NHS
Bristol, North Somerset and South Gloucestershire
Integrated Care Board

DIPHTHERIA

PRESENTATION FOR INVESTIGATION & MANAGEMENT: SLIDE SET FOR PRIMARY CARE

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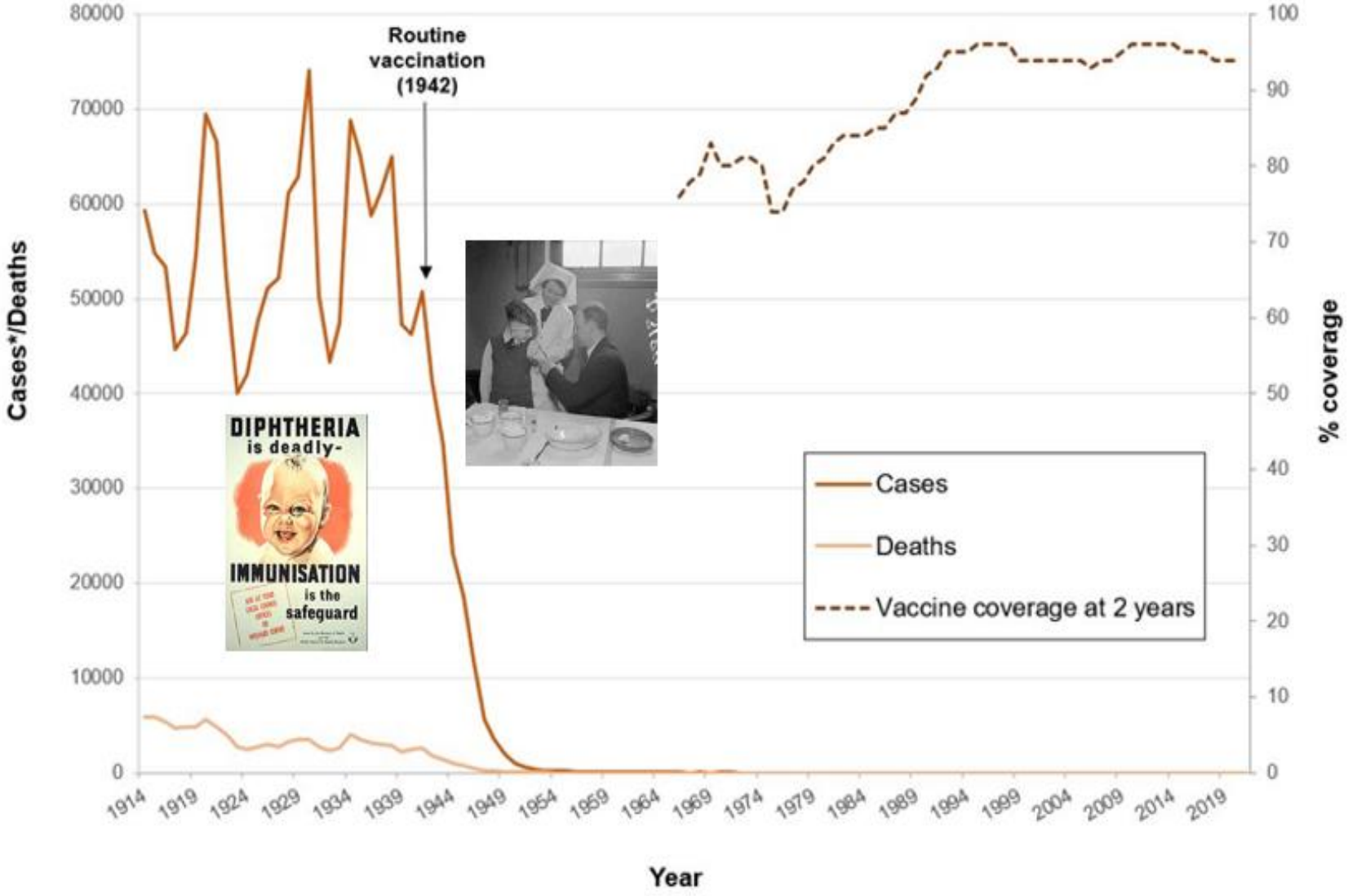
Diphtheria: Executive Summary & Overview

- Affects upper respiratory tract and/or skin.
- Caused by action of diphtheria toxin produced by toxigenic Corynebacterium diphtheriae or Corynebacterium ulcerans, both rare in the UK since the 1940s, cases often travel related but epidemiology is changing.
- Acute respiratory diphtheria requires early diagnosis & prompt, live saving-administration of diphtheria anti-toxin.
- UKHSA Health Protection Teams play an important role in the risk assessment of toxigenic cases: contact tracing, management investigation of source and outbreak management.

