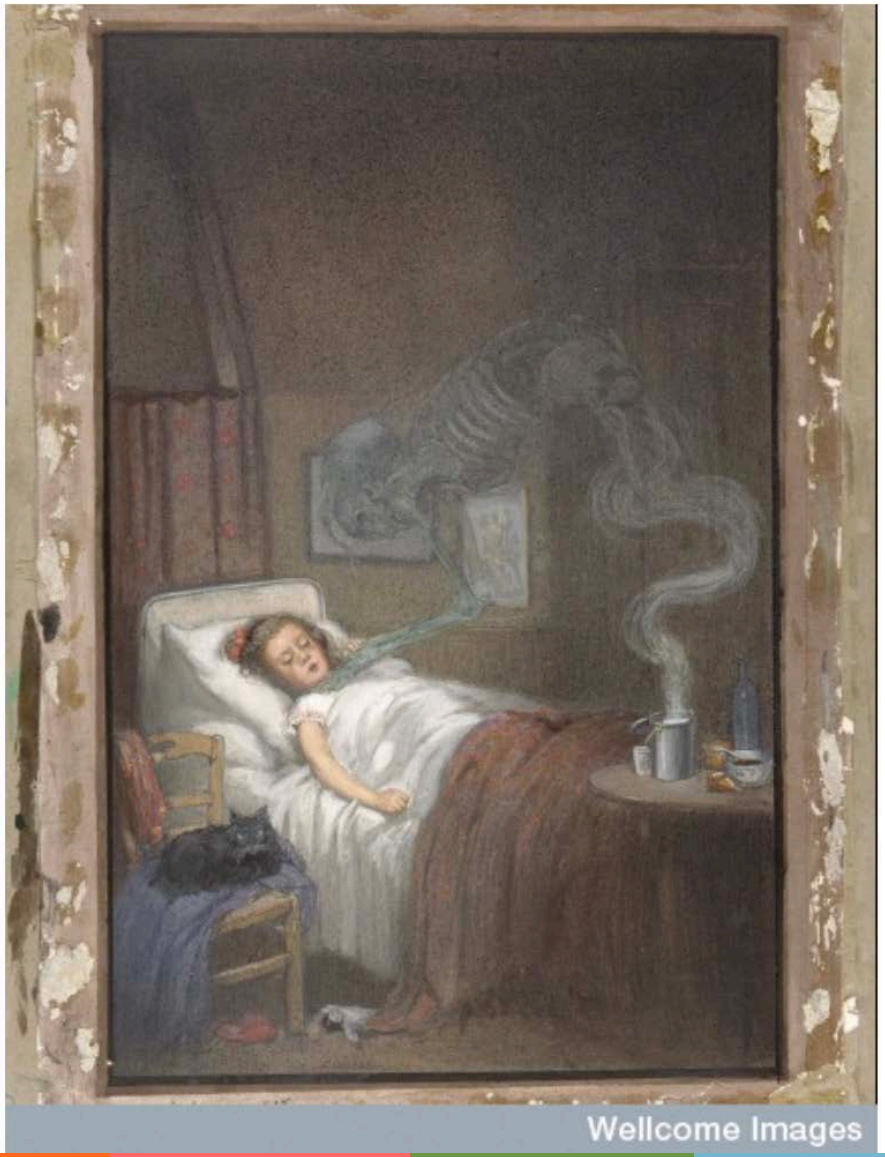
CHU Saint-Pierre
UMC Sint-Pieter

INFECTIOUS DISEASES
DEPARTMENT
HIV REFERENCE CENTRE

ULB UNIVERSITÉ LIBRE DE BRUXELLES



Diphtheria: clinical picture and management

Severine Noirhomme, Camille Marlière, Leila Belkhir, Johan Van Laethem, Lucie Seyler, Maya Hites, Charlotte Martin

"the strangling angel of children"

