UK Health Security Agency

Public health control and management of diphtheria in England

2025 guidelines

Contents

Executive summary

These guidelines were first developed in 1999 following the re-emergence of diphtheria in the former Soviet Union and Eastern Europe [1]. A revision of the guidance published in 2015 was prompted by changes in local epidemiology, including an increasing number of toxigenic *Corynebacterium ulcerans* cases, the introduction of routine quantitative real-time PCR (qPCR) testing of potentially toxigenic corynebacteria isolates by the national reference laboratory in April 2014 and the identification of circulating non-toxigenic toxin gene-bearing (NTTB) *C. diphtheriae* strains in England. Further revision followed an audit of the clinical, laboratory and public health management of toxigenic *C. diphtheriae*, toxigenic *C. ulcerans* and NTTB infections in England between 2014 and 2017 following the introduction of the revised guidelines. In addition, the updated guidelines were informed by the results from antimicrobial susceptibility testing of recent isolates and whole genome sequencing of NTTB strains to assess risk of reversion to toxigenic strains.

This 2025 revision updates the epidemiology of infection with toxigenic and non-toxigenic strains of diphtheria causing corynebacteria . It also expands the scope to include the principles of management of clusters of non-toxigenic C. *diphtheriae.*

These guidelines present the rationale and recommendations for the control of diphtheria in England. These guidelines complement existing guidance from the World Health Organization (WHO) [1, 2].

The updated guidelines are intended for those involved in the public health control of diphtheria, including:

- health protection teams (HPTs) in UKHSA
- National Health Service (NHS) staff at local and national levels in England

These guidelines are split into 3 main sections:

- Part 1. Background and rationale
- Part 2. Investigation and management of cases and close contacts
- Part 3. The management of outbreaks of toxigenic and non-toxigenic diphtheria causing corynebacteria .

Part 1. Background and rationale

1.1 Clinical features of diphtheria

Classical respiratory diphtheria is characterised by the insidious onset of membranous pharyngitis with fever, enlarged anterior cervical lymph nodes, and oedema of the surrounding soft tissue, giving rise to the ‘bull neck’ appearance. Although not always present, the membrane is typically grey, thick, fibrinous, and firmly adherent. Laryngeal diphtheria is characterised by gradually increasing hoarseness and stridor and most commonly occurs as an extension of pharyngeal involvement in children [3, 4]. Nasal diphtheria, usually mild and chronic, is marked by unilateral or bilateral nasal discharge, which is initially clear and later becomes bloody. Cutaneous diphtheria usually appears on exposed limbs, particularly the legs. The lesions start as vesicles and quickly form small, clearly demarcated and sometimes multiple, ulcers that may be difficult to distinguish from impetigo [5]. The classic description of diphtheritic lesions is that they are usually covered with an eschar, a hard bluish-grey membrane that is slightly raised. Individuals may have both respiratory and cutaneous symptoms.

Diphtheria is no longer easily diagnosed on clinical grounds as classic respiratory diphtheria is now rare in the UK due to the success of the routine immunisation programme. However, when healthcare systems are disrupted and vaccine coverage declines, diphtheria is one of the first of the vaccine preventable diseases to emerge as was the case in the former Soviet Union in the 1990s and, more recently, in camps of displaced Myanmar nationals in Bangladesh [6, 7].

Mild respiratory cases of the disease resemble streptococcal pharyngitis and the classical pseudomembrane of the pharynx may not develop, particularly in people who have been vaccinated. With vaccine coverage for the routine childhood vaccination programme having been maintained at around 95% for the last 2 decades, the majority of cases within the UK now are mild infections in partially immunised individuals, or in adults that have been fully immunised but have waning immunity. Infections may still occur in fully vaccinated individuals as the diphtheria toxoid vaccine prevents the clinical manifestations of toxigenic strains but does not prevent acquisition of carriage [8]. As the disease is increasingly rare, most clinicians will not have encountered a case before and therefore may miss the clinical diagnosis [3 to 5, 8, 9]. For example, potentially toxigenic corynebacteria infections are rarely included in the differential diagnosis of pharyngitis. Care should be taken when interpreting the presence of diphtheroids as representing coincidental commensals. Not all laboratories routinely culture pharyngeal swabs for corynebacteria and wound swabs in particular may contain additional potentially causative organisms, further increasing the potential for missed or delayed diagnosis [8, 10].

1.2 Microbiology

Respiratory or cutaneous diphtheria is caused by toxigenic strains (those expressing diphtheria toxin) of *C. diphtheriae* and *C. ulcerans*, and, very rarely, *C. pseudotuberculosis*. *C. diphtheriae* is a non-sporing, non-encapsulated, and non-motile Gram positive bacillus [11]. *C. ulcerans* and *C. pseudotuberculosis* are zoonotic pathogens. There are many (at least 115) other species of corynebacteria including *C. pseudodiptheriticum* which are not able to carry the toxin gene and are thus unable to cause diphtheria. Four biovars of *C. diphtheriae* can be distinguished by colonial morphology and biochemical characteristics: gravis, intermedius, mitis, and belfanti [12]. The biovar belfanti was reported to be clearly separated phylogenetically from *C. diphtheriae* biovar mitis and gravis and a new species, *Corynebacterium belfantii* sp. nov. proposed [13]. The predominant toxigenic *C. diphtheriae* biovar in the UK between 2015 and 2020 was biovar mitis (77% of cases, followed by biovar gravis with 23% of cases; between 1986 and 2008 81% of cases involved biovar mitis and 17% biovar gravis [14] (Fry and others, unpublished data). The clinical and public health management of patients and contacts is identical for all toxigenic strains; however, potentially zoonotic infections also require the involvement of colleagues in the APHA. The microbiology of *C. ulcerans* is discussed in section 1.5.

Toxigenic strains are lysogenic for a family of corynebacteriophages that carry the structural gene for diphtheria toxin, *tox*. The toxin is a 535 amino-acid 58 kDa exotoxin whose active form consists of 2 polypeptide chains linked by a disulphide bond [11, 15]. Following infection, secretion of this exotoxin can cause local tissue necrosis and, when absorbed into the bloodstream, systemic manifestations including demyelinating peripheral neuritis and myocarditis can occur as late complications. Non-toxigenic strains of *C. diphtheriae* can cause severe infections, including myocarditis, endocarditis, bacteraemia, septic arthritis, osteomyelitis, neuritis and epiglottitis [15 to 26]. Similarly, non-toxigenic strains of *C. ulcerans* have been isolated from ulcerative lesions. However, the mechanisms of the pathogenicity of non-toxigenic strains are not well understood. This is further discussed in section 1.6.

1.2.1 Laboratory confirmation

Laboratory confirmation is typically by a combination of culture, bacterial isolation and preliminary identification of *C. diphtheriae, C. ulcerans or C. pseudotuberculosis* in a clinical laboratory followed by confirmation and toxigenicity testing at a reference laboratory. 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 local diagnostic laboratory for bacterial culture.

The swab containers should be labelled accordingly with unique identifiers, source of the specimen and collection date, clinical details should accompany the specimen.

The common isolation methods in use in most laboratories are microbiological culture on standard blood agar (or tellurite-containing media, such as Hoyle’s agar). These tellurite

containing media are both partially selective and differential for the isolation of toxigenic corynebacteria. The potassium tellurite inhibits a variety of both Gram negative and Gram positive bacteria and allows for the detection of tellurite reduction, resulting in colonies with a grey-black appearance, which is typically, but not exclusively found in corynebacteria. Putative corynebacterial colonies which prove to be catalase positive, Gram-positive coryneform rods may be further identified by conventional biochemical testing using commercial systems, such as API Coryne (bioMèrieux), VITEK microbial identification system (bioMeriéux) or Matrix Assisted Laser Desorption/Ionization – Time of Flight Mass Spectrometry (MALDI-TOF MS) (for example, Bruker, BioMèrieux, Shimazdu) [27].

Primary diagnostic laboratories should be able to putatively identify the potentially toxigenic corynebacteria *C. diphtheriae* and *C. ulcerans* to species level. If laboratories do not have access to MALDI-TOF or API Coryne, we recommend that in addition to Hoyle's agar they also stock Tinsdale agar. This would assist in the identification of the potentially toxigenic corynebacteria species which are cystinase positive so would appear as grey-black colonies, surrounded by a brown-black halo on the agar whilst other corynebacterial species would not. If primary diagnostic laboratories that do not have access to primary and selective agars such as Hoyle's agar, then primary swabs may be sent to UKHSA clinical network laboratories (CNL). Any isolate with an identification of *C. ulcerans*/*C. diphtheriae*/*C. pseudotuberculosis* should be sent promptly to the national reference laboratory.

All of the above methods can have good specificity but the confirmation of identification, and the determination of toxigenicity requires submission of the isolate to the Respiratory and Vaccine Preventable Bacteria Reference Unit (RVPBRU), UK Health Security Agency, London. The front-line test for confirmation of identification and the presence of the *tox* gene is qPCR. This assay uses DNA extracts from submitted isolates to identify *C. diphtheriae*, *C. ulcerans*/*C. pseudotuberculosis* targets, plus the presence of the *tox* gene [28]. The assay targets the RNA polymerase β-subunit-encoding gene (*rpoB*) and the A-subunit of the diphtheria toxin gene (*tox*). When the *tox* gene is detected, the isolate undergoes an Elek immunoprecipitation test to confirm expression of the diphtheria toxin [28].

Review of the European literature [29] from the 2022 to 2023 outbreak of diphtheria among asylum seekers (AS) prompted some concern around a small number of multi-drug resistant isolates associated with the Sequence Type (ST)377 strain, harbouring a Class 1 integron. This integron conveyed aminoglycoside, macrolide, sulphonamide, tetracycline and trimethoprim resistance. In addition, a beta lactam gene (blaOXA-2) 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. It is strongly recommended that local laboratories undertake antimicrobial susceptibility testing on all *C. diphtheriae*/*C. ulcerans*/*C. pseudotuberculosis* isolates, to include as a minimum, sensitivity to penicillin and erythromycin (according to local methods and reported using the European Committee on Antimicrobial Susceptibility Testing (EUCAST) Clinical Breakpoint Tables v.13.1 [30]. If resistance to either penicillin (R> 1mg/L) or erythromycin (R> 0.06mg/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 the isolate should be referred for typing and antimicrobial susceptibility confirmation.

Sending isolates for toxigenicity testing

Please ensure the isolate and not the sample itself is sent for toxigenicity testing, as this would cause substantial delays. Submission of additional samples (such as membrane) should be discussed with the reference laboratory. Please notify the laboratory RVPBRU (telephone 0208 327 7887, Bacteriology triage or 0208 327 7331 Vaccine Preventable Bacteria Section) before sending potentially toxigenic isolates for toxigenicity testing within working hours on a weekday.

Outside these hours, please notify the Colindale duty doctor on 0208 200 4400. Always use the Vaccine Preventable Bacteria Section request form R3 and ensure full contact telephone numbers are provided on the form to allow timely reporting of results.

Send isolates to:

UK Health Security Agency Colindale
Vaccine Preventable Bacteria Section
Bacteriology Reference Department
Respiratory and Vaccine Preventable Bacteria Reference Unit (RVPBRU)
61 Colindale Avenue
London NW9 5HT

Isolates may also be sent by Hays DX, in which case the following address should be used:

Vaccine Preventable Bacteria Section
UKHSA Colindale
Bacteriology
DX 6530002
Colindale NW

1.2.2 Laboratory safety

Although rare, laboratory-acquired infections have been reported [31, 32]. In the UK toxigenic *C. diphtheriae*, *C. ulcerans* and *C. pseudotuberculosis* are classified by the UK Advisory Committee on Dangerous Pathogens (ACDP) as Hazard Group 2. Laboratories should have their own local safety and risk assessment documentation and staff be made aware of the risks involved in working with toxigenic corynebacteria prior to work. Staff must comply with personal protective equipment regulations for that laboratory, wear suitable protective clothing when handling these organisms and must be deemed competent to perform the relevant Standard

Operating Procedures. Wherever practical and for all procedures which may potentially generate an aerosol, a microbiological safety cabinet (MSC) should be used. The use of sterile disposable loops is recommended for the spreading of sample material onto culture media. All staff that routinely handle cultures of potentially toxigenic corynebacteria should be fully vaccinated (including booster vaccinations).

1.2.3 Immunisation of laboratory staff

Recommendations for immunisation to protect against diphtheria are as per Green Book Chapter 12: Immunisation of healthcare and laboratory staff. Recommended diphtheria antitoxin antibody levels are 0.1 IU/mL for those handling or regularly exposed to toxigenic strains.

Note: these antibody levels and interpretive criteria are based on those described by the World Health Organization's recommendations using a functional (toxin neutralisation) assay [27]. The Vaccine Preventable Bacteria Section also offers testing for the determination of diphtheria antitoxin antibody levels using a toxin neutralisation assay. All requests should be submitted using the R3: vaccine preventable bacteria section request form.

1.3 Transmission and carriage of diphtheria-causing organisms

The incubation period for diphtheria is usually 2 to 5 days [33], but may be longer, with duration of up to 10 days reported [25, 34]. The common mode of transmission of *C. diphtheriae* is via droplet spread from a person with respiratory diphtheria. Alternative modes of transmission are direct contact with cutaneous diphtheria lesions, infected secretions or via contact with infected animals (*C. ulcerans*), or consumption of unpasteurised dairy products (*C. ulcerans*).

Closeness and duration of contact are important in determining the likelihood of spread of the disease, and prolonged close contact is usually required for spread, as reported in a study showing greater risk in children sharing a dormitory [35]. In the absence of clear evidence on transmission of diphtheria, principles used in the public health management of meningococcal disease can be applied [36]. Contacts considered at risk are those who have had prolonged close contact with a case or known carrier in a household-type setting, or those who have had transient close contact if they have been directly exposed to large particle droplets or secretions. Cutaneous diphtheria may be spread by direct contact with cutaneous lesions. Contact with articles soiled with the discharge of infected people or animals may play a role in transmission [24, 28, 33, 37].

Asymptomatic carriage of toxigenic corynebacteria may occur during the incubation period of diphtheria, during convalescence, or for an unknown duration in healthy people. Patients convalescing from diphtheria may harbour corynebacteria in the pharynx or nose for many weeks [15]. Carriage can be eradicated by antibiotic treatment: macrolides (erythromycin,

clarithromycin and azithromycin) and penicillin are all likely to be effective but antimicrobial susceptibility testing is required (see section 2.6.4).

