

# Public health control and management of diphtheria in England

Supplementary guidance for cases and outbreaks in asylum seeker accommodation settings

November 2023

# **Contents**

	Scope	of this document	3
	Backg	round and rationale	3
	Part 1.	Investigation and management of individual cases	
	1.2	Case definitions	5
	1.3	Testing	6
	1.4	Isolation of cases	7
	1.5	Treatment of possible, probable or confirmed cases	9
	1.6	Management of asymptomatic carriers	. 11
	1.7	Immunisation	. 12
	1.8	National Surveillance	. 12
		lanagement of close contacts of confirmed cases and close contacts of asymptomatic	
	2.1	Risk assessment for close contacts of confirmed cases	. 13
	2.2	Isolation of close contacts	. 13
	2.3	Definition of healthcare exposure	. 14
	2.4	Chemoprophylaxis of close contacts	. 15
	2.5	Immunisation of close contacts	. 15
	2.6	IPC and cleaning	. 15
P	art 3. C	outbreaks	. 18
R	eferend	ces	. 20
		x 1. Risk assessment checklist for probable or confirmed cases of diphtheria in AS (for use in IMT)	. 21
	_	x 2. Warn and inform letter	
	-	x 3. Data collection form	
		κ 4. Staff letter template	
	-	x 5. GP letter template for clearance swabs	
• •	r 12		

# Scope of this document

This is a supplementary guide for use by health protection teams (HPTs) to support the control and management of diphtheria in asylum seeker (AS) accommodation settings to be used alongside:

<u>Diphtheria: public health control and management in England</u> Diphtheria anti-toxin (DAT): information for healthcare professionals

# **Background and rationale**

Since June 2022, there has been an increase in confirmed cases of diphtheria caused by toxigenic *Coynebacterium diphtheriae* among migrants in Europe (1). Cases have predominantly been among young adult males presenting with cutaneous lesions, although cases of respiratory diphtheria have also been reported.

Between 1 January 2022 and 31 October 2023 there have also been 85 confirmed cases of diphtheria (caused by toxigenic *C. diphtheriae*) and one probable case, identified among AS in England (2, 3). Most of these were identified in 2022, with only 13 of the 86 cases notified in 2023. These individuals are considered likely to have acquired their infection before reaching the UK with cases originating from diphtheria endemic countries (where vaccine coverage is sub-optimal) but also spending many weeks travelling across Europe in challenging circumstances, prior to arrival by small boat to the south-east coast of England.

UKHSA issued a national briefing 28 September 2022 to alert colleagues, including NHS staff, on the evolving epidemiology and to highlight the importance of early diagnosis and prompt treatment of suspected cases in line with <u>national guidance</u>.

Accommodation settings for AS were considered high risk for transmission of infectious diseases and challenges with contact tracing were recognised. Population based control measures were therefore put in place in mid-November 2022, with mass antibiotic prophylaxis (with azithromycin) and vaccination recommended within 10 days of arrival for those who had transited through an initial reception centre.

The level of risk of diphtheria for asylum seekers following this migrant journey is lower than previously estimated in 2022 but remains significant and greater than that for the wider UK population. This reduction is likely due to a combination of factors including a reduction in infection in the AS population in Europe, reduced numbers of new arrivals, a reduction in overcrowding in accommodation pathways and ongoing establishment of more robust health assessment, testing and early treatment of symptomatic individuals. Basic health checks undertaken on disembarkation, the availability of health services at reception settings and clinicians having an increased awareness of the signs and symptoms of diphtheria mean many cases are now identified on arrival.

It is not possible to quantify the contribution of mass prophylaxis to diphtheria control since November 2022 but with the ongoing identification of macrolide resistant cases and limited alternative antibiotic options available, this population level control strategy is not the preferred option in the long-term.

This document therefore includes updated recommendations from November 2023, which are based on a reversion to individual level disease control measures but with the continued recommendation of an early offer of diphtheria vaccination at reception, to protect all new arrivals against severe infection.

# Part 1. Investigation and management of individual cases

#### 1.1 Risk assessment of cases

All new arrivals at a setting (such as an Initial Accommodation Centre (IAC) or large-scale site) should ideally have a clinical review by a nurse or a medical practitioner. Those with respiratory symptoms or cutaneous lesions should be discussed with a clinician and appropriate treatment and testing undertaken. Clinicians should have a high index of suspicion for diphtheria infection when clinically assessing individuals with compatible cutaneous and/or respiratory symptoms. Risk assessment should be undertaken as per section 2.1 of the <u>national guidance</u> (see <u>Appendix 1</u> for risk assessment checklist template) with further consideration of the following clinical and epidemiological features.

#### Clinical presentation

Individuals may present with lesions typical of cutaneous diphtheria with raised edges and a blueish/grey eschar. In these settings however, chronic wounds and skin lesions are common and therefore consideration for further investigation should also be given to:

- chronic wounds or lesions or wounds that do not heal as expected
- other common cutaneous presentations for example lacerations, ulcers, abscesses, infected insect or animal bites
- the presence of other organisms such as Staphylococcus spp. and Streptococcus spp., as isolation from wound sites or lesions does not exclude co-infections with *C. diphtheriae*, which has been observed in this population.