Plan

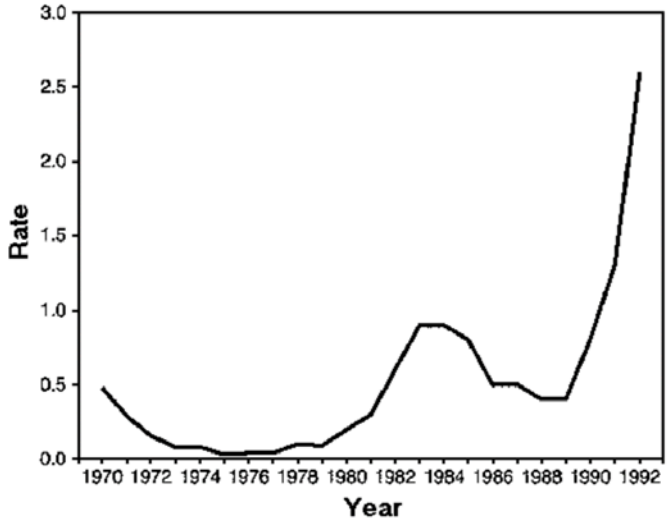
- Epidemiology
- Clinical vignette(s)
- Clinical presentation
- Diagnosis
- Clinical management

Epidemiology

Epidemiology

- 18th- 20th century: large outbreaks in Europe, America, Russia and Eastern Europe
- today still endemic in many countries

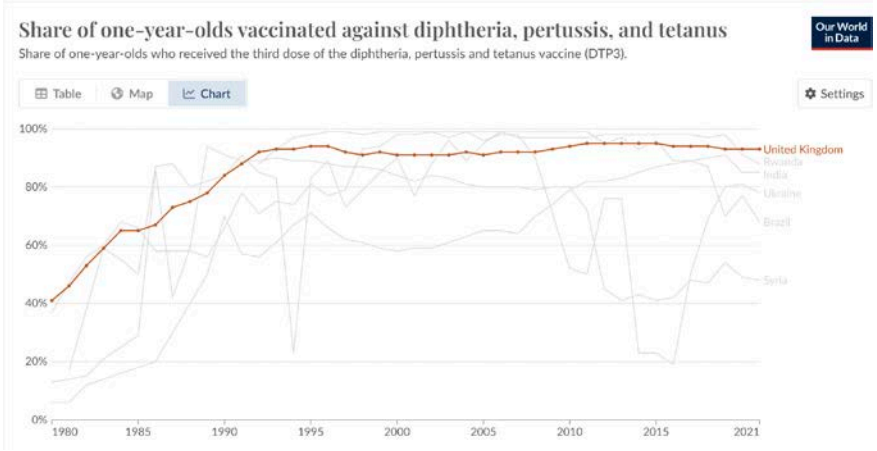
FIGURE 1. Rate* of reported diphtheria cases, by year – Russian Federation, 1970-1992

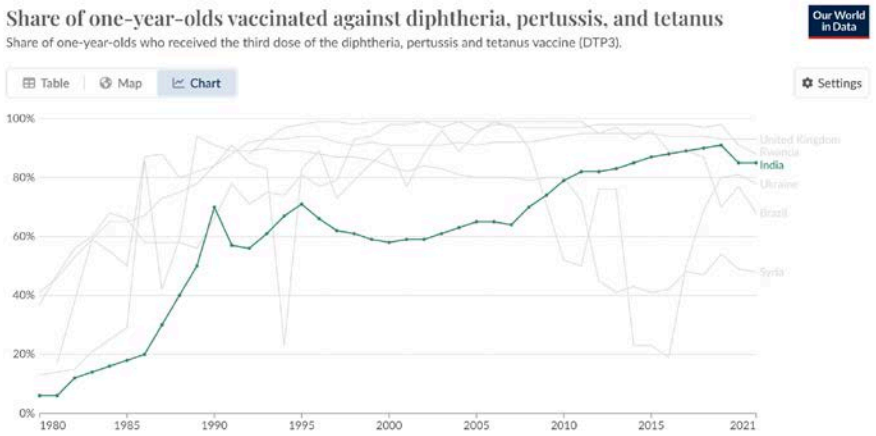


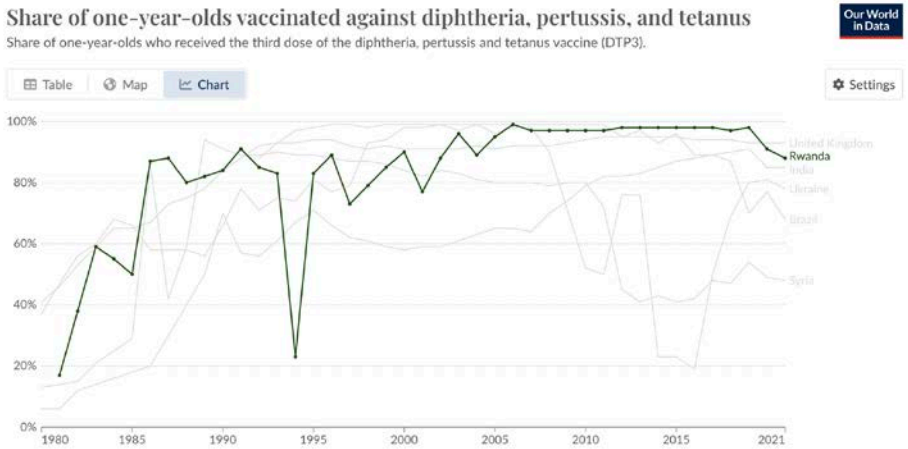
*Per 100,000 population.

