

Update Diphtherie – back in Europe  
conference SSTMP & SSTTM  
Kursaal Bern | 11.November 2022

PD Dr. med. Cornelia Staehelin



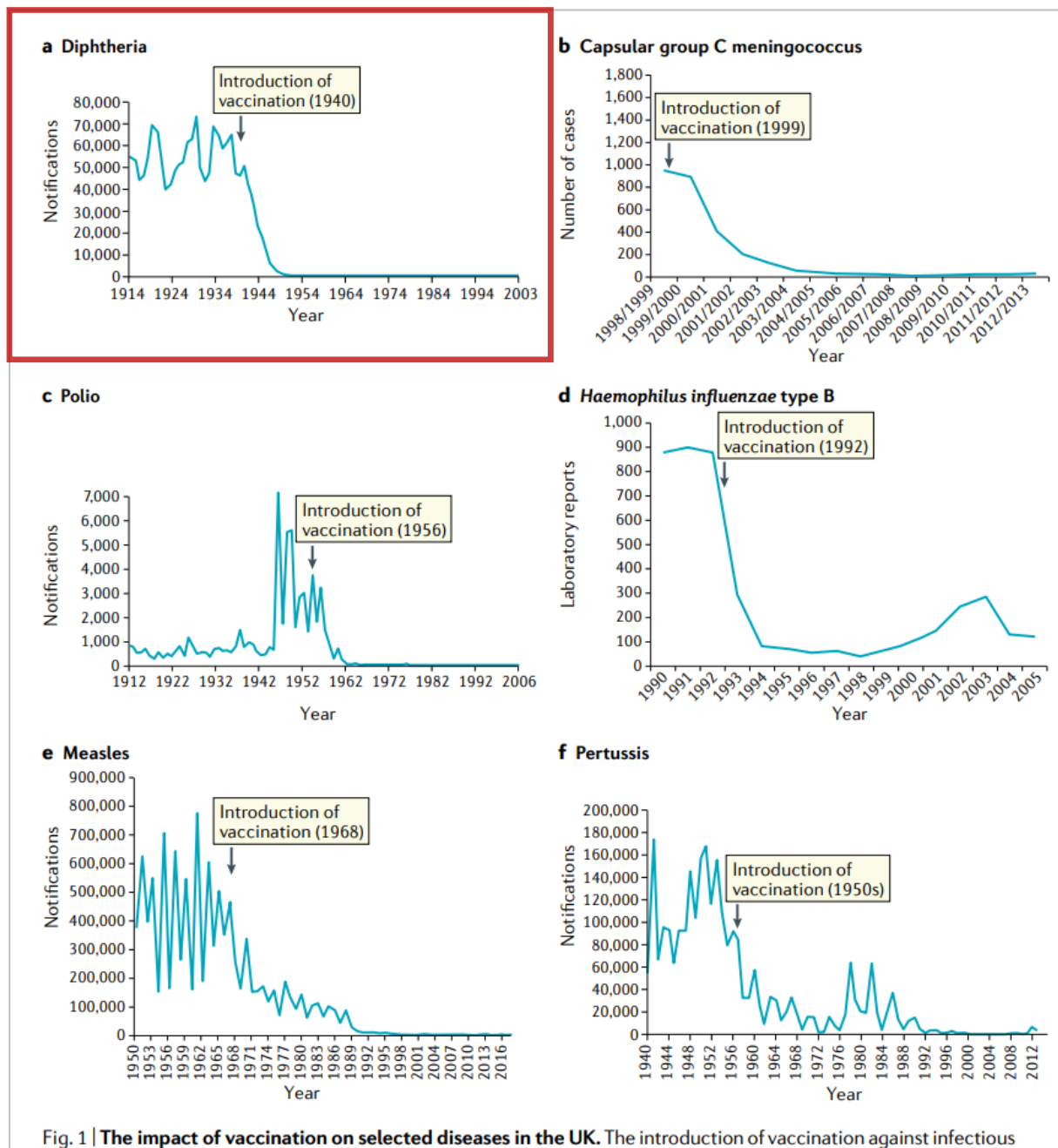


Fig. 1 | The impact of vaccination on selected diseases in the UK. The introduction of vaccination against infectious

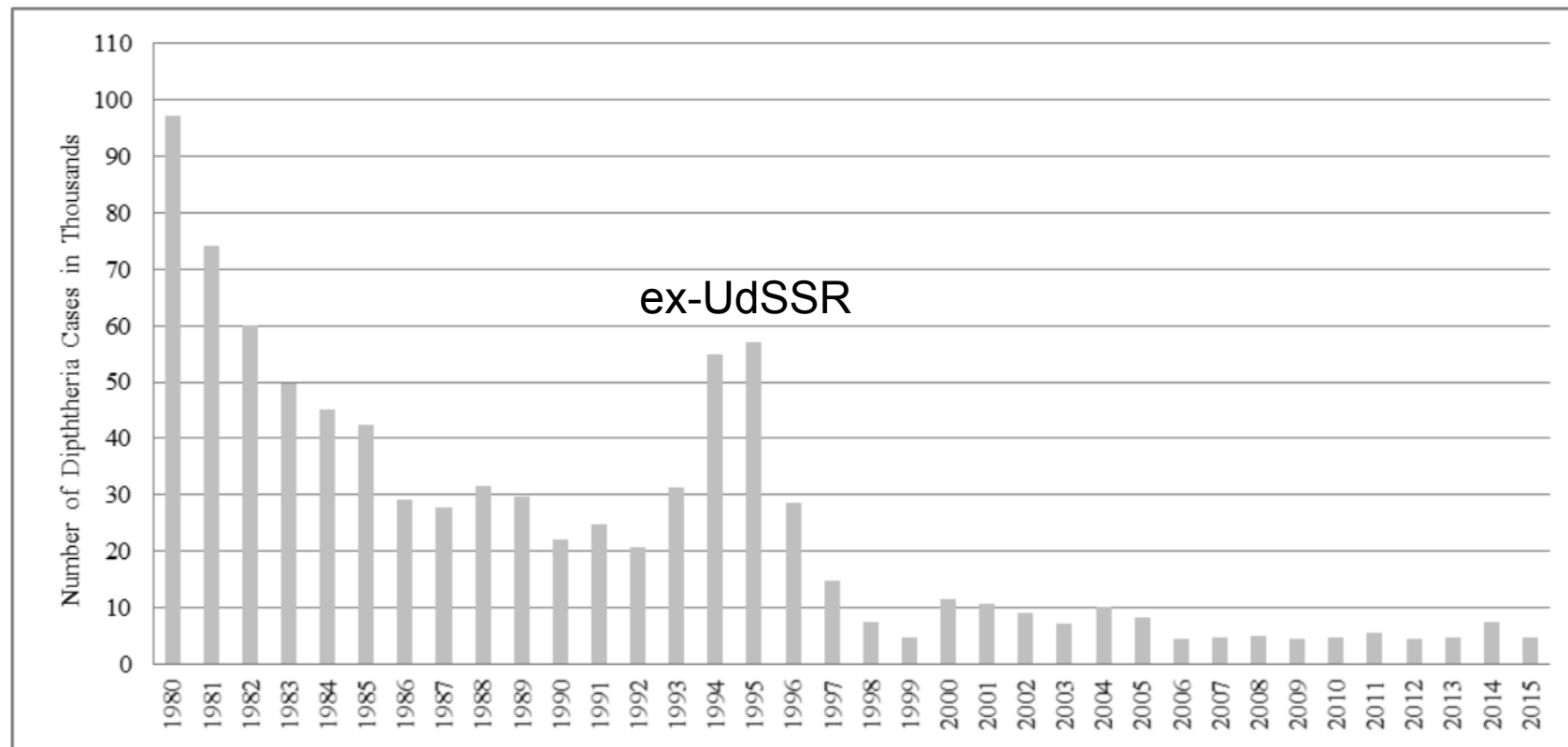
1880-er Jahre USA and Europe: CFR up to 50%!

