

Diphtheria Epidemiology in Indonesia During 2010 - 2017

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ABSTRAK

Latar belakang: dewasa ini, difteria telah muncul kembali di beberapa negara termasuk Venezuela, Yemen, Bangladesh dan Haiti. Serupa dengan hal tersebut, Indonesia juga menunjukkan peningkatan kasus difteria pada tahun 2010 hingga 2017 meski program imunisasi difteria, tetanus dan pertusis (DPT) untuk anak-anak telah dilaksanakan di Indonesia. Penelitian ini bertujuan untuk mengevaluasi epidemiologi kasus difteria yang terjadi di Indonesia pada tahun 2010-2017. **Metode:** penelitian ini merupakan penelitian retrospektif tentang kasus difteria di Indonesia. Sumber data mengenai beban penyakit difteria dan cakupan vaksinasi diperoleh dari Kementerian Kesehatan Republik Indonesia, Ikatan Dokter Anak Indonesia dan Kantor Regional Asia Tenggara Badan Kesehatan Dunia (World Health Organization). **Hasil:** kasus-kasus difteria di Indonesia yang tersebar di 30 propinsi seluruhnya berjumlah 811 kasus pada tahun 2011; 1.192 kasus pada tahun 2012; 296 kasus pada tahun 2014; dan 939 kasus pada tahun 2017. Berdasarkan kelompok usia, jumlah kasus dengan tingkat fatalitas tertinggi terdapat pada kelompok usia 5-9 tahun. Cakupan imunisasi difteria pada anak di Indonesia berfluktuasi dan dilaporkan sebanyak 67,7% pada tahun 2007, 61,9% pada tahun 2010, 75,6% pada tahun 2013 dan 61,3% pada tahun 2018. Selain itu, organisasi ilmu penyakit dalam telah merekomendasikan booster imunisasi setiap 10 tahun untuk anak-anak yang telah mendapatkan vaksinasi DPT lengkap selama masa kanak-kanaknya; namun rekomendasi ini belum terlaksana. Sebagai langkah untuk mengatasi kecenderungan ini, Kementerian Kesehatan telah melakukan tiga putaran Imunisasi sebagai Respons terhadap Kejadian Luar biasa atau Outbreak Response Immunization (ORI) yang ditujukan untuk kelompok usia 0-1-6 bulan dan 1-18 tahun pada tahun 2017 dan penyesuaian pendekatan (tailored approach) untuk dewasa yang terpapar kasus tersebut. Banten, DKI Jakarta dan Jawa Barat merupakan tiga propinsi pertama yang melaksanakan program ini mengingat populasinya yang padat serta tingginya risiko penularan penyakit. **Kesimpulan:** di Indonesia, terdapat peningkatan kasus difteria yang dramatis pada tahun 2010-2017, sedangkan imunisasi pada anak perlu digiatkan kembali dengan meningkatkan cakupan hingga lebih dari 95% dan pendekatan booster vaksinasi pada dewasa perlu dimulai untuk mencegah penyebaran penyakit difteria yang bersifat fatal ini di Indonesia.

Kata kunci: difteria, epidemiologi, imunisasi.

ABSTRACT

Background: in recent years, diphtheria has reemerged in several countries including Venezuela, Yemen, Bangladesh, and Haiti. Similarly, Indonesia also showed an increased number of diphtheria cases in 2010-2017 despite the Diphtheria, Tetanus, Pertussis (DTP) immunization program applied in Indonesia for children. This study

aimed to evaluate the epidemiology of diphtheria cases which occurred in Indonesia during 2010-2017. **Methods:** this was a retrospective study of diphtheria cases in Indonesia. The following source of data about diphtheria disease burden and vaccine coverage was obtained from Ministry of Health Republic of Indonesia, Indonesian Pediatric Society and World Health Organization South East Asia Regional Office. **Results:** the number of diphtheria cases in Indonesia were distributed across 30 provinces with a total of 811 cases in 2011; 1,192 cases in 2012; 296 cases in 2014; and 939 cases in 2017. Based on age group, the highest number of case fatality rate were in age group of 5-9 years old. Diphtheria immunization coverage in Indonesia among children was fluctuated, reported as 67.7 % in 2007, 61.9 % in 2010, 75.6% in 2013 and 61.3% in 2018. In addition to that, the organization of internal medicine has recommend booster of DPT immunization every 10 years for those children that had received complete DPT vaccination during childhood, however this was not applied. As the countermeasure towards this trend, the Ministry of Health implemented three rounds of Outbreak Response Immunization (ORI) targeted for the age group of 0-1-6 months old and 1-18 years old in 2017 and tailor approached for adults that had exposed to cases. Banten, DKI Jakarta and West Java were the first three provinces to implement this program considering their condensed population and high risk of disease transmission. **Conclusion:** in Indonesia, there was dramatic increase of diphtheria case in 2010-2017, where immunization in children should be reinforced by increasing coverage more than 95% and adult boosted vaccination approaches should be initiated to prevent the spread of these fatal diphtheria diseases in Indonesia.

