Public health action following an outbreak of toxigenic cutaneous diphtheria in an Auckland refugee resettlement centre

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Abstract

Global forced displacement has climbed to unprecedented levels due largely to regional conflict. Degraded public health services leave displaced people vulnerable to multiple environmental and infectious hazards including vaccine preventable disease. While diphtheria is rarely notified in New Zealand, a 2 person outbreak of cutaneous diphtheria occurred in refugees from Afghanistan in February 2015 at the refugee resettlement centre in Auckland. Both cases had uncertain immunisation status. The index case presented with a scalp lesion during routine health screen and toxigenic *Corynebacterium diphtheriae* was isolated. A secondary case of cutaneous diphtheria and an asymptomatic carrier were identified from skin and throat swabs. The 2 cases and 1 carrier were placed in consented restriction until antibiotic treatment and 2 clearance swabs were available. A total of 164 contacts were identified from within the same hostel accommodation as well as staff working in the refugee centre. All high risk contacts (n=101) were swabbed (throat, nasopharynx and open skin lesions) to assess C. *diphtheriae* carriage status. Chemoprophylaxis was administered (1 dose of intramuscular benzathine penicillin or 10 days of oral erythromycin) and diphtheria toxoid-containing vaccine offered regardless of immunisation status. Suspected cases were restricted on daily monitoring until swab clearance. A group of 49 low risk contacts were also offered vaccination. Results suggest a significant public health effort was required for a disease rarely seen in New Zealand. In light of increased worldwide forced displacement, similar outbreaks could occur and require a rigorous public health framework for management. *Commun Dis Intell* 2016;40(4):E475–E481.

Keywords: diphtheria, cutaneous, outbreak, refugees, vaccination

Introduction

The global displaced population has climbed to unprecedented levels with a worldwide total of 59.5 million individuals forcibly moved by 2014 and no simple resolution in sight.[1,2] Public health measures are critical for these humanitarian emergencies including management of vaccine preventable diseases (VPD) since displaced people are more likely to be inadequately immunised.[3] Recent studies by the World Health Organization (WHO) reveal 'varied and non-standardised criteria' used by various government agencies to control vaccine preventable outbreaks.[4,5]

Diphtheria is a rare disease in New Zealand primarily due to high immunisation coverage.[6] Diphtheria is caused by a polypeptide exotoxin of *Corynebacterium diphtheria*.[7] Severe clinical illness results from absorption of the toxin to the pharynx, nasal lining or skin, producing low grade fevers, and a pharyngeal pseudomembrane can classically develop over 2 to 3 days.[8] Cutaneous disease can also occur with indolent non-healing skin lesions that ulcerate. Diphtheria antitoxin (DAT) developed in the 1890s in horses hyperimmunised with diphtheria toxoid has dramatically reduced mortality.[9] DAT is used prophylactically in the treatment of diphtheria while the advent and widespread use of diphtheria toxoid containing vaccines makes the disease vanishingly rare in the developed world.[10] Cases are largely observed among unimmunised individuals or their contacts with recent travel history to countries where diphtheria remains endemic.[11] These countries include Afghanistan, Bangladesh, Cambodia, China, India, Indonesia, Malaysia, Nepal, Pakistan, Papua New Guinea, the Philippines, Thailand, Vietnam and the Pacific Islands.

Guidance for the management of diphtheria cases and contacts had been previously developed by the New Zealand Ministry of Health (MoH) following the Centers for Disease Control and Prevention (CDC) recommendations.[12] The disease is notifiable with a confirmed case definition of clinically compatible respiratory and/or cutaneous illness that is laboratory confirmed with a toxigenic isolate of *C. diphtheriae* or epidemiologically linked to a laboratory confirmed case. A probable case is a clinically compatible illness that is not laboratory confirmed.

A recent review of national surveillance data in New Zealand showed 1 case of diphtheria was reported in each of the years 1987, 1998, 2002 and

2008[6] and 2 unrelated cases in 2014.[13] The last recorded outbreak occurred in 2009 consisting of 2 cases in Wellington following the incomplete treatment of a person returning with disease from Samoa and resulting in contact tracing of 27 people.[6] This paper reports the public health response to an outbreak of 2 cases of cutaneous diphtheria in a group of Afghani refugees who had recently arrived in New Zealand from Pakistan, resulting in the follow up and contact tracing of 164 people at the Mangere Refugee Resettlement Centre (MRRC).