Respiratory presentations of diphtheria may be more common than expected in asylum seekers compared to the general UK population due to low vaccination rates in this group. Respiratory symptoms include:

- presence of classic respiratory symptoms (presence of sore throat, fever, adherent greyish membrane (bleeds when manipulated or dislodged) of the tonsils, pharynx or nose (but noting a membrane may not always be present)
- carriage of *C. diphtheriae* may occur in the throat in the absence of respiratory symptoms and has been isolated in individuals with cutaneous lesions; all individuals with cutaneous lesions where diphtheria is suspected should also have a nose and throat swab to determine presence of respiratory carriage

Review of local *C. diphtheriae* positive wound and throat isolates sent to the reference laboratory for PCR and Elek toxigenicity testing in 2022 has highlighted that the majority of locally C. *diphtheriae* positive isolates are toxigenic. Clinicians should therefore note that the positive predictive value (PPV), of either a locally positive wound or throat swab, is 84%.

Where alternative diagnoses are considered, cases should also be treated and excluded as appropriate.

#### 1.2 Case definitions

Cases among asylum seekers should be classified according to case definitions outlined in section 2.2 of <u>national guidance</u> but with an additional criteria for probable cases. The probable case definition has been extended for the AS population based on 2022 calculations of the positive predictive value (PPV) of a locally positive throat swab being 85% and a locally positive wound swab being 84%.

#### Confirmed case of toxigenic infection

- classic respiratory diphtheria [note 1] and
- either laboratory confirmation of a toxigenic strain or
- epidemiological link to a laboratory-confirmed case with a toxigenic strain [note 2, below]

Or:

 laboratory confirmation of a toxigenic strain [note 2] with other presentations of diphtheria including mild respiratory or cutaneous lesions [note 3]

#### Probable case of toxigenic infection

- classic respiratory diphtheria [note 1] and
- no laboratory confirmation (*C. diphtheriae, C. ulcerans* or *C. pseudotuberculosis* has not yet been isolated from a relevant swab, or where a strain has been isolated **but** toxigenicity status has not yet been confirmed) **and**
- no epidemiological link to a laboratory-confirmed case with a toxigenic strain

Or:

• a severely unwell patient with *C. diphtheriae*, *C. ulcerans* or *C. pseudotuberculosis* isolated from a relevant swab, but toxigenicity status has not yet been confirmed (for example laryngeal disease)

Or:

cases with other presentations of diphtheria [note 3] – and

- *C. diphtheriae* isolated from a relevant swab, but toxigenicity status has not yet been confirmed,
- **and** a confirmed epidemiological link to a laboratory confirmed case [note 2] **or** an epidemiological link to a high volume AS initial reception centre

#### Possible case of toxigenic infection

 clinical presentation consistent with diphtheria (where no other infection/diagnosis is considered more likely) pending local laboratory isolation of *C. diphtheriae* or *C. ulcerans / C. pseudotuberculosis*

#### Asymptomatic carrier of toxigenic strain

- no symptoms and
- laboratory confirmation of toxigenic strain [note 2] from any anatomical site

#### **Notes**

[Note 1] Classic respiratory diphtheria: a patient with an upper respiratory tract illness characterised by sore throat, low grade fever, and an adherent membrane of the tonsils, pharynx or nose. Many clinicians will not have seen a classical presentation of diphtheria with a membrane. Clinical assessment of the likelihood of *C. diphtheriae* should include consideration of the likely source, with increased risk associated with recent travel from a diphtheria endemic country or over land travel to the UK along a migrant route with periods of stay in a migrant camp. A high prevalence of diphtheria has not been documented in settled migrant populations in the UK.

[Note 2] Laboratory identification and confirmation of diphtheria: Isolation of diphtheria toxin-producing corynebacteria (indicated by toxin gene PCR detection and confirmed by Elek test) from a clinical specimen by a reference laboratory. For the purposes of public health action, a strain with tox gene detected by PCR is considered to be laboratory confirmed.

[Note 3] Other presentations of diphtheria: a patient with mild respiratory symptoms but no membrane or a patient with a skin lesion, in whom a laboratory report of an isolate of *C. diphtheriae* or *C. ulcerans* from a nose or throat swab or skin lesion swab has been obtained. Very rarely, endocardial, laryngeal, conjunctival, optic and genital involvement may be seen. If local laboratory testing is negative for *C. diphtheriae*, but the patient fails to either clinically improve or deteriorates, and diphtheria remains clinically likely, then further testing should be discussed with the local and reference laboratory and treatment reviewed, including whether treatment with DAT is appropriate.

## 1.3 Testing

Appropriate swabs should be collected for all suspected cases irrespective of clinical presentation and before starting treatment with antibiotics:

nose and throat swabs should be taken for all suspected cases (including screening)

for respiratory carriage in cutaneous cases)

- skin swabs of wounds and lesions (if present)
- where a membrane is present, swabs from underneath the membrane or a piece of membrane

Dacron, Viscose or flocked applicator swabs should be used to collect samples from each suspected case and placed in a routine semi-solid transport medium, such as Amies, immediately after collection and sent to the hospital microbiology laboratory for culture.

Review of the <u>European literature</u> (4) has prompted some concern around a small number of multi-drug resistant isolates associated with the ST377 strain, harbouring a Class 1 integron. This integron conveyed aminoglycoside, macrolide, sulphonamide, tetracycline and trimethoprim resistance. In addition, a beta lactam gene (*bla*<sub>OXA-2</sub>) was detected, although not expressed phenotypically. Class 1 integrons play a major role in the dissemination of antibiotic resistance via horizontal gene transfer into a diversity of bacterial species.

The evidence is evolving around the epidemiology of this strain, including the implications for antibiotic treatment regimes. Whilst this is under review it is strongly recommended that local laboratories undertake antimicrobial susceptibility testing on <u>all C. diphtheriae</u> isolates, to include as a minimum, sensitivity to penicillin and erythromycin (according to local methods and reported using the EUCAST Clinical Breakpoint Tables version 13.1 (29 June 2023).

