# Diphtheria

#### ***1. The Organisms & Toxin***

* *Corynebacterium diphtheriae*, *C. ulcerans*, rarely *C. pseudotuberculosis*; only toxigenic strains cause classical disease.
* Diphtheria toxin (DT) is an A‑B exotoxin that ADP‑ribosylates EF‑2 → inhibition of protein synthesis → local necrosis plus systemic effects (myocarditis, neuritis, adrenal damage).
* Natural immunity after sub‑clinical infection is unreliable; UK serosurvey 2021 showed 11 % of the population lacked basic protection, highest susceptibility in ≥70 y (26 %)

#### ***2. Clinical Picture***

|  |  |  |  |
| --- | --- | --- | --- |
| **Form** | **Key features** | **Complications** | **Infectious period** |
| **Respiratory** | Pseudomembranous pharyngitis, “bull‑neck”, low‑grade fever | Airway obstruction, myocarditis, cranial & peripheral neuropathies | Up to 4 w untreated |
| **Cutaneous** | Vesicle → sharply demarcated ulcer with grey eschar; often lower limbs | Secondary bacterial infection | Prolonged colonisation |
| **Carriage** | Asymptomatic | Source of outbreaks | Variable |

Incubation 2–10 days (commonly 3–5). Transmission: droplets, contact with soiled fomites, and (for *C. ulcerans*) raw dairy or companion animals.

#### ***3. Epidemiology (UK focus)***

* Pre‑vaccine era (1940): > 61 000 cases, 3 283 deaths. Introduction of immunisation (1940) caused rapid decline.
* 1986‑2023: 233 toxigenic cases; shifting pattern from *C. diphtheriae* to *C. ulcerans* in 1990s‑2000s, then rise in cutaneous *C. diphtheriae* 2009‑17.
* 2022 UK outbreak: 73 toxigenic *C. diphtheriae* in newly arrived asylum seekers; mainly cutaneous, 2 severe respiratory cases, 1 death.

#### ***4. Laboratory Diagnosis (exam‑level detail)***

1. **Specimens** – throat/nasal swabs from membrane edge, skin lesion swabs, and close contacts’ throat swabs.
2. **Primary culture** – selective tellurite agar (black colonies).
3. **Species ID** – MALDI‑TOF, biochemical tests.
4. **Toxigenicity** – modified Elek test (immunoprecipitation), or real‑time PCR for *tox* gene (faster, higher sensitivity).
5. **Additional tests** – AST (penicillin/erythromycin resistance rare but emerging), MLST for outbreak linkage.

*(Points 2–5 are core FRCPath knowledge; not explicitly in Green Book.)*

#### ***5. Case Management***

* **Isolation & notification** – immediately notifiable; manage in side‑room with droplet precautions.
* **Antitoxin (DAT)** – equine; give urgently on clinical suspicion (do not await culture). Test for horse‑serum hypersensitivity; monitor for anaphylaxis.
* **Antibiotics** – first‑line benzyl‑penicillin IV then oral erythromycin/azithromycin for 14 d; alternatives guided by AST.
* **Immunisation** – start/complete course once recovered (see section 7).

#### ***6. Public‑Health Actions***

|  |  |
| --- | --- |
| **Measure** | **Detail** |
| Case | DAT + antibiotics + clearance cultures (after 48 h treatment & at ≥24 h intervals) |
| Close contacts (household, kissing, healthcare if exposure to secretions) | Throat swab; chemoprophylaxis (erythromycin 10 d); reinforce vaccination (single booster if completed course ≥12 m ago; complete schedule if partial/unimmunised); exclude from nursery/school/work pending first negative culture if ≥5 y and incomplete vaccination |
| Outbreak | Incident Control Team, enhanced surveillance, mass vaccination if immunity gap |

#### ***7. Vaccines – Core Facts***

|  |  |  |  |
| --- | --- | --- | --- |
| **Product group** | **Antigen dose** | **Age indication** | **Examples** |
| **“D” (full dose)** | ≥30 IU DT | <10 y for priming | Hexavalent DTaP/IPV/Hib/HepB (Infanrix Hexa, Vaxelis) |
| **“d” (low dose)** | ≈2 IU DT | ≥10 y & boosters | dTaP/IPV (Boostrix‑IPV, Repevax), Td/IPV (Revaxis) |

**UK schedule (as of 1 July 2025):**

* **Primary** (8, 12, 16 wk): DTaP/IPV/Hib/HepB ×3
* **18 mo** (hexavalent) booster – Hib‑driven; *does not count* as long‑term diphtheria booster.
* **Booster 1** (3 y 4 m): dTaP/IPV
* **Booster 2** (~13‑14 y): Td/IPV
* **Adults/travel/lab staff**: ensure 5 lifetime doses; give Td/IPV if >10 y since last.

**Special groups**

* **Pregnancy** : give dTaP/IPV (pertussis programme) regardless of trimester; good safety record.
* **Premature infants ≤28 wk**: vaccinate on chronologic schedule but observe 48‑72 h for apnoea.
* **Immunocompromised/HIV**: standard schedule; may need re‑vaccination post‑therapy.
* **Latex anaphylaxis**: avoid Adacel (latex tip‑cap); use Boostrix‑IPV/Repevax.

**Contra‑indications** – confirmed anaphylaxis to previous dose/component only. Minor illness ≠ reason to defer.

#### ***8. Vaccine Handling & Administration***

* Store 2–8 °C, protect from light; do **not** freeze.
* IM injection: anterolateral thigh (<1 y) or deltoid. If co‑administered with other vaccines use separate sites (≥2.5 cm if same limb).

#### ***9. Adverse Events & Safety***

* Common: pain, swelling, low‑grade fever.
* Rare: HHE, febrile convulsion, large local swelling (more likely after 4th‑5th doses).
* Anaphylaxis ≈1 per million doses.
* Report via MHRA Yellow Card.

#### ***10. Antimicrobial & Laboratory Alert Points (Exam Pearls)***

* **Tellurite agar** is essential; *C. ulcerans* may grow poorly on Loeffler’s.
* Always perform *tox* PCR on any *Corynebacterium* from throat/wound if diphtheria clinically possible.
* Notify public‑health immediately on suspicion – statutory requirement.
* Clearance: two consecutive negative cultures required (nose & throat or lesion), ≥24 h apart and ≥48 h after completion of antibiotics.

**Mnemonic for exam recall – “DIPHTHERIA”**

**D** roplet spread **I** ncubation 2–10 d **P** seudomembrane **H** orse‑derived antitoxin

**T** oxin‑mediated myocarditis/neuritis **H** igh‑dose vs low‑dose vaccines

**E** pidemiology shift (*ulcerans*, asylum seekers 2022) **R** einforcing boosters (3y4m & teen)

**I** solate on tellurite, PCR *tox* **A** ction – notify, antibiotics, antitoxin, immunise contacts