Case presentations

Three Afghani children were identified with culture-proven toxigenic *C. diphtheriae;* 2 with cutaneous lesions and 1 with asymptomatic pharyngeal carriage. All had spent the proceeding 4 years in Pakistan prior to arrival in New Zealand in January 2015.

Index case

A 7-year-old Afghani girl was identified at the MRRC when she had her routine health screening, which is mandatory for all new arrivals. She was noted to have an impetigous scalp lesion, which was cultured. Initial microbiology results identified *Staphylococcus aureus*, *Streptococcus pyogenes* and *C. diphtheriae*. This was reported 6 days later to be a *C. diphtheriae* toxin-producing strain by the National Reference Laboratory, Institute of Environmental Science and Research (ESR). This index case had no written record of immunisation. She had been started on flucloxacillin initially with significant resolution of the lesion, and on advice from the paediatric infectious diseases physician she was restricted with her family under voluntary consent and changed to amoxicillin/clavulanate for a further 14 days. She was assessed for consideration of prophylactic DAT but this was not available within New Zealand. The scalp infection improved and she did not develop any clinical signs of respiratory diphtheria. Pharyngeal carriage of *C. diphtheriae* was also noted so she remained in consented restriction until 2 sets of negative swabs from the nasopharynx, throat and scalp lesion were obtained 24 hours apart after completion of the antibiotic course.

Secondary case

A 6-year-old refugee Afghani girl from Pakistan had a small bullious lesion on the plantar surface of her right foot which developed after arrival in New Zealand and while resident at the MRRC. Toxigenic *C. diphtheriae* was isolated from it. She was from the same contact group, hostel block and attended the same school classes as the index case. Throat and nasopharyngeal swabs were both negative. She had been given intramuscular benzathine penicillin the day before the lesion swab result was known and vaccinated with diphtheria toxin containing vaccine (tetanus–diphtheria–acellular pertussis (Tdap) Boostrix© GSK). She remained in consented restriction on 14 days of erythromycin for eradication until 2 sets of clearance negative swabs from the nasopharynx, throat and foot lesion were obtained 24 hours apart on completion of the antibiotic course.

Asymptomatic carrier

The 11-year-old sister of the index case was identified during the contact tracing with asymptomatic pharyngeal carriage of toxigenic *C. diphtheriae*. She had been given intramuscular benzathine penicillin and Tdap vaccine 24 hours before the swab result was known as part of the screening. She remained in consented restriction for 7 days until 2 sets of clearance swabs were obtained from the nasopharynx and throat 24 hours apart.

Public health action

A public health response was initiated on the date of notification (2 February 2015) and managed as per MoH protocols.[12] A total of 164 contacts were identified, of which 1 became the secondary case. There were 3 rounds of contact tracing completed according to priority (Figure).

Group 1 – High risk close contacts including family, people with respiratory symptoms or skin lesions, other contacts in the same hostel, children in the MRRC school class and their families, as well as contact staff (n=101).