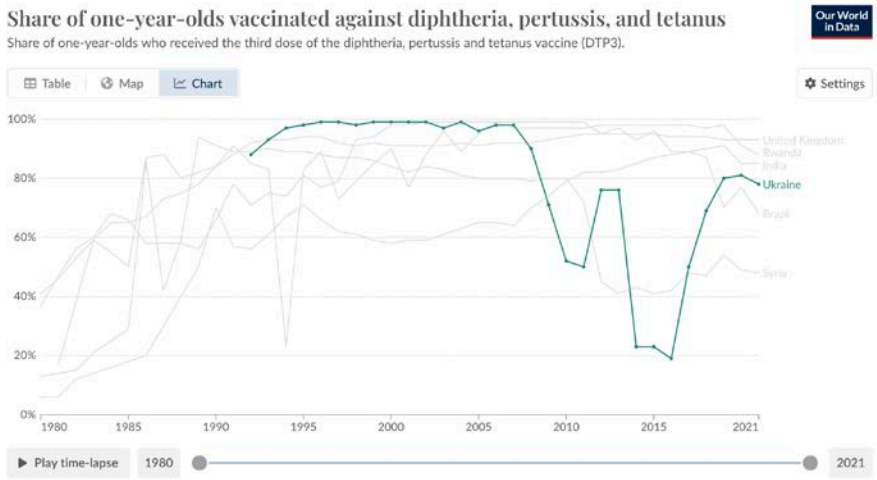
low socioeconomic status
inaccessibility to public health (conflicts)
displacement of human population
poor immunization programmes
interruption of childhood vaccination schedules worldwide due to COVID-19

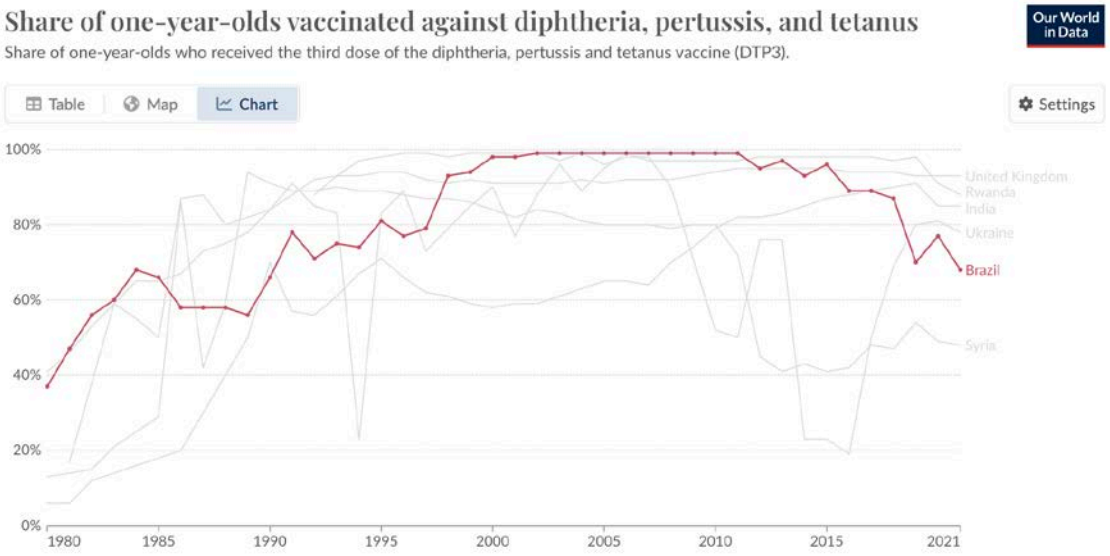
What is the diphtheria vaccination coverage?