Europe WW I: CFR reduced to 15% thanks to anti-toxin

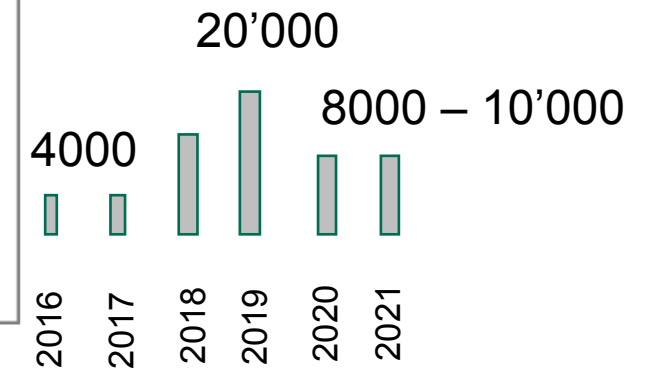
1970-ies worldwide 1 mio. cases und 50'000 – 60'000 deaths (prior to broad availability of Di-toxoid containing vaccines)

1974 inclusion into Expanded Programme of Immunization (EPI) → one of 6 EPI vaccines → cases reduced by > 90% after 1980

Figure 1 Diphtheria Reported Cases, 1980-2015 (World Health Organization)



Source: World Health Organization



<https://www.unicef.org/supply/sites/unicef.org.supply/files/2019-06/diphtheria-antitoxin-market-update.pdf>



[Home](#) / [News](#) / COVID-19 pandemic fuels largest continued backslide in vaccinations in three decades



“The percentage of children who received three doses of the vaccine against diphtheria, tetanus and pertussis (DTP3) – a marker for immunization coverage within and across countries – fell 5 percentage points between 2019 and 2021 to 81 per cent.

**As a result, 25 million children missed out on one or more doses of DTP through routine immunization services in 2021 alone.”**

## COVID-19 pandemic fuels largest continued backslide in vaccinations in three decades

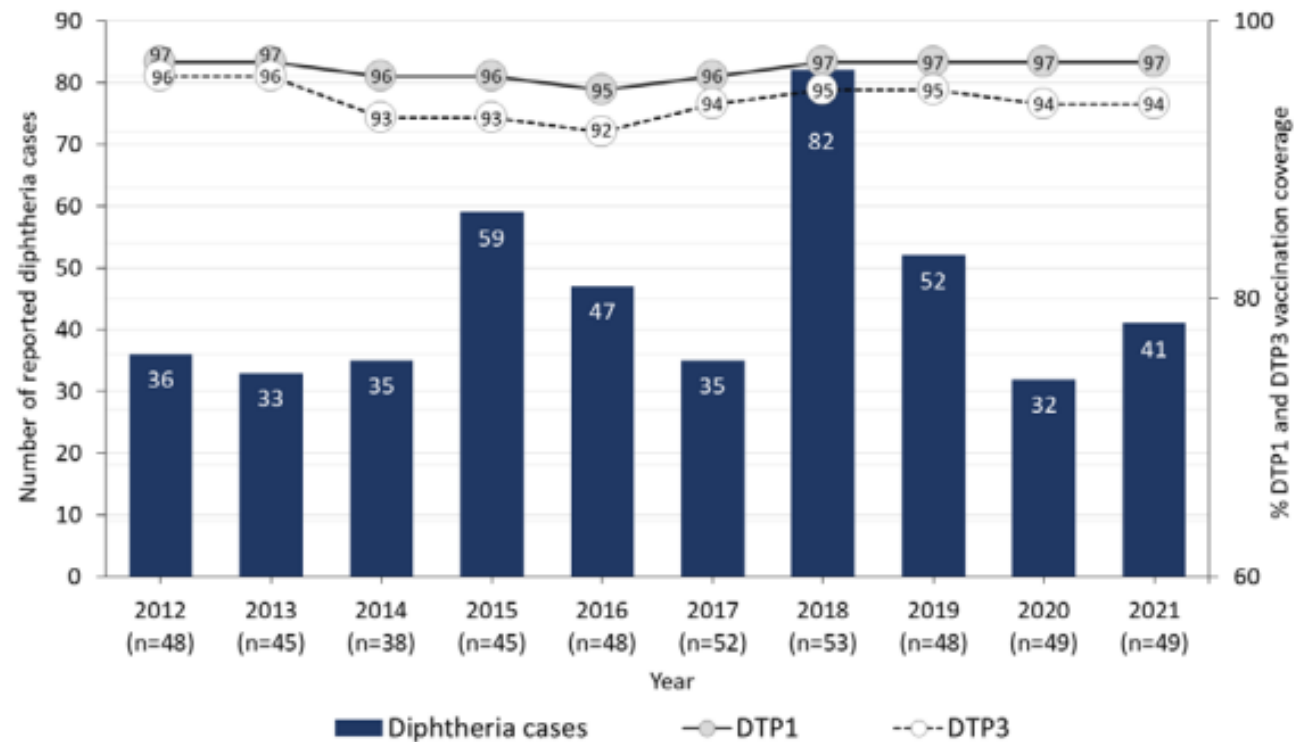
**WHO and UNICEF sound the alarm as new data shows global vaccination coverage continued to decline in 2021, with 25 million infants missing out on lifesaving vaccines**

15 July 2022 | Joint News Release | Geneva/New York | Reading time: 6 min (1581 words)

<https://www.who.int/news/item/15-07-2022-covid-19-pandemic-fuels-largest-continued-backslide-in-vaccinations-in-three-decades>