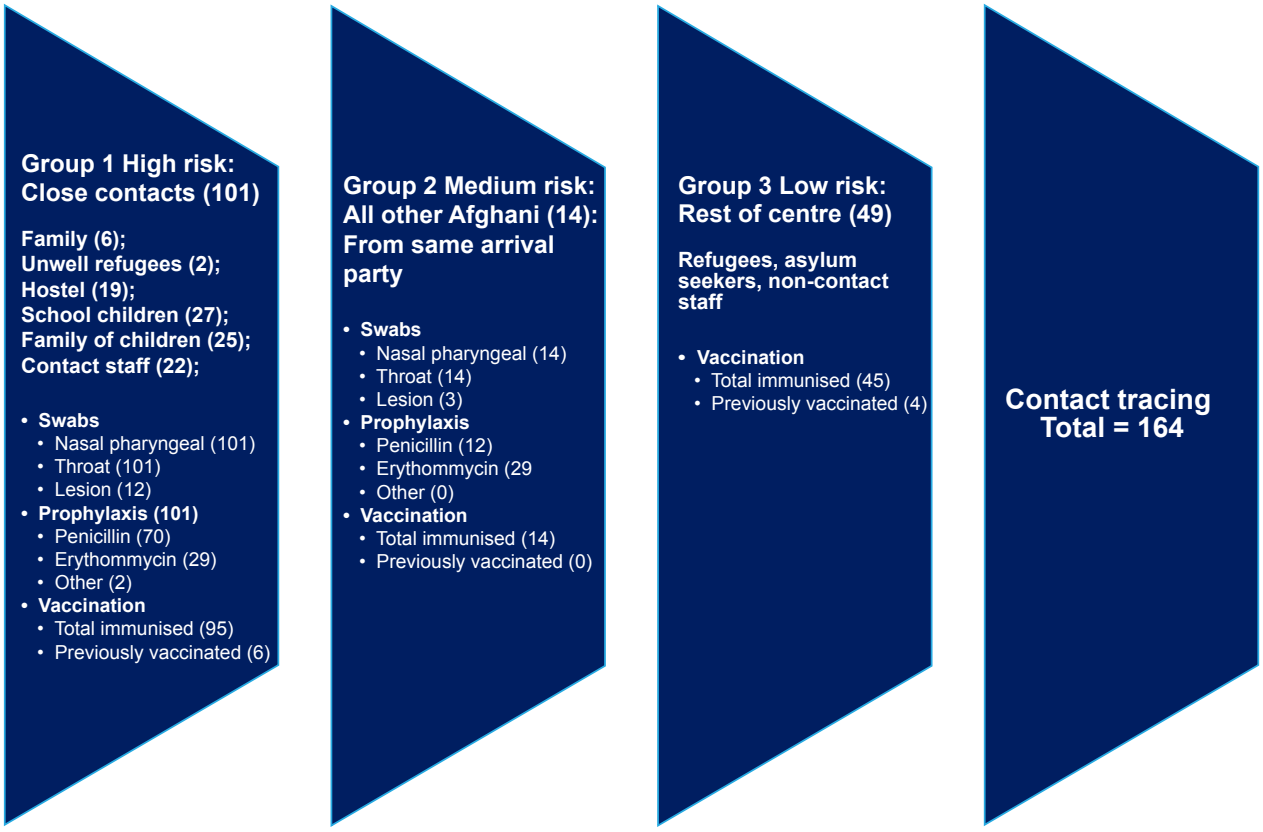
Group 2 – Medium risk contacts included all other Afghani people at the centre who arrived in the same party from Pakistan though not in direct close contact (n=14).

Group 3 – Deemed low risk, were the rest of the MRRC refugees and asylum seekers and non-contact staff (n=49).

Groups 1 and 2 had nasopharyngeal and throat swabs collected for screening for *C. diphtheriae* and open lesion skin wounds were swabbed regardless of history. Groups 1 and 2 were given antibiotic prophylaxis and immunised with Tdap after swabbing. The low risk contact group 3 were offered Tdap vaccine unless they had previously documented vaccine in the past 5 years.

The MRRC is an area that is fenced and gated allowing only staff or pre-approved visitors to have access to the site. Refugees who did not require vol-

Figure: Risk groups for diphtheria contact tracing, Mangere Refugee Resettlement Centre, Auckland, 2015



A total of 164 contacts were followed up at the MRRC in 3 contact tracing rounds according to risk. Groups were classified as high, medium and low risk of toxigenic diphtheria including; high risk close contacts of the Afghani case (group 1), medium risk all other Afghani refugees in the same arrival party (group 2) and low risk, all other refugee, asylum seekers and non-contact staff at the MRRC (group 3).

untary consented restriction, were free to come and go from the centre and so had access to the local community. During the outbreak routine medical assessment, including screening and health care continued as normal.

Outbreak information and the process of informed consent required the use of appropriate interpreters in 4 language streams. All refugees are routinely invited to consent to the collection of health information to provide the appropriate care; plan for and fund health services; carry out teaching and research; and monitor quality. Where their information was used for research or monitoring quality, it would not be published in a manner that identified that person. Approval from a human research ethics committee was not required but extra informed consent was invited for the outbreak management. Full ethical permission is not required for a public health action.

Skin, nasopharyngeal and throat swabs from the 164 contacts were cultured on sheep blood agar plates incubated at 35º C for 24–48 hours in 5% CO_2-enriched atmosphere. Suspicious Gram positive bacilli resembling *Corynebacterium* species morphologically were identified by MALDI-TOF (bioMerieux MS, Durham, NC, US). Isolates confirmed as *C. diphtheriae* were then sent to the ESR for detection of toxigenic strain using polymerase chain reaction amplification of the toxin gene (*tox*).

While the *C. diphtheriae* can persist for several days after antibiotics,[14] the preferred chemoprophylaxis was a single dose of intramuscular benzathine penicillin or 10 days of oral erythromycin where intramuscular doses were impractical or there was penicillin hypersensitivity. Many of the refugee children received oral erythromycin due to practical constraints related to correct intramuscular benzathine penicillin dosing.

