UK Health Security Agency

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Evolving cluster of severe infective endocarditis with non-toxigenic C. *diphtheriae* involving people experiencing homelessness and people with substance misuse (including powder or crack cocaine)

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Authorised by:
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IRP Level: Routine

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Instructions for Cascade

- UKHSA Regions Directorate and Regional Deputy Directors for onward cascade to:
  - UKHSA Field Services
  - UKHSA Health Protection Teams
  - Directors of Public Health
- UKHSA Lab Management Teams
- UKHSA microbiologists/Consultants in Public Health Infection to cascade to non-UKHSA labs (NHS labs and private) and NHS Trust infection leads
- **NHS labs/NHS infection leads/NHS microbiologists/NHS infectious disease specialists** to cascade to ID, ED, cardiology, cardiothoracic teams, microbiology departments
- UKHSA Health Equity & Inclusion
- UKHSA Regional Communications
- DHSC CMO, DCMOs
- OHID Regional Directors of Public Health and Drug & Alcohol teams
- Local Authority colleagues to cascade via Local Drug Information Systems and Professional Information networks
- **NRC to circulate to:**
  - Royal College of Emergency Medicine - president@rcem.ac.uk
  - Royal College of General Practitioners - Chair-RCGP@rcgp.org.uk
  - Royal College of Physicians - sarah.clarke@rcp.ac.uk
  - Faculty of Public Health - president@fph.org.uk
  - Faculty for Homeless and Inclusion Health
  - Royal College of Surgeons of England - president@rcseng.ac.uk
- **Devolved Administrations & Crown Dependencies**

Summary:

The UKHSA are currently investigating reports of non-toxigenic C. *diphtheriae* presenting with severe, fulminant infective endocarditis (IE). Initial case finding has identified 5 cases with onsets from July 2024 to the present date. The majority are young males (30 median; range 23–52 years) with a history of inhalation, smoking or nasal insufflation of heroin or crack cocaine/powdered cocaine. All cases report no intravenous drug use (IVDU), although one acknowledged past use. A significant proportion (60%) have been street homeless in London, although single cases are noted to be resident in the East of England and South-East England.

Cases had rapid disease progression with large vegetations and marked tissue destruction requiring valvular surgery and multiple embolic episodes despite appropriate intravenous antibiotic therapy. One case has died.

Non-toxigenic C. *diphtheriae* has been isolated in blood cultures from all cases in this investigation and strain typing is underway.

Background and Interpretation:

Non-toxigenic C. *diphtheriae* may be associated with severe endocarditis, but it is uncommon and has historically been associated with underlying cardiac risk factors and often a history of intravenous drug use. Cutaneous *C. diphtheriae* skin colonisation has been associated with street homelessness[i].

Case series of IE have been reported from New Zealand (10 cases in 14 years)[ii] and Australia, (7 in a single year in 1993, including one death)[iii]. More recently a case series was reported from South Africa describing five clinically severe IE cases with a high case fatality (80%) and associated with a novel sequence type of non-toxigenic *C. diphtheriae* (ST885). Whilst these cases were all reported in 2021 from the same area, no other epidemiological links were found. One individual reported polysubstance misuse and only one had cardiac risk factors[iv].

Individual case reports detail the speed of disease progression and severity. De Santis et al report a young male cocaine user, who reported no IVDU, with an acute presentation of endocarditis and septic shock, with no previous cardiac risk factors[v]. The authors postulate direct injury to the nasal mucosa providing a point of entry within an airway colonized with non-toxigenic C. *diphtheriae* leading to bacteraemia.

A routine incident has been stood up. UKHSA will work with partners to:

- Raise awareness amongst clinicians to ensure early diagnosis and treatment
- Raise awareness amongst drug and alcohol services and those working with the homeless population to facilitate access to appropriate care
- Undertake rapid case finding to investigate the extent of the issue
- Establish enhanced surveillance to better understand the epidemiology, risk factors for severe infection and contributing factors
- Characterise the organism further to support epidemiological assessment
- Investigate the prevalence of non-toxigenic C. *diphtheriae* in high-risk communities
- To work with partners to review potential common sources of C. *diphtheriae* infection including the possible microbiological contamination of products.

Implications & Recommendations for UKHSA Regions:

- HPTs are asked to continue to inform the national diphtheria team of clinically suspected diphtheria cases or reports of local isolates of C. *diphtheriae* being sent to the reference lab on: diphtheria_tetanus@ukhsa.gov.uk. HPTs are asked to document on CIMS available information on clinical presentation,

including consideration of IE, and basic risk factor information e.g. substance misuse and homelessness or rough sleeping.

- Cases with C. *diphtheriae* isolated from a **sterile** site that are found to be non-toxigenic in the reference lab will be referred back to the HPT to collate further information. An ES questionnaire is being developed and HPTs/Field Services will be asked to support completion with the supervising clinician.
- Cases and contacts should be managed in line with current national diphtheria guidance (noting contact tracing and prophylaxis is not required around non-toxigenic cases).

Implications & Recommendations for UKHSA sites and services:
Microbiologists are reminded of the importance of further testing/investigation of Corynebacterium species identified in blood and their potential clinical significance.

To refer all local isolates of C. *diphtheriae* to the RVPBRU for toxin-gene testing and to undertake local sensitivity testing to inform antibiotic treatment.

Implications & Recommendations for NHS:
Clinicians are asked to:

- Consider C. *diphtheriae* isolates from sterile sites, including blood cultures as significant and refer isolates to the RVPBRU
- To consider early echocardiography in cases with C. *diphtheriae*, even in the absence of classical cardiac risk factors for IE or a history of intravenous drug use
- To discuss all cases of IE with non-toxigenic C. *diphtheriae* with regional cardiology/cardiothoracic specialist centres, as early surgical intervention is key to improved outcomes
- To report cases of IE with non-toxigenic C *diphtheriae* to the local health protection team to allow further monitoring and characterisation of cases through enhanced surveillance.

Implications and recommendations for Local Authorities:
To cascade this alert through Local Drug Information Systems (LDIS) and Professional Information Networks (PINS). Additional advice will follow on further investigation of this incident.

References/Sources of information

[i] Lowe et al, 2011 zjm2664.pdf
[ii] Corynebacterium diphtheriae endocarditis: a case series and review of the treatment approach
[iii] National diphtheria guidance Public health control and management of diphtheria
[iv] Lovelock et al 2024 Non-toxigenic Corynebacterium diphtheriae endocarditis: A cluster of five cases - PMC
[v] Santis et al 2020 Non-toxigenic Corynebacterium diphtheriae infective endocarditis with embolic events: a case report - PMC