In Western Europe, carriage and disease has become very uncommon since the introduction of routine immunisation and isolation of the organism from healthy individuals is extremely rare. Although vaccination does not eliminate carriage it reduces transmission by up to 60% in an outbreak setting [38]. A carriage study conducted during a 7 month period in 2007 to 2008 in 10 European countries identified only 6 toxigenic strains of *C. diphtheriae*: 2 were from symptomatic patients in Latvia (the country with the highest reported incidence of diphtheria in the European Union) and 4 (2 cases, 2 carriers) were from Lithuania where the previously last reported case was in 2002 [10].

There is some evidence that cutaneous diphtheria may be more transmissible than respiratory diphtheria [39]. In tropical countries, cutaneous diphtheria lesions may act as reservoirs of infection. Both cases and contacts of cutaneous diphtheria may develop respiratory diphtheria [11, 39]. In the UK and Europe, most cutaneous cases are caused by imported toxigenic *C. diphtheriae* infections [14, 40 to 44], although cutaneous *C. ulcerans* infections are increasingly being reported [8,14, 45, 46]. Occasionally patients have developed respiratory diphtheria following cutaneous infection [47]. More detailed information on transmission of *C. ulcerans* is in section 1.5.

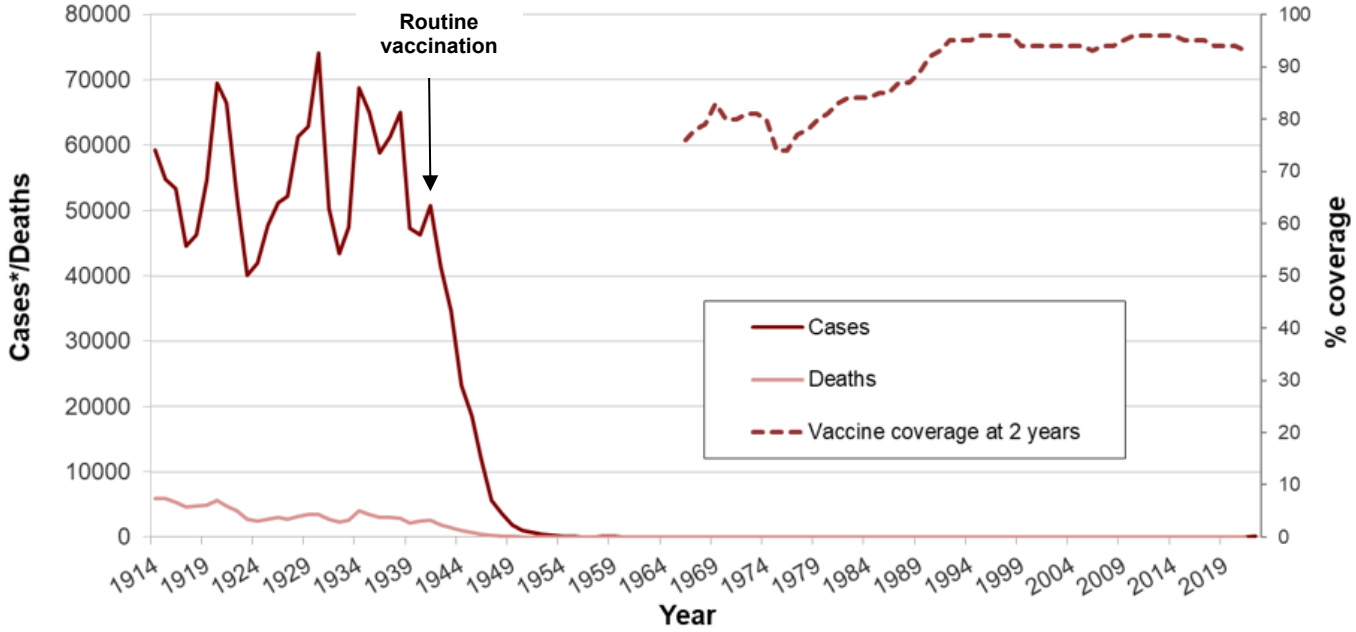
1.4 Epidemiology and control of diphtheria in England

Diphtheria is a notifiable disease under the Infectious Disease (Notification) Act of 1889 and the updated 2010 regulations. Doctors in England have a statutory duty to notify a ‘proper officer’, usually through the HPT, of all forms of diphtheria diagnosed clinically, including cutaneous [10].

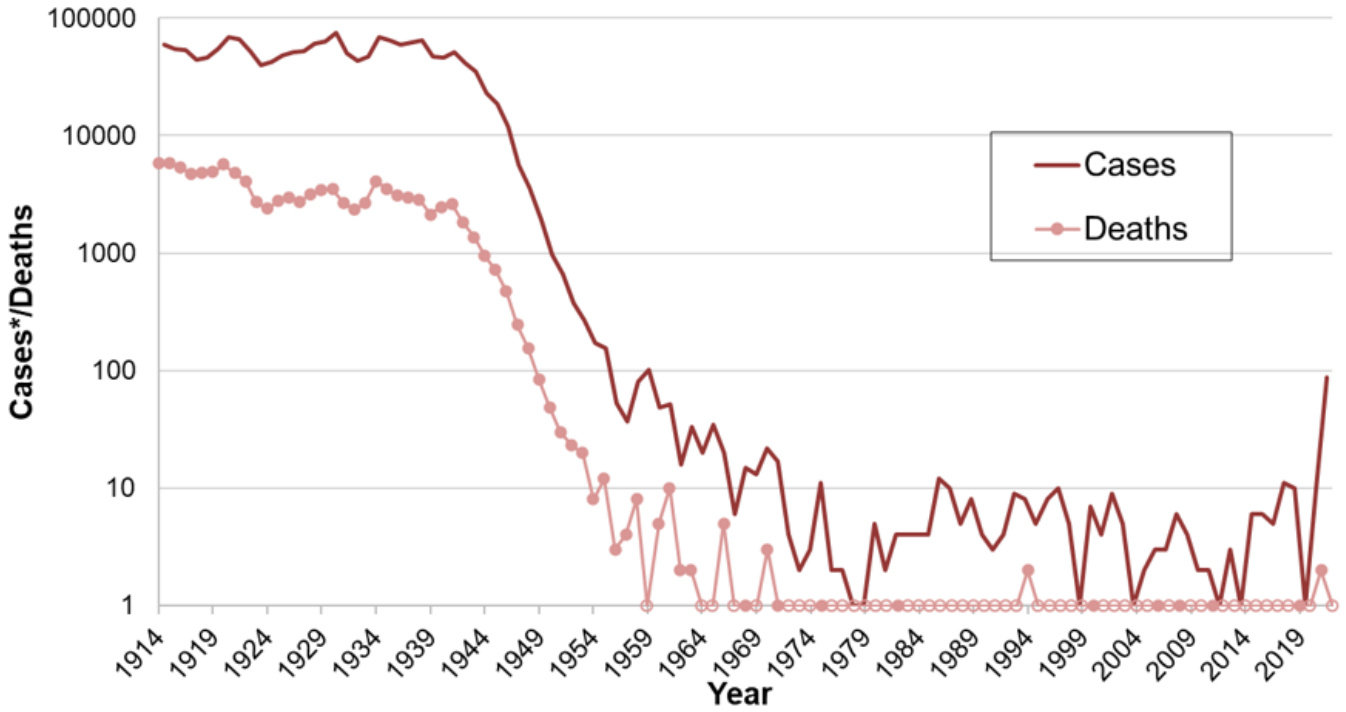
Also under these regulations, laboratories have a duty to notify human isolates of *C. diphtheriae* and *C. ulcerans* [48]. UKHSA also requests notification of human isolates of *C. pseudotuberculosis* [49]. Laboratories should notify the HPT for the case, and all potentially toxigenic isolates from these 3 species should be referred promptly to the national reference laboratory for toxigenicity testing (see section 2.3.2).

Diphtheria was once one of the most feared childhood diseases in the UK, with more than 61,000 cases and 3,283 deaths in 1940 [50], this has dramatically reduced following introduction of mass immunisation in 1942 and by 1957 there were only 38 cases and 6 deaths [50, 51].

Diphtheria cases* and deaths, England and Wales†, 1914 to 2022



Diphtheria cases* and deaths, England and Wales†, 1914 to 2022



* Notifications up to 1985, laboratory confirmed cases 1986 to 2021.
† From 2016, data from England only.

Diphtheria vaccine is made from inactivated diphtheria toxin (toxoid) and protects individuals from the effects of toxin-producing corynebacteria. In the UK, diphtheria toxoid is included in the immunisation schedule at 8, 12 and 16 weeks of age followed by 2 boosters (at approximately 3 and 14 years of age), with further boosters recommended for travel and as part of the maternal pertussis immunisation programme due to inclusion in the pertussis booster vaccine [50, 52]. In

addition, CRM_{197} containing vaccines (a non-toxigenic mutant of diphtheria toxin used as a carrier protein), such as pneumococcal conjugate vaccine provide additional boosting [53].

Data on the duration of the protective effectiveness conferred by a complete diphtheria vaccine course is limited [54], however, serological studies have demonstrated that vaccine-derived immunity wanes over time for both fully immunised and partially immunised individuals. The proportion of individuals with fully-protective antibody levels declines by approximately 0.6% per year since vaccination [38]. Full vaccination with 3 or more doses has been shown to be 87% effective against symptomatic disease (up to 99% with 5 doses) and 81% effective in preventing severe disease. Diphtheria toxoid vaccines do not prevent colonisation (estimated 17% effective) but 3 doses have been estimated to reduce transmission by 60% [38].

Diphtheria vaccine coverage in the UK remains high; annual coverage of the primary course evaluated at one and 2 years of age was at 94% and 96% in 2010 but there has been a gradual small decline since this time, to 91 and 92% in 2023 to 2024 [55]. Assessment of preschool booster coverage started in 1999 to 2000; coverage remained between 78% and 82% during the following decade, before increasing to 89% in 2012 to 2013, and then following a declining trend to 83% in 2023 to 2024. .

Coverage assessment of the tetanus, diphtheria and polio adolescent booster began in 2016. The coronavirus (COVID-19) pandemic impacted coverage but this has somewhat recovered to 72% in children aged 14 to 15 years [56].

There have been significant changes in diphtheria epidemiology over time in the UK, including the identification of the zoonotic risk of *C. ulcerans* (see section 1.5) and changes in disease presentation, such as the increase of mild respiratory disease in partially vaccinated individuals and a relative increase in the reports of cutaneous cases [8, 14]. From the start of laboratory surveillance in 1986 until the end of 2023, there have been 233 toxigenic cases of diphtheria in England and Wales with the number of cases per year varying from one to 87.

An increase in notifications of diphtheria since 1992 was due to a rise in isolations of non-toxigenic strains of C. diphtheriae which do not cause classical diphtheria disease [21]. These may be associated with a mild sore throat without signs of toxicity.

Until the early 1990s, toxigenic infections were more commonly caused by *C. diphtheriae* than *C. ulcerans*, whereas between the 1990s and 2008, *C. ulcerans* became the predominant cause, responsible for more than two-thirds of cases. Between 2009 to 2017, whilst overall incidence remained low, there was a large increase in the proportion of cutaneous cases, particularly caused by *C. diphtheriae* [8]. Around 2014 there was a significant increase in the proportion of referred isolates from wounds and changes to local testing practices in NHS laboratories, both of which may have contributed to this rise [8]. From 2018 to 2021, the proportion of cases caused by *C. ulcerans* increased again. Both species may be isolated from both respiratory and cutaneous presentations.

From the start of laboratory surveillance in 1986 until 2013, the clinical presentation in over 85% of toxigenic infections was non-classical respiratory diphtheria for both *C. diphtheriae* (59 of 68 isolates; 87%) and *C. ulcerans* (59 of 66 isolates; 89%) (see section 2.2 for case definitions). However, both *C. ulcerans* and *C. diphtheriae* resulted in severe or fatal disease with 6 deaths between 1986 and 2013, 4 of which were caused by *C. ulcerans* [41].

In the surveillance period 2014 to 2021, 52% of toxigenic diphtheria infections were cutaneous. Cases with toxigenic *C. diphtheriae* have been more likely to be cutaneous in presentation, (14 of 22 isolates, 64%), with 2 cases with mild respiratory presentation, 4 asymptomatic cases, one case with other presentation and one case with classical respiratory diphtheria. There was a further clinical case of classical respiratory diphtheria in 2018; no diphtheria organism was isolated; however, the case responded well to treatment with DAT. Cases with toxigenic *C. ulcerans* have similarly been more likely to be cutaneous in presentation (12 of 28 isolates, 43%), with 8 cases being of mild respiratory presentation, 3 cases with classical respiratory diphtheria, 2 asymptomatic cases and 3 cases with other presentation. Three cases died during this period, all with *C. ulcerans infection* and all of whom were inadequately immunised.

Eighteen NTTB *C. diphtheriae* (see section 1.6.1) were also detected between the introduction of PCR testing until the end of 2021. An increase in the detection of cutaneous cases has coincided with an increase in the submission for testing of isolates from wound swabs (see Section 1.7), suggesting changes in testing and identification methods at frontline laboratories such as the use of MALDI-TOF MS may be at least partially responsible.

Risk factors for acquisition of the 2 species do partially differ. Assessment of risk factors is based on standardised risk factor information collected since 1995; companion animal information was added in 2003 following recognition of risk [57]. The main risk factor for all diphtheria cases is being unvaccinated; between 2009 and 2017, 67% of cases were inadequately vaccinated [8]; and 69% from 2018 onwards. However, 43% of cases during this time period were fully vaccinated, mostly younger individuals presenting with mild cutaneous or mild respiratory forms of both *C. diphtheriae* and C. *ulcerans*. *C. ulcerans* was more commonly seen in older individuals with unknown or partial vaccination history. Suboptimal diphtheria vaccination status for both toxigenic *C. diphtheriae* and *C. ulcerans* infections was strongly associated with the risk of hospitalisation and death.

Diphtheria cases continue to be reported in South-East Asia, South America, Africa, Oceania and India. A large number of UK citizens travel to and from these regions, maintaining the possibility of the reintroduction of toxigenic *C. diphtheriae* infections into the UK. Between 2009 and 2017, 78% of cases were characterised as imported [8].