Diphtheria cases* and deaths, England and Wales†, 1914 to 2021



Epidemiology 2000-2022

- Increase in C. diphtheria – travel associated, mostly cutaneous, may be vaccinated D. ulcerans mostly associated with pets, lower % of non-toxigenic strains.
- MALDI-TOF MS* is increasingly being used by local laboratories to identify gram-positive coryneforms. This may partly be responsible for the increase in the number of referred isolates and confirmed toxigenic isolates from the National Reference Laboratory.
- National incident March 2022

***Matrix Assisted Laser Desorption/Ionization – Time of Flight Mass Spectrometry*

Background

- **Distribution**

  Endemic in many countries, highest in low-income areas with low vaccine uptake.

- **Source**

  C. diphtheriae – nose or throat of human case or carrier. In the Tropics, infected lesions are common from person to person close contact with infected secretions.

  C. ulcerans – historically cattle, now in companion animals.

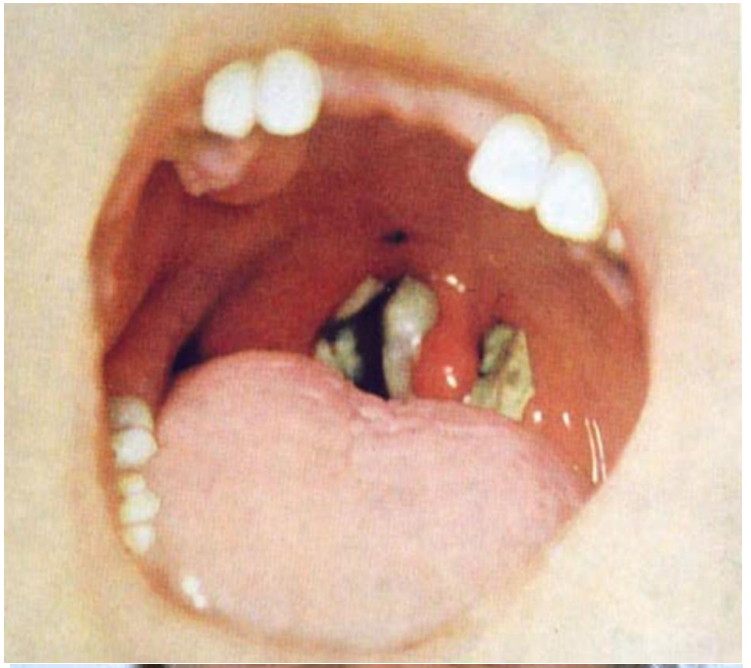
- **Spread**

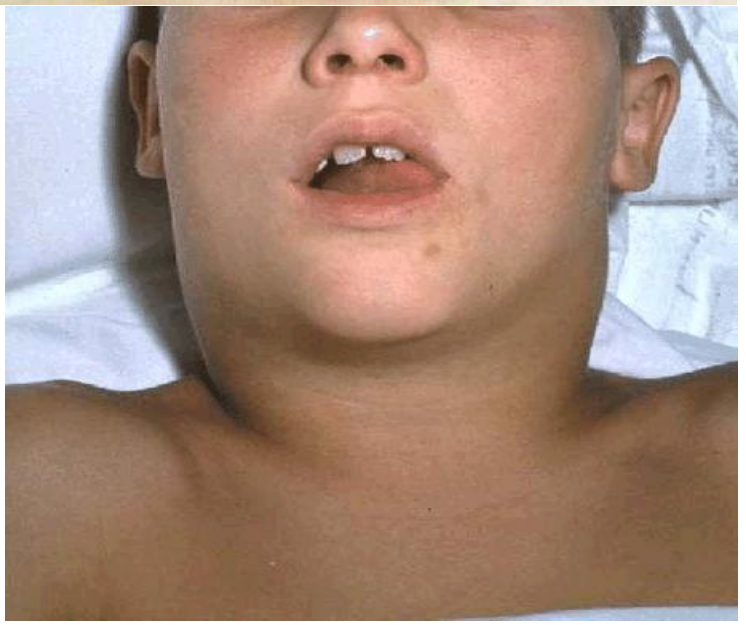
  C. diphtheriae – person to person close contact with infected secretions.