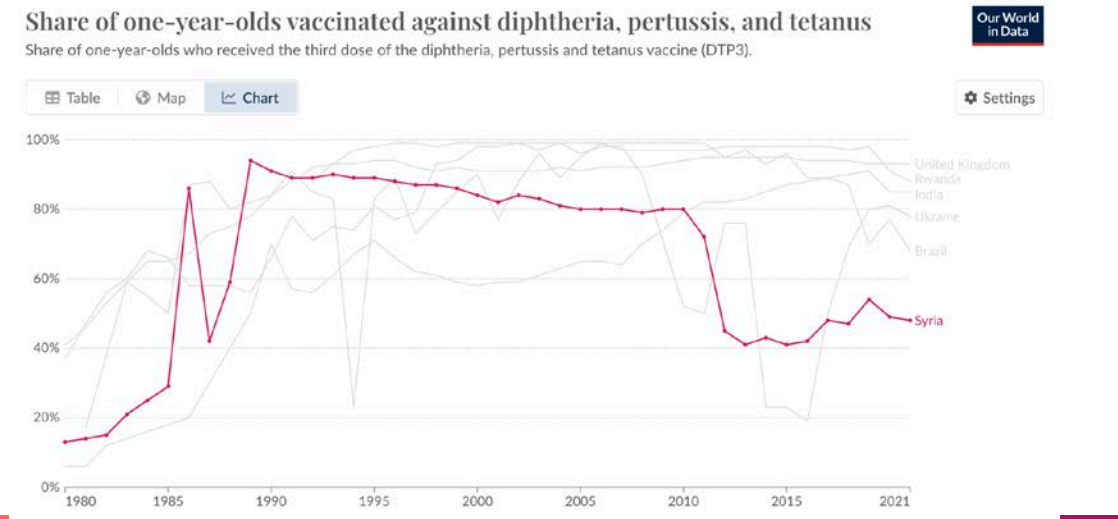









Share of one-year-olds vaccinated against diphtheria, pertussis, and tetanus
Share of one-year-olds who received the third dose of the diphtheria, pertussis and tetanus vaccine (DTP3).
Our World in Data
Table
Map
Chart
Settings
100%
80%
60%
40%
20%
0%
1980
1985
1990
1995
2000
2005
2010
2015
2021
United Kingdom
Rwanda
India
Ukraine
Brazil
Syria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March 2024

Shoreland's *Travax News Alert* Service

Czech Republic: Significant Diphtheria Increase

According to the Czech Republic's Ministry of Health, 6 cases of diphtheria (including 1 death), a significant increase over average incidence, have been reported since early January 2024, including in Prague. All travelers should be current with a diphtheria-containing vaccine (primary series or booster within the last 10 years). Diphtheria should be considered in any traveler presenting with pharyngitis within 10 days of returning from the Czech Republic.

Diphtheria outbreak in Nigeria

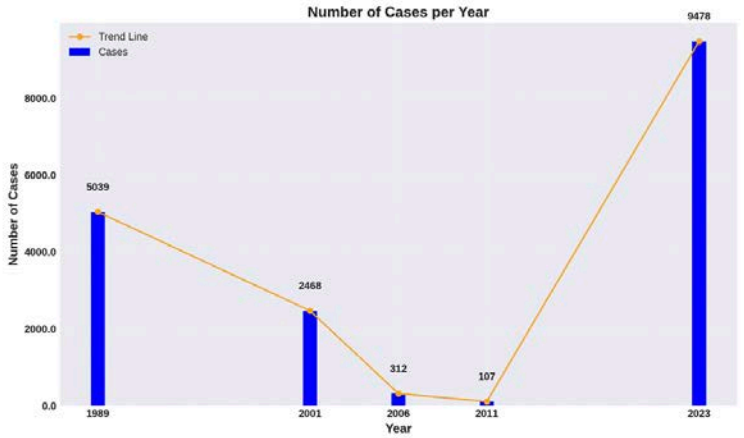
Published Online
November 8, 2023
https://doi.org/10.1016/
S2666-5247(23)00330-0

At a Médecins Sans Frontières (MSF) hospital in Kano, Nigeria, Dr Hashim Juma Omar encounters at least six children daily with diphtheria

To enhance surveillance, the NCDC deployed National Rapid Response Teams to identify and treat diphtheria cases in communities and health-

laboratory equipment being installed in Kaduna, Katsina, and Bauchi States, according to Adetifa.