Toxigenic *C. ulcerans* infections were previously associated with consumption of raw dairy products, but have become more recently associated with contact with companion animals. In a review of 62 cases of *C. ulcerans* between 1986 and 2008, 7 of 59 (12%) *C. ulcerans* cases were recorded as having consumed raw milk or dairy products, one of these had also had contact with cattle [14].

In the surveillance period 2009 – 2021, all 34 *C. ulcerans* cases reported contact with domestic animals; contact with non-domesticated animals was also noted for 7 cases and 4 reported a history of consuming unpasteurised dairy products. The evidence on companion animal transmission to humans is limited because of the relatively small number of cases, high exposure prevalence to companion animals in the general population, and lack of (or timing of) swabbing of animal contacts [41]. However, evidence is slowly accumulating. In England, in a surveillance period from 2009, swabs were taken from 42 companion animals in 23 cases, most commonly from dogs and cats; in 7 cases, at least one companion animal screened positive for toxigenic *C. ulcerans* (4 dogs and one cat; 3 cases had contact with the same positive dog). *Corynebacterium ulcerans* was not detected in any of the other companion animals that underwent swabbing although a zoonotic source of infection was considered most likely in these incidents.

The first documented transmission of toxigenic *C. diphtheriae* in the UK for over 30 years occurred in the East of England in 2017, when a contact of a case with cutaneous *C. diphtheriae* infection who had recently returned from Africa, but had not herself travelled, developed a mild respiratory diphtheria infection [58]. There was also a cluster of cases in South Yorkshire in 2017 and 2018 which were found to belong to the same Sequence Type by multi-locus sequence typing (MLST) with further cases confirmed from late 2021 in the same geographical region. This suggested there may be low level transmission in an under-vaccinated community, although there is no evidence this has been sustained (PHE, 2017; UKHSA 2021).

This incident represented the largest cluster of toxigenic diphtheria in the UK in recent years, and only the second suspected event of onward transmission in 3 decades. Other positive contacts have been identified for cases of *C. diphtheriae* with a shared history of travel and for household contacts of *C. ulcerans* with a shared infected domestic animal, but it is not possible to state in these cases whether human-to-human transmission had occurred.

From June 2022, there was an increase in cases of diphtheria caused by toxigenic *C. diphtheriae* reported among asylum seekers arriving by small boats to England, mirroring a wider situation across a number of European countries [59, 60]. Between 1 January 2022 and 30th June, 87 confirmed cases and one probable case, were reported. Most of these cases were identified in 2022 (n=73),13 cases notified in 2023, no cases in 2024 and 2 cases in 2025 (to 30th June) [61]. Cases were predominantly among young males, with toxigenic *C. diphtheriae* isolated from skin lesions or injuries sustained en route to England [61, 62], and included a small number of cases with a macrolide-resistant strain. Supplementary guidance on the management of these cases is available on the UKHSA website.

The most effective treatment of severe cases of diphtheria involves the prompt administration of DAT which binds to and neutralises circulating toxin which has not yet bound to tissue [49]. Clearance of the organism is also achieved with appropriate antibiotics (see section 2.6.3). DAT was first produced in the late 19th century and is still produced using serum from horses

hyperimmunized with diphtheria toxoid. Currently there is one equine DAT product available in the UK for treatment of probable or confirmed diphtheria cases [63].

Public health management of clinical cases of diphtheria in the UK is provided by HPTs, including identification, assessment and prophylaxis of close contacts (see Section 2). Guidance on the use of DAT can be found on the UKHSA website.

1.5 Corynebacterium ulcerans

The first report of the isolation of *Corynebacterium ulcerans* was in January 1920 when the organism was cultured from a patient who had clinically recovered from diphtheria previously that year [64]. It has been associated with a range of clinical symptoms including, relatively mild respiratory (for example, sore throat) and/or cutaneous to classical respiratory diphtheria with pseudomembrane [45, 65 to 73]. Several deaths in the UK have been attributed to this infection [8, 14].

Corynebacterium ulcerans may infect the bovine udder and previously an association between human *C. ulcerans* infection and drinking raw milk and unpasteurised milk products was observed [69, 70]. The organism has a wide host range and has been isolated from domestic, wild and captive animals [74]. More recently an increase in toxigenic *C. ulcerans* infections associated with close contact to domestic [75] and companion animals has been reported [8, 40, 76 to 80]. Person-to-person spread has not been definitively documented and the majority of swabs taken from close contacts have been culture-negative for *C. ulcerans* [66, 69, 72, 81]. However, a number of incidents have raised this as a possibility. In 1996 and 1998 toxigenic *C. ulcerans* was isolated from asymptomatic contacts of cases [14]. In more recent cases in Germany and Belgium, in 2014 and 2016 respectively, asymptomatic contacts also tested positive for toxigenic *C. ulcerans* which belonged to the same DNA sequence type (by MLST) as the index cases [82, 83]. In Germany, the contact was a grandmother living on the same farm as the symptomatic index case, who had limited contact with the animals on the farm, including the suspected animal source. The contact of the Belgian case was a nurse caring for the patient, suggesting that a shared animal source was unlikely, further supporting the possibility of person-to-person transmission of *C. ulcerans.*

In 1997, following 2 reports of cases of membranous pharyngitis caused by toxigenic *C. ulcerans*, the US Centers for Disease Control and Prevention recommended that people exposed to the index case should be treated along similar lines to cases exposed to toxigenic *C. diphtheriae*. This was later revised in 2011 to advise vaccination of unimmunised contacts rather than provision of prophylactic antibiotics. This advice was given because there was inadequate information about human-to-human transmission of this organism [84, 85]. In the UK, because possible person-to-person transmission of toxigenic *C. ulcerans* has been observed [14], chemoprophylaxis of contacts of a case, from whom isolation of a toxigenic strain has been confirmed, is recommended.

1.6 Non-toxigenic C. diphtheriae and C. ulcerans

There are more than 115 species of Corynebacterium described to date, isolated from a wide range of human, veterinary and environmental sources [86]. Approximately 50% have been isolated from human clinical specimens, many of which are considered part of the normal flora, but may also opportunistically cause disease [87]. It is well established that the ability of *C. diphtheriae*, *C. ulcerans* and *C. pseudotuberculosis* to produce diphtheria toxin is mediated by infection of these species by bacteriophages carrying the *tox* gene. However, the mechanism of pathogenicity of non-toxigenic strains of *C. diphtheriae* and *C. ulcerans* in humans is not well understood although a number of additional (potential) virulence factors have been described, including pili in both species and phospholipase D in *C. ulcerans* [68, 88, 89].

Examples illustrating the diverse clinical presentations of non-toxigenic corynebacteria include 2 historical cases who accidentally ingested non-toxigenic *C. diphtheriae* biovar mitis in a laboratory, developing clinical diphtheria with a sore throat and tonsillar membrane (80). In Australia, 7 aggressive cases of endocarditis due to non-toxigenic *C. diphtheriae* biovar gravis were reported in a single year in 1993, including 4 major vascular complications and one death [23]. Other cases of endocarditis caused by non-toxigenic strains have been reported in India [16], the USA [17], Poland [26], Germany [25], New Zealand [18] and England [19]. Non-toxigenic strains have also been associated with disease in immunocompromised individuals [20], and with recurrent pharyngitis in young adults [21]. For example, cutaneous lesions have been reported in a Canadian homeless population [22], and there was an increase in identification of disease-causing non-toxigenic strains of *C. diphtheriae* in Scotland reported in 2011, all presenting with persistent sore throat [90].

A multi-centre European carriage study identified that carriage rates of non-toxigenic corynebacteria ranged from zero (Bulgaria, Finland, Greece, Ireland, Italy) to 4.0 per 1,000 (95% CI 2.0 to7.1) in Turkey, though the zero estimates may have been due to small sample sizes [10].

Five cases of severe, fulminant infective endocarditis (IE) caused by C. diphtheriae were reported in England between July 2024 and January 2025, including one fatality [91]. These cases reported substance use, although did not report recent intravenous drug use and the majority were experiencing homelessness or were residing in a hostel setting at the time of onset of symptoms [91]. Case finding as part of the public health investigation suggested these were likely to represent the more serious cases within a range of disease presentations with non-toxigenic C. diphtheriae, from mild skin infection (often with coinfections with Staphylococcus aureus or Group A Streptococcus), to blood stream infections. A review of available data also suggested cases may be clustered in some city hostel settings for those experiencing homelessness. Sequencing of non-toxigenic strains of C. diphtheriae is not routinely performed but a non-toxigenic C. diphtheriae, ST559 was responsible for 4 out of 5 of the cases with IE.

An increase in the number of cases of non-toxigenic C. diphtheriae infection in people with substance use who experience homelessness has also been reported since 2023 in some cities in the EU (personal communication UKHSA 2025). Cases have predominately presented with skin infections but also bloodstream infections and more rarely with IE.

Clinical management of non-toxigenic corynebacteria depends on case presentation and site of disease: detailed instructions for individual treatment are outside the scope of these guidelines. Contact tracing is not required around cases of non-toxigenic C. diphtheriae. Contacts do not require postexposure prophylaxis. Any individual with an infected skin wound or lesions should have routine swabs taken and antibiotics prescribed, guided by local antibiotic susceptibility testing.

There is no public health action required for individuals either with a non-toxigenic strain or NTTB *C. diphtheriae* or *C. ulcerans* (see section 1.6.1). However, HPTs should provide advice where clusters of infection with non-toxigenic C. *diphtheriae* (most likely skin or soft tissue infections) arise in settings for vulnerable groups, for example homeless hostels and shelters, see section 3.

Routine laboratory surveillance began in England and Wales in 1986 and allows monitoring of non-toxigenic *C. diphtheriae* and *C. ulcerans* in addition to diphtheria cases. Data from 1986 onwards is available on the UKHSA website [41]. This surveillance data shows that between 1986 and 2013, 2,662 *C. diphtheriae* isolates were received, of which 68 (2.6%) were toxigenic.

An increase in laboratory reports of non-toxigenic *C. diphtheriae* was observed from 58 in 1992, peaking to 294 in 2000 before falling to 39 in 2009 and remaining around 30 to 60 isolates per year up to 2022. This increase in reports may have been attributed to increased case ascertainment as public health laboratories were encouraged at this time to routinely screen pharyngeal swabs for corynebacteria following the resurgence of diphtheria in the former Soviet Union [21]. Between 2014 and 2021, 448 human *C. diphtheriae* isolates were received, of which 22 (4.9%) were toxigenic. Between 2014 and 2021, 48 human *C. ulcerans* isolates were received, of which 31 (64.6%) were toxigenic. Most isolates are from throat swabs, but an increasing proportion of isolates from wound swabs is noted.

Analysis of the total index case isolates submitted for species identification and toxigenicity since 2009 highlighted a significant difference in toxigenicity rates between *C. diphtheriae* and *C. ulcerans*, with approximately 5% of samples being toxin-producing for *C. diphtheriae* and 50% to 60% toxin-producing for *C. ulcerans.* Since submissions to the RVPBRU are based on isolates from symptomatic cases, they are not useful for estimation of overall non-toxigenic corynebacteria carriage rate in the UK, but a minimum incidence rate of carriage in symptomatic cases of 0.73 cases per 100,000 population per year was estimated, which is in line with estimates from other European countries [10]. It should be noted that proportions of toxigenic to non-toxigenic strains of C. diphtheriae evolved dramatically during the outbreak of diphtheria in the AS population in 2022.

1.6.1 Non-toxigenic toxin gene-bearing C. diphtheriae and C. ulcerans (NTTB)

Non-toxigenic strains *C. diphtheriae*, *C. ulcerans* (and *C. pseudotuberculosis*) usually lack the entire *tox* gene. Exceptionally some non-toxigenic strains can also carry variants of the tox operon such that the diphtheria toxin cannot be expressed phenotypically. These strains are designated non-toxigenic toxin gene-bearing (NTTB) and to date NTTB clinical isolates of both *C. diphtheriae* and more rarely in *C. ulcerans* have been reported. The qPCR employed by the RVPBRU is able to detect some of these non-functional *tox* gene variants, so an NTTB will usually appear qPCR tox positive, Elek-negative. These NTTB strains were originally described during the diphtheria epidemics in countries of the former Soviet Union within the WHO European region in the 1990s [87]. In a study of 828 *C. diphtheriae* non-toxigenic strains isolated in different regions of Russia between 1994 and 2002, approximately 14% were found to be NTTB and differed from the epidemic toxin producing strains in both biovar and ribotype.

Four NTTB strains of *C. diphtheriae* were isolated from humans in the UK between March 2011 and June 2012. From August 2014 to March 2021, 8 NTTB *C. diphtheriae* strains were isolated from 6 epidemiologically linked cases in the UK [92]. Since 2014, 5 other NTTB *C. diphtheriae* strains were isolated in the UK with geographical, but no known epidemiological links. The WHO Collaborating Centre for Diphtheria and Streptococcal Infections, Colindale, London has also confirmed 2 non-UK NTTB isolates: a *C. diphtheriae* from a cat from Belgium in 2021 [57], and a *C. ulcerans* from a human case from Sweden in 2015.

Retrospective analyses of culture collections have revealed NTTB *C. diphtheriae* in Canada (from 1999 to 2003) [93] and Romania (from 1963 to 2007) [94]. Similar NTTB strains of *C. ulcerans* have also been isolated from game animals in Germany indicating potential reservoirs for human infection [95, 96]. As described earlier, discovery of these NTTB strains has been largely due to the use of PCR assays (both standard and real-time) targeting the *tox* gene together with use of the Elek test, and also retrospective testing. (section 1.2).
In an investigation of a cluster and subsequent transmission of NTTB (with a deletion in *tox*) over a 7 year period, no evidence of reversion to diphtheria toxin expression or isolation of toxigenic strain was observed [92]. The likelihood of NTTB gaining the ability to become toxigenic is considered highly unlikely and therefore updated advice included in these guidelines is to manage such cases as non-toxigenic.