  C. ulcerans – milk borne, contact with animals or possible person to person.

Presentation

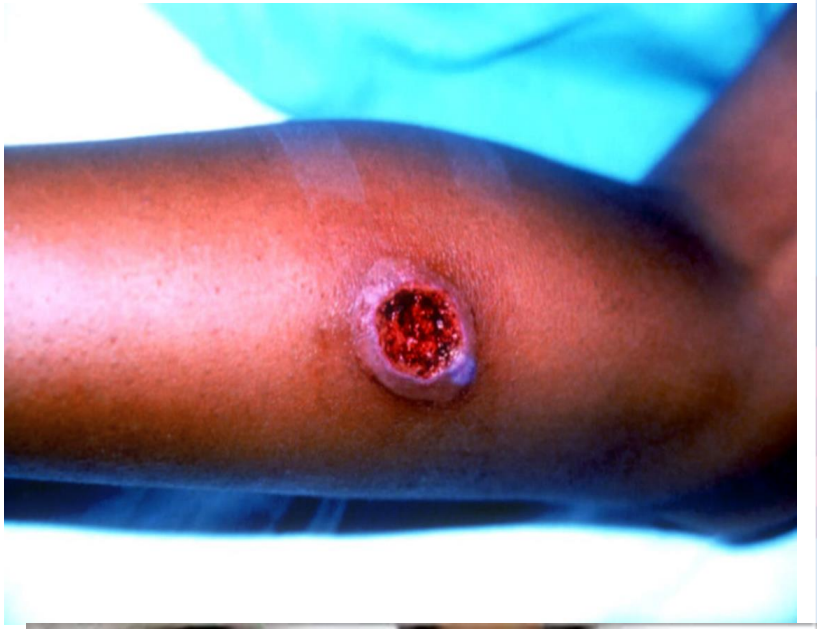
- **Classical Respiratory Diphtheria:**
  Inflammatory pseudo-membrane on tonsils, oropharynx & pharynx, ”bull neck”, sore throat, fever, potentially death.
- **Laryngeal Diphtheria:**
  Hoarseness – stridor.
- **Nasal Diphtheria:**
  Mild or chronic nasal discharge – clear to bloody.



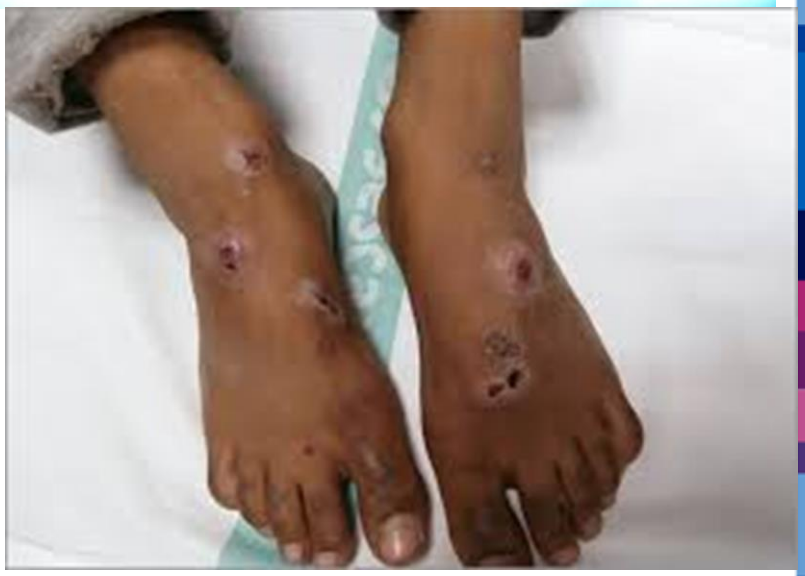


Presentation

- **Cutaneous Diphtheria:**
  Usually on exposed limbs. Lesions start as vesicles – form small, clearly demarcated, sometimes multiple.