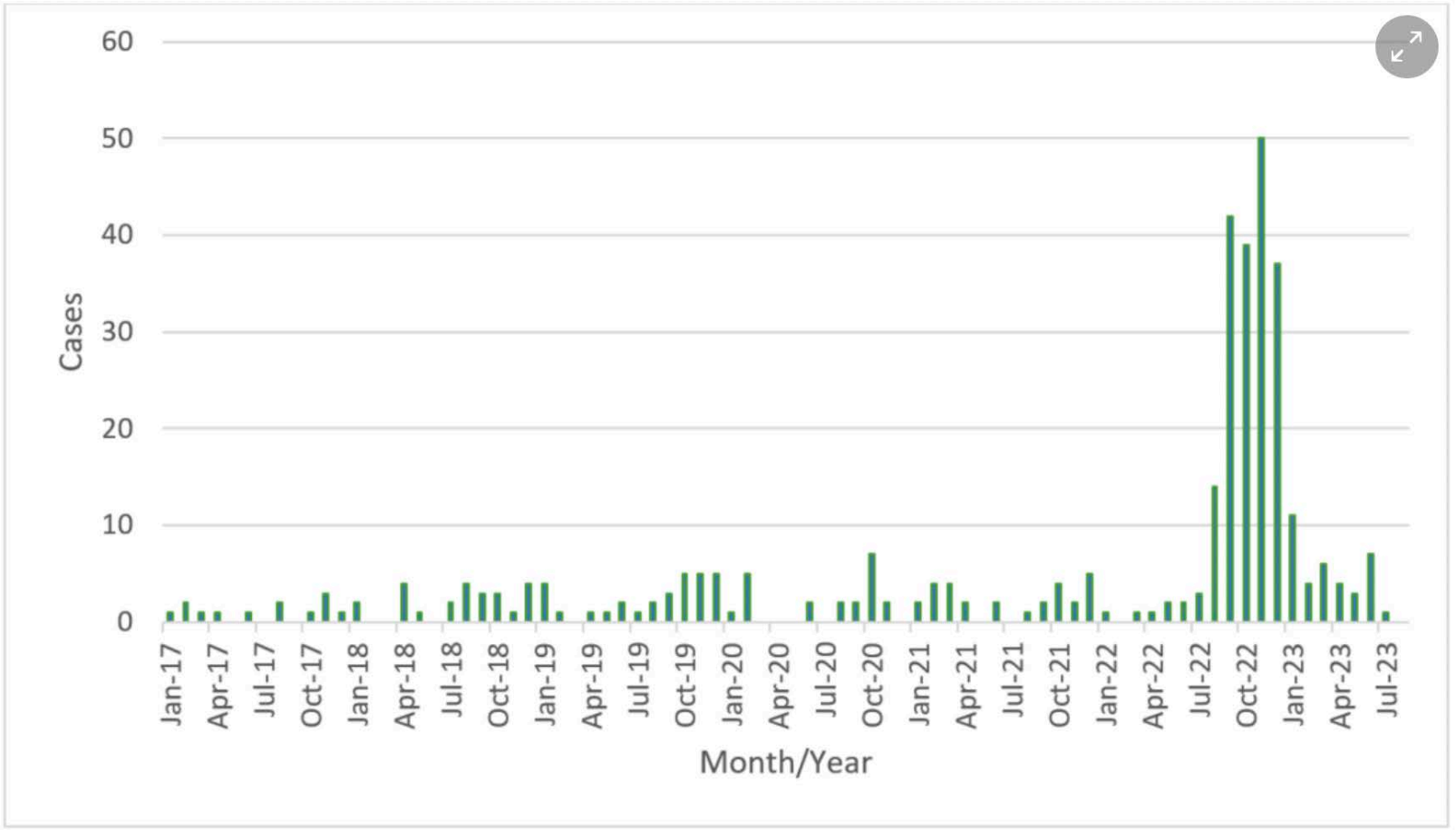
Some of the isolates collected during



ECDC

« Since January 2022, and as of 11 August 2023, 281 confirmed diphtheria cases, as per the EU case definition (2022: 224 cases, 2023: 57 cases), and four deaths were reported in the EU/EEA through the European Surveillance System (TESSy), compared to an average of 55 cases reported annually between 2017 and 2021. »
« The majority of cases in 2022 were diagnosed in migrant-related facilities, with onward transmission documented in a few instances. »

Figure 1. Number of *C. diphtheriae* cases reported to ECDC via TESSy, and month/year, 1 January 2017-11 August 2023