Keywords: diphtheria, epidemiology, immunization.

INTRODUCTION

Since the introduction of vaccination program in 1970s, the number of diphtheria cases, one of the leading causes of death in children during pre-vaccine era, quickly declines. However, there were still 5,000 cases of diphtheria reported worldwide each year.¹ Potential outbreaks may also occur when a community has both a large population of non-immune adults and poor vaccination coverage among children, such as occurred in the Russian Federation and the former Soviet Republics in 1990s.¹ Even so, patterns of diphtheria disease epidemiology are known to have altered over time depending on vaccination coverage and socioeconomic condition of the countries.²

Several countries experienced diphtheria outbreaks during the last few years, including Bangladesh, Haiti, Venezuela, and Yemen.³ While disruption of primary health care facilities, crowded urban populations, and migrations were the main contributing factors for these outbreak, low community vaccination coverage is also the stated risk factors for the increased incidence of diphtheria.⁴ Similarly, Indonesia was also reported to have an increase in diphtheria incidence in 2017.⁵

In Indonesia, diphtheria becomes a public health problem as diphtheria incidence has

increase in 2010 and continue to rise until 2017.⁶ Therefore, this study is aimed to evaluate the epidemiology trend of diphtheria cases in Indonesia during 2010-2017.

METHODS

The study reviewed data on diphtheria cases reported in Indonesia during 2010-2017 which was obtained from: 1) Ministry of Health Republic of Indonesia, 2) Indonesian Pediatric Society, and 3) World Health Organization South East Asia Regional Office. The data related to diphtheria or *Corynebacterium diphtheria* were reported in terms of case definition and classification based on Indonesia national diphtheria guidelines published by Ministry of Health Republic of Indonesia.

The definition of diphtheria case were: 1) "Suspected diphtheria" if it is found with pharyngitis, tonsillitis, laryngitis, tracheitis, or a combination with not sub-febrile and a grayish white pseudo-membrane that is difficult to remove but easily bleeds when manipulated or removed; 2) "Probable diphtheria" is suspected of having diphtheria with one of the following symptoms: contact with other cases (<2 weeks), incomplete immunization including no booster, lives in diphtheria endemic areas, having stridor and bullneck, there are complications such as

submucosal bleeding or petechiae, heart failure, acute renal failure, myocarditis until death; 3) “Laboratory-confirmed diphtheria case” is a case of diphtheria suspicion with positive *Corynebacterium diphtheriae* culture results on toxigenic strains or positive PCR (polymerase chain reaction) *Corynebacterium diphtheriae* confirmed by Elek test; 4) “Epidemiological relationship-confirmed diphtheria case” is a case that meets the criteria for suspected diphtheria and has an epidemiological relationship with laboratory-confirmed cases; 5) “Clinically compatible diphtheria case” is a case that meet the criteria for suspected diphtheria but do not have a link with laboratory-confirmed cases or epidemiological relationships-confirmed case; 6) Contact diphtheria cases” are people at home, playmates, schoolmates, including teachers and co-workers who are close contact with the

case; 7) “Carrier diphtheria cases” are people who have no clinical symptoms, but the results of laboratory tests are positive.^{6,7} Additionally, case fatality rate (CFR) of diphtheria was also described in this study defined as the percentage of cases who died from diphtheria in all cases of clinical diphtheria reported.⁸ All of these data were collected during surveillance procedure by ministry of health directorate of Disease Control and Environmental Health.