Refugees with no documented vaccination history are generally considered non-immune. Tdap was offered rather than adult diphtheria-tetanus (ADT) for vaccination because they would normally be offered Tdap as a catch-up within the

first 4 weeks of arrival. A total of 154 contacts were immunised (137 refugees and 17 staff); while a further 10 contacts who had documented evidence of Tdap or ADT and were not offered a booster. Staff involved in the response were required to know their own vaccine history, but vaccination history was checked via occupational health records where possible. Tdap was also administered to public health outbreak response staff who had not been vaccinated in the previous 5 years.

The public health nurse team donned full personal protective equipment (PPE consisting of gowns, gloves and surgical masks) to swab, administer chemoprophylaxis and immunise the high risk group. All high risk contacts received follow-up daily symptom checks by the public health nurse for 7 days from their last contact with the case. Skin lesions were covered with dressings and the public health nurse assessed them during their daily symptom checks

Probable cases (n=6) who displayed potential clinically compatible diphtheria pharyngeal or cutaneous symptoms were identified, reviewed and treated by medical staff. They were then restricted until negative swab cultures were obtained (usually 2–3 days) in accordance with MoH and CDC manual guidelines.[12]

All contacts were educated on transmission prevention methods and effective hand hygiene measures. A health protection officer from the public health unit assessed the MRRC and provided environmental cleaning recommendations to staff. Extensive commercial cleaning of high risk areas was undertaken, including the hostel accommodation the cases used as a restriction facility, the medical centre and school classroom.

Discussion and public health significance

This outbreak involved 2 cases of confirmed toxigenic cutaneous diphtheria and an asymptomatic throat carrier of toxigenic *C. diphtheriae,* which did not satisfy the case definition though a reservoir for disease. The public health response to this outbreak was the largest recorded group contact trace for diphtheria in New Zealand history since the notification process began in 1956 and involved intensive resource allocation. The emergency action in this refugee resettlement centre for such a rarely notified disease highlights 4 internationally pertinent issues for any future VPD outbreaks occurring in these vulnerable refugee populations. These concerns are detailed in the sections below.

1. *A diphtheria outbreak could readily happen again with international pressure to increase refugee intakes and could involve other VPD, including polio and measles.*

Arriving refugees are a heterogeneous group with varied medical needs based on the country of origin and country of transit, the length of time as a refugee and quality of healthcare prior to arrival.[15] All displaced people are at increased risk of VPD due to poor vaccine availability and failing public health systems in their country of origin.[3] The rapidly increasing annual rate of forced global displacement, more markedly over the last 3 years,[16] in regions of conflict and political instability makes a VPD outbreak more likely at borders and refugee intake centres.

Unlike other immigrants, refugees tend to arrive with minimal documentation of immunisation as well as very limited history of previous clinical illness. Re-vaccination as soon after arrival as practical is recommended within New Zealand where there is no valid documentation.[17] Previous studies have shown it is cost effective to re-start catch-up immunisation soon after resettlement rather than using screening measures such as serological testing.[18] While the MRRC protocol allowed for fully funded catch-up immunisation within the first 4 weeks of arrival at the centre, full immunisation prior to arrival in New Zealand would be preferable. There are a number of logistical barriers to preclude this option including funding, consistent vaccine supply, cold chain and vaccine delivery into areas of political instability.

An extensive public health response was more feasible and manageable because the refugees all reside in 1 site for the first 6 weeks after arrival in New Zealand and would provide further challenges if it had occurred in the community. A purpose built resettlement centre for all refugees and asylum seekers entering the country allowed consistent and strategic health screening soon after arrival. It has the added advantage of quick diagnosis and management of any VPD outbreaks.

2. *There is a need for a consistent and rigorously tested framework for planning and managing of rare VPD emergencies including diphtheria.*

Since diphtheria is rare, testing the disease management framework for best practice has been difficult. For this reason the protocol was risk averse[12] and included a rigorous public health intervention of consented restriction of the cases and infection prevention and control (Standard and Contact Precautions), swabbing, chemoprophylaxis and a complete course of vaccine or a booster as appropriate for all close contacts. A more tested public

health response might be less risk averse and result in more efficient resource allocation. Testing the framework would require an international effort and rely on good communication and formal debrief after such outbreaks, to identify any issues. Internationally sharing information would help to optimise management in future situations.