1.7 History of guidelines

These guidelines were first developed in 1999 following the re-emergence of diphtheria in the former Soviet Union and Eastern Europe [97]. A revision of the guidance, published in 2015, was prompted by changes in disease epidemiology, including the increasing number of *C. ulcerans* cases, the introduction of routine qPCR testing of potentially toxigenic corynebacteria isolates by the national reference laboratory in April 2014, and the identification of circulating NTTB *C. diphtheriae* strains in England.

The 2015 guidelines were assessed during an audit of the clinical, laboratory and public health management of qPCR diphtheria toxin gene positive *C. diphtheriae* and *C ulcerans* cases and NTTB *C. diphtheriae* infection in England between 2014 and 2017 [98]. The audit concluded that there was good recording of clinical presentation and case definitions, and in most cases, appropriate public health actions were initiated according to the case definition. Travel, animal contact and immunisation history risk factors were well-documented, but other factors such as occupation, contact with other travellers less so. There was limited documentation of clearance swabs having been taken or clinical details, such as whether patients had been hospitalised, type of antibiotic received and whether they had been assessed for anti-toxin, although this may reflect record keeping rather than an absence of this having taken place. Only one-third of cases were formally notified via the Notifications of infectious diseases (NOIDs) system. All HPTs collected information on close contacts, but healthcare workers (HCWs) were not always included at early stages. It was concluded that timeframes for public health actions should be more clearly specified in the UKHSA guidance, including a need for incident management teams (IMTs) to be convened, preferably within 24 hours. There should be improved efforts to consider and identify HCW contacts (both at primary and secondary care) and improved documentation of infection control and emphasis on the importance and role of anti-toxin and antimicrobial therapy.

These guidelines have been updated in 2025 to include a new section detailing the principles of managing severe cases of non-toxigenic C. *diphtheriae* infection and also clusters of non-toxigenic diphtheria causing corynebacteria in vulnerable populations. The opportunity has been taken to update the epidemiology of diphtheria infection where there are significant changes.

1.8 Rationale for the guidelines

Incidents of confirmed diphtheria are rare and it would be unusual for a local health protection lead to have personal experience of managing a case. Delay in starting treatment could prove fatal for the case and wider spread of the agent could occur in the community if control measures are not promptly initiated. Conversely, there is a risk of inappropriate use of antibiotics and very limited supplies of antitoxins. These guidelines therefore aim to:

- maintain awareness amongst clinicians and prompt consideration of diphtheria as a part of the differential diagnoses
- assist health protection leads in undertaking the risk assessment
- provide clarity as to the clinical and public health actions that should be taken on the basis of the risk assessment for the different potentially toxigenic corynebacteria
- provide advice on the management of cases of non-toxigenic C. diphtheriae with severe presentation and clusters in vulnerable populations or settings for example hostels or shelters for those experiencing homelessness or those with substance use

Part 2. Management and investigation of cases and close contacts

The NHS clinician will notify UKHSA of a suspected case. This notification may come to the local HPT or the national centre at Colindale. The UKHSA duty doctor at Colindale will provide public health management support to the NHS and local HPT and coordinate the issuing of DAT, if required. For advice regarding clinical management of suspected cases, please contact the UKHSA duty doctor on 0208 200 4400. For other queries relating to the treatment (including antibiotics) of suspected cases during office hours, please contact the Bacteriology Reference Department Office, UKHSA Colindale on 0208 327 7887. Out of hours please contact the UKHSA duty doctor on call on 0208 200 4400 for all queries and advice.

2.1 Risk assessment of cases

The public health management of suspected diphtheria involves a risk assessment to determine whether public health actions should be commenced prior to laboratory confirmation of a toxigenic strain. The local HPT should undertake the risk assessment ideally in discussion with the UKHSA Immunisation and Vaccine Preventable Diseases team or duty doctor out of hours. Information that should be collected on each case to inform the risk assessment includes the following.

Demographics:

- name, date of birth, sex, ethnicity, birthplace, NHS number
- current address including postcode, phone number
- GP name and contact details (address and phone number)

Clinical details:

- symptoms and signs – date of onset and severity of symptoms*, presence of classic respiratory symptoms (presence of sore throat, fever, adherent greyish membrane (bleeds when manipulated or dislodged) of the tonsils pharynx or nose), other presentations (such as otic, genital, laryngeal), skin lesions
- results of laboratory investigations (local and/or reference laboratory) – anatomical site of samples, antimicrobial sensitivity results, toxigenicity results if available or when these can be expected and any other organisms detected
- differential diagnoses considered
  - the most common respiratory presentation for non-toxigenic C. *diphtheriae* is presentation of a patient with sore throat to a GP with the presence of another causative pathogen: for example, Lancefield Group A *Streptococcus* (or other Lancefield type C, G and so on)

  - common cutaneous presentations are wounds, ulcers, abscesses, infected insect or animal bites from which toxigenic or non-toxigenic *C. diphtheriae* or *C. ulcerans* may be isolated; other causative pathogens may also be present: for example, *Staphylococcus* spp., *Streptococcus* spp.
  - drugs – some drugs may rarely cause a membrane (for example, methotrexate)

* Note that a previously immunised or partially immunised case may only have a sore throat even when infected with a toxin-producing strain.

Epidemiological details:

- immunisation history (primary course and boosters, including dates)
- occupation, for example work in a clinical microbiology laboratory, or similar occupation, where potentially toxigenic *Corynebacterium* spp. may be handled
- membership of community with sub-optimal immunisation coverage and/or frequent travel links to high-risk areas
- within the 10 days prior to onset of symptoms whether the patient has:
  - had contact with a confirmed case
  - travelled abroad to a high-risk area (particularly Indian subcontinent, South East Asia, Africa, South America, former Soviet States and/or Eastern Europe)
  - had contact with someone who has been to a high-risk area
  - had contact with any animals (including household pets or visiting a farm or petting zoo)
  - recently consumed any type of unpasteurised milk or dairy products

2.2 Case definitions

Cases should be classified according to clinical and laboratory criteria (see below). For suspected cases in asylum-seeker settings, please see section 1.2 of the Supplementary guidance. These are adapted from previous surveillance reporting definitions (5, 86) [note 1] and so on refer to notes at the end of this section.

Confirmed case of toxigenic infection:

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

OR

- laboratory confirmation of a toxigenic strain [note 2] with other presentations of diphtheria including mild respiratory or cutaneous [note 1]

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

- other presentations of diphtheria [note 3] with a confirmed epidemiological link to a laboratory confirmed case [note 2]

Possible case of toxigenic infection:

- other presentations of diphtheria [note 3] (see section 2.1) **and**
- isolation of *C. diphtheriae, C. ulcerans* or *C. pseudotuberculosis* in a pharyngeal, skin, or other appropriate swab, but toxigenicity status has not yet been confirmed

OR

- respiratory diphtheria being considered as part of a wider differential diagnosis (for example respiratory symptoms and suspected membrane), pending isolation of C. *diphtheriae*, C. *ulcerans* or C. *pseudotuberculosis*, but where epidemiological factors and/or vaccine history make diphtheria unlikely

Asymptomatic carrier of toxigenic strain:

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

Case of non-toxigenic toxin gene-bearing (NTTB) Corynebacteria infection:

- other presentations of diphtheria [note 3] (see section 2.1) **and**
- isolation of NTTB corynebacteria (PCR toxin gene positive, Elek negative) in a pharyngeal, skin, or other appropriate swab

Asymptomatic carrier of NTTB strain:

- no symptoms **and**
- laboratory confirmation of NTTB corynebacteria (PCR toxin gene positive, Elek negative) strain from any anatomical site

Confirmed non-toxigenic case:

- isolation of *C. diphtheriae, C. ulcerans* or *C. pseudotuberculosis* in a pharyngeal, skin, or other appropriate swab and toxigenicity status negative

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.

[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, throat or skin lesion swab has been obtained. Very rarely, endocardial, laryngeal, conjunctival, otic and genital involvement may be seen.

2.3 Laboratory confirmation and timing of public health actions (see Appendix 1)

Following isolation of corynebacteria at the local microbiology laboratory, confirmation will be based on further testing by UKHSA RVPBRU. It is sometimes appropriate to initiate public health actions before the confirmatory toxigenicity result is available from RVPBRU. The decision should be made in consultation with UKHSA Immunisation and Vaccine Preventable Diseases team or out-of-hours duty doctor, and on the basis of the risk assessment as follows:

For a confirmed or probable diphtheria case or asymptomatic carrier of toxigenic *C. diphtheriae, C. ulcerans* or *C. pseudotuberculosis*, initiate full public health actions immediately without waiting for toxigenicity results.

For a possible case of diphtheria, public health actions can usually be delayed until toxigenicity results are available, at which point the case will either be reclassified as confirmed toxigenic infection or NTTB corynebacteria, or will be discarded. For a possible case of diphtheria due to *C. ulcerans* in a hospitalised (or other community healthcare setting) individual, infection control measures should be implemented as per section 2.6.1 for confirmed and probable cases pending toxigenicity testing results. This is due to the high proportion of *C. ulcerans* isolates in the UK being confirmed as toxigenic.

In certain situations, some public health actions, such as initiating swabbing and chemoprophylaxis and exclusion of close contacts in high risk occupations, should be considered for a possible case of diphtheria before toxigenicity results are available, such as:

- if there are epidemiological factors that increase likelihood of toxigenicity (see section 2.1) or
- if there is a high public health risk but inconsistent or absent clinical or epidemiological information, for example suspected case in a healthcare worker with undetermined immunisation status and travel to an endemic region and
- toxigenicity results are unlikely to be available within 24 hours

Following toxigenicity results:

- for a case that is confirmed as a toxigenic strain, there should be complete management of close contacts
- for a case with NTTB corynebacteria (PCR *tox* positive, Elek negative), management of close contacts is not necessary and public health actions can be stopped
- for a case that is non-toxigenic, management of close contacts is not necessary and public health actions may be stopped – in the rare event that a contact has been swabbed and grown *C. diphtheriae*, *C. ulcerans* or *C. pseudotuberculosis*, toxigenicity testing should be performed and a risk assessment undertaken
- see section 2.10 if cases are presenting with severe infection (for example bacteraemia or IE)
- see section 3 for the management of outbreaks of toxigenic diphtheria
- see section 3 for the principles of the management of clusters of cases with a non-toxigenic diphtheria-causing organisms where cases are epidemiologically linked to a setting with vulnerable individuals, for example a hostel for people experiencing homelessness

2.3.1 Culture

Swabs (nose, throat, wound or skin lesions) should be obtained for culture before starting treatment. Where a pseudomembrane or membrane is present, if possible, swabs should be taken from underneath the pseudomembrane or a piece of the membrane should be removed. A single swab from each of the nose and throat should also be taken in cases of cutaneous diphtheria to exclude respiratory carriage of toxigenic strains. 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.

The swab containers should be labelled accordingly with unique identifiers, source of the specimen and collection date.

If antibiotics have already been commenced, specimens for culture should still be taken if within 24 hours of the first dose. Beyond this point, if on appropriate treatment, cultures will likely be negative. On occasion, there may be benefit in taking swabs beyond this time point; for example, confirmed cutaneous diphtheria with no respiratory screen. In such circumstances, please discuss the case with the Immunisation and Vaccine Preventable Diseases Division team who will advise on further appropriate sampling, including the use of molecular tests. Clinicians should alert the local laboratory that diphtheria is suspected (or from a confirmed case, as appropriate).

2.3.2 Antibiotic susceptibility testing

Local laboratories are recommended to undertake antimicrobial susceptibility testing on all *C. diphtheriae*/*C. ulcerans*/*C. pseudotuberculosis* isolates, to include as a minimum, sensitivity to penicillin and erythromycin (according to local methods and reported using the EUCAST Clinical Breakpoint Tables v.13.0 [30]. If resistance to either penicillin (R>1mg/L) or erythromycin (R> 0.06mg/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.

In the event of resistance to both macrolides and penicillin, clinicians should be guided by susceptibility testing. In empirical management of severe cases, including treatment of possible pan-resistant clones, vancomycin and linezolid are likely to remain active agents. Macrolide resistance should be reported to the local HPT, and the isolate should be referred for typing and antimicrobial susceptibility confirmation. An IMT is recommended for these cases to inform treatment or prophylaxis decisions for cases and contacts.

2.3.3 Toxigenicity testing

All isolates of potentially toxigenic corynebacteria (*C. diphtheriae, C. ulcerans* or *C. pseudotuberculosis*) should be submitted promptly to the Vaccine Preventable Bacteria Section (VPBS), (within the UKHSA RVPBRU) for confirmation of identification and toxigenicity testing using the R3 laboratory request form.

Identification or confirmation and toxigenicity testing is performed initially by qPCR on a DNA extract of the submitted isolate. This qPCR assay targets the RNA polymerase β-subunit-encoding gene (*rpoB*) and the A subunit of the diphtheria toxin gene (*tox)* to detect and identify C*. diphtheriae,* C*. ulcerans* or C*. pseudotuberculosis* and presence of the tox gene. All isolates which are qPCR positive for the *tox* gene will also be tested by the Elek immunoprecipitation test for toxin expression.

Although all *C. diphtheriae, C. ulcerans* or *C. pseudotuberculosis* toxin gene PCR positive results will be confirmed by the Elek test, a toxin gene PCR positive result should be acted upon immediately without waiting for the Elek result.

As already described, isolates of *C. diphtheriae* may be *tox* gene positive by PCR but not express toxin and so they are negative on the Elek test (NTTB, see section 1.6.1). These are rare in the UK and no UK NTTB *C. ulcerans* have been reported (unpublished data) [49]. Strains of NTTB do not cause diphtheria and so patients are not treated with antitoxin. Individuals identified with a NTTB strain should be managed as non-toxigenic strains with antibiotic therapy only if clinically indicated (see section 2.9).

Sending an isolate for toxigenicity testing

Please ensure the isolate and not the sample itself is sent for toxigenicity testing, as this would cause substantial delays. Submission of additional samples (for example, membrane) should be discussed with the reference laboratory. Please notify the laboratory RVPBRU (telephone 0208 327 7887, via the Bacteriology Reference Department triage or 0208 327 7331 Vaccine Preventable Bacteria Section) before sending potentially toxigenic isolates for toxigenicity testing within working hours on a weekday. Outside these hours, please notify the Colindale duty doctor on 0208 200 4400. Always use the Vaccine Preventable Bacteria Section request form (R3) and ensure full contact telephone numbers are provided on the form to allow timely reporting of results.