RESULTS

In 2011, there were 811 cases of diphtheria reported in Indonesia, spread across 18 provinces with 38 deaths in North Sumatra, Bengkulu, South Sumatra, Bangka Belitung, Lampung, DKI Jakarta, Banten, West Java, Central Java, Yogyakarta, East Java, West Borneo, South Borneo, East Borneo, South Sulawesi, Southeast

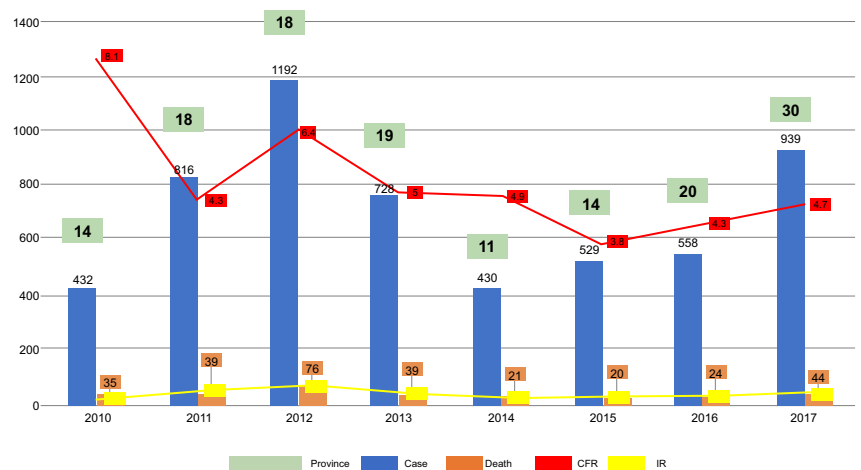


Figure 1. Development of diphtheria cases in Indonesia

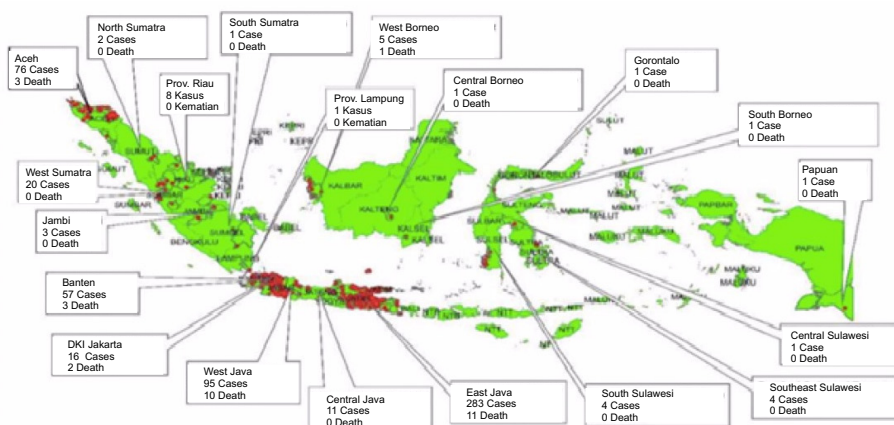


Figure 2. Distribution of diphtheria cases in Indonesia 2017

Sulawesi and Bali (CFR 4.71%). The cases of diphtheria were mostly reported from East Java with 663 cases (82.3%), followed by East Borneo and West Java with 52 cases (6.5%) and 45 cases (5.6%), respectively. These cases were found mostly in the age group of 1-9 years old with 279 cases (72.47%) in 2010 and 524 cases (65%) reported in 2011.^{9,10}

Diphtheria incidence in Indonesia has fluctuated in the period of 2010 to 2017 (**Figure 1**), where in 2012 there was an increase of 1,192 diphtheria cases with the highest case fatality rate (CFR) 6.38%. East Java was reported to have 954 cases (80%), followed by South Borneo and South Sulawesi with 61 cases (5.1%) and

50 cases (4.2%), respectively.¹¹ In 2017, the case reemerged to 954 cases with CFR 4.61% in 30 provinces. East Java and West Java were the area most severely affected, reported to have 331 cases and 167 cases, respectively.¹² Based on data from the Research and Development Ministry of Health Republic of Indonesia, there were 686 suspected or probable diphtheria cases, with 58 toxigenic and 13 non-toxigenic cases respectively (excluding contacts).¹³

Based on the age group, the highest number of cases occurred in the age group of 5-9 years old and followed by 1-4 years old which accounted in consecutive for 32.5% and 19.1% of overall diphtheria cases in 2017. This description