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. The UKHSA reference laboratory (RVPBRU) is investigating the sensitivity profiles of all ST377 strains received prior to this recommendation.

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.

#### 1.4 Isolation of cases

All probable and possible cases should be advised to restrict their contact with others<sup>1</sup> pending confirmation of toxigenicity testing by the UKHSA reference laboratory (RVPBRU). Particular consideration should be given to restricting contact with others who may be un- or partially immunised and in an AS reception centre or other accommodation setting this will mean that isolation in their own room and not sharing communal facilities on site.

<sup>&</sup>lt;sup>1</sup> Restricting contact with others may be interpreted as minimising contact with those who are un- or partially immunised. In an accommodation setting this may include restriction in the use of communal facilities on-site.

For possible cases based on clinical presentation alone, this restriction of movements may cease if the case is recovering and local microbiology laboratory is unable to isolate a Corynebacterium species (and therefore onward submission of isolate to RVPBRU is unwarranted) unless the possible case has had, or is likely to have had, recent prophylaxis when the restriction of movement should be continued until the first 6 days of a treatment course is completed. Please note that *C. diphtheriae*, *C. ulcerans* and *C. pseudotuberculosis* are toxin producing Corynebacterium species. Other Corynebacterium species identified using a reliable local method of confirmation such as MALDI-TOF are commensal organisms that do not require further testing or further action.

If a probable or confirmed case is well and not hospitalised they should be advised to continue to restrict their contact with others (including isolation to their room if in an AS accommodation setting) for the first 6 days of an appropriate course of antibiotics.

Due to the highly vulnerable population residing in these settings, the period of restricted interaction with others should be observed as far as possible even for cutaneous cases where lesions are healed or almost healed. A wound assessment taken at a point in time might not indicate risk is mitigated as wounds can breakdown or become disrupted on contact. Direct contact with cutaneous lesions can be as infectious as exposure to respiratory droplets. All confirmed cases should undergo microbiological clearance at the end of their treatment course although they do not need to restrict their interactions beyond day 6 of effective antibiotic treatment.

A single swab from each of the following sites – nose, throat and wound (where applicable) should be obtained at least 24 hours after completing antibiotics and once again after (at least) a further 24 hours (that is, at 24- and 48-hours to ensure elimination of carriage).

If clearance is not achieved (including from the site it was originally detected) a further course of antibiotics should be prescribed following the advice of the local microbiologist (in consultation with UKHSA colleagues as appropriate), as guided by local susceptibility testing. Ideally, a different antibiotic class from that used in the original course is recommended. Resistant isolates should be referred on to the RVPBRU (as per section 1.2.1 of the <u>national guidance</u>).

Probable cases, where original isolation of a local *Corynebacterium diphtheriae / ulcerans / pseudotuberculosis*, or reference laboratory of confirmation of a toxigenic *Corynebacterium* species has not been possible (for example, due to prior receipt of antibiotics), do not require clearance swabs.

#### 1.4.1 Issues with isolation or restricting movements

Where there are reported issues with movement restrictions that cannot be resolved, consideration should be given to factors such as the condition or stage and site of lesions, whether they can be covered and compliance with antibiotics, on a case by case basis.

#### 1.4.2 Transfer of individuals out of setting

Transfer of any individual out of the setting while awaiting microbiological results should be avoided, if it is safe for the individual to stay in the setting; this includes all possible or probable cases as well as asymptomatic close contacts awaiting results from screening swabs. However, this decision should be weighed against other priorities including the wellbeing of the individual and opportunity of longer-term placement in a foster family. Where transfer is being considered, review may occur on a case-by-case basis and should consider safe-guarding issues.

Additional measures to mitigate potential transmission in the community should be considered such as: ensuring recipient family are aware of the situation, have no family members that are high-risk or immunocompromised, and are up to date with their vaccinations according to the <a href="UK immunisation schedule">UK immunisation schedule</a>. It may be favourable for an individual (in particular, an unaccompanied minor) to be moved to a setting where they are supported with completing their antibiotic therapy and with appropriate restriction of movements.

# 1.5 Treatment of possible, probable or confirmed cases

#### 1.5.1 Diphtheria anti-toxin (DAT)

All probable and confirmed cases of diphtheria presenting with respiratory symptoms and/or large cutaneous lesions (that is, greater than 2cm²) should be promptly assessed by a clinician with access to advice from an ID specialist, for treatment with DAT, in line with the <u>national guidance</u>. In light of the high proportion of presentations with mild cutaneous infection in this population, the clinical review may be undertaken by a Primary Care or non-specialist physician for cutaneous cases, but with a low threshold for discussion with, and/or referral to an ID clinician, should there be any signs of systemic infection and for all those with respiratory symptoms.

When indicated, treatment with DAT should not be delayed and should be undertaken in a hospital setting to ensure appropriate sensitivity testing and monitoring of hypersensitivity can occur.

Clinicians are reminded that management should proceed based on the clinical assessment, even in the absence of laboratory confirmation and where there is no alternative diagnosis, particularly in those who have previously received antibiotic prophylaxis. If local laboratory testing is negative for *C. diphtheriae*, and diphtheria remains clinically likely, then further testing should be discussed with the local microbiologist and national reference laboratory and treatment reviewed, including whether treatment with DAT is appropriate.

The UKHSA Colindale duty doctor should be contacted in and out-of-hours if considering the use of antitoxin (0208 200 4400). They will advise on details of current stock and dosing and will issue DAT as indicated. Further details are provided in <u>Clinical guidance for the use of diphtheria anti-toxin</u> and <u>Information for healthcare professionals</u>.