A recent review of literature by WHO[4] confirms a range of criteria used by organisations and government agencies to plan and implement urgent public health responses such as vaccination in outbreak situations. Very little data are available to evaluate the process of how decisions are made to assess rare disease and VPD management frameworks. There is a clear need for a framework to ensure a standardised and consistently applied methodology for decision making both nationally and internationally. The use of such a framework would minimize mortality, maximize resources, reduce wastage, ensure equity, and ultimately improve accountability to the population at risk and other stakeholders.[4]

3. *Readiness and preparedness of public health services for VPD emergencies including rarely accessed medical treatments such as DAT.*

The readiness and preparedness of public health services to manage and plan for VPD outbreaks needs regular review. This requires the training and availability of staff to diagnose, then manage the acute outbreak with the resultant temporary reduction in other services. The sharing of information and strong communication networks are vital when such a rare disease is involved. Health care workers working with refugees need to have a thorough knowledge of the causes of communicable diseases in developing countries to facilitate the appropriate collection of clinical specimens, avoiding diagnostic delay and result in timely, appropriate management. Mechanisms also need to be in place to deliver this information on a national basis to all primary care health workers who will have long-term care of the refugee populations.

Maintaining high levels of immunity for all New Zealanders, particularly those travelling to high risk areas is recommended. Despite high levels of community and refugee health worker immunity to diphtheria, only a small group of the total number of health workers at the centre had documented immunisation status reflecting the lack of application of the health and safety policies and procedures. There were also special occupational health requirements identified for interpreters, teachers and administrators not usually at high risk of contact.

A national shortage of anti-toxin in New Zealand and neighbouring Australia was identified by this outbreak and global access to DAT continues to be restricted. Despite ongoing efforts to secure supplies, rapid access to DAT would currently not be possible. While a case of clinical pharyngeal or cutaneous diphtheria with systemic manifestations would be unlikely, the MoH's CDC manual 2012 recommends DAT "before laboratory confirmation when there is strong clinical suspicion of diphtheria". While the literature regarding anti-toxin (DAT) in cutaneous diphtheria is unclear,[19] antitoxin is not usually given due to lack of pseudomembranes or cardiac involvement.[20] These 2 children clinically had no evidence of systemic disease and so anti-toxin was not indicated.

Neither case of cutaneous diphtheria identified in this outbreak had typical features. *C. diphtheriae* is a well-recognised cause of skin infections in children both in New Zealand and in Pacific Island countries though the isolates are largely non-toxigenic. While invasive disease has also been reported,[21] cutaneous diphtheria usually presents as indolent, non-healing lesions often with no characteristic features. Children with cutaneous diphtheria rarely develop the pharyngeal form of the disease or systemic manifestations, probably due to a brisk antibody response, but the ulcer acts as a reservoir to infect susceptible hosts. This makes timely diagnosis very important, particularly in situations where there is a closed community with a large number of vulnerable refugee families with suboptimal vaccination and often significant health issues.

4. *There are implications from this diphtheria outbreak for the wider public health and emergency response policy framework including non-VPD outbreaks.*

This outbreak of rarely notified and potentially life threatening diphtheria has implications for wider public health emergency response and planning. Policy needs to include consideration of:

1. the varied needs of this vulnerable group of people about to resettle in a different country;
2. the temporary arrival into a single screening facility is a good model and highlights the need for the appropriately funded purpose built infrastructure for refugees;
3. appropriate information technology infrastructure for the sharing of knowledge and experience after rare VPD and non-VPD outbreaks to the national and international scientific and medical community can direct best practice protocols for management;

4. a well trained group of health professionals that recognise the specific needs of refugees will also be aware of the array of communicable diseases from other parts of the world and their treatment;
5. adequately funded and trained public health units that are equipped to respond to VPD and non-VPD emergencies; and
6. agencies caring for newly arrived refugees need to have a robust health and safety policy to keep their staff and other refugees safe against VPD and non-VPD hazards.

Summary

We describe a 2 person outbreak of diphtheria in a New Zealand refugee centre resulting in the follow-up of 164 contacts and this is timely with the rapid increase in global displacement. It highlights the need for rigorous policy for countries who are receiving refugee populations as these events could readily happen again. The outbreak shows that a rare VPD can be imported from areas of humanitarian need and requires clear systems and protocols for management. Finally it emphasises the need for readiness and preparedness and the importance of integration of VPD and non-VPD into emergency planning.

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