# WHO: current epidemiology Europe

**Fig. 1.** Number of diphtheria cases\* (n=452) and DTP1 and DTP3 coverage in the WHO European Region, 2011–2021



2022

9/12 months

1  
4  
4

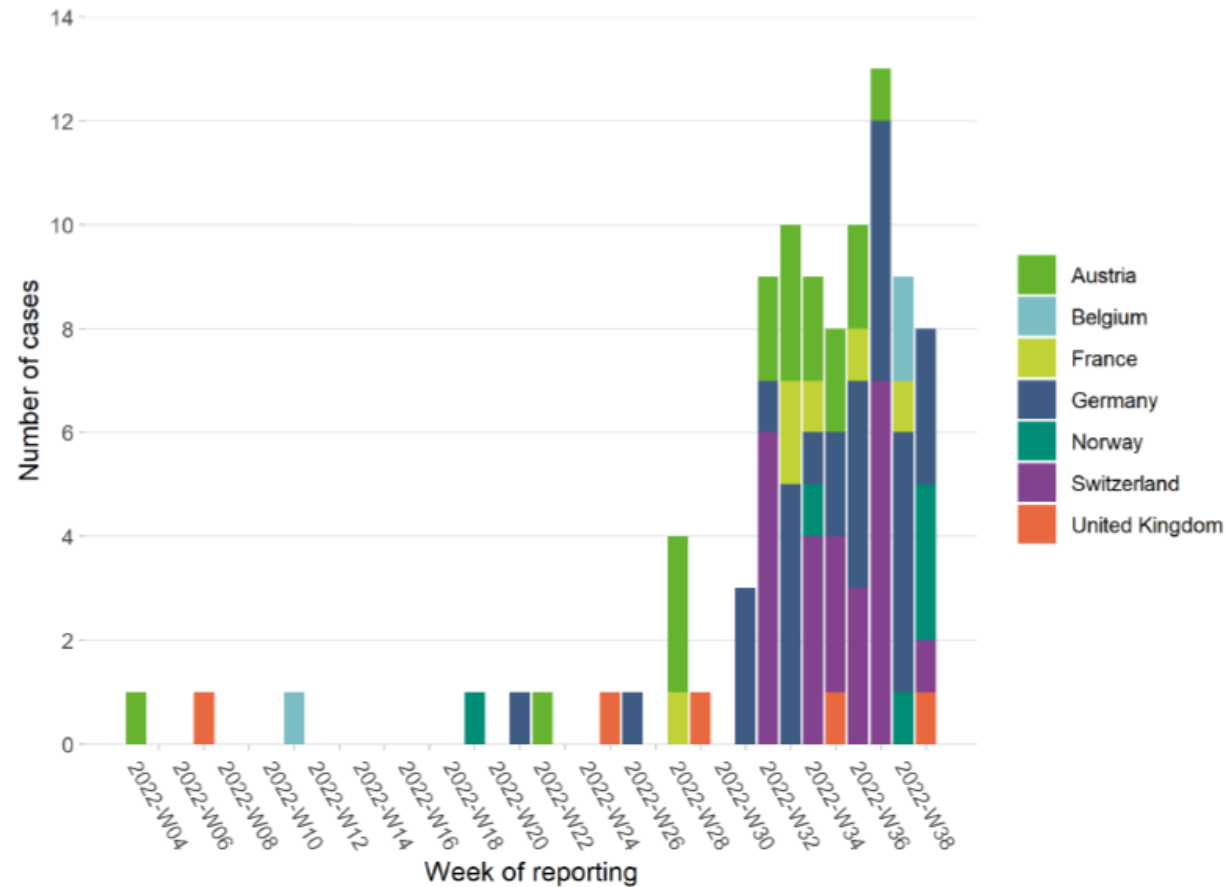
A, CH, D, F, IT, NO, UK

63% asylum seekers

DTP1: first dose of diphtheria, tetanus and pertussis vaccine; DTP3: third dose of diphtheria, tetanus and pertussis vaccine.  
\*The number of countries that submitted reports (including zero reporting) on diphtheria cases are shown in parentheses below the year.

# ECDC: current epidemiology Europe

**Figure 1. Number of diphtheria cases among migrants per week, by country, and date of reporting in 2022.**



Source: EpiPulse; direct communication with countries and official reports.

Note: Date of reporting for Switzerland is the date of publication of official or media reports.

Note 2: There is an inherent delay between the date of disease onset, the date of detection and the date of reporting, resulting in a reporting lag. This should be taken into consideration when interpreting this figure.

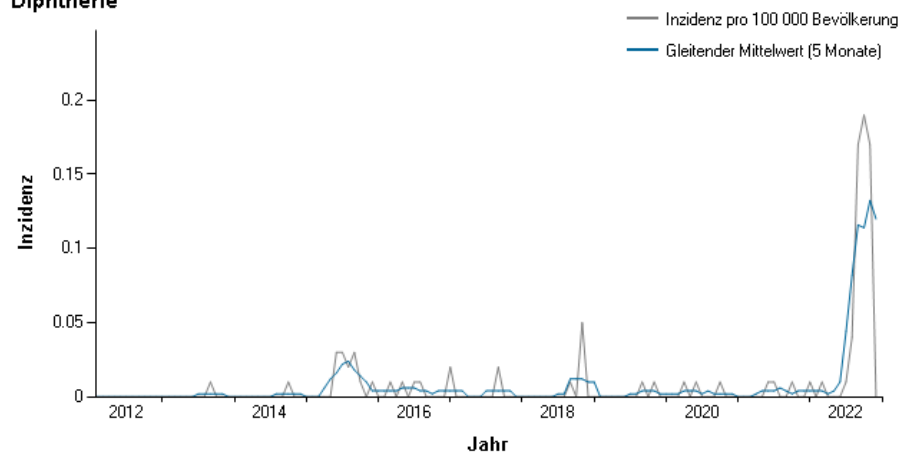
Note 3: Figure includes cases of respiratory diphtheria from Austria (4), Germany (1) and Switzerland (10).