#### 1.5.2 Antibiotic treatment

For guidance on the administration of antibiotics, please refer to sections 2.6.4 and 2.7 of the <u>national guidance</u>. Ensure probable and possible cases are commenced on a prophylactic course of antibiotics while awaiting toxigenicity confirmation by the RVPBRU. For cases where toxigenicity is confirmed, the prophylactic course should be changed to a treatment course. For cases who have previously completed a prophylactic course, consideration of the timing between completion and the exposure event will be required to determine the appropriate antibiotic course.

Where diphtheria is one of several possible diagnoses, and/or co-isolated with other organisms requiring treatment, advice should be sought from a local microbiologist with regards appropriate antibiotic treatment, guided by local antibiotic sensitivities.

Elimination of the organism, from the site it was originally detected (including wound, throat, nose) should be attempted with 2 sets of clearance swabs taken a minimum of 24 hours apart with the first sample taken at least 24 hours after the completion of the recommended antibiotic course.

If clearance is not achieved a further course of antibiotics should be prescribed following the advice of the local microbiologist (in consultation with UKHSA colleagues as appropriate), as guided by local susceptibility testing. Ideally, a different antibiotic class from that used in the original course is recommended.

#### 1.5.3 Principles for the management of macrolide resistant strains

Macrolide resistant C. diphtheriae, in combination with resistance to additional antibiotics, has been detected in a small number of cases in asylum seekers in England. It is recommended 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. 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).

Table 1. Antibiotic options for macrolide resistant C. diphtheriae isolates

Case treatment and contact prophylaxis	Severity	Adult dose	Duration
Linezolid*	All	600 mg every 12 hours IV/PO	10 to 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 to 12 hours by intravenous infusion (maximum per dose 2g) adjusted according to plasmaconcentration monitoring.	IV to oral switch when possible

<sup>\*</sup> 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.

HPTs are asked to request for all clearance swabs to be sent for testing through their regional Public Health laboratory. Request forms and clearance swabs should be clearly labelled as 'Diphtheria clearance swabs' to ensure correct processing and communication of these results. A template request letter to GPs can be found in Appendix 5 as an example that local teams may wish to use as a guide when requesting clearance samples. If this process has already been established locally, there is no requirement for HPTs to use this template.

## 1.6 Management of asymptomatic carriers

Asymptomatic carriers of toxigenic strains should be managed as per confirmed or probable cases. Where an asymptomatic individual tests positive for *C. diphtheriae* (either through testing as a contact of a confirmed case, or through enhanced surveillance testing), they should be started on a prophylactic course of antibiotics while awaiting toxigenicity confirmation by the RVPBRU. For individuals where toxigenicity is confirmed, the prophylactic course should be changed to a treatment course with the same regime and dosage as for symptomatic cases

<sup>\*\*</sup> 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.

<sup>\*\*\*</sup> 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.

(please refer to section 2.6.4 and 2.8 of the <u>national guidance</u>), and offered immunisation. A single swab from each of the following sites – nose, throat as well as skin swabs (if appropriate) should be taken on completion of therapy to ensure eradication of the organism.

If the asymptomatic carrier remains clinically well and not hospitalised, they should be advised to restrict their contact with others (including isolation to their room if in an AS accommodation setting) for the first 6 days of an appropriate course of antibiotics.

#### 1.7 Immunisation

For guidance on immunisation of cases and asymptomatic carriers, please refer to section 2.6.5 of the national guidance.

Immunisation status of cases and asymptomatic carriers should be reviewed and all attempts should be made for catch up immunisations once clinically stable. Where possible it is recommended that catch-up courses of vaccination are commenced in the accommodation setting prior to an individual taking up an onward placement. It is important that continuity of care is maintained once the individual is transferred out of the setting so that immunisations as per the <u>UK schedule</u> can be completed.

#### 1.8 National Surveillance

To support enhanced surveillance of diphtheria in the asylum seeker population to inform ongoing case and outbreak management, health protection teams are asked to complete the data collection form for asylum seekers for all confirmed toxigenic cases and asymptomatic carriers and upload this to the HPZone record for the case or email it to the UKHSA Immunisation and Vaccine Preventable Diseases Division: diphtheria tetanus@ukhsa.gov.uk or phe.diphtheria.tetanus@nhs.net. This supersedes the national enhanced surveillance form for follow-up of confirmed toxigenic cases.

#### Additional details to be included:

- country of birth
- travel history or route to the UK
- travel history within the UK (including details of processing centres and accommodation settings if multiple)
- dates and duration of stay in each location
- mode of transportation between locations
- details of any potential high-risk settings stayed in

# Part 2. Management of close contacts of confirmed cases and close contacts of asymptomatic carriers

# 2.1 Risk assessment for close contacts of confirmed cases

For guidance on the risk assessment for close contacts and management, please refer to section 2.10.1 of the <u>national guidance</u>.

For AS accommodation settings, examples of contacts who should be considered for prophylaxis are:

- those sleeping in the same room as the index case
- residents that may have had direct exposure to open wounds, or particle droplets (via shared food or drinks)
- those sharing bathroom facilities

The incubation period for *C. diphtheriae*, *C. ulcerans* and *C. pseudotuberculosis* is usually 2 to 5 days, but may be longer, with duration of up to 10 days reported (<u>6</u>, <u>7</u>). The infectious period is not well-defined pre-symptom onset; therefore, all individuals that had contact with the case in the time from 10 days prior to symptom onset should be considered for risk assessment. The rationale for using this time frame is to identify the possible infection source and eliminate established carriage, thereby reducing onward transmission (from both source and confirmed case).

