UK Health Security Agency

Serial number **2023/026** **Date** **15th September 2023**

Event: **Updated guidance on the management of cases of diphtheria amongst asylum seekers and an update on enhanced surveillance**

Notified by: **Immunisations and Vaccine Preventable Diseases Division, UKHSA**

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NIERP Level: **National Standard**

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Instructions for Cascade

- **Devolved Administrations** to cascade to Medical Directors and other DA teams as appropriate to their local arrangements
- **Regional Deputy Directors** to cascade to Directors of Public Health, Local Authority Public Health teams, NHS Screening and Immunisation teams and ICBs for onward cascade to primary care
- **CPHIs/Regional Heads of Operations** to cascade to NHS microbiology laboratories, laboratory managers and microbiologists
- **UKHSA microbiologists** to cascade to non-UKHSA labs (NHS labs and private)
- **UKHSA microbiologists** to cascade to NHS Trust infection leads
- **NHS labs/NHS infection leads/NHS microbiologist/NHS infectious disease specialists** to cascade to NHS hospital ED, ID, ENT, paediatric and general medicine physicians, Infection Prevention and Control teams, Directors of Infection Prevention and Control laboratories, microbiologists, and others who may be involved in the testing and treatment of suspected cases of diphtheria

Background and Interpretation:

This is an update to BNs 2022/082, 2022/089 and 2022/93, published September and November 2022, and BN 2023/007, published February 2023

Recent Epidemiology

The incidence of diphtheria caused by toxigenic *Corynebacterium diphtheriae* amongst asylum seekers (AS) in England declined in early 2023, with only 1 case identified in January and then none further until an uptick over the summer with 3 confirmed cases in August 2023 and a further 4 cases identified as of 14th September (1 cutaneous and 3 mild respiratory).

These individuals are largely being identified during early medical assessments on arrival, with only two initially asymptomatic or mildly symptomatic individuals being picked up

through enhanced surveillance. Surveillance was established in July 2023 to estimate prevalence in unaccompanied asylum-seeking children (UASC) arrivals and to inform future recommendations (see below).

From 1st January – 8th August 2023, 57 cases of diphtheria have been reported in the EU/EEA through the European Surveillance System (TESSy)[2]. Cases have been reported in Germany (35), Belgium (6), Czechia (5), the Netherlands (5), Latvia (3), Norway (1), Slovakia (1) and Sweden (1). This represents an increase of 7 cases since the previous update on 10th July 2023. 36 of these cases were caused by C. *diphtheriae* although no distinction is made between those identified in the asylum seeker versus wider population, although the report notes there remains no information on community transmission or outbreaks in the broader EU or EEA population. 2 fatal cases have been reported during this period, both respiratory presentations of C. *diphtheriae*.

Whilst the majority of cases of toxigenic diphtheria in AS in England last year were generally mild in presentation, three severe respiratory cases were identified. The deaths in Europe are a reminder of the potential seriousness of this infection and the need for early diagnosis, prompt assessment for the need for DAT treatment, antibiotic therapy, and vaccination.

Laboratory Testing

It is strongly recommended that local laboratories undertake antimicrobial susceptibility testing on all *C. diphtheriae* isolates, to include as a minimum, susceptibility to penicillin and erythromycin (according to local methods and reported using the EUCAST Clinical Breakpoint Tables version 13.1 (29 June 2023)[13]. All erythromycin resistant isolates (R> 0.06 mg/L) should be referred to the UKHSA Respiratory and Vaccine Preventable Bacteria Reference Unit (RVPBRU) for confirmation of resistance and testing of alternative agents and the local health protection team informed urgently.

Macrolide resistant strains

Macrolide resistant *C. diphtheriae*, in combination with resistance to additional antibiotics, has been detected in two recent cases in asylum seekers in England. As per supplementary AS guidance, it is recommended that, for such macrolide resistant cases, an incident management team (IMT) is stood up with representation from regional and national UKHSA teams, as well as NHS and ICB colleagues as appropriate[7]. This is to ensure appropriate clinical oversight, treatment and clearance.

Principles for macrolide resistant C. diphtheriae confirmed on susceptibility testing:

- For mild or asymptomatic cases, where EUCAST clinical breakpoints v.13.1 have indicated susceptibility (increased exposure) to either penicillin or amoxicillin, amoxicillin 1g tds for 14 days may be used.
- All macrolide resistant strains received in the reference laboratory to date have remained susceptible to linezolid. Consideration should be given to the drug cautions, interactions, side effects and safety information as outlined in the BNF. A Full blood count (including platelet count) is required after 7 days to monitor for blood disorders. Patients should be warned to report symptoms of visual impairment.
- It is recommended that the clinical management of macrolide resistant cases be supervised by infectious diseases teams.

- Post treatment clearance swabs x 2 sets (nose, throat and any lesion), to commence 24 hours after completion of antibiotic course and a minimum of 24 hours apart
- Screen and arrange prophylaxis for all close contacts (as directed by IMT)
- Re-screen all close contacts post clearance of case (if ongoing exposure to case in household setting during clearance).

Antibiotic options for macrolide resistant C. diphtheriae isolates

Case treatment & contact prophylaxis	**Severity**	**Adult dose**	**Duration**
Linezolid*	All	600 mg every 12 hours IV/PO	10-14 days
High dose amoxicillin** (when susceptible on EUCAST testing)	Asymptomatic – mild	1g 3 times a day PO	14 days
Vancomycin***	Moderate – severe in-hospital management	15-20 mg/kg every 8-12 hours by intravenous infusion (maximum per dose 2g) adjusted according to plasma-concentration monitoring.	IV to oral switch when possible

*prescription of linezolid should be supervised by a microbiologist or ID physician to ensure appropriate monitoring is in place. **The IMT will advise on repeat swabs for PCR testing during linezolid treatment which may support shorter course duration.**
** isolates "susceptible, increased exposure" (I) to benzylpenicillin can be reported susceptible to amoxicillin. Isolates resistant to benzylpenicillin should be tested for susceptibility to amoxicillin or reported resistant.
*** in the absence of EUCAST clinical breakpoints for vancomycin for *C. diphtheriae* EUCAST guidance 'When there are no breakpoints in the breakpoint tables' should be followed.