# Epidemiology CH

## Monatliche Inzidenz pro 100 000 Bevölkerung bis Woche 44/2022

### Diphtherie



BAG OFSP UFSP SFOPH

Stand 08.11.2022

## Jährliche Fallmeldungen und Inzidenzen der letzten 10 Jahre und aktuelles Jahr bis Woche 44/2022

\* aktuelles Jahr mit annualisierter Inzidenz

	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Fallmeldungen	0	1	1	10	6	2	5	2	3	4	52

	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022*
Inzidenz pro 100 000 Bevölkerung	0	0.01	0.01	0.12	0.07	0.02	0.06	0.02	0.03	0.05	0.7

In Bern alone: 37 cases

## RAPID COMMUNICATION

# Ongoing toxin-positive diphtheria outbreaks in a federal asylum centre in Switzerland, analysis July to September 2022

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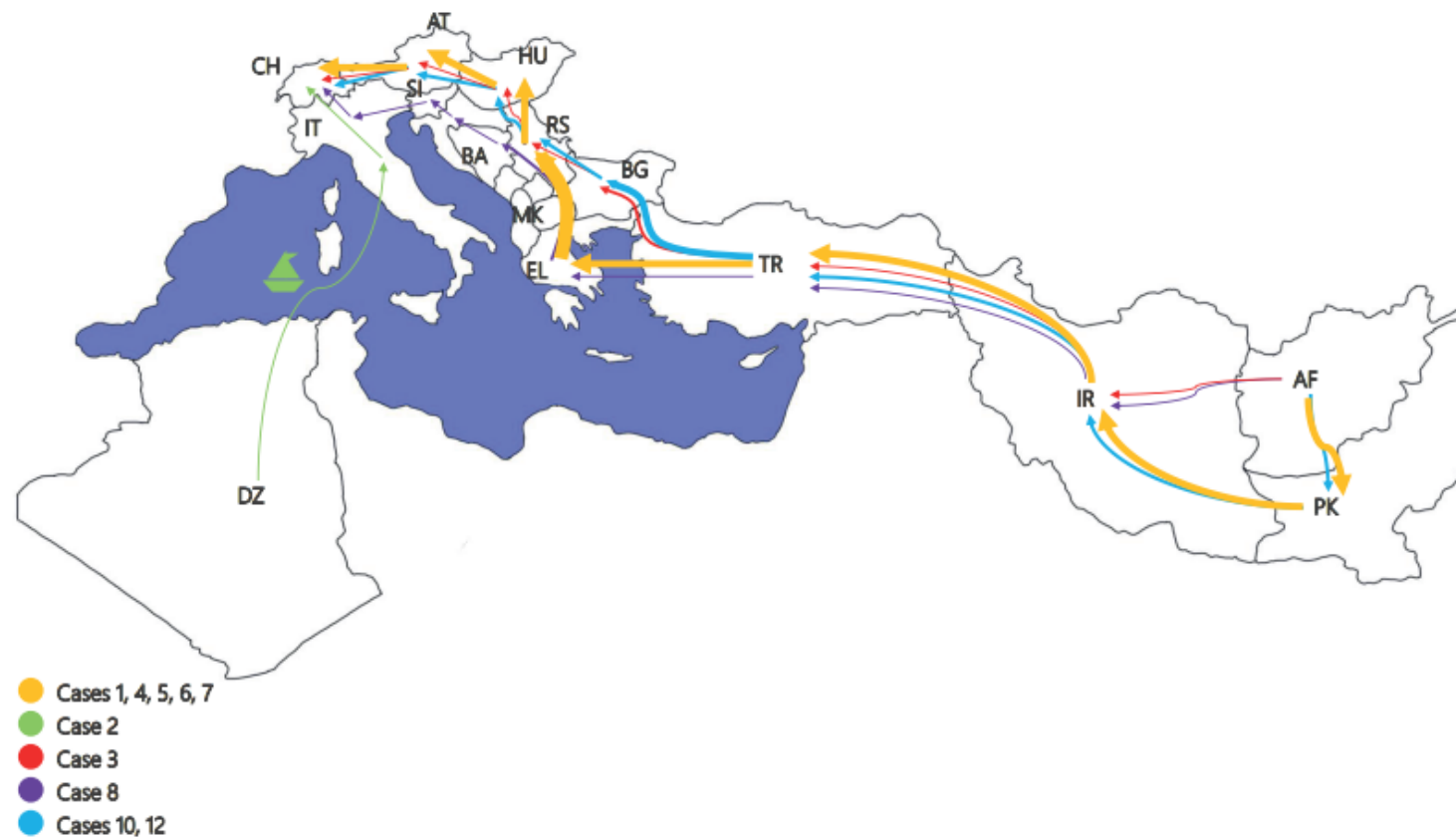
### Citation style for this article:

Kofler Jacob, Ramette Alban, Iseli Patricia, Stauber Lea, Fichtner Jens, Droz Sara, Zihler Berner Annina, Meier Anna Bettina, Begert Michelle, Negri Sabine, Jachmann Anne, Keller Peter Michael, Staehelin Cornelia, Grützmacher Barbara. Ongoing toxin-positive diphtheria outbreaks in a federal asylum centre in Switzerland, analysis July to September 2022. *Euro Surveill.* 2022;27(44):pii=2200811. <https://doi.org/10.2807/1560-7917.ES.2022.27.44.2200811>