#### 2.1.1 Issues identifying close contacts

Where it is difficult to identify close contacts (for example, reception tents, boats, transfer coaches), a warn and inform letter (translations are available on GOV.UK) should be given to all those staying in the same setting (where possible), with appropriate translations. Information on signs and symptoms of diphtheria should be included and instructions to seek medical assessment if any concerns. A low threshold for referral for clinical assessment and testing should be considered for symptomatic individuals, and restriction of contact with others is advised.

## 2.2 Isolation of close contacts

All close contacts of confirmed and probable cases and close contacts of asymptomatic carriers identified within 10 days post exposure should be swabbed (see <u>section 1.3 Testing</u>), started on

chemoprophylaxis (see section 2.10.2 of the <u>national guidance</u>) and should restrict their movements pending microbiological results. Particular consideration should be given to restricting contact with others who may be un- or partially immunised and in an AS reception centre or other accommodation setting this will mean that they are isolated in their own room as they should not share communal facilities on site.

Asymptomatic close contacts identified outside the 10 day post exposure window should be tested but are not required to restrict their movements pending test results if they remain well. Antibiotic prophylaxis is not routinely recommended for close contacts identified outside the 10 day eligibility period (see section 2.4 Chemoprophylaxis of close contacts).

If *C. diphtheriae*, *C. ulcerans* or *C. pseudotuberculosis* is identified by local laboratory testing, then the close contact needs to restrict their movements until toxigenicity testing is undertaken by RVPBRU. In the case that RVPBRU confirm toxigenicity, the close contact should be managed according to the confirmed case definition; this includes a change from the prophylactic course to the treatment course of antibiotics and to continue to restrict their movements until completion of the first 6 days of appropriate antibiotic treatment.

If *C. diphtheriae, C. ulcerans* or *C. pseudotuberculosis* is not identified by local laboratory testing and the individual is recovering, then close contact does not require further restriction on their movements. However, completion of chemoprophylaxis is recommended.

## 2.3 Definition of healthcare exposure

For guidance on the risk assessment for healthcare workers (HCW), please refer to section 2.10.1 of the national guidance.

The risk of infection is directly related to the closeness and duration of contact. For healthcare workers to be considered a close contact, direct exposure to a cutaneous wound or respiratory droplets without the appropriate personal protective equipment (PPE) is required. As a minimum, HCW attending a case should wear a fluid-repellent surgical face mask, disposable gloves and aprons for wound care. Eye protection should be worn where there is a risk of blood or body fluids splashing into the face and eyes.

HCW that are close contacts should be swabbed (see <u>section 1.3 Testing</u>), started on chemoprophylaxis (see section 2.10.2 of <u>national guidance</u>) and should be excluded from work pending microbiological results due to their contact with high-risk individuals.

If *C. diphtheriae*, *C. ulcerans* or *C. pseudotuberculosis* is not identified by local laboratory testing and the HCW remains well, then they can return to work while completing the antibiotic course.

## 2.4 Chemoprophylaxis of close contacts

For guidance on chemoprophylaxis of close contacts please refer to section 2.10.2, part ii of the national guidance.

The recommended agents for chemoprophylaxis are a 6-day course of azithromycin or 7-day course of clarithromycin. As an alternative, in certain circumstances when more easily administered, a single intramuscular (IM) dose of benzathine benzylpenicillin can be given with dosing according to the British National Formulary. **Benzathine benzylpenicllin should never be administered by the IV route**.

In the case that RVPBRU subsequently confirm toxigenicity, the close contact should be managed according to the confirmed case definition; this includes a change from the prophylactic course to the treatment course of antibiotics.

Asymptomatic close contacts identified outside the 10 day post exposure window should be tested (nose and throat) and offered vaccination; antibiotic prophylaxis is not routinely recommended outside the 10 day eligibility period. These contacts are not required to restrict their movements pending test results if they remain well.

#### 2.5 Immunisation of close contacts

For guidance on vaccination of close contacts please refer to section 2.10.2, part iv of the <u>national guidance</u>.

Immunisation status of close contacts should be reviewed and all attempts should be made for catch up immunisations.

# 2.5.1 Immunisation for staff and healthcare workers in AS accommodation settings

All staff and HCW involved in the care of recent arrivals should have their immunisation status reviewed and those with incomplete schedules should be brought up to date.

## 2.6 IPC and cleaning

Diphtheria is most easily spread by direct contact with a person with infection or carriage, such as to those directly exposed to large particle droplets or secretions and direct contact with an undressed wound. It is more rarely spread through contact with articles soiled by discharges from lesions on infected people. There is limited published evidence of transmission through fomites, but the evidence does suggest that individuals with cutaneous diphtheria are more likely to contaminate the environment than those with respiratory infection.

All employers have a duty to ensure safe systems of working are in place in the workplace and that they meet their duty of care to their employees under Health and Safety legislation and COSHH regulations.

#### 2.6.1 Personal Protective Equipment (PPE)

Healthcare and cleaning staff should receive appropriate training and be competent in the use of PPE and hand hygiene. Staff should know their local procedures for reporting any PPE breach or other risk contact with a confirmed or probable case so that they can be assessed for follow-up.

For possible, probable and confirmed cases, the minimum PPE is:

- fluid-resistant surgical facemask (FRSM) for routine care and FFP3 for aerosol generating procedures)
- gloves
- apron
- eye protection (where contamination to the eyes or face is anticipated or likely, for example during aerosol generating procedures)

#### 2.6.2 Hand hygiene

Hand hygiene is important and should be encouraged for all residents and staff. Staff should follow best practice regarding hand hygiene including when removing PPE. Alcohol-based hand sanitiser can be used as an alternative to soap and water for visibly clean, dry hands.

