n=4). *C. ulcerans* strains were mostly recovered from humans (n=4), elderly and female, and mainly from the lower limbs (n=5). Although all strains were susceptible to linezolid, tetracycline and vancomycin, penicillin resistance was detected in both *C. diphtheriae* (n=2) and *C. ulcerans* (n=3) isolates. Resistance to clindamycin (n=4) and ciprofloxacin (n=1) was also found among *C. ulcerans* strains. Intermediate susceptibility to ciprofloxacin was detected in 3 strains of each species. Data showed that diphtheria bacilli remain circulating in all Brazilian regions, which may represent a risk for the appearance of diphtheria and other severe infections. Finally, resistance to antimicrobials, particularly to penicillin, the first-line agent for the treatment of *C. diphtheriae* and *C. ulcerans* infections, alerts to the possibility of therapeutic failure in empirical treatment.

Keywords: *Corynebacterium diphtheriae*, *Corynebacterium ulcerans*, diphtheria toxin, drug resistance, mass spectrometry.

Development Agency: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - CAPES; Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro - FAPERJ.