Send isolates to:

Vaccine Preventable Bacteria Section
Respiratory and Vaccine Preventable Bacteria Reference Unit (RVPBRU)
Bacteriology Reference Department
UK Health Security Agency, Colindale
61 Colindale Avenue
London, NW9 5HT

Isolates may be sent by Hays DX in which case the following address should be used:

Vaccine Preventable Bacteria Section
UKHSA Colindale
Bacteriology
DX 6530002
Colindale NW

However, depending on the urgency a same-day courier may be required.

Service

Monday to Friday before midday (in the normal working week): isolates are processed same day with the qPCR result available by the end of the working day.

Monday to Friday after midday (in the normal working week): this is contingent on time of arrival in the laboratory and if possible will be processed same day with the qPCR result available by the end of the working day. If late arrival precludes this, then the results will be reported on the following day.

Out-of-hours Saturday and bank holidays (this is usually a Monday but may on occasion be a Tuesday or Friday): this may also apply to isolates arriving late on a Friday. If sending an urgent isolate on Saturday for the Saturday service or on a Bank Holiday please ensure it arrives by midday to allow processing or reporting time.

Out-of-hours Sunday: the Colindale site is manned 24/7 so isolates may be sent to Colindale on Sunday to be tested first thing on Monday morning. The packages will be placed in the out-of-hours fridge by the security team.

For the out-of-hours service it is essential that you telephone prior to sending isolates for Saturday or bank holiday testing as otherwise they will not be processed. If you require any further details out of hours, please contact the Colindale duty doctor (0208 200 4400). Test results will be reported by phone to the telephone number provided on the Request Form (R3). Please ensure that full contact details to assist reporting are provided (including out-of-hours numbers if required).

2.4 Notification of cases

Notification must be undertaken as per the statutory duties outlined in section 1.4. Clinicians should notify all cases, whether confirmed, probable or possible, or asymptomatic carriers, by phone on the same day to the local HPT.

Microbiology departments should notify all *C. diphtheriae*, *C. ulcerans*, and ideally *C. pseudotuberculosis* isolates by phone to the local HPT.

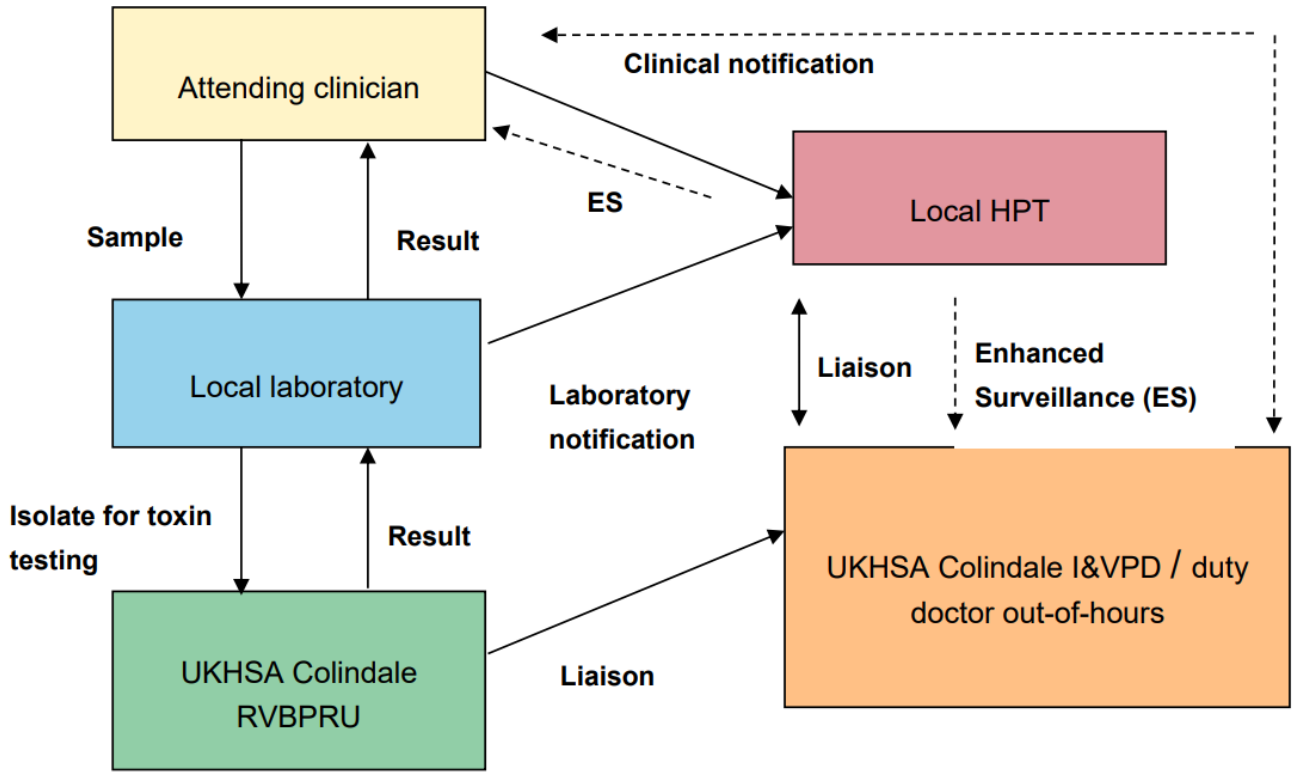
HPTs should ensure the case is formally notified in the case management system to ensure they are counted by the NOIDs system. In addition to mandatory notifications, there should be good communication between the HPT, microbiology team, infectious disease physicians, other hospital doctors, general practitioners and the relevant team at UKHSA Colindale (Immunisation and Vaccine Preventable Diseases Division and/or Emerging Infections and Zoonoses Team, and RVPBRU). The local HPT should discuss out-of-hours cases with the duty doctor at UKHSA Colindale (0208 200 4400).

Enhanced surveillance of diphtheria for England is also carried out by the Immunisations and Vaccine Preventable Diseases Division, UKHSA. We ask HPTs to complete the national surveillance form and send it to diphtheria_tetanus@ukhsa.gov.uk or phe.diphtheria.tetanus@nhs.net

HPTs may need to consult NHS clinical colleagues to complete the form.

Figure 1 details the various interactions of the local laboratory, local health protection service, the reference laboratory and Immunisation and Vaccine Preventable Diseases Division at UKHSA Colindale.

Figure 1. Case notification flowchart and interaction between departments



Text equivalent of Figure 1

The attending clinician should send samples to the local laboratory and await the result from the laboratory. They should also notify their local HPT. The local laboratory will receive the sample from the attending clinician and will share the results with them. The local laboratory should notify the local HPT via a laboratory notification and they will send the isolate to the UKHSA Colindale RVPBRU for confirmation toxigenicity testing.

The local HPT will receive a clinical notification from the attending clinician and/or receive a laboratory notification from the local laboratory. They will liaise with the UKHSA Colindale Immunisation and Vaccine Preventable Diseases Division (in hours) and the duty doctor (out-of-hours). In addition, the local HPT will conduct enhanced surveillance in conjunction with the UKHSA national diphtheria surveillance team and the attending clinician.

The UKHSA Colindale RVPBRU will receive the isolate for toxigenicity testing from the local laboratory and will share the result from toxigenicity testing with the local laboratory. They will also liaise with the UKHSA Colindale Immunisation and Vaccine Preventable Diseases Division (in hours) and the duty doctor (out-of-hours).

The UKHSA Immunisation and Vaccine Preventable Diseases Division will liaise with the patient's GP and attending clinician (if DAT was administered) to complete the remaining enhanced surveillance forms for follow up of confirmed cases.

2.5 Incident management team

For most cases of confirmed or probable diphtheria, an IMT or outbreak control team (OCT) should be convened within 24 hours of the PCR toxigenicity result. However, an IMT may be convened earlier if it is deemed necessary, particularly where epidemiological or clinical suspicion is high or where resistance to first line macrolide has been identified on antibiotic susceptibility testing. Membership of the team will vary depending on local circumstances, but would typically include:

- consultant in communicable disease control or consultant in health protection
- local consultant microbiologist (NHS)
- regional microbiologist or consultant in public health infection (UKHSA)
- local authority public health team
- consultant physician responsible for care of the patient
- consultant in infectious disease
- infection control nurse
- representation from UKHSA Colindale
- communications team
- APHA as appropriate (see section on zoonotic source investigations)

2.6 Management of confirmed or probable cases of diphtheria due to C. diphtheriae, C. ulcerans, or C. pseudotuberculosis (see Appendix 2)

For advice regarding clinical management of suspected cases, please contact the UKHSA duty doctor on 0208 200 4400. For other queries relating to the treatment (including antibiotics) of suspected cases during office hours, please contact the Bacteriology Reference Department Office, UKHSA Colindale on 0208 327 7887. Out of hours, please contact the UKHSA duty doctor on call on 0208 200 4400 for all queries and advice.

2.6.1 Isolation

For those confirmed or probable cases admitted to hospital institute precautions appropriate for droplet borne infection and/or direct contact measures, for example single en-suite room, apron, gloves, fluid resistant surgical facemask (FRSM) for routine care and FFP3 for aerosol generating procedures. [99, 100].

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. Isolation should continue until clearance cultures are negative for toxigenic *C. diphtheriae, C. ulcerans* or *C. pseudotuberculosis* [12].

If the case is well and not hospitalised, advise to restrict contact with others for the first 6 days of an appropriate course of antibiotics. During this time the case should not attend GP practice for further tests. Clearance swabs should be obtained 24- and 48-hours after completion of antibiotics to ensure elimination of carriage. In the rare event that the case remains positive following completion of the recommended antibiotic course, further advice on additional treatment should be sought from the national team. It is also advisable to take nose and throat swabs from close contacts of the index case (see section 2.9).

2.6.2 Referral

All probable or confirmed cases must be referred to the local specialist infectious disease (ID) unit or consultant for a face to face clinical review and assessment of whether anti-toxin treatment is required. The responsibility of the HPT is to check that this clinical review has taken place.

2.6.3 Antitoxin treatment

DAT should only be used in a hospital setting for confirmed or probable cases of diphtheria. DAT should be given to classic respiratory cases without waiting for laboratory confirmation. Early treatment with DAT is critical to neutralise free-circulating toxin before it can irreversibly bind to tissues causing organ damage. The effectiveness therefore declines with time since onset of symptoms.

In most cutaneous infections, large-scale toxin absorption is unlikely and therefore the risk of giving antitoxin is usually considered to be substantially greater than any benefit. Nevertheless, if the ulcer in cutaneous diphtheria infection were sufficiently large (for example, more than $2cm^2$) and especially if it were membranous, then antitoxin would be justified [50].

DAT is based on horse serum and therefore severe, immediate anaphylaxis occurs more commonly than with human immunoglobulin products. However, from our experience in England of treating patients with DAT, anaphylaxis is very rare. Tests to exclude hypersensitivity to horse serum should be carried out as described in the summary of product characteristics (SPC). Local policies for the management of anaphylaxis should be followed.

Contact the UKHSA Colindale duty doctor in and out of hours if considering the use of antitoxin (0208 200 4400). They will advise on details of current stock and dosing as suppliers change and dosing is product-specific and will issue DAT as indicated. Find more details in Guidance on the use of DAT on the UKHSA website.

2.6.4 Antibiotic treatment

Antibiotic treatment to eliminate the organism and prevent spread is not a substitute for antitoxin treatment if indicated. All specimens should be collected BEFORE antibiotic treatment is started if possible. If antibiotics have already been started then samples should still be taken if within 24 hours of the first dose. On occasion, there may be benefit in taking swabs beyond this time

point; for example, confirmed cutaneous diphtheria with no respiratory screen. In such circumstances, please discuss the case with the Immunisation and Vaccine Preventable Diseases Division team who will advise on further appropriate sampling, including the use of molecular tests (see also section 2.3.1). Guidance for antibiotic administration is shown in tables 1a and 1b (see also Appendix 3). For mild disease, such as small cutaneous lesions with no evidence of systemic toxicity, the preferred empirical antibiotic is a macrolide (either clarithromycin, azithromycin or erythromycin).

For severe disease, intravenous benzylpenicillin sodium at the maximum appropriate dose should be combined with a macrolide. In patients who are extremely systemically unwell, consider a third agent such as IV vancomycin or linezolid until local susceptibility results are available.

Table 1a. Guidance for the administration of antibiotics for confirmed or probable cases: mild disease or community treatment

Antibiotic	Dose	Duration (days)
First line		
Clarithromycin		
Adult (and children 12 to 17 years)	500mg twice a day	14
Child (1 month to 11 years)	7.5 mg/kg twice a day (maximum per dose 500mg)	14
Or		
Azithromycin		
Adult (and children 12 to 17 years)	500mg once a day	7 to 10
Child (6 months to 11 years)	12mg/kg once a day (maximum per dose 500mg)	7 to 10
Or		
Erythromycin[1,2,3]		
Adult (and children 12 to 17 years)	500mg 4 times a day	14
Child (1 month to 11 years)	10 to 15mg/kg 4 times a day (maximum per dose 500mg)	14
Neonate	10 to 15mg/kg 4 times a day	14

[1] Erythromycin is the preferred antibiotic for use in pregnancy.
[2] Total daily dose may alternatively be given in 2 divided doses.
[3] Dose increase may be used in severe infections; see BNF.

Consult the BNF or the BNF for children for cautions, interactions and side-effects prior to prescribing. If unable to take macrolide, consider non-macrolide options as listed below and discuss with UKHSA.

Table 1b. Guidance for the administration of antibiotics for confirmed or probable cases: severe disease or hospital treatment

Antibiotic	Dose	Duration (days)
First line		
IV Benzylpenicillin sodium (plus macrolide as above)		
Adult	1.2 to 2.4g every 6 hours	14
Child	25mg/kg every 6 hours; increased if necessary to 50mg/kg every 4 to 6 hours (maximum per dose 2.4g every 4 hours)	14
Add vancomycin or linezolid if extremely systemically unwell Dose as per BNF (duration 14 days)		
Second line: discuss with UKHSA		
Once patient improves clinically, stepdown to oral antibiotics		

Minimum inhibitory concentration (MIC) distribution for toxigenic isolates of *C. diphtheriae* and *C. ulcerans* received between 2017 and 2022 are shown in tables 2a and 2b. Susceptibility testing was performed using gradient strips and MICs were interpreted using the European Committee on Antimicrobial Susceptibility Testing (EUCAST) v13 breakpoints tables where available.