For further information on the use of PPE and hand hygiene best practice please refer to the National infection prevention and control manual.

It remains important to reduce the risk of transmission from the contaminated environment. The risk can be reduced by following agreed cleaning methods based on standard cleaning and disinfection using usual products in accordance with manufacturer's instructions.

Increased cleaning is likely to reduce risk of all infections, including the risk of transmission of diphtheria. Regular cleaning will also minimise the build-up of dust.

Anyone cleaning a room of a suspected or confirmed case of diphtheria should wear PPE (as per minimum requirements listed above). Any used cloths and mop heads (if used) must be disposed of and should be put into waste bags after each cleaning of the room in accordance with the local waste disposal policy.

Once the person is recovered then a final clean of their room should be undertaken while wearing PPE (as per minimum requirements listed above) using the standard cleaning detergent and disinfection products:

- remove all disposable items and dispose of in waste bags
- bag and transfer used laundry in accordance with the laundry providers procedures for the management of contaminated laundry
- clean all hard surfaces including floors, chairs, bed frame, mattress, frequent hand touch surfaces and ensuite facilities
- any soft furnishings should be steam cleaned or vacuumed; where possible, use a vacuum cleaner with HEPA filtration

Multiple occupancy rooms require regular cleaning, with particular attention given to bathroom facilities and frequent hand touch surfaces.

#### 2.6.3 Waste management

All waste produced by the case in isolation (whilst infectious) should be bagged. This bag should be placed into another waste bag outside the room for transport to the appropriate waste collection bin for usual domestic waste management in accordance with local policy.

Usual protective equipment should be worn by people handling waste and hands washed on disposal of PPE.

Waste generated by healthcare should be disposed of as healthcare waste according to the National infection prevention and control manual.

#### 2.6.4 Contaminated linen

There is a potential risk that infections such as diphtheria can be spread via contact with clothing or linens (such as bedding or towels) used by an infected person therefore handling should be minimised. Linens and bedding should be carefully lifted and rolled to prevent dispersion of infectious particles from lesions and body fluids.

Laundries handing potentially infectious linen should operate safe systems of working to minimise the exposure risk posed to laundry staff. This will include the appropriate use of PPE but should also consider other options to minimise handling of potentially infectious linen (for example, soluble laundry bags or soluble seal bags which can be placed directly into the washer without the need for manual pre-sorting). It is therefore essential to discuss these processes with the laundry service provider and to ensure that procedures for packaging of potentially infectious laundry are agreed and implemented.

Where possible, such linen should ideally be bagged (preferably in a water-soluble bag) by the infected or recovering person. This bag should be placed directly into a clean plastic bag immediately outside the room prior to these being transported to the laundry.

Laundry providers should have a validated process for cleaning and disinfection of contaminated linen.

## Part 3. Outbreaks

Over recent years there have been many outbreaks of diphtheria within displaced populations and where health infrastructure is sub-optimal (8). The largest of these occurred in Rohingya refugees in Bangladesh in November 2017 where there were over 8,000 cases and 45 deaths. Outbreak management within challenging environments requires a move away from an individual targeted approach involving contact tracing, testing and prophylaxis which becomes unsustainable and ineffective, towards mass control measures that can be implemented at scale and pace. Evidence suggests a similar impact on transmission may be achieved by applying control measures to a larger at risk population whilst also alleviating pressure on stretched healthcare provision.

In models of outbreak scenarios, mass vaccination reduces transmission likely through reduced symptomatic shedding ( $\underline{8}$ ).

Vaccination with a diphtheria containing vaccine stimulates the production of anti-toxin antibodies. Full vaccination with 3 or more doses has been shown to be around 87% effective overall against symptomatic disease (up to 99% with 5 doses). Full vaccination is 81% effective in preventing severe disease and 93% effective in preventing death.

Diphtheria toxoid vaccines do not prevent colonisation but 3 doses have been estimated to reduce transmission by 60% during outbreaks (8).

The mean incubation period of diphtheria is 1.4 days (from infection to prodromal symptoms) and the serial interval in outbreaks is estimated at 7.8 days (that is the time between symptom onset in successive cases). Untreated cases are colonised for an average of 18.5 days (with 5% colonised for more than 48 days). Evidence suggests colonisation times do not vary between those with asymptomatic and symptomatic infections. It is estimated that asymptomatic throat carriers cause around 76% fewer onward cases over their course of infection than those who are symptomatic respiratory cases. A case will clear respiratory colonisation within 5.2 days (range 4.4 to 6.1 days) of commencing treatment thus reducing infectiousness by around 2 weeks (8).

In an outbreak setting, all new arrivals to the setting require a basic assessment. Those with acute medical needs, including those with symptoms suggestive of diphtheria infection should be referred to the onsite services for clinical review.