Note: ulcers may be difficult to distinguish from impetigo lesions, usually covered with an eschar; a hard slightly raised bluish-grey membrane.



More likely after respiratory diphtheria

- **Cardiac** - Myocarditis
- **Neurological** - Polyneuropathies (may mimic Guillain-Barre)
  - Palatal palsy
  - Ocular muscle palsies
  - Limb weakness
  - Diaphragmatic palsy
- **Respiratory** - Airway obstruction

Immunisation protects against toxic manifestations but not necessarily against acquisition of infection.

Diphtheria Transmission

- **C. diphtheriae:** - droplet
  - contact with infected animals
- **C. ulcerans:** - contact with infected animals
  - unpasteurised dairy products consumption
  - Cases & contacts of cutaneous diphtheria (both C. diphtheriae & C. ulcerans) may AA develop respiratory diphtheria incubation 2-5 days (up to 10 days).

    Close prolonged contact.

Lab Investigation:

Local lab – some potential for missed or delayed diagnosis.

- Not all labs routinely culture pharyngeal swabs for corynebacterial.
- Care should be taken when interpreting presence of diphtheroid as representing co-incidental commensals.
- Wound swabs may contain additional causative organisms.
- Isolates – original sample should be sent to the national reference lab for toxigenicity testing.
- Ensure all samples being taken are labelled correctly, swabs are in-date and request made for diphtheria and not a routine MC+S.

Laboratory Investigations PCR

- Lab confirmation informs public health Action.
- To decrease time to result, a real-time PCR (qPCR) assay developed for confirmation of both identification of C. diphtheria and C. ulcerans / C. pseudotuberculosis, and detection of the diphtheria toxin gene (April 2014).
- Target Genes: RNA polymerase beta-subunit-encoding gene (rpoB), a sub-unit of the diphtheria toxin gene (tox), green fluorescent protein DNA (gfp) as an internal process control.
- Elek immunoprecipitation test used to confirm expression of diphtheria toxin in qPCR toxin gene (tox positive isolates).

Laboratory Investigations PCR

- Time to result: 3-4 hours after receipt of isolate.
- High diagnostic sensitivity and specificity.
- Limitations:

  Inability to to distinguish between C. ulcerans and C. Pseudotuberculosis.

  Presence of toxin gene may not always predict toxin expression, therefore confirmation of expression of diphtheria toxin in qPCR toxin gene positive isolates is always determined using the phenotypic Elek tests.

Diphtheria Laboratory Services

- Monday to Friday: normal working hours. Isolates received by midday, result by close of play. Isolates received late afternoon, results by close of play or next day.
- Saturday / Bank Holiday service out of hours. Isolates received by midday, result by close of play.
- For queries out of hours, check UKHSA CSA/CMA out of hours on call rota, which will provide contact details of diphtheria senior scientist on call.

Management of suspected cases

- PROBABLE and CONFIRMED CASES require public health action.
- RISK ASSESS POSSIBLE OR PROBABLE CASES.
- POSSIBLE cases – public health action may be delayed unless concerning features or Epifactors increasing likelihood of toxogenicity.
- Immunisation history.
- Occupation.
- Travel or contact with traveller.
- Contact with animals.
- Raw Dairy produce consumption.

Management of Cases

- If PCR toxin gene positive and confirmed Elek positive (that is toxigenic).
- If unwell, consider requirement for admission, isolate and barrier nurse, if well and /or symptomatic provide isolation advice and safety netting advice on what to do if they become unwell.
- Consider antitoxin (DAT), this can be discussed with local Infection specialist and UKHSA HPT.
- Give antibiotic treatment for 14 days (7 days if asymptomatic).
- Target Genes: RNA polymerase beta-subunit-encoding gene (rpoB), a sub unit of the diphtheria toxin gene (tox), green fluorescent protein DNA (gfp) as an internal process control.
- Identify & manage close contacts with support from UKHSA HPT and BNSSG IPM Cell Team.
- If PCR toxin gene positive and Elek negative, **STOP** public health action.