There are no clinical breakpoints for azithromycin and clarithromycin therefore formal categorisation of the MIC is not possible. Erythromycin MICs were interpreted using EUCAST clinical breakpoints (S ≤0.06mg/L and R >0.06mg/L). The macrolide MICs determined between 2017 and 2022 mostly ranged from ≤0.016mg/L to 0.5mg/L suggesting that macrolides remained active.

Table 2a. Penicillin and macrolide MIC distributions for toxigenic *C. diphtheriae* and *C. ulcerans* received between 2017 and 2022: number of isolates with indicated MIC (mg/L) – toxigenic *C. diphtheriae* (n = 17)

	≤0.016	0.032	0.064	0.125	0.25	0.5	1	Non-tested
Penicillin (S ≤0.001mg/L; R >1mg/L)				7	7	1	2	
Clarithromycin	7	1			2			7
Erythromycin (S ≤0.06mg/L and R >0.06mg/L)	9	6				1		1
Azithromycin	1	5	1	4				6

Table 2b. Penicillin and macrolide MIC distributions for toxigenic *C. diphtheriae* and *C. ulcerans* received between 2017 and 2022: number of isolates with indicated MIC (mg/L) – toxigenic *C. ulcerans* (n = 35)

	≤0.016	0.032	0.064	0.125	0.25	0.5	1	Non-tested
Penicillin (S ≤0.001mg/L; R >1mg/L)	4		6	16	8			1
Clarithromycin	8	8	6					13
Erythromycin (S ≤0.06mg/L and R >0.06mg/L)	7	15	12				1	
Azithromycin		2	2	9	7	6		9

The local clinical microbiology laboratory should undertake susceptibility testing according to their local method. Antimicrobial susceptibility testing can also be confirmed by UKHSA Colindale, with a published turnaround time of 15 days (Bacteriology reference department user manual). Antibiotic treatments are outlined in Table 1 (or Appendix 3).

For azithromycin, given the long half-life, a reduced course can be given. Elimination of the organism should be confirmed after antibiotic treatment has been completed by obtaining a single swab from each of the following sites – nose and throat, or in cases of cutaneous diphtheria nose, throat and skin swabs for culture at least 24-hours after completion of antibiotic treatment course and once more after

(at least) a further 24 hours (that is, at 24- and 48-hours). If microbiological clearance is not achieved an additional 10 day course of an alternative antibiotic should be prescribed following discussion with local microbiologists.

Treatment of confirmed or probable cases of cutaneous diphtheria also includes thorough cleaning of the lesion.

For further guidance on the management of macrolide resistant infections see the Supplementary guidance for cases and outbreaks in asylum seeker accommodation settings , section 1.5.3

2.6.5 Immunisation

Infection does not always induce adequate levels of anti-toxin so confirmed or probable cases should receive a booster dose of a diphtheria-toxoid containing vaccine or immunisation appropriate to their age and immunisation history (see below). For adults with a complete immunisation history (5 doses of diphtheria-containing vaccine) this is likely to be tetanus, low dose diphtheria or inactivated polio vaccine (Td/IPV). No booster dose is required if the last dose was given within the last 12 months.

Cases should be immunised once they are clinically stable. For further details on diphtheria immunisation, see Chapter 15 in UKHSA's Green Book: Immunisation against Infectious Disease. For further advice on travel vaccination, refer to the National Travel Health Network and Centre website.

Recommended immunisations according to age and status for cases of confirmed or probable diphtheria

If a dose of diphtheria-containing vaccine has not been given in the last 12 months to:

- immunised children up to 10 years of age – one injection of adsorbed diphtheria-containing vaccine (either Td/IPV, dTaP/IPV or DTaP/IPV)
- immunised children aged 10 years and over, and adults – one injection of adsorbed low-dose diphtheria-containing vaccine for adults (for example, Td/IPV)
- unimmunised children under 10 years of age – 3 injections of adsorbed full dose diphtheria-containing vaccine (for example DTaP/IPV/Hib/HepB) at monthly intervals
- unimmunised children aged 10 years and over, and adults – 3 injections of adsorbed low-dose diphtheria-containing vaccine (for example, Td/IPV) at monthly intervals
- a person with unknown immunisation status – where there is no reliable history of previous immunisation, it should be assumed that they are unimmunised and follow as above

Laboratory and pathology staff: recommendations for immunisation to protect against diphtheria are as per the Immunisation of healthcare and laboratory staff: the Green Book, chapter 12.

2.6.6 Fomites

There is little evidence of transmission of diphtheria through fomites and it can be assumed to be very rare. Depending on circumstances, an individual risk assessment should be undertaken based on vulnerability of contacts and level of potential risk (for example, extensive skin shedding). It is recommended that bedding or toys in close contact with infected person or animals, in particular ulcerative wounds, should be hot (>60°C) washed.

2.7 Management of possible cases of diphtheria due to C. diphtheriae, C. ulcerans or C. pseudotuberculosis (see Appendix 1)

The following actions should be taken:

1. **Isolation.** Isolate possible cases who are in hospital (or other community healthcare settings) as per section 2.6.1, and dress cutaneous lesions. Possible cases who are well at home should be advised to restrict contact with those outside their immediate household until further microbiological results are obtained. Ensure isolates are sent to the UKHSA RVPBRU for toxigenicity testing (see section 2.3.2). Liaise with the relevant microbiologists (local and reference laboratories).
2. **Referral.** Possible cases should be assessed by a local clinician to ensure that they do not have clinical symptoms compatible with classic diphtheria (and should therefore be reclassified as a probable case). This should be confirmed by HPT and documented on the case management system.
3. **Treatment.** Treatment of the case is undertaken on clinical grounds only. Please see antibiotic treatment section outlined in Table 1 or Appendix 3. For possible cases in asylum seeker settings, please see section 1.5.2 of the Supplementary guidance.
4. **Immunisation.** Most possible cases will be reclassified following toxigenicity results and immunisation can be decided accordingly. If not possible to reclassify, ensure individuals are up to date with immunisation with diphtheria-toxoid containing vaccine (Figure 2).

2.8 Management of asymptomatic carriers

Asymptomatic carriers of toxigenic strains should be managed in the same way as confirmed cases including treatment with the same antibiotic regime and dosage, and immunisation offer (see Table 1 or Appendix 3). 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.

2.9 Management of cases of non-toxigenic toxin gene-bearing (NTTB) corynebacteria

Individuals identified with a NTTB strain should be managed as non-toxigenic strains with antibiotic therapy only if clinically indicated. In the event of the report of a suspected cluster of NTTBs, please discuss with UKHSA Immunisation and Vaccine Preventable Diseases Division.

2.10 Management of cases of non-toxigenic corynebacteria

The clinical significance of positive *C. diphtheriae* isolates should be discussed with a microbiologist. Confirmed cases of non-toxigenic *C. diphtheriae* in community settings with mild cutaneous infection are not required to isolate however they should be promptly commenced on appropriate antibiotic treatment (as directed by local antibiotic susceptibility testing) and have their wounds dressed to reduce onward transmission. Where in the community, single room accommodation with en-suite facilities is recommended, if possible. Microbiological clearance is not required.

Clinicians are recommended to have a low threshold for referral of all cases with suspected deep seated wound infections and/or systemic infection to secondary care for further investigation and prompt treatment. Early echocardiography should be considered in cases with systemic infection with *C. diphtheriae*, even in the absence of classical cardiac risk factors for IE or a history of intravenous drug use. All cases of IE with non-toxigenic C. *diphtheriae* should be discussed with a regional cardiology or cardiothoracic specialist centre, as surgical intervention is key to improved outcome.

Be vigilant for *C. diphtheriae* skin and soft tissue infections:

- take samples from all infected wounds
- request that testing includes *C. diphtheriae* and local antibiotic sensitivities to inform treatment
- discuss with microbiologists clinical significance of positive *C. diphtheriae* isolates and onward referral of isolates to the UKHSA national reference laboratory, RVPBRU
- treat skin infections and wounds, including those caused by *C. diphtheriae*, as directed by antibiotic sensitivities
- consider early referral to hospital if signs of systemic infection
- consider early echocardiography in cases with systemic infection with *C. diphtheriae*, even in the absence of classical cardiac risk factors for IE or a history of intravenous drug use

- discuss all cases of IE with non-toxigenic *C. diphtheriae* with regional cardiology or cardiothoracic specialist centres, as early surgical intervention is key to improved outcomes
- report outbreaks of non-toxigenic *C. diphtheriae* to the local health protection team to allow advice to be disseminated to those at risk

2.11 Management of close contacts of toxigenic diphtheria cases and close contacts of asymptomatic carriers (see Appendix 2)

2.11.1 Definition of close contacts

As the risk of infection is directly related to the closeness and duration of contact, prophylaxis is required if the contact:

- is with a case or known carrier in a household type setting
- has been directly exposed to large particle droplets or secretions (following the same principles of meningococcal disease)
- has been exposed to an undressed wound of a cutaneous case

Examples of contacts who should be considered for prophylaxis are:

- those sleeping in the same household as the index case
- students in a hall of residence in the same corridor, flat or shared kitchen facilities with the index case – adapt to local situation (needs to mimic household contact)
- kissing or sexual contacts of the index case
- a childminder or carer having regular close contact with the case for 6 or more hours

Principles for risk assessment of healthcare workers (HCW) who should be considered for prophylaxis

This will depend on the presentation of diphtheria in the index case, which body sites were positive on swabbing, and what personal protective equipment (PPE) the HCW wore while attending the case. As a minimum, HCW attending to a case (possible, probable or confirmed) of diphtheria should wear disposable gloves and aprons for wound care and depending on the situation either a fluid repellent surgical face mask or a FFP3 mask for any aerosol generating procedures.

Individual risk assessment can be performed, that is, if no gloves were worn during wound assessment but there was likely no splash or droplet contamination and prompt hand washing occurred, prophylaxis may not be indicated.

For respiratory cases, HCW who have given mouth to mouth resuscitation to or intubated the index case (without appropriate PPE) would normally be considered as close contacts.

Types of contact who are unlikely to require prophylaxis:

- friends, relations and caregivers who have visited the home during the infectious period
- school classroom contacts
- those who share the same room at work
- healthcare staff that have had contact with the index case without exposure to droplets or open wounds
- laboratory workers if they are following their best practice for handling and culturing respiratory pathogens

The risk of transmission in other types of settings should be assessed on a case-by-case basis by the IMT chair or consultant in health protection.

Experience of other droplet-spread infectious diseases suggests that the risk of transmission of disease on an aircraft is low, and contact tracing is not recommended [101]. Contact with a case on public transport is also likely to carry a low risk.

The maximum incubation period for diphtheria is 10 days; however, there may be longer duration of carriage in asymptomatic carriers but there is little evidence. Therefore, close contacts should be identified from 10 days before onset of diphtheria symptoms in a case. For asymptomatic carriers, identify current close contacts; if there was a suspected time of acquisition, identify close contacts since that time and any recent vulnerable contacts.

2.11.2 Control measures for close contacts of confirmed and probable toxigenic diphtheria cases, and close contacts of asymptomatic carriers (see Appendix 2)

This will be led by the local HPT.

i) Investigation and monitoring of close contacts

Inform and self-monitor. Health protection staff should inform the close contacts that they may have been exposed to diphtheria, and should explain the symptoms (fever, sore throat, swollen neck glands, development of a membrane, skin lesions) and advise them to seek urgent medical attention if they become unwell. Travel history should be obtained as the close contact may be the source of the case's infection. Close contacts should be advised to self-monitor for 10 days from the date of the last contact with the case. After 10 days, the HPT should check that the contact has remained well and this information should be documented on the case management system. For those unable to self-monitor the health protection staff should follow up daily with the contact or their carer.

Swabbing. Health protection staff should inform the GP of the situation, and provide the fact sheet on diphtheria (Appendix 5). They should then arrange for swabbing of the close contact. This should include a nose and a throat swab and swabs of any skin lesions, taken before chemoprophylaxis. This will identify any asymptomatic carriers. For more details of types of swabs, where to send them and methods of identification please see section 1.2.

ii) Chemoprophylaxis of close contacts

After nose and throat swabs have been taken, close contacts of confirmed or probable diphtheria cases and asymptomatic carriers should be given prophylactic antibiotics, regardless of culture result, to:

- treat incubating disease in recently exposed contacts
- eliminate carriage and thereby reduce the risk of exposure to other susceptible contacts

The recommended agents for chemoprophylaxis are macrolides (see Table 3 or Appendix 4). As an alternative, in certain circumstances when more easily administered, a single intramuscular (IM) dose of benzathine benzylpenicillin can be given. Benzathine benzylpenicllin should never be administered by the IV route.

Table 3. Guidance for the administration of antibiotics for close contacts of confirmed and probable diphtheria cases and close contacts of asymptomatic carriers

Antibiotic	Dose	Duration (days)
First line		
Clarithromycin		
Adult (and children 12 to 17 years)	500mg twice a day	7
Child (1 month to 11 years)	7.5 mg/kg twice a day (maximum per dose 500mg)	7
Azithromycin		
Adult (and children 12 to 17 years)	500mg once a day	6
Child (6 months to 11 years)	12mg/kg once a day (maximum per dose 500mg)	6
Alternative regimes		
Benzathine benzylpenicillin IM		
Adult (and children over 30kg)	1.2 MIU single dose	Single dose
Child (under 30kg)	600 000 IU single dose	Single dose
Benzathine benzylpenicllin should never be administered by the IV route; inadvertent administration by the IV route may be associated with cardiorespiratory arrest and death		
Or		
Erythromycin[1,2,3]		
Adult (and children 12 to 17 years)	500mg 4 times a day	7
Child (1 month to 11 years)	10 to 15mg/kg 4 times a day (maximum per dose 500mg)	7
Neonate	10 to 15mg/kg 4 times a day	7
Please consult the BNF or the BNF for children for cautions, interactions and side-effects prior to prescribing.		

[1] Erythromycin is the preferred antibiotic of choice in pregnancy.
[2] Total daily dose may alternatively be given in 2 divided doses.
[3] Dose increase may be used in severe infections; see BNF.