In November 2022, the UKHSA incident management team recommended mass antibiotic prophylaxis and mass vaccination due to a high prevalence of toxigenic diphtheria infection in high volume reception settings where individual case and contact management was not possible. During 2023 the level of risk for AS following their migrant journey has been lower than previously estimated. This reduction is likely due to a combination of factors including reduced numbers of new arrivals, a reduction in infection in the AS population in Europe,

improved capacity in accommodation pathways and ongoing establishment of more robust health assessment, testing, and early treatment of symptomatic individuals. With the ongoing identification of a small number of macrolide resistant cases and limited antibiotic options available, mass antibiotic prophylaxis is not the preferred option in the long-term. Therefore, following review in October 2023, the following updated recommendations have been made based on a reversion to individual level control measures:

- **early identification of cases**; this requires continued provision of the basic health check at port of entry to identify symptomatic individuals, allow early testing, treatment and isolation of suspected cases
- **empirical treatment** for respiratory symptoms (including sore throats), and skin lesions which includes cover for diphtheria
- early offer of diphtheria vaccination; this requires continued delivery at reception to protect all new arrivals against severe infection. This is recommended in the reception facility for adults and families and in UASC hotel/accommodation settings, as has been established. It is recommended that this provision is further strengthened to improve coverage.
- on arrival into initial accommodation (contingency hotel or large site), to ensure all asylum seekers are registered with a GP and have timely access to a baseline medical assessment (as set out in the Migrant Health Guide). This should include a review of all immunisations as soon as possible, to allow timely catch-up to the UK schedule.
- on identification of a case, to follow national guidelines and implement a multiagency, multi-disciplinary response, which is particularly important for cases with macrolide resistant infection
- suspected cases will require assessment for DAT treatment with appropriate clinical supervision and oversight (<u>see section 1.5.1</u>)
- contact tracing will be required with testing, prophylaxis and vaccination arranged for close contacts
- local laboratories to monitor antibiotic susceptibilities and to ensure antibiotic treatment and prophylaxis schedules are amended for suspected macrolide resistance as per supplementary guidance. Linezolid treatment to be supervised by ID/ or alternative in community as required

The epidemiology of diphtheria and issues arising with individual case and contact management will remain under evaluation and these recommendations will be reviewed as necessary into Spring/Summer 2024.

19

<sup>&</sup>lt;sup>2</sup> Where the recommended first line antibiotic is not suitable, alternative options may be considered as guided by the <u>World Health Organization 'Operation Protocol for the clinical management of Diphtheria, 2017'</u>

### References

- 1. ECDC (2022). 'Increase of reported diphtheria cases among migrants in Europe due to Corynebacterium diphtheriae, 2022'
- 2. UKHSA (2022). 'Diphtheria: cases among asylum seekers in England, 2022'
- 3. UKHSA (2022). 'Diphtheria in England: 2022' Health Protection Report
- 4. Kofler J and others. 'Ongoing toxin-positive diphtheria outbreaks in a federal asylum centre in Switzerland, analysis July to September 2022' Eurosurveillance 2022: volume 27 number 44
- 5. European Committee on Antimicrobial Susceptibility Testing. 'Corynebacterium diphtheriae and ulcerans: Breakpoint tables for interpretation of MICs and zone diameters version 13' EUCAST, 2022
- 6. Dangel A and others. 'Geographically diverse clusters of nontoxigenic corynebacterium diphtheriae infection, Germany, 2016 to 2017' Emerging Infectious Diseases 2018: volume 24 number 7
- 7. CDC (2015). 'Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book)'
- 8. Truelove SA and others. 'Clinical and Epidemiological Aspects of Diphtheria: A Systematic Review and Pooled Analysis' Clinical Infectious Diseases 2020: volume 71 number 1

# Appendix 1. Risk assessment checklist for probable or confirmed cases of diphtheria in AS settings (for use in IMT)

Case		
Name		
Date of birth		
Nationality		
ID number (from Home Office)		
Current setting and location in setting (for example, room or tent number)		
Collate information for <u>Data collection form for asylum seekers</u> including:		
<ul><li>travel history (arrival at and travel between UK settings</li><li>symptoms and date of onset</li></ul>		
swabs obtained and local results		
check appropriate antibiotics prescribed (as per national guidance) and date commenced		
Advise restriction of movements of the case until completion of 6 days of appropriate antibiotic treatment		
Document date that isolation will end.		
Clearance swabs: Advise that clearance swabs should be taken 24 and 48 hours after the case has finished antibiotics.		
Inform setting that this is nose and throat swab, and wound swab if case has cutaneous diphtheria. These can be done with standard swabs that GP or healthcare will have in stock. The swabs should be sent to the Regional Public Health laboratory and clearly labelled as clearance swabs (see GP letter template in Appendix 5 Supplementary guidance).		
Identify infectious period: 10 days before onset of symptoms and up to 6 days of appropriate antibiotic course		
Collate a timeline of dates for case and consider if transmission could have occurred in the setting:		
<ul><li>arrival in UK</li><li>arrival at and travel between settings</li></ul>		
Request Home Office to provide the case's travel history prior to UK arrival and country of origin and share this information with national team at <a href="mailto:diphtheria_tetanus@ukhsa.gov.uk">diphtheria_tetanus@ukhsa.gov.uk</a> or <a href="mailto:phe.diphtheria.tetanus@nhs.net">phe.diphtheria.tetanus@nhs.net</a>		

Case	
Clinician should arrange clinical review of case by local secondary care Infectious Disease team to discuss requirement of diphtheria anti-toxin (See SOP for notes on this)	
If incomplete or unknown vaccination status, clinician to arrange for case to receive diphtheria-containing vaccine once clinically stable (within full course of childhood immunisations if needed)	
Request the Home Office / social workers to inform the HPT if any welfare or mental health concerns arise with extended period of isolation	
Send diphtheria factsheet to the case	
Advise that transferring case to a new setting should be avoided while isolation/restriction on movement in place. If transfer is necessary, then Home Office must inform current HPT and the HPT supporting the new setting.	
For cases who are no longer within the region where identified, obtain details through Home Office (HPT inform Local Authority Safeguarding lead - if unaccompanied child) and refer to appropriate HPT	