**FIGURE 3**

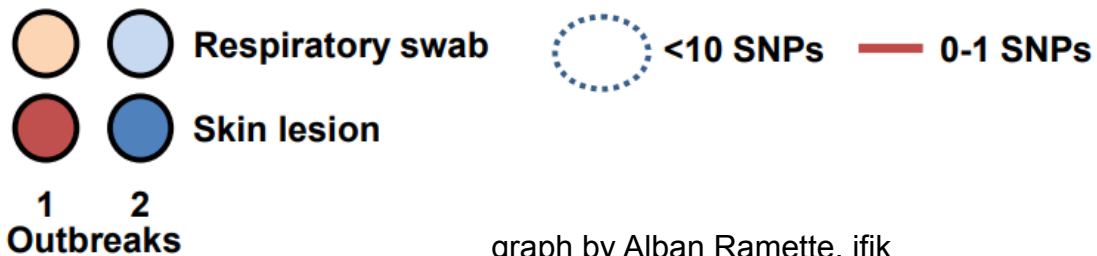
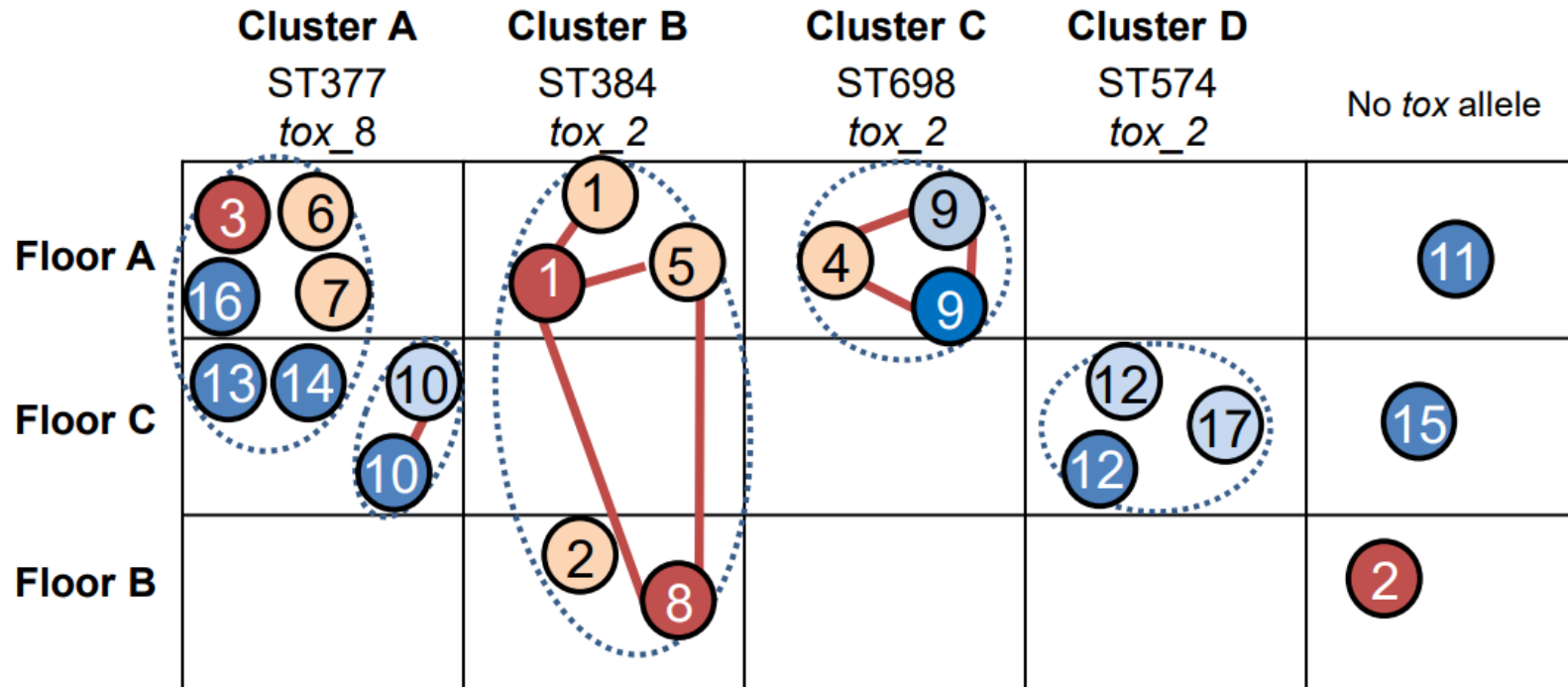
Reported travel routes to Switzerland of *Corynebacterium diphtheriae* positive cases in two outbreaks at an asylum centre, Switzerland, July–September 2022 (n = 10)



AF: Afghanistan, AT: Austria, BG: Bulgaria, BA: Bosnia and Herzegovina, CH: Switzerland, DZ: Algeria, EL: Greece, HU: Hungary, IR: Iran, IT: Italy, MK: North Macedonia, PK: Pakistan, RS: Serbia, SI: Slovenia, TR: Türkiye.

Data were collected through epidemiological surveys (Supplementary Table S1B).

Data on Cases 9, 11 and 13 to 20 were not available.



graph by Alban Ramette, ifik

as of 12.10.22

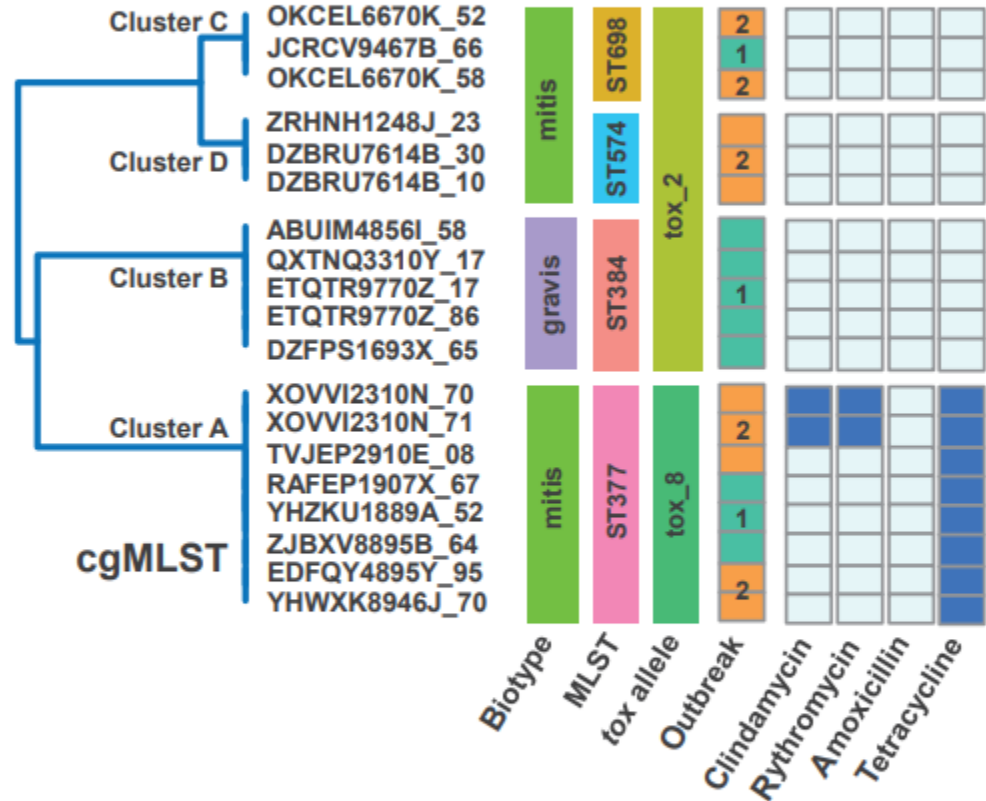
outbreak 1 n=8  
outbreak 2 n=16

WGS so far analysed up to  
end September

- «molecular clock» (Badell; Lancet Microbe 2021)
- 0 SNPs expected up to 6 weeks
  - first (1) SNP after 1.75 months (7 weeks)
  - 2 SNPs after 5 months (19 weeks)
  - 5 SNPs after 1.1 years (57 weeks)
  - 10 SNPs after 2.3 years (119 weeks)

**FIGURE 2**

Relationships between cgMLST clusters, *Corynebacterium diphtheriae* biotypes, MLST types, tox alleles, outbreak, and antimicrobial resistance profiles of commonly used drugs<sup>a</sup> to treat *C. diphtheriae* infections in two outbreaks at an asylum centre, Switzerland, July–September 2022 (n = 19)



■ Outbreak 1      ■ Outbreak 2  
■ Non-susceptibility      ■ Susceptibility

cgMLST: core genome multi-locus sequence typing; MLST: multi-locus sequence typing.

<sup>a</sup> Non-susceptibility is indicated in dark blue colour.