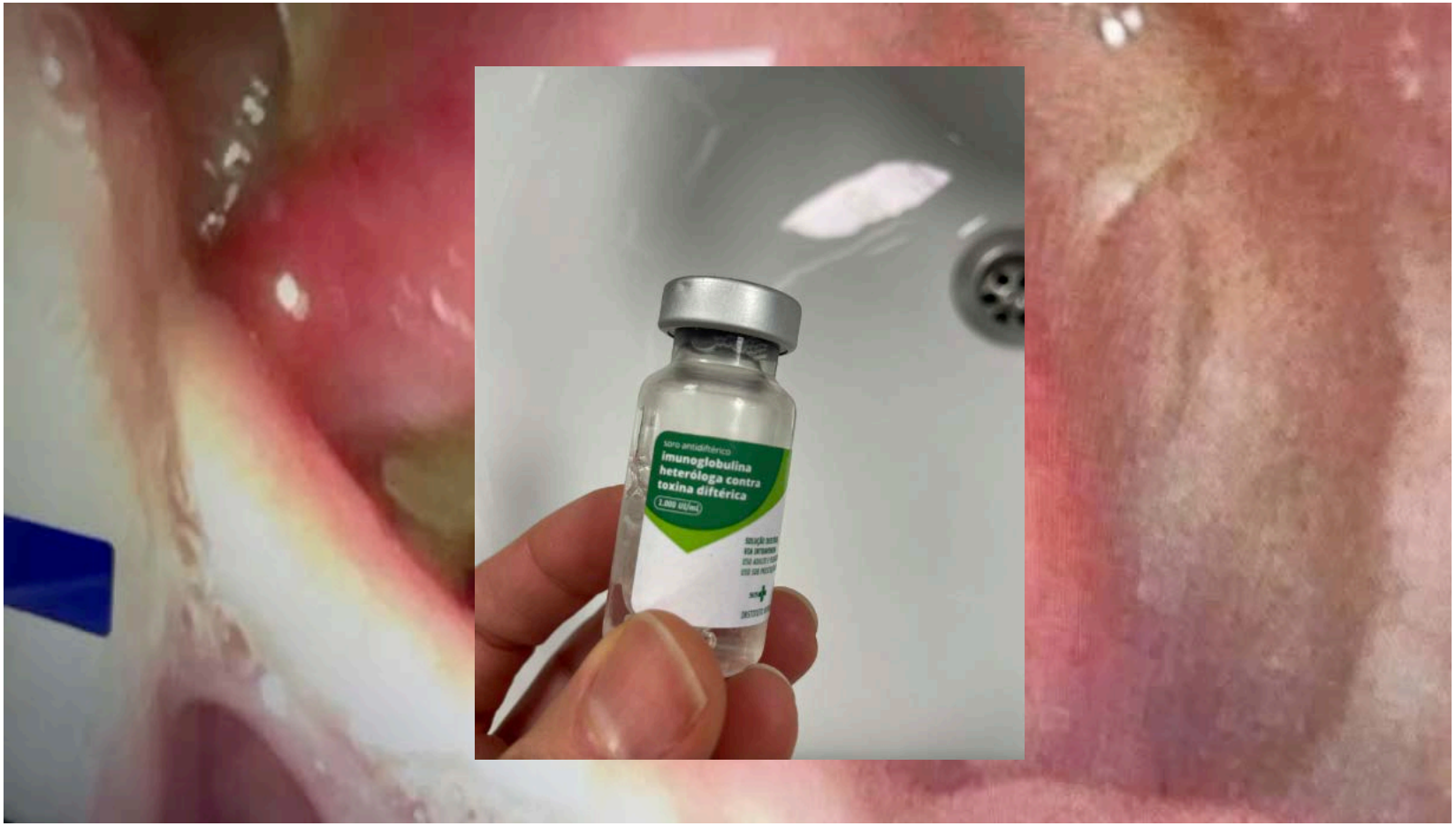
Clinical vignettes

September 2022 CHU Saint-Pierre

27 yo man from Afghanistan
Fever, rash
Mpox suspicion

Streptococcus pyogenes, *Staphylococcus aureus*
Oxa-R and …*Corynebacterium diphtheriae!* (tox +)

December 2022: Cliniques Universitaires Saint-Luc



June 2023: CHRSM Namur

- L. 16 yo, from Iran, lives in Red Cross center <4 y
- Day 1: consultation with GP at Red Cross Centre: pharyngitis started on oral amoxicillin
- Day 2: ED due to poor evolution. Hospital admission for IV amoxiclav
- Day 5: desaturation and major swelling of tonsils leading to tonsillectomy. Post-operative extubation impossible.
- Day 6: Multi-organ failure with bilateral pulmonary image, ARF, thrombocytopenia, DIC. Cardiac arrest, ECCMO, transfer to paediatric ICU in Woluwé. Diphtheria suggested by ENT following review of the file after patient transferred.
- Day 7: death. Post-mortem diagnosis based on throat swab cultures and autopsy. PCR + for *Corynebacterium diphtheriae,* tox +

- no documentation of vaccination.
- Anti-toxin antibody: minimal protection (>0.01 and < 0.05) => evidence of incomplete vaccination?