#### **Contacts** Identify close contacts and document where are they located. See national guidance chapter 2.10.1 and section 2.1 of Supplementary guidance for close contact definition. If case is sharing a living space with a large number of people (for example, tent), consider identifying only contacts who have close or intimate contact, are part of a family unit, or other similar group. Send details of any contacts who have been transferred out of the setting to the Home Office. For UASC, HPT to inform the Local Authority Safeguarding Lead. If any close contacts are identified: 1. Inform contact, check they are well and inform GP (if in setting – ask setting staff to do this) 2. Request nose or throat swabs and swabs of any skin lesions, arrange chemoprophylaxis with antibiotics, immunise as appropriate 3. Advise restriction of movements if contact is resident at asylum seeker accommodation, or hospitalised. If this is not possible, advise setting to reduce mixing and consider cohorting contacts. 4. If any safeguarding concerns regarding restriction of contact with others, discuss how this can be managed within RA meeting/ IMT 5. If the contact becomes symptomatic arrange urgent clinical assessment. Ascertain when their last contact was and whether they need active follow up for 10 days.

Contacts	
Identify potential close contacts or lower risk contacts not meeting the full definition (Including but not limited to small boat passengers, initial Reception Centre, Taxi driver and passengers, health care providers)	
Consider sending warn and inform letter to lower risk contacts, usually via the Home Office.	
Advise that staff working in the setting should ensure they are up to date with their childhood immunisations (5x diphtheria containing vaccinations). There is no need for additional booster doses.	

# **Appendix 2. Warn and inform letter**

You can download a <u>warn and inform letter</u> in English and other languages.

# **Appendix 3. Data collection form**

The <u>data collection form</u> for cases among asylum seekers is available to download. Please note that for cases in asylum seekers, the 'Diphtheria: data collection form for asylum seekers (for HPTs)' should be used and not the original 'Diphtheria: national surveillance form for follow-up of confirmed toxigenic cases (for HPTs)'.

# **Appendix 4. Staff letter template**

Recipient's name

Address 1

Address 2

Address 3

Address 4

Postcode

Dear [name],



Diphtheria is a serious disease that usually begins with a sore throat and can quickly cause breathing problems. It can damage the heart and nervous system, and in severe cases, it can kill. The same bacteria can also cause nasty ulcers on the skin, particularly the legs. Diphtheria bacteria can live in the mouth, nose, throat or skin of people with the infection. It is spread through close and prolonged contact.

Everyone arriving to claim asylum in the UK is currently being offered a dose of a diphtheria containing vaccine to reduce the risk of diphtheria and some other infections. This is after a number of cases have been detected in centres for asylum seekers in both Kent and in other parts of the UK. No cases have been identified in staff working in these centres. You are not at risk from diphtheria if you are fully vaccinated. You can read the patient leaflet online:

#### https://www.gov.uk/government/publications/diphtheria-vaccination-resources

Diphtheria vaccination was introduced into the routine childhood immunisation programme in the UK in 1940 and now used worldwide. The vaccine is very effective and thanks to the highly successful vaccination programme, the disease is rare in the UK. In countries where immunisation services have been disrupted, however, the infection is more common.

The level of contact you would have with clients as part of your work is considered to be an extremely low risk for catching diphtheria. As a precaution, however, we are advising all staff working in AS settings to make sure they are up to date with all their immunisations including diphtheria containing vaccinations as per the UK schedule:

www.gov.uk/government/publications/the-complete-routine-immunisation-schedule

If you are unsure if you are up to date, please check with your GP practice.

Yours sincerely,

**Public Health Team** 

# Appendix 5. GP letter template for clearance swabs



#### Diphtheria: case management and clearance

Dear Dr [name],

The patients below have been identified as confirmed cases of diphtheria, resident at [name of hotel or residence], and require clearance.

Name: [case name]
Date of birth: [date of birth]
Address: [address]

As per the guidance, confirmed cases of diphtheria should:

- be immunised once they are clinically stable, see <u>Diphtheria</u>: the green book, chapter 15
- undergo microbiological clearance at the end of their treatment course

Two sets of clearance swabs are required to ensure elimination of the organism from the site where it was originally detected. A single swab from each of the following sites – nose, throat and wound (where applicable) should be obtained at least 24 hours after completing antibiotics and once again after (at least) a further 24 hours (that is, at 24 and 48 hours). These swabs can be sent as normal to your local microbiology lab, who can then send on to the regional Public Health laboratory for microbiological testing. Please ensure that these swabs and request forms are clearly labelled as 'Diphtheria Clearance swabs' (in addition to routine patient identifiers; name, surname, date of birth) to ensure correct processing and communication of these results.

Please see <u>Diphtheria</u>: <u>public health control and management</u> in England and <u>Supplementary</u> <u>guidance for cases and outbreaks in asylum seeker accommodation settings for further information</u>.

Please get back in touch with [HPT name] on [HPT contact details] if you have any further questions.

Kind regards, [name and position]

# About the UK Health Security Agency

UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation's health secure.

<u>UKHSA</u> is an executive agency, sponsored by the <u>Department of Health and Social Care</u>.

© Crown copyright 2023 Version 5

For queries relating to this document, please contact: <a href="mailto:immunisation.lead@ukhsa.gov.uk">immunisation.lead@ukhsa.gov.uk</a>

Published: November 2023

Publishing reference: GOV-15710

#### **OGL**

You may re-use this information (excluding logos) free of charge in any format or medium, under the terms of the Open Government Licence v3.0. To view this licence, visit <u>OGL</u>. Where we have identified any third party copyright information you will need to obtain permission from the copyright holders concerned.



UKHSA supports the Sustainable Development Goals