Updates to mass antibiotic and vaccination programme

The mass antibiotic and vaccination programme was implemented from November 2022 due to increasing difficulties in maintaining individual-level case management and contact tracing in high-volume settings. These arrangements remain in place over this summer and autumn whilst new arrival numbers remain high and pending reassurance that individual case and contact management can be reliably delivered. Details of the interventions are outlined in the Supplementary guidance for cases and outbreaks in AS accommodation settings (see Guidance page on GOV.UK).

Enhanced surveillance

Prevalence of diphtheria amongst new arrivals to the UK is influenced by their country of origin which changes over time, as will travel routes, settings stayed in and access to healthcare during long journeys. UKHSA, together with Home Office and NHS colleagues, established enhanced surveillance within a subgroup of accommodation settings for AS to monitor prevalence of toxigenic diphtheria, particularly in asymptomatic individuals. This commenced in July 2023 in hotel settings for unaccompanied AS minors in Kent. Over 200 individuals were screened, and 2 individuals were identified with toxigenic C.

diphtheriae that had not been detected through health checks undertaken prior to this screening. This surveillance is now being implemented at the Manston Reception Facility for single adult males, and families with small children. A maximum of 200 samples each week will be taken from an opportunistic sample of new arrivals. These samples are being taken at the point at which they are offered antibiotic prophylaxis and vaccination for diphtheria (see Appendix A). Any individuals with a positive result will be notified to the SE HPT and the enhanced surveillance team and their current location identified via the Home Office, to allow onward notification to the appropriate HPT for case and contact management.

Updates to guidance and resources

There are two key sets of national guidance to support the management of diphtheria, the Public health control and management of diphtheria in England and Supplementary guidance for cases and outbreaks in AS accommodation settings (see Guidance page on GOV.UK). The following updates have been made to the national guidance:

- New antibiotic treatment dosing tables for confirmed cases and close contacts (including guidelines for paediatric dosing).
- Importance of anti-microbial susceptibility testing for all *Corynebacterium* isolates
- Clarification of risk assessment for contact with cutaneous cases and updates to IPC measures
- Clarification on swabs required for clearance testing (both guidance documents)

And in the Supplementary guidance for AS:

- Guidance on the management of asymptomatic carriers and their close contacts

In addition, a diphtheria training slide set for laboratory staff will be available on the Diphtheria page on GOV.UK later this month.

Implications and Recommendations for UKHSA Regions

UKHSA Regions should implement the amended guidance as described above. All suspected cases should be notified to the local HPT. **HPTs are requested to add the context Diphtheria 2022/23 to all cases and situations on HPZone.**

Further advice can be sought from the UKHSA Colindale duty doctor in and out of hours (020 8200 4400) if DAT is being considered, following a local clinical assessment. Additional resources are available on GOV.UK webpages including general information and clinical guidance on the use of diphtheria anti-toxin (DAT) and a training slide set for clinicians and HPTs.

Implications for UKHSA sites and services

Laboratories may receive increased requests for diphtheria testing and should be aware that regional labs can accept referrals where necessary to facilitate this increase. Public Health regional labs should expect to receive clearance samples from confirmed cases.

As a minimum, all confirmed *C. diphtheriae* isolates should undergo susceptibility testing against erythromycin and penicillin according to local methods, and reported using the EUCAST Clinical Breakpoint Tables v.13.0. If resistance to either penicillin (R> 1 mg/L) or erythromycin (R> 0.06 mg/L) is detected, further antimicrobial susceptibilities are recommended to include amoxicillin, tetracycline, trimethoprim-sulfamethoxazole, and fluoroquinolones (ciprofloxacin). If the patient requires parenteral antibiotics, then

vancomycin +/- linezolid should ideally be tested. Macrolide resistance should be reported to the local HPT, and when these isolates are submitted for toxigenicity testing, typing and antimicrobial susceptibility confirmation will also be performed on these isolates.

Samples from the enhanced surveillance are being tested in the UKHSA PH laboratories in Bristol and Cambridge.

Implications and recommendations for local authorities

HPTs are asked to work with LA and NHS colleagues and others to enable appropriate messaging and training for those responsible for the health of asylum seekers and migrants in their local area.

HPT regions are asked to disseminate information about the enhanced surveillance work (DAiSiES) to local authority colleagues, Directors of Public Health and Integrated Care Boards.

References/ Sources of information

1. Irregular migration to the UK, year ending March 2023
2. ECDC Communicable Disease Threats: week 32
3. Vaccination of individuals with uncertain or incomplete immunisation status
4. Diphtheria anti-toxin (DAT): information for healthcare professionals
5. Diphtheria anti-toxin: clinical guidance
6. Diphtheria training slide sets for clinical management and laboratory testing
7. Supplementary guidance for cases and outbreaks in asylum seeker accommodation settings
8. Information for HCP
9. Link to posters, leaflets
10. National Surveillance form for toxigenic cases in asylum seekers
11. Migrant health guide
12. Diphtheria Factsheets
13. EUCAST: Breakpoint tables for interpretation of Corynebacterium species v.13
14. Regions Directorate - Asylum Seeker & Migrant Health Resources - All Documents (sharepoint.com)

Appendix A

SEPT 2023 DAISIES briefing note for LAs