E., boy 10 yo

- Day8 admission of her sister : febrile pharyngitis
- R/ amoxicillin IV + azithromycin per os + DAT (70 000 IU)
- Favourable evolution in 48h, back home, R/ AB 14 days
- Throat smear: *Corynebacterium diphtheriae*+, tox neg

- No documentation of vaccination.
- Anti-toxin antibody: minimal protection (>0.01 and < 0.05) => evidence of incomplete vaccination?
- primary vaccination started after the acute episode

M., 2,5 yo

- Day 10: ED younger brother for febrile pharyngitis despite antibiotic prophylaxis
- Moderate oropharyngeal presentation but thrombocytopenia on admission
- Administration of amoxicillin IV + azithromycin per os + DAT 100,000 IU

- Throat smear: *Corynebacterium diphtheriae +* , tox +
- Documented history of vaccination (child born in Belgium)

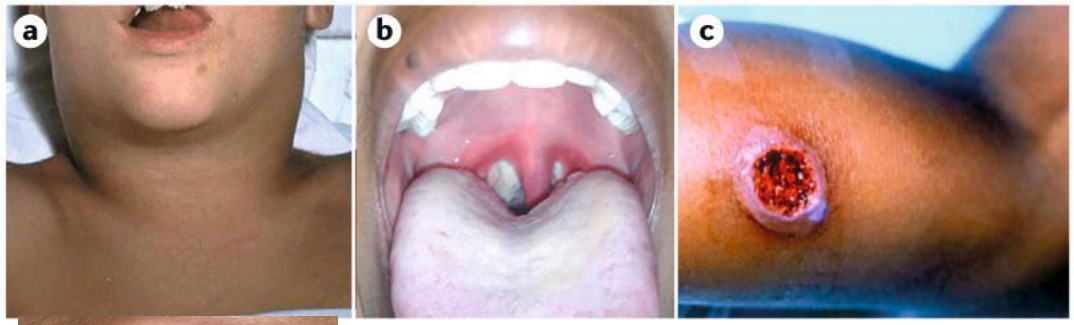
- Rapidly favourable course. R/ 14 days AB

Nurse

- Day 10: nurse from the Red Cross centre who initially examined and referred L. to ED
- Pharyngitis seems viral
- Normal blood test
- Amoxicillin + DAT 100,000 IU
- Negative throat smear => antibiotic therapy withdrawn
- Sick serum syndrome reaction after DAT requiring corticosteroid therapy

Clinical presentation

Clinical presentation



➢Clinical hallmark : Pseudomembranous pharyngitis, sometime with enlarged lymph nodes in the neck (bull neck)

➢Cutaneous diphtheria: painful lesion(s) with greyish adherent membrane

Clinical presentation (2)

- incubation: 1-10 d (2-5)

Complications

- Myocarditis myocardial dysfunction, bradyarrhythmias, tachyarrhythmias and complete heart block
- Polyneuropathy (10 d to 3 mo) paresis of the soft palate, distal paraesthesia, respiratory muscle pareses, hyporeflexia or areflexia and hypotonia, sensory symptoms, facial palsy, nerve palsy (DD Guillain-Barre S)

Diagnosis

Diagnosis

- Clinical suspicion → inform the lab!