Schweizerische Eidgenossenschaft  
Confédération suisse  
Confederazione Svizzera  
Confederaziun svizra

Eidgenössisches Departement des Innern EDI  
**Bundesamt für Gesundheit BAG**  
Direktionsbereich Öffentliche Gesundheit

2020

leer lassen



## Diphtherie

Meldung zum klinischen Befund

Bitte ausgefüllt innerhalb 24h  
an Kantonsärztin/-arzt senden  
(nicht direkt ans BAG).<sup>a</sup>

### Patient/in

Name/Vorname: \_\_\_\_\_ Geburtsdatum: \_\_/\_\_/\_\_\_\_ Geschlecht:  w  m  
Strasse: \_\_\_\_\_ PLZ/Wohnort: \_\_\_\_\_ Kanton: \_\_\_\_\_ Tel.: \_\_\_\_\_  
Nationalität:  CH  andere: \_\_\_\_\_ Wohnsitzland, falls nicht CH: \_\_\_\_\_

### Diagnose und Manifestation (Bitte alle beobachteten Symptome ankreuzen)

Manifestationen:  Erkrankung der oberen Luftwege mit  Laryngitis  Nasopharyngitis  Tonsillitis  
 adhärente Membran/Pseudomembran  
 Hautläsion, wo? \_\_\_\_\_  
 Läsion Augenbindehaut oder Schleimhäute  
 andere: \_\_\_\_\_  keine  unbekannt

Manifestationsbeginn: Datum: \_\_/\_\_/\_\_\_\_  unbekannt

Labor: Name/Tel.: \_\_\_\_\_

Anlass:  klinischer Verdacht  Exposition  Zufallsbefund  anderer: \_\_\_\_\_

Entnahme: Datum: \_\_/\_\_/\_\_\_\_ Material:  Rachenabstrich  Hautabstrich  anderes: \_\_\_\_\_

### Verlauf

Hospitalisation:  ja, Eintrittsdatum: \_\_/\_\_/\_\_\_\_ Austrittsdatum: \_\_/\_\_/\_\_\_\_  nein  unbekannt

Zustand:  Tod, Datum: \_\_/\_\_/\_\_\_\_

Behandlung Antitoxin:  ja, Datum Beginn: \_\_/\_\_/\_\_\_\_ Dosis: \_\_\_\_\_  nein  unbekannt

### Impfstatus vor Krankheitsbeginn

Gemäss:  Impfausweis  Anamnese

Geimpft gegen Diphtherie:  ja, mit total \_\_\_\_\_ Dosen  nein  unbekannt

1. Dosis im Jahr: \_\_\_\_\_ mit Impfstoff: Markenname: \_\_\_\_\_

Notifiable disease within 24h!

# clinical pictures

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*Tibia li*



*Tibia re*



*Wade rechts*



# clinical pictures



Bild: Ph. Agyeman



Bild: K. Klingberg

# clinical pictures



Photo:  
A. Eichenberger  
A. Hachfeld



**FIGURE 10-5**  
Clinical findings in diphtheria.  
**A**, Pharyngeal pseudomembranes.  
**B**, Bull neck.

Panel A reprinted with permission from MacGregor RR.<sup>91</sup> © 2015 Elsevier.

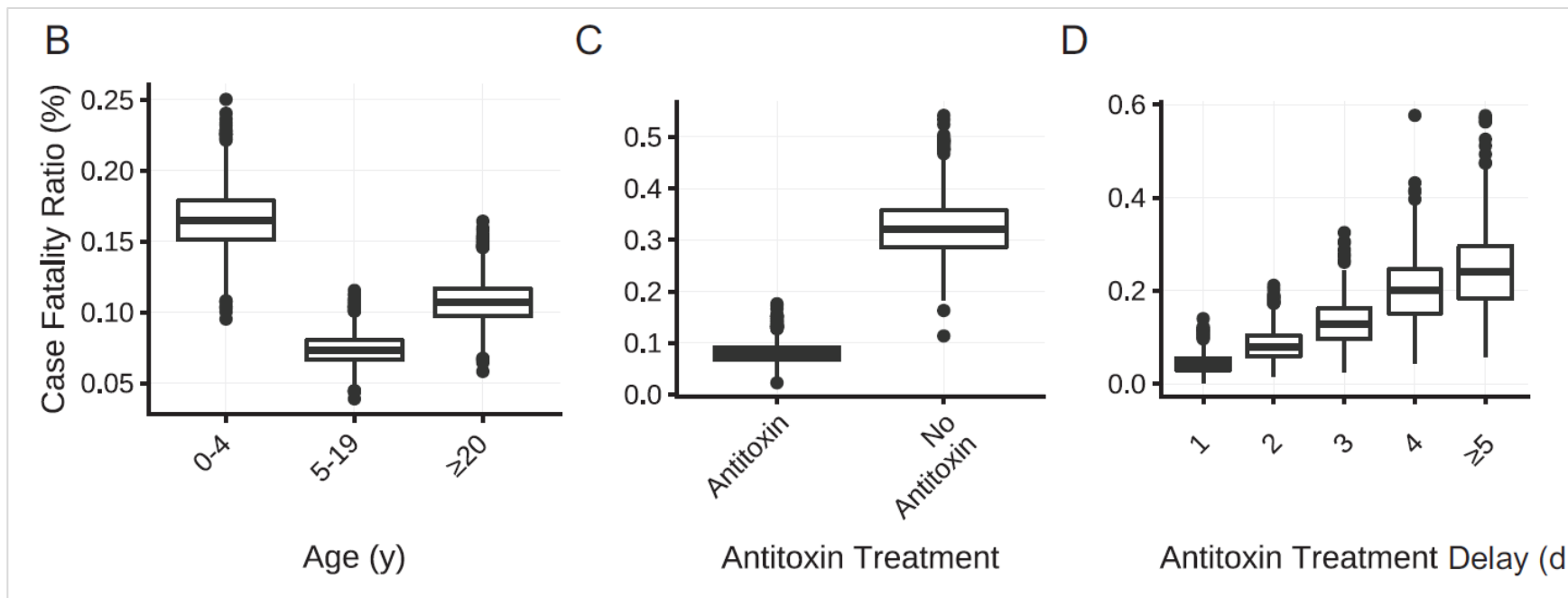
Panel B reprinted from the Centers for Disease Control and Prevention.<sup>105</sup>

DOI:10.1056/NEJMicm1814405



# Predictors of mortality I

- Administration of **diphtheria anti-toxin (DAT)**: reduces mortality by 76%
- DAT only neutralises circulating toxin, not intracellular toxin → effectiveness depends on timely administration to prevent intracellular uptake!
  - 4% probability of mortality if given within 24 – 48h
  - doubles with each day of delay
  - 24% if administered day 5 or later



