



CONSULTATIVE SIGNAL ASSESSMENT
PRIMARY RISK ASSESSMENT
 EVIDENCE BASED RISK ASSESSMENT
 PUBLIC HEALTH EVENT ASSESSMENT

**CORYNEBACTERIUM DIPHTHERIAE INFECTION CASES AMONG
 ASYLUMSEEKERS IN EUROPE AND IN BELGIUM**

Date of the signal	Date of the PRA	Signal provider	Experts consultation	Method
27/06/2023	28/06/2023	FOD VVL	Permanent experts: Karin Cormann (DGOV), Caroline Boulouffe (AViQ), Jorgen Stassijns (Sciensano), Adrae Ataame (COCOM), Stefaan Van Der Borgh (FOD Volksgezondheid), Bart Hoorelbeke (FOD Volksgezondheid), Naïma Hammami (Departement Zorg) Specific experts: Lien Bruggeman (Fedasil), Laura Cornelissen (Sciensano), Stéphanie Jacquinet (Sciensano), Helena Martini (NRC), Dorine Claes (Croix Rouge)	E-mail consultation
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Signal

On the 27th June, 2 cases of respiratory diphtheria were notified to AVIQ, including 1 fatal case. The cases occurred in 2 unvaccinated sisters (aged 15 and 11 years), originally from Pakistan, who entered Belgium in February 2020 and had been living for several years in a centre for applicants of international protection in Namur.

Symptom onset for case 1 (15y) was on 18th June when empiric antibiotic treatment with Amoxicilline was initiated. The following day, she was hospitalized in the ENT department with a worsening clinical condition. There was no clinical suspicion of diphtheria and an amygdalectomy was performed with the aim to control infection. Finally, she died in the early hours of 24th of June as a result of multiple organ failure. Upon autopsy, pseudo-membranes typical for diphtheria were discovered and *C. diph* tox+ was retrospectively confirmed from the swabs. Case 2 presented with symptoms on 26th June. Because of the epidemiological link with the first case, she quickly received antitoxin. Throat swabs, taken after initiation of antibiotic therapy, are weakly positive for *C. diph*. Case 3, a child of 2.5y belonging to the same family, has been fully vaccinated through ONE medical consultations. He equally presented with respiratory symptoms on 25/6 and was treated with antibiotics. Due to worsening clinical condition on 29/6, the boy was hospitalized and DAT was administered. Due to the setting of the cases, a high number of persons have been potentially exposed.

Description

Cause known?

Diphtheria is a disease caused by **bacteria** *Corynebacterium diphtheriae* and *Corynebacterium ulcerans*. It can lead to difficulty breathing, heart rhythm problems, and even death. Transmission occurs through respiratory droplets, or contact with infected open sores or ulcers.

Unexpected/unusual

Unusual. The last reported death related to respiratory diphtheria in Belgium occurred in 2016 in a 3-year-old girl with delayed clinical diagnosis.

Between 2015-2021, 0 to 3 cases have been reported each year. However, in 2022 an outbreak of over 300 cases of diphtheria has been reported among immigrants in Europe, including in Belgium. In Belgium, a total of 25 cases has been reported in 2022 among asylum seekers. Among these cases, the majority was caused by *C. diphtheriae*. Most patients presented with the cutaneous form, but 2 respiratory cases were reported and sequelae are expected to be life-long for one of these cases. In response to the outbreak, a risk assessment was performed on 27/09/2022 and updated on 16/10/2022. In those assessments, the risk of a fatal respiratory case in unvaccinated children was highlighted, and there was a strong recommendation to accelerate vaccination of asylum seekers, in particular children, and to raise awareness among clinicians likely to treat asylum seekers.

Since January 2023 no more cases had been notified.

Severity

The case fatality rate of respiratory diphtheria in unvaccinated individuals can be high if no availability of diphtheria antitoxin (DAT), and in a context of lack of knowledge of the disease by health practitioners.

Dissemination Low/medium

Low for general population, in a context of a high vaccination coverage in Belgium (coverage >90% for DTP4 since >10 years) severe cases should be rare. However, carriage (and thus transmission) of toxin producing strains of *Corynebacteria* is possible among both unvaccinated and vaccinated healthy individuals, as the vaccine protects against the toxin but not against the bacterium.