If initial swabs for contacts are culture positive for *C. diphtheriae, C. ulcerans or C. pseudotuberculosis* the individual should be managed as per Appendix 1 and samples should be submitted to RVPBRU for confirmation and toxigenicity testing (section 2.3.2).

Note: DAT is no longer used in the UK for diphtheria prophylaxis because of the risk of hypersensitivity.

iii) Exclusion of close contacts in high-risk occupations

Close contacts of confirmed or probable cases of diphtheria and close contacts of asymptomatic carriers who work in the following high-risk occupations should be excluded from work and started on chemoprophylaxis:

- health and social care workers
- those who work with unimmunised children
- those involved in milk production (for *C. ulcerans*)

This list is not exhaustive and there may be other instances where exclusion would be appropriate. The decision to exclude close contacts should be made by the IMT based on an individual risk assessment.

All should have a nose and a throat swab taken prior to the start of antibiotics. If the initial culture is negative they can go back to work while completing the course. In cases where the initial culture is positive for *C. ulcerans, C. diphtheriae*, or *C. pseudotuberculosis* they must remain excluded from work until the toxigenicity result is known. If toxigenic, they should be managed as per guidance for confirmed cases (see section 2.6).

iv) Immunisation of close contacts

Vaccination status of close contacts should be assessed. For those who are appropriately immunised for age, close contacts of confirmed or probable diphtheria cases and asymptomatic carriers should be immunised with a diphtheria-toxoid containing vaccine, unless a diphtheria-toxoid containing vaccine has been given within the previous 12 months [1]. Please refer to schedule outlined in section 2.6.5. For those who are not appropriately immunised, a diphtheria-containing dose should be given immediately, and the schedule completed according to the guidelines available on vaccination of individuals with uncertain or incomplete immunisation status.

2.12 Management of close contacts of asymptomatic and symptomatic non-toxigenic toxin gene-bearing (NTTB) corynebacteria cases

No public health follow up of contacts is required. In cases where public health actions have commenced in response to a positive PCR toxigenicity result, these can be stood down when a negative Elek test result is received.

2.13 Investigation into zoonotic sources of infection for confirmed human toxigenic C. ulcerans cases

Where a case of toxigenic *C. ulcerans* is identified, investigations should aim to identify any history of exposure to animals or unpasteurised dairy products. Consideration should be given

to domestic settings, where companion animals may be present, as well as farms, where there is potential for contact with multiple animals or species. Where contact with animals is identified, the species of animals, nature of the contact, and presence of symptoms in the animals should be noted, for example wound infections or nasal discharge. If a zoonotic source of infection is suspected for a confirmed toxigenic *C. diphtheriae* or *C. pseudotuberculosis* case, the same process should be followed.

APHA should be invited to attend the IMT meetings where a zoonotic source of infection may exist. The IMT will risk assess settings where animals are present and agree on appropriate actions to manage potential animal sources of infection. It may be necessary to determine carriage in potential animal sources by taking samples from animals; this includes animals in close contact with the case or unpasteurised milk or dairy products.

C. ulcerans is not a notifiable disease in animals and investigation and treatment is unlikely to be covered by pet insurance policies if the animal is otherwise healthy. Therefore, prior to testing animal contacts, it is important to discuss who will cover the costs of swabbing by the private veterinary surgeon (PVS) and the implications of a positive test with the owner. This may include:

- the cost of any private veterinary consultations
- the cost and potential outcome of antibiotic treatment, including possible side effects
- clearance swabs
- potential for further treatment

It is appropriate for veterinary staff from APHA to discuss veterinary issues with the owners or PVS.

The natural history of *C. ulcerans* in animals is not fully understood and animals may pass on the infection to humans without exhibiting signs of illness themselves. As it can be difficult to obtain good quality swabs from some animals and they may no longer be carrying the infection when swabbed, it may not always be possible confirm the presence of toxigenic *C. ulcerans* infection in an animals that appears to be the likely source of a human infection.

2.13.1 Sample collection and testing

APHA, with UKHSA, will advise on collection and analysis of animal samples.

Sample collection usually involves taking throat swabs from companion animals within the case's household or animals with which the case has regular close contact. Any skin lesions present should also be swabbed. Charcoal swabs should be used for bacterial culture. The swabbing is carried out through the animal's PVS, but swabs are then sent to the APHA Regional Laboratory in Starcross, Devon where cultures to identify the presence of *C. ulcerans* are undertaken. If *C. ulcerans* is confirmed the positive isolates should be sent to UKHSA

RVPBRU for toxigenicity testing. Testing of potentially toxigenic isolates from animal samples at RVPBRU will generally only be carried out during routine working hours.

2.13.2 Antibiotic treatment

APHA will advise on appropriate antibiotic treatment of animals found to be positive for *C. ulcerans*. Antimicrobial sensitivity results will guide appropriate antibiotic choices. In 2 cases where an indistinguishable strain was identified from a dog and human, a 10 day course of a combination of spiramycin and metronidazole was found to successfully clear the organism from the dog (89). Where daily administration of tablets is not possible, a long-acting antibiotic injection may be advised. To confirm clearance of toxigenic *C. ulcerans*, repeat swabs should generally be taken 5 to 7 days following completion of the antibiotic course.

Where there is more than one companion animal present in a defined setting but only one tests positive for toxigenic *C. ulcerans*, APHA may recommend treatment of all animals due to the risk of transmission of infection through close contact or sharing of food or water bowls.

2.13.3 Cost of animal investigations

While APHA will cover the costs of culturing the swabs taken from animals, there are other costs associated with investigating animals as a zoonotic source of toxigenic *C. ulceran*s and these will usually need to be covered by the owner. The initial costs will include PVS consultation with swab collection, but consideration should be given to how antibiotics will be paid for if the animal tests positive for *C. ulcerans* on swabbing and the likely costs of subsequent clearance swabs.

Unfortunately, it is not possible to give an accurate estimate for these costs, as they will vary depending on the size and number of animals involved, the number of appointments needed, type and amount of antibiotic required, and the PVS involved. The IMT should discuss alternative funding options in the event that the owner is unable to cover the costs.

For the public health management of suspected and confirmed toxigenic *C. ulcerans* cases in animals where there are no associated human infections, please see the separate guidance document.

Part 3: Outbreaks of toxigenic and non-toxigenic diphtheria

3.1 Management of outbreaks of toxigenic diphtheria

Please see Supplementary guidance for the management of cases and outbreaks of toxigenic diphtheria in asylum seeker accommodation settings.

3.2 Management of clusters of non-toxigenic C. diphtheriae

Outbreaks of non-toxigenic *C. diphtheriae* should be reported to the local HPT to allow advice to be disseminated to those at risk. Small clusters of skin and wound infections are common in accommodation settings for those experiencing homelessness or in unstable housing situations and clusters often involve the transmission of several organisms and many cases of co-infection.

The general principles of outbreak management should include:

- ensuring all residents have access to clinical review
- ensure all those with systemic symptoms are urgently referred for further investigation and treatment
- ensure cutaneous wounds or lesions are appropriately dressed
- ensuring all those with wounds have microbiological swabs taken and C. diphtheriae detection is included in the test request
- requesting antibiotic sensitivities are performed for all positive isolates to inform treatment plans
- recommending cases refrain from sharing rooms and drug equipment
- encouraging hostels to implement systematic cleaning of rooms and shared facilities
- encouraging settings to disseminate appropriate health advice to clients and display posters with key information

Where there is co-circulation of other pathogens, management of cases or clusters of infection should also follow appropriate national guidance:

- UK guidelines for the management of contacts of invasive group A streptococcus (iGAS) infection in community settings
- PVL-Staphylococcus aureus infections: diagnosis and management

- UKHSA guidelines for the management of scabies cases and outbreaks in communal residential settings
- Migrant health guide

Part 4. Communications

Disseminate information promptly and appropriately to contacts to aid understanding, minimise anxiety and control rumours (see the factsheet in Appendix 5).

Consider informing institutions such as schools and nurseries, and in some situations, the wider community, as appropriate.

For confirmed toxigenic cases, a reactive press statement should be prepared (see Appendix 6). Main messages could include:

- a case has occurred
- the chance of another case is very small as most people are protected by immunisation
- advice for close contacts of cases including the importance of having swabs taken and completing the appropriate antibiotic course
- immunisation status of close contacts will be checked and immunisation will be offered if necessary

The local health protection lead should use this opportunity to emphasise the general importance of immunisation in the prevention of infectious diseases.

If a case has recently travelled to another country or a contact has left the UK, it may be necessary to share information with that country to enable them to take appropriate public health actions. International information sharing for public health purposes is communicated securely through the UK International Health Regulations national focal point (IHRNFP) to the equivalent IHRNFP in the other country. Contact the UK IHRNFP (IHRNFP@ukhsa.gov.uk) with details of the country involved, details of the individual who has travelled, dates of travel and relevant contact details.

Abbreviations

Abbreviation	Meaning
APHA	Animal and Plant Health Agency
CI	confidence interval
DAT	diphtheria anti-toxin
Defra	Department for the Environment, Food and Rural Affairs
DTaP/IPV	diphtheria, tetanus, acellular pertussis, inactivated polio vaccine
EUCAST	European Committee on Antimicrobial Susceptibility Testing
GP	general practitioner
HPT	health protection team
IHBSD	Immunisation, Hepatitis and Blood Safety Department
I&VPDD	Immunisation and Vaccine Preventable Diseases Division
IE	Infective endocarditis
IHRNFP	International Health Regulations national focal point
IM	intramuscular
IMT	incident management team
IU	international units
IU/mL	international units per millilitre
M unit	mega unit
kDa	kilodaltons
NHS	National Health Service
NTTB	non-toxigenic toxin gene-bearing
PCR	polymerase chain reaction
PHE	Public Health England
RVPBRU	Respiratory and Vaccine Preventable Vaccine Bacteria Reference Unit
Td/IPV	Tetanus, low dose diphtheria, inactivated polio vaccine
UK	United Kingdom
UKHSA	United Kingdom Health Security Agency
US	United States
WHO	World Health Organization

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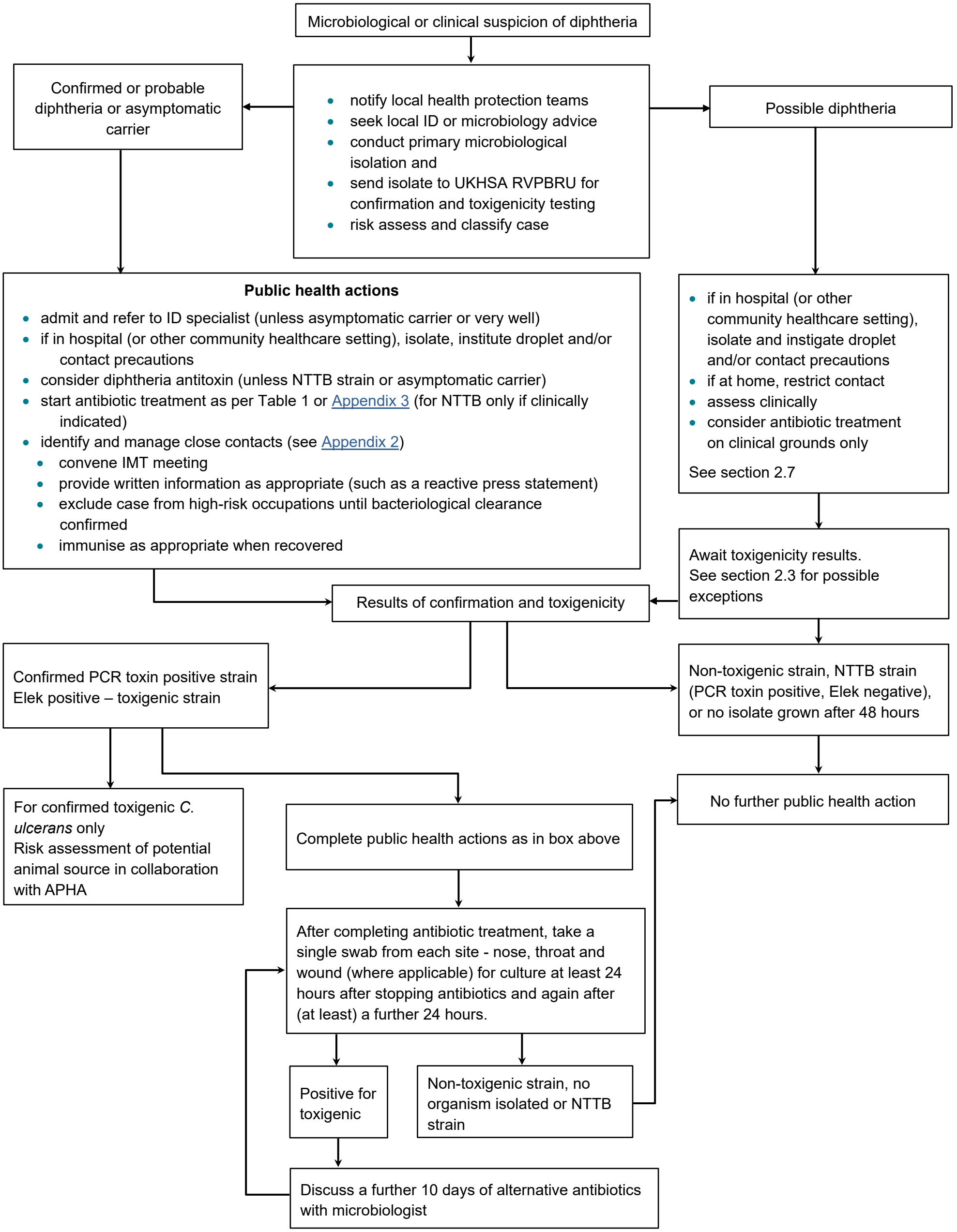
Appendix 1. Algorithm for management of a suspected diphtheria case



Accessible text version of Appendix 1

1. When there is a microbiological or clinical suspicion of diphtheria, the first actions are:

- notify local health protection teams
- conduct primary microbiological isolation and
- send isolate to UKHSA RVPBRU for confirmation and toxigenicity testing
- risk assess and classify case as either possible or probable or confirmed or asymptomatic carrier

2. If the case is possible, then please see section 2.7 and carry out the following actions while awaiting results of toxigenicity testing:

- if in hospital (or other community healthcare setting), isolate and instigate droplet and/or contact precautions (see NIPCM).
- if at home, restrict contact for the first 6 days of appropriate antibiotic course
- assess clinically
- consider antibiotic treatment on clinical grounds only
- wait for toxigenicity results, please see section 2.3 for possible exceptions

3. If the case is confirmed or probable or an asymptomatic carrier, then carry out these public health actions (see section 2.6 or 2.8):

- admit and get ID or microbiology advice (unless asymptomatic carrier or very well)
- if in hospital (or other community healthcare setting), isolate and instigate droplet and/or contact precautions (see NIPCM).
- consider antitoxin (unless NTTB strain or asymptomatic carrier)
- start antibiotic treatment as per Table 1 or Appendix 3 (for NTTB only if clinically indicated)
- identify and manage close contacts (see Appendix 2)
- convene IMT meeting
- provide written information as appropriate (such as a reactive press statement)
- exclude case from high-risk occupations until bacteriological clearance confirmed
- immunise as appropriate when recovered

4. Once there are PCR results and the possible case is confirmed as a PCR toxin gene positive then carry out public health actions in step 3.