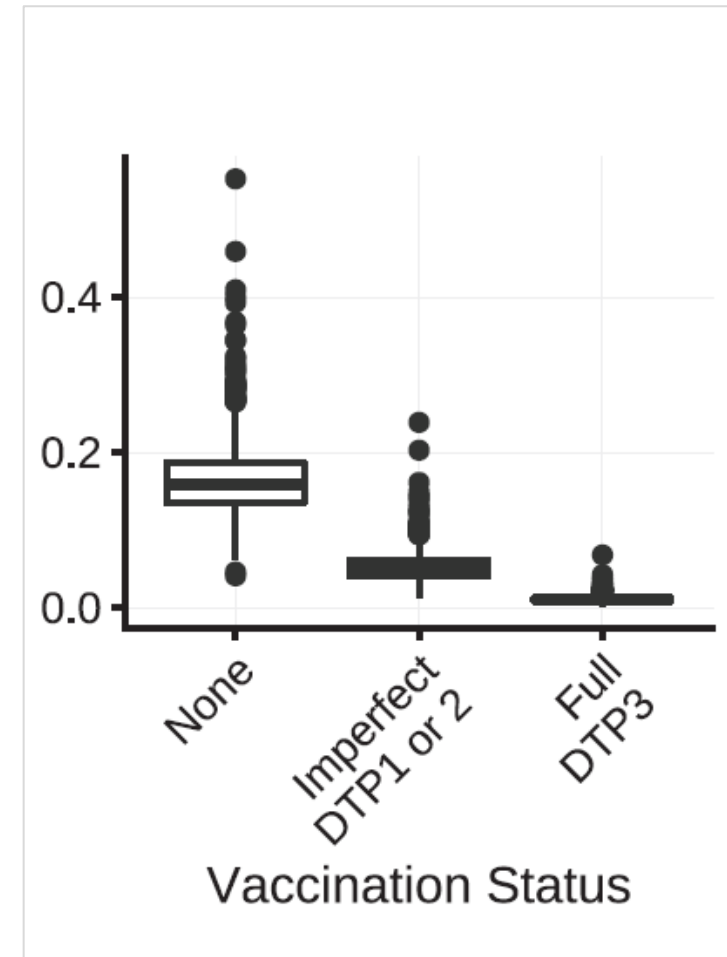
# Predictors of mortality II

## DPT $\geq$ 3 doses

- 85% (95% CI, 68-97%) effectiveness vs symptomatic disease
- 93% (95% CI, 90-96%) effectiveness vs death

## DPT $\geq$ 5 doses

- 99% (95% CrI, 68-97%) effectiveness vs symptomatic disease



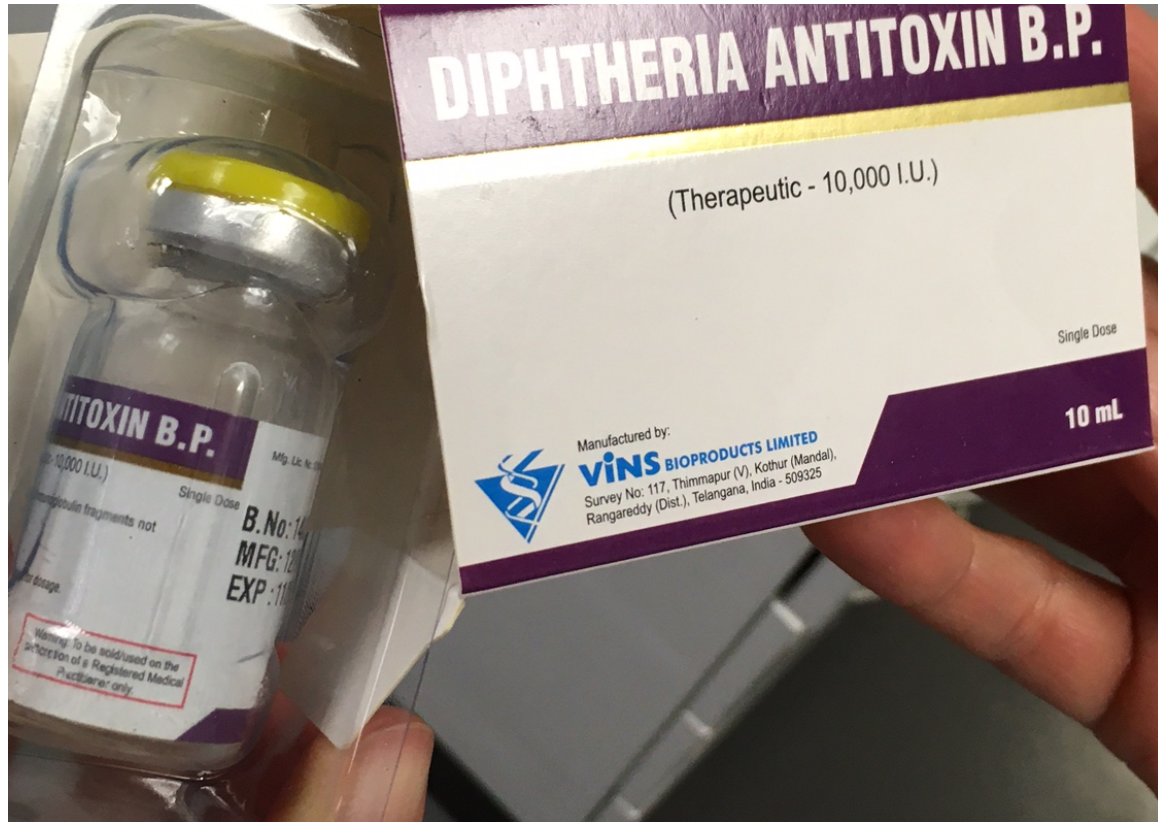
# THINK: Diphtheria ANTITOXIN?

## 2.6.3 Antitoxin treatment

Diphtheria antitoxin should only be used in a hospital setting for CONFIRMED or PROBABLE cases of diphtheria. Diphtheria antitoxin 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<sup>2</sup>) and especially if it were membranous, then antitoxin would be justified (47).