Medium for the specific population in migrant reception centres, including the staff, especially if immunosuppressed or without a completed vaccination scheme. Coverage for one (booster) dose in adults is 70% in the centre in the centre where the

	<p>cases were living. It is unclear how many of these adults have previously received primary vaccination in their country of origin. There is currently no information on vaccination coverage for children and adolescents. Coverage for small children (<6 years) is expected to be reasonable, as there is a good collaboration with the well-baby clinics of ONE. Coverage for children aged 6-17y is expected to be low, as vaccination through school health services is more challenging. Generally, about 85% of adults going through the medical dispatching at Fedasil are vaccinated with a first dose of dTap, but coverage for supplementary doses is much lower. Additionally, about 2,000 people do not yet have a place in a reception centre and have not passed through dispatching. There are no displaced people from Ukraine living in the affected centre but the Ukrainians do form another risk population as uptake of vaccination is low. In this setting, more cases can be expected in the coming weeks/months. The overall number of cases should remain limited if adequate action is taken.</p>
<p>Risk of (inter)national spread</p>	<p>Infection certainly occurred within Belgium, as the family had entered the country several years ago. However, further international spread is possible as the refugee population is a mobile population with international connections.</p> <p>Information has been shared through EpiPulse.</p>
<p>Preparedness and response</p>	
<p>Preparedness</p>	<ul style="list-style-type: none"> - <i>Clinical diagnosis</i> <p>Diphtheria has become a rare disease and many Belgian physicians lack experience with the disease. The diagnosis was not made for case 1, leading to incorrect treatment. Following the outbreak in 2022, efforts were made to raise awareness particularly among clinicians in contact with the refugee population, but this seems to have been insufficient.</p> <ul style="list-style-type: none"> - <i>Microbiological diagnosis</i> <p>Each laboratory of Clinical Biology should be able to cultivate <i>C. diphtheriae</i> and <i>C. ulcerans</i> and refer the strain for confirmation of toxigenicity and further characterization to the National Reference Centre (NRC). However, it is very important that the prescribing physician informs the lab of a suspicion of diphtheria, as corynebacteria are often present in a mixed flora and will not always be detected without the use of selective media, or at least awareness of the technician. However, many labs lack experience and prefer to refer the samples. As a result of contact tracing, a very high number of samples is expected in the coming days. Collaboration between labs will be essential to cope with the high number of samples.</p> <p>As a result of the outbreak in 2022, recommendations are in place for the Refugee Medical Point and the dispatching of Fedasil to take swabs of skin wounds and test for cutaneous diphtheria. The number of tested samples has drastically reduced in recent months, but this seems due to a general reduction in skin lesions, rather than an absence of awareness.</p> <ul style="list-style-type: none"> - <i>Treatment</i> <p>The Superior Health Council made guidelines about treatment and prophylaxis of contacts in 2019.</p> <p>Following the outbreak in 2022, stock of DAT is now available for 15 cases and the procedure on how to procure DAT is updated and available. Once the suspicion of respiratory diphtheria was established for case 2, DAT was rapidly dispensed by the FPS Public Health.</p> <ul style="list-style-type: none"> - <i>Prophylaxis</i>