Management of Cases

- After completion of antibiotic treatment, take two throat nasopharyngeal swabs (as well as skin swabs for cutaneous cases). Swabs should be taken after 24 hours after completion of antibiotics and at least 24 hours apart.
- If swabs are positive for toxigenic strain, discuss further 10 days of antibiotics with local microbiologist.
- Asymptomatic carriers of toxigenic strains should be treated with the same antibiotic regime, as cases with appropriate swabs taken on completion of therapy, to ensure eradication.

Management of Cases: Immunisation

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 dose of absorbed diphtheria containing vaccine, either Td/IPV, dTaP/IPV or DTaP/IPV.
- Immunised children aged 10 years and over and adults – one dose of adsorbed low-dose diphtheria containing vaccine for adults e.g. Td/IPV.
- Unimmunised children under 10 years 3 doses of adsorbed full dose diphtheria containing vaccine e.g. Td/IPV at monthly intervals.
- In a person with unknown immunisation history, assume they are unimmunised and follow above.

Infection Control & PPE

Follow droplet and airborne transmission based precautions contained in the National Infection Prevention and Control Manual for England, Appendix 11a, Immunised children up to 10 years of age, one dose of absorbed diphtheria containing vaccine, either Td/IPV, dTaP/IPV or DTaP/IPV.

- **PPE:**

  Fluid repellent surgical facemask

  Eye protection

  Apron

  Gloves

  Hand hygiene

Management of Cases: DAT Vaccine

Mortality rates for clinical diphtheria frequently exceeded 50% in pre anti-toxin era.

Dramatic declines in mortality in those treated (mortality 3.3% in treated, compared with 12.2% in untreated, in one clinical trial).

EARLY TREATMENT IS CRITICAL

- Discuss with ID clinician.

  DAT only for confirmed or probably cases.

  Give DAT without waiting for laboratory confirmation for classical respiratory diphtheria presentations.

  DAT is extracted from horse serum – check for allergies.

- **Supplies are limited**

Management of Cases: Contact Tracing

UKHSA HPT can support with contact tracing:

- **Classification of contacts:**

  Members of household type settings.

  Kissing or sexual contacts.

  Childminder or carer with regular contact for 6 hours or more.

  Exposure to respiratory droplets or secretions.

  Exposure to undressed wound of cutaneous case.

  Healthcare and outreach workers should be risk assessed (considering PPE use).

Management of Contacts - Actions

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

- Inform contact (and other GP, Occupational health etc…) as appropriate.
- Advise self-monitoring for 10 days from date of last contact with case and provide safety netting advice, and actions to take, if they become unwell.
- Perform nasopharyngeal and throat swabs as well as swabs of any skin lesions (if present).
- Offer chemoprophylaxis with antibiotics for 10 days.
- Exclude from high-risk occupations until bacteriological clearance is confirmed.
- Immunise as appropriate.

Management of Contacts

- Immunise as appropriate.
- If the contact becomes symptomatic, then arrange urgent clinical assessment.
- If a contact is tested positive for a toxigenic strain, manage them as a confirmed case.
- If the index case is discarded, then **stop public health actions**.

Contact Tracing of C. ulcerans

- If a contact is positive for a toxigenic strain, then manage as a confirmed case
- If contact becomes symptomatic, arrange urgent clinical assessment.
- If the index case is discarded, then stop public health actions.
- Perform risk assessment of potential animal source in collaboration with APHA and local vet colleagues (nature of contact, symptoms in animal, consider need to determine carriage in animal via testing).
- APHA advise on appropriate antibiotic treatment for animals found to be positive for C. ulcerans. Confirm clearance in the animal, testing 5 to 7 days following completion of antibiotics.

Reporting

- Diphtheria is a NOID.
- If you **suspect** diphtheria, you must inform the UKHSA Health Protection Team.
- Further links can be found via the two links below:

https://www.gov.uk/guidance/notifiable-diseases-and-causative-organisms-how-to-report

https://www.gov.uk/government/collections/diphtheria-guidance-data-and-analysis#:~:text=For%20symptoms%20and%20general%20information,protection%20teams%20of%20suspected%20cases

Support & Advice

- BNSSG IPM Cell Team

  Email: *bnssg.covid.ipc@nhs.net*

- UKHSA Southwest, Health Protection Team

  Email:swhpt@phe.gov.uk

  Telephone 0300 303 8162 (option 1, then option 1).

  Out of hours advice 0300 3038162 (option 1).