Diphtheria antitoxin 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



**INSTITUTO BUTANTAN**  
A serviço da vida

## PRODUCTION OF SERA AND VACCINES

São Joaquim Farm

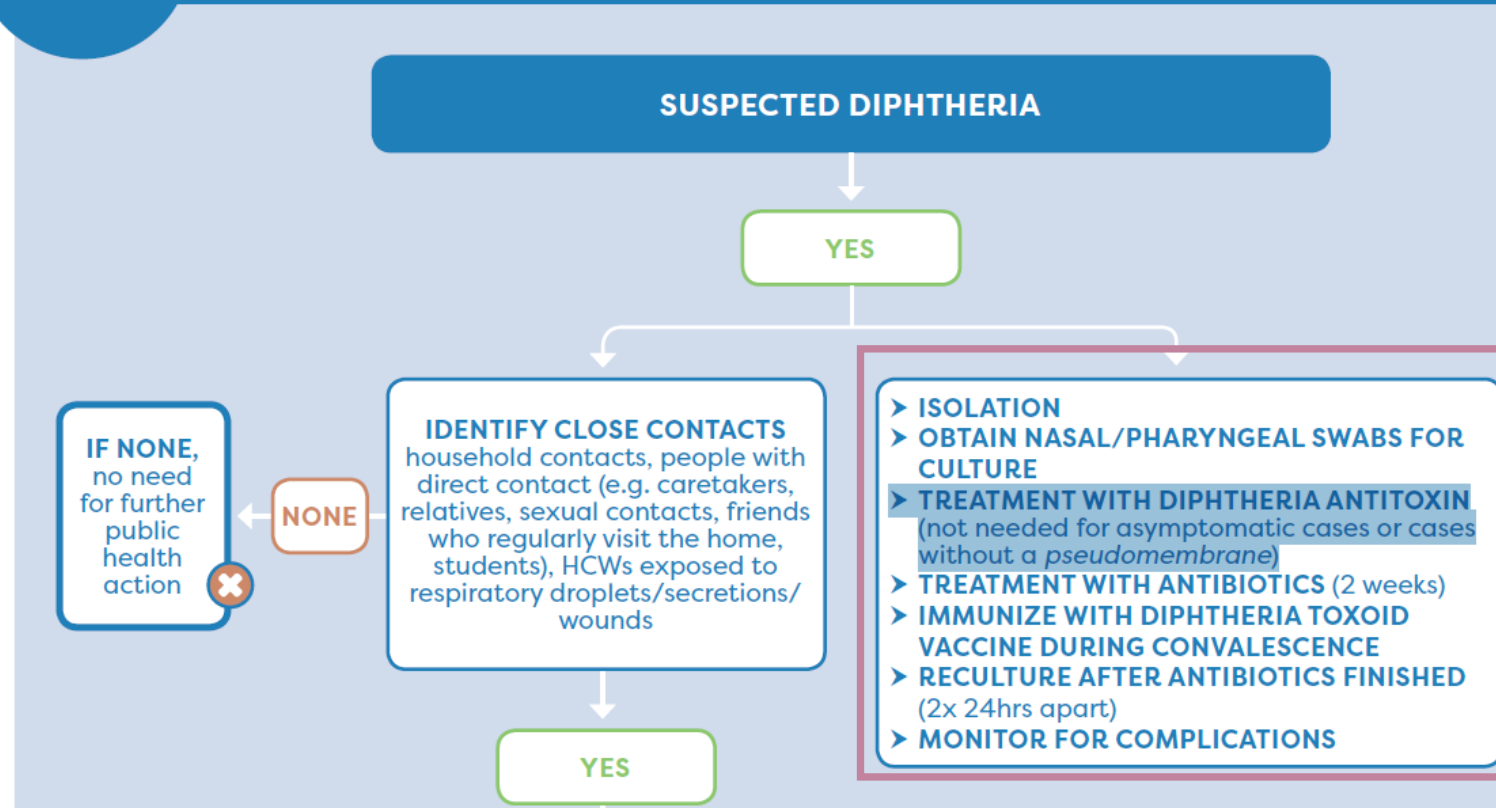
Against **venomous animals**, **bacterial toxins**, and the **rabies virus**

**560K**  
Vials of serum  
per year

In 2019, the **process of equine plasma collection** was automated through **plasmapheresis**, thus improving the quality of the sera's raw material

FIGURE  
2

## Case management and contact tracing



# Diphtheria Antitoxin – UK

Type of diphtheria	Dosage adults and children	Number of ampoules (10,000 IU/ampoule)
Severe diphtheria, for example, extensive membrane or severe oedema ('bull neck')	100,000 IU	10
Laryngeal or pharyngeal or nasopharyngeal disease of more than 48 hours	100,000 IU	10
Laryngeal or pharyngeal or nasopharyngeal disease of less than 48 hours	70,000 IU	7
Skin lesions	40,000 IU	4

**“Sensitivity testing in people with a negative history for animal allergy and no prior exposure to equine-derived immunoglobulin:**

**Do not perform sensitivity testing and proceed with a slow IV infusion of full recommended dose.”**

dosing, how to administer DAT incl. Procedures in case of anaphylaxis very well described

# Vaccine

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Vaccine coverage required: 80 – 85% to maintain population protection

# Vaccination plan CH

Tabelle 1  
**Empfohlene Basisimpfungen 2022**  
Stand 2022

Alter	Diphtherie (D/d) <sup>1)</sup> Tetanus (T) <sup>2)</sup> Pertussis (P <sub>a</sub> /p <sub>a</sub> ) <sup>1)</sup>
<b>2 Monate</b>	DTP <sub>a</sub>
<b>4 Monate</b>	DTP <sub>a</sub>
<b>9 Monate</b>	
<b>12 Monate *</b>	DTP <sub>a</sub>
<b>4–7 Jahre</b>	DTP <sub>a</sub> <sup>1)</sup>
<b>11–14/ 15 Jahre</b>	dTp <sub>a</sub>
<b>25 Jahre</b>	dTp <sub>a</sub> <sup>3)</sup>
<b>45 Jahre</b>	dT <sup>3)</sup>
<b>≥ 65 Jahre</b>	dT <sup>3)</sup>

Only available in combination

inactivated toxoid  
adjuvant (aluminium based)

D – children’s dose min. 30 IU/dose

d – adult dose min. 2 IU/dose  
(minimizes reactogenicity at injection  
site but sufficient to provoke antibody  
response in this age group)

Tabelle 2  
**Schema für die Nachholimpfungen bei ungeimpften Kindern und Erwachsenen**  
Stand 2022

Impfstoff Alter	Anzahl Dosen <sup>1)</sup>
<b>DTP<sub>a</sub></b>	
3–5 Monate	5
6–11 Monate	5
12 Monate–3 Jahre	5
4–7 Jahre	4
<b>dTp<sub>a</sub> / dT <sup>6)</sup></b>	
8–10 Jahre	4
11–24 Jahre	3
25 Jahre	3
26–64 Jahre <sup>5)</sup>	3
≥ 65 Jahre	3

<sup>3)</sup> Auffrischimpfungen mit 25 (dTp<sub>a</sub>), 45 (dT) und 65 (dT) Jahren (d. h. alle 20 Jahre) und alle 10 Jahre nach 65 Jahren (dT). Bei Patienten mit einer Immuninsuffizienz sind dT-Auffrischimpfungen alle 10 Jahre empfohlen.

Reisende: Kürzere Intervalle (als 10 oder 20 Jahre) können je nach Risikosituation indiziert sein (z. B. hochendemische Diphtheriegebiete, begrenzter Zugang zu medizinischer Versorgung).



# Thank you for your attention!