•The lab should perform a culture on blood agar and on selective medium

•Labs are asked to send the strains of *C. diphtheriae, C. ulcerans, or C. pseudotuberculosis* to the NRC (UZ-Brussel), where a PCR testing is done on all strains, followed by confirmation by Elek test, to confirm toxin production

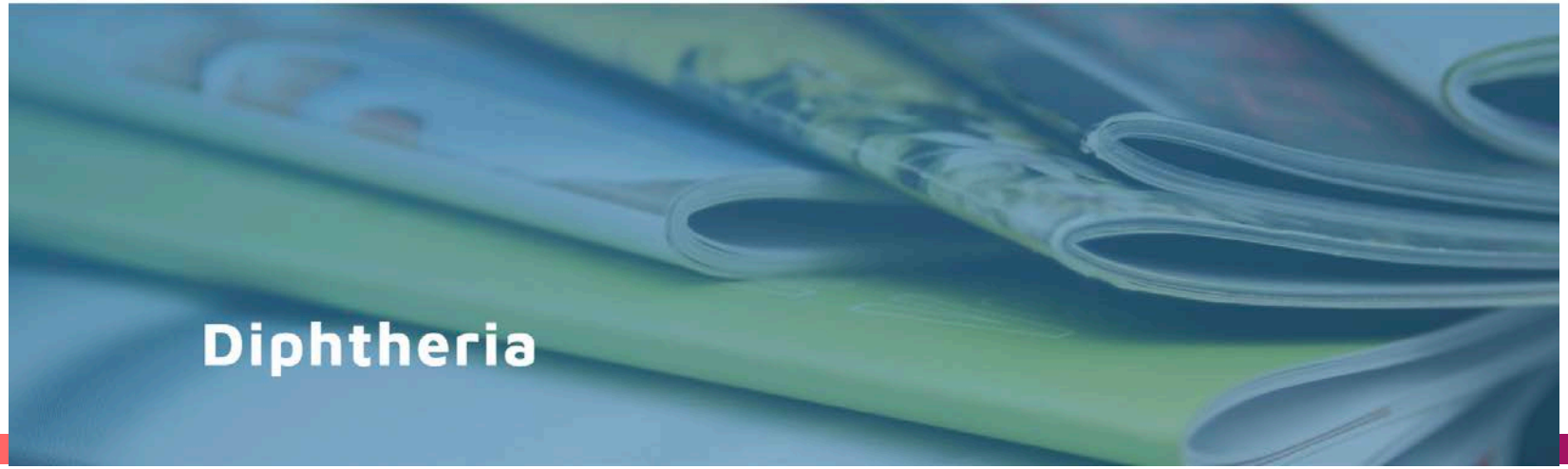
•If prior AB: PCR for tox genes

Clinical management

BVIKM/SBIMC
Belgische Vereniging voor Infectiologie en Klinische Microbiologie
Société Belge d'Infectiologie et de Microbiologie Clinique

WHO WE ARE | WORKING GROUPS | EVENTS | PAST EVENTS | TRAINING | GUIDELINES

DIPHTHERIA



Clinical management

1. BACKGROUND

2. PATHOGEN AND TRANSMISSION

3. HOW TO RECOGNISE DIPHTHERIA?

4. DIAGNOSTICS TESTS FOR DIPHTHERIA

5. TREATMENT OF DIPHTHERIA (THERAPEUTIC AND PROPHYLACTIC)

6. VACCINATION AGAINST DIPHTHERIA

7. INFECTION CONTROL MEASURES

8. ORDERING DIPHTHERIA ANTITOXINS

Clinical management: cutaneous diphtheria

If confirmed and not severe: antibiotics alone

Confirmed case (= toxin-positive)	Cutaneous (not severe)	**Antibiotics alone:** **Amoxicillin** Adults: 1g x3/day (IV or PO) for 14 days Children: 100mg/kg/dag div in 3 doses IV or PO or **Penicillin** Adults: IV Penicillin G 1 million IU x6/day, or PO feneticillin (Broxil) 500mg x6/day for 14 days Children: Pen G: 100.000-400.000IU/kg/day div in 6 doses IV (max 24 million IU/day); or PO Broxil:<2j

+ vaccination

Clinical management: ENT presentation

Confirmed case (or strong ENT suspicion) → DAT administration ASAP + AB combined therapy

Diphtheria antitoxin is an antiserum produced in horses;
Hypersensitivity reactions to the antitoxin are observed in approximately 10% of patients

TO ORDER ANTI-TOXINS, CONTACT THE HEALTH INSPECTOR OF THE REGION WHERE THE PATIENT IS TREATED:

+ vaccination during convalescence

Take home messages

- Think of diphtheria in the case of *pseudomembranous pharyngitis/cutaneous lesion with adherent membrane* in a person living in promiscuity or poverty, or in a migrant

- DAT asap in case of ENT diphtheria

- Excellent collaborative work to develop Belgian clinical management guidelines

Thank You !

Respect Innovation Engagement Solidarity Quality