	<p>Guidelines regarding contact tracing and antibiotic prophylaxis exist and AVIQ is in charge of contact tracing. However, due to the context there is a particularly large number of contacts to be followed up, which might stretch the available human resources as well as lab resources.</p> <p>A large-scale catch-up vaccination campaign is planned, but it is as of yet unclear whether the required number of vaccine doses will be available at short notice.</p> <p>Diphtheria is entirely preventable by vaccination but both cases were unvaccinated, despite a prolonged stay in Belgium, indicating weaknesses in the system. Indeed, although the importance of correctly vaccinating incoming asylum seekers has been repeated in multiple recent risk assessment (e.g. measles, <u>diphtheria</u>, displaced people from Ukraine), vaccination coverage in this population is too low. The vaccination of children is often delayed, as they need to go through well-baby clinics or school health services. Especially the role and responsibility of school health services in FWB is often unclear. Moreover, follow-up of vaccination status of children is made very difficult by the absence of registration of vaccination in electronic health records. For adults, even if vaccination is initiated upon registration (which is not always the case), further follow up for administration of the next doses is challenging.</p>
<p>Specific control measures (surveillance, control, communication)</p>	<p>The following measures have already been taken or are planned:</p> <ul style="list-style-type: none"> • Communication: <ul style="list-style-type: none"> ○ All medical teams of Fedasil have been warned to be vigilant ○ Following the 2022 outbreak, all staff has been pro-actively informed and been invited to update their vaccination status (but uptake low) • Contact tracing: <ul style="list-style-type: none"> ○ The other family members have been tested and received antibiotic prophylaxis. ○ Close contacts at the hospital are being followed up by the Service d'Hygiène hospitalier (swab + prophylaxis if necessary). ○ Contacts that were exposed during work are being followed up by the occupational health services (swab + prophylaxis if necessary). ○ All contacts at the centre will be tested on 29/6 and receive a one-off AB prophylaxis. ○ Both girls attended the same school, where the school health services are busy assessing vaccination status and need for additional interventions. • Vaccination: <ul style="list-style-type: none"> ○ Following the 2022 outbreak, Fedasil dispatching is vaccinating children from the age of 6 years upon registration (previously 12 years). ○ A large scale catch-up vaccination campaign for all residents (both children and adults) on-site at the concerned centre is planned for Monday 3/7.
Public health impact	
<p>Public health impact in Belgium Medium</p>	<p>There has been already one death in a young person, and these severe, respiratory cases indicate undetected transmission of <i>C. diphtheria</i> in Belgium. The disease is associated with a high case fatality rate if no rapid administration of curative DAT, hence timely diagnosis is critical. Overall, there is a global lack of awareness in health practitioners regarding rare infectious diseases (notification, case management, diagnostic and treatment).</p> <p>However, the disease is entirely preventable by vaccination and vaccination coverage in the general population is high. Thus, the total number of cases in Belgium is expected to remain limited.</p>

Recommendations
(surveillance, control,
communication)

Recommendations overlap with those made in 2022, but resources need to be urgently made available to improve implementation:

- Inform physicians on the risk of Diphtheria in asylum seekers.
- Continued vigilance for skin lesions at the intake of asylum seekers and testing of wound swabs for cutaneous diphtheria. Treat adequately if presence of toxinogenic corynebacteria.
- Vaccination of all immigrants (including displaced adults from Ukraine not passing through Fedasil reception centres) should be available free of charge in all regions.
 - Timelines for catch-up vaccination of children should be as short as possible. In order to make this possible, clear information on the vaccination status is required (preferably in an electronic format), as well as clearly defined roles and responsibilities.
 - Catch-up vaccination of adults without documented immunity should be initiated asap upon arrival in Belgium.
 - Catch-up vaccination schedules should be completed (administration of multiple doses over several months) even if the person changes their place of residence.
- Make sure all staff in contact with refugee population is fully vaccinated, including a booster dose if last vaccination >10 years ago.

Actions

- Communication on the current cases and the guidelines in Belgium to physicians
 - through the Flash (early July) -> Sciensano/regions.
 - through a uniform communication distributed through the professional associations for GPs (SSMG, CMG, Domus Medica), to hospitals through the HOST and to ENT-specialists → Sciensano (prep com)/regions(distribute)
- Continue specific control measures as outlined above
 - mobilize sufficient vaccine doses (Fedasil, with possible help of Flanders)
 - distribute lab testing capacity (AVIQ/NRC)
- Clearly define roles & responsibilities in vaccination of immigrant population and improve coverage:
 - children 0-5 years → ONE consultations / K&G
 - children/adolescents 6-17 years: first dose upon registration, but further active follow-up required → ONE through PSE/CMPS (current procedure insufficient) / CLB
 - adults: 1st dose upon registration, further doses??
- Facilitate follow-up of vaccination status through use of electronic registries that are interoperable and easy-to-use → ONE/AVIQ/COCOM/DZ
- Follow-up of actions taken and progress made on vaccination of immigrant population and vaccination registry: RMG
- Epidemiological follow-up of situation and international reporting of relevant results → Sciensano, with info from regions/NRC