5. If the results of the confirmation testing show the case is a non-toxigenic strain or there is no isolate grown after 48 hours then no further public health action is needed. If the Elek test shows that the strain is NTTB, then stop public health actions.

6. For confirmed toxigenic *C. ulcerans* only, carry out a risk assessment of potential animal source in collaboration with APHA.

7. For all confirmed cases, after completing antibiotic treatment, take a single swab from each site - nose, throat and wound (where applicable) for culture at least 24 hours after stopping antibiotics and again after (at least) a further 24 hours.

8. If the clearance swabs are non-toxigenic strain, no organism isolated or NTTB strain, then no further public health action.

9. If the clearance swabs are positive for a toxigenic strain, then discuss a further 10 days of an alternative antibiotic with a microbiologist.

Appendix 2. Algorithm for the management of close contacts of confirmed and probable diphtheria cases*, and close contacts of asymptomatic carriers

1. Identify all close contacts of the index case of confirmed or probable diphtheria (see section 2.10.1), or of the asymptomatic carrier. If the case is possible, please see section 2.3. Close contacts include:

- contacts in a household type setting
- kissing or sexual contacts
- healthcare workers who have had direct exposure to respiratory droplets or exposed to undressed wounds of cutaneous cases where splash or droplet contamination has occurred

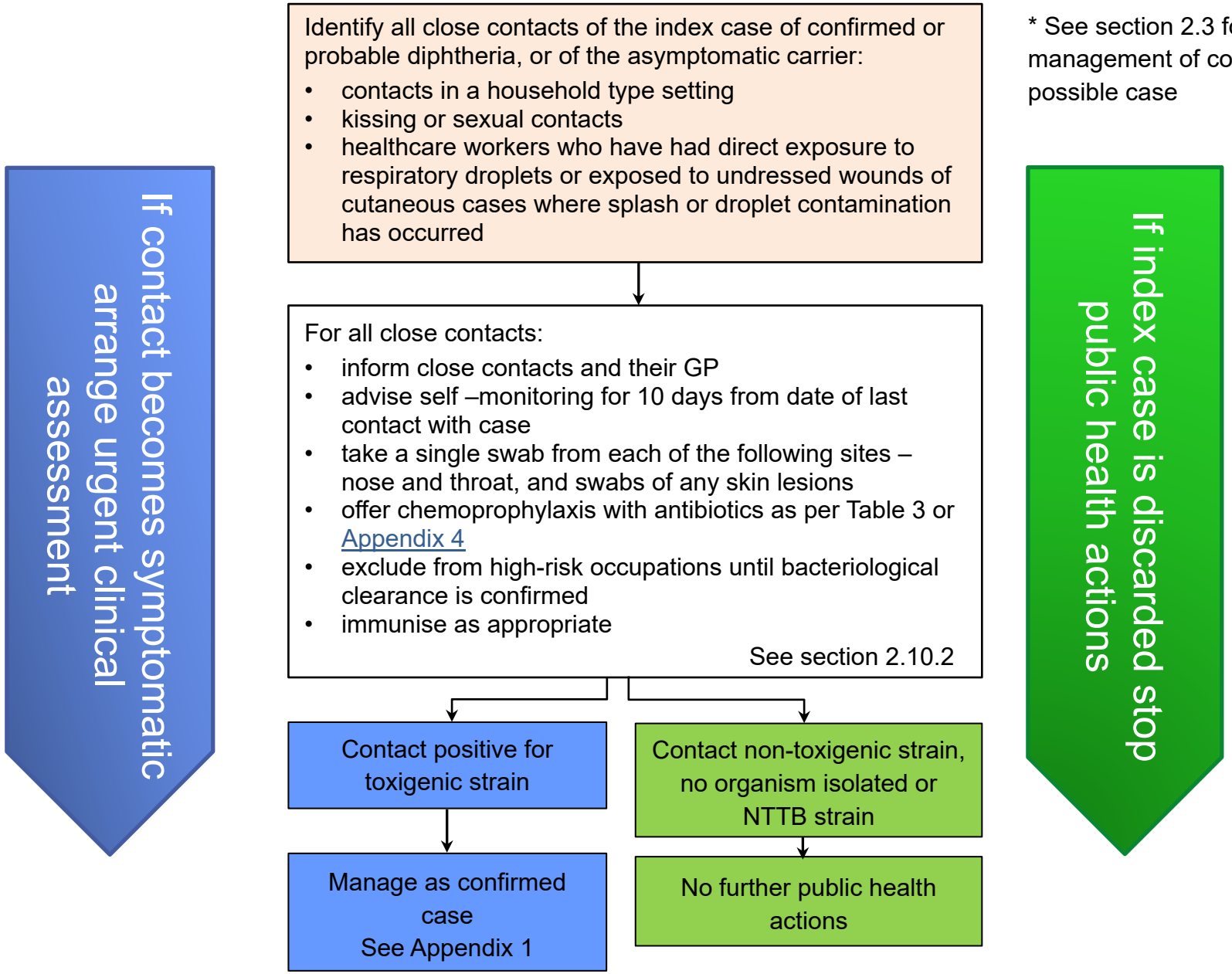
2. Carry out these actions for all close contacts (see section 2.10.2):

- inform close contacts and their GP
- advise self-monitoring for 10 days from date of last contact with case
- take a single swab from each of the following sites – nose and throat, and swabs of any skin lesions
- offer chemoprophylaxis as per Table 3 or Appendix 4
- exclude from high-risk occupations until bacteriological clearance is confirmed
- immunise as appropriate
- if the contact becomes symptomatic then arrange urgent clinical assessment

3. If a contact is positive for a toxigenic strain, then manage them as a confirmed case (Appendix 1).

4. If a contact has a non-toxigenic strain, no organism isolated or NTTB strain, then stop public health actions.

5. If the index case is discarded, then stop public health actions.



* See section 2.3 for the management of contacts of a possible case

Appendix 3. Guidance on the administration of antibiotics for confirmed or probable cases

Antibiotic	Dose	Duration (days)
Mild disease or community treatment		
Clarithromycin		
Adult (and children 12 to 17 years)	500mg twice a day	14
Child (1 month to 11 years)	7.5 mg/kg twice a day (maximum per dose 500mg)	14
Or		
Azithromycin		
Adult (and children 12 to 17 years)	500mg once a day	7 to 10
Child (6 months to 11 years)	12mg/kg once a day (maximum per dose 500mg)	7 to 10
Or		
Erythromycin[1,2,3]		
Adult (and children 12 to 17 years)	500mg 4 times a day	14
Child (1 month to 11 years)	10 to 15mg/kg 4 times a day (maximum per dose 500mg)	14
Neonate	10 to 15mg/kg 4 times a day	14

[1] Erythromycin is the preferred antibiotic for use in pregnancy.
[2] Total daily dose may alternatively be given in 2 divided doses.
[3] Dose increase may be used in severe infections; see BNF.

For cautions, interactions and side-effects prior to prescribing, consult the BNF or the BNF for children. If unable to take macrolide, consider non-macrolide options as listed below or discuss with UKHSA.

Severe disease or hospital treatment		
First line		
IV Benzylpenicillin sodium (and macrolide as above)		
Adult	1.2 to 2.4g every 6 hours	14
Child	25mg/kg every 6 hours; increased if necessary to 50mg/kg every 4 to 6 hours (maximum per dose 2.4g every 4 hours)	14
Add vancomycin or linezolid if extremely systemically unwell Dose as per BNF (duration 14 days)		
Second line – discuss with UKHSA		
Once patient improves clinically, stepdown to oral antibiotics		

For further guidance on the management of macrolide resistant infections see the Supplementary guidance for cases and outbreaks in asylum seeker accommodation settings , section 1.5.3

Appendix 4. Guidance on the administration of antibiotics for close contacts of confirmed or probable cases and close contacts of asymptomatic carriers

Antibiotic	Dose	Duration (days)
First line		
Clarithromycin		
Adult (and children 12 to 17 years)	500mg twice a day	7
Child (1 month to 11 years)	7.5mg/kg twice a day (maximum per dose 500mg)	7
Or		
Azithromycin		
Adult (and children 12 to 17 years)	500mg once a day	6
Child (6 months to 11 years)	12mg/kg once a day (maximum per dose 500mg)	6
Alternative regimes		
Benzathine benzylpenicllin IM		
Adult (and children over 30kg)	1.2 MIU single dose	Single dose
Child (under 30kg)	600,000 IU single dose	Single dose
Benzathine benzylpenicllin should never be administered by the IV route; inadvertent administration by the IV route may be associated with cardiorespiratory arrest and death		
Erythromycin[1,2,3]		
Adult (and children 12 to 17 years)	500mg 4 times a day	7
Child (1 month to 11 years)	10 to 15mg/kg 4 times a day (maximum per dose 500mg)	7
Neonate	10 to 15mg/kg 4 times a day	7
Please consult the BNF or the BNF for children for cautions, interactions and side-effects prior to prescribing		

[1] Erythromycin is the preferred antibiotic for use in pregnancy.
[2] Total daily dose may alternatively be given in 2 divided doses.
[3] Dose increase may be used in severe infections; see BNF.

Appendix 5. Diphtheria fact sheet: for cases and close contacts

You are receiving this fact sheet because you have been diagnosed with an infectious disease called diphtheria, or you have recently been in contact with someone who has been diagnosed with this infection.

Although diphtheria can be a serious illness, there are effective treatments available including antibiotics. There are also steps that you can take to prevent yourself from spreading diphtheria to your friends and loved ones, and to prevent yourself from catching diphtheria if you are a close contact. These steps are included in this fact sheet.

What diphtheria is

Diphtheria is a infectious disease, caused by a toxin (poison) made by a bacteria (from the *Corynebacteria* family). Diphtheria can be life-threatening if it is left untreated, but can be treated using antibiotics. It can also be prevented by vaccinating people against it, and babies and children are vaccinated against this disease as part of the routine childhood vaccine programme.

Most people who catch diphtheria in the UK have either not been fully vaccinated against the disease, or they are older adults who have been vaccinated but their immune system is not as good at fighting off the infection any more. These people will usually only have mild symptoms if they catch diphtheria.

Symptoms of diphtheria

Symptoms usually begin 2 to 5 days after being in contact with the diphtheria bacteria. Symptoms will depend on where on your body the bacteria has infected, but the most severe form of diphtheria affects the throat and tonsils. This is known as respiratory diphtheria.

The first symptoms of respiratory diphtheria are usually a sore throat, loss of appetite and a mild fever (high temperature). Within 2 to 3 days, a membrane may form over the throat and tonsils that can make it hard to swallow and breathe. The infection can also cause the lymph glands and tissues on both sides of the neck to swell (sometimes referred to as a ‘bull neck’).

Diphtheria can also cause small skin sores that form larger ulcers, which usually appear on exposed skin on the limbs, particularly the legs. This is known as cutaneous diphtheria.

How diphtheria spreads

Diphtheria bacteria can live in the mouth, nose, throat or skin of people with the infection. It is commonly spread when a person comes into contact with airborne droplets after an infected person has sneezed or coughed, or touching things they have sneezed or coughed on. Less

frequently, the infection can be passed on by touching the skin lesions of someone who has the infection. Prolonged close contact (such as living in the same household) is normally required for the infection to be transmitted to others.

Diphtheria caused by *Corynebacterium ulcerans* bacteria has been linked to prolonged close contact with animals (for example through having pets in the home or working on a farm or as a vet), or by eating or drinking milk and dairy products made from unpasteurised milk.

Diphtheria vaccination

Diphtheria vaccination protects against the disease and is very effective. It gives protection against disease by producing antibodies to the diphtheria toxin. This means that that if the vaccinated person comes into contact with diphtheria later in life, the body's immune system will be able to fight off the disease.

Diphtheria vaccination is given as part of the UK's childhood immunisation programme. All babies should receive 3 doses of a diphtheria-containing vaccine in the first year, usually given at 8, 12 and 16 weeks of age. Children should receive a first booster dose when they are between 3.5 and 5 years old and a second booster when they are between 13 and 18 years old.

Diagnosis

Diphtheria is diagnosed after an examination by a doctor, and by testing swabs usually taken from the throat but also sometimes from sores if someone has a skin infection. Special laboratory tests are needed to detect the toxin and confirm the diagnosis.

Treatment of diphtheria

A doctor will prescribe antibiotics to treat diphtheria. In cases of severe respiratory diphtheria they will also advise the person with diphtheria takes other medicines (such as anti-toxin) to stop the effects of toxins produced by the bacteria. People who have diphtheria will be advised to isolate away from other people until they have completed their antibiotics and follow up swabs have shown that they don't have the bacteria in their body any more.

People who share a house or who have been in close contact with the infected person will be offered a swab to test for diphtheria infection. All close contacts will also be treated with antibiotics as a precautionary measure.

If you have not been fully vaccinated against diphtheria, that is, you have not previous had 5 doses of a diphtheria vaccine, you will be offered additional vaccines to complete the course by your GP. If you have been fully vaccinated previously but this was more than 12 months ago, you will be offered a booster dose to boost your immunity against the infection. If you are unsure about your vaccine status, please check with your GP.

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Approval

This guidance was approved and signed off by the UK Health Security Agency Vaccine Science and Surveillance Group and the UK Public Health Network for Zoonoses.

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.

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

Version 21

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