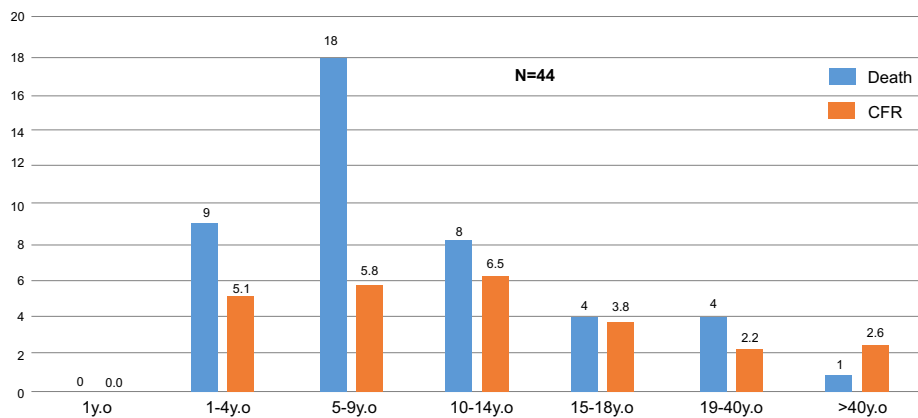


Figure 3. Case fatality rate of diphtheria based on age in 2017

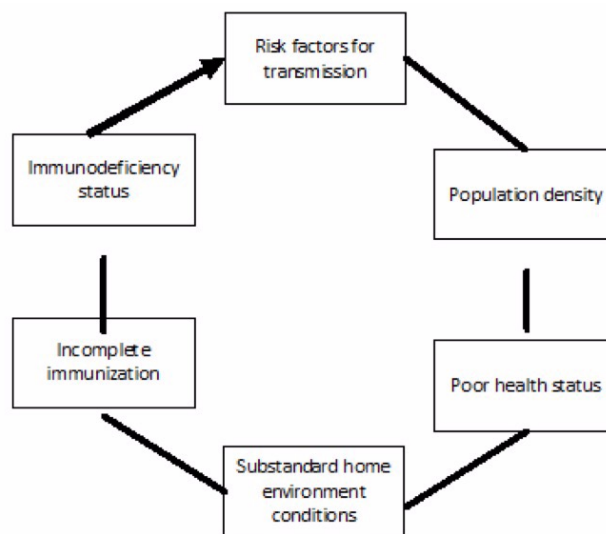
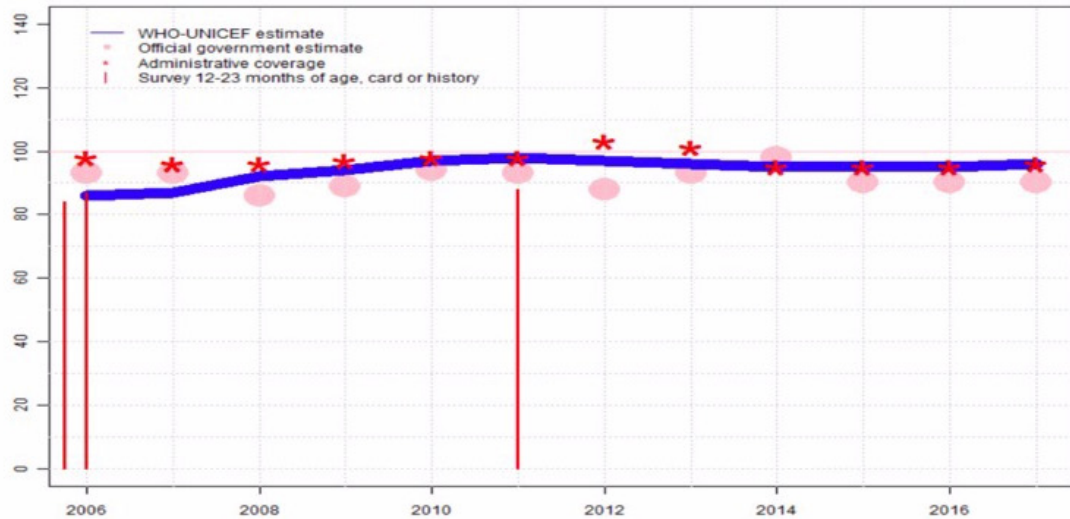


Figure 4. Chart of diphtheria outbreak causes

showed that routine immunization coverage has yet to reach the target and distributed equally across the regions. The case distribution was also reported among the adults aged 19-40 years old accounting for 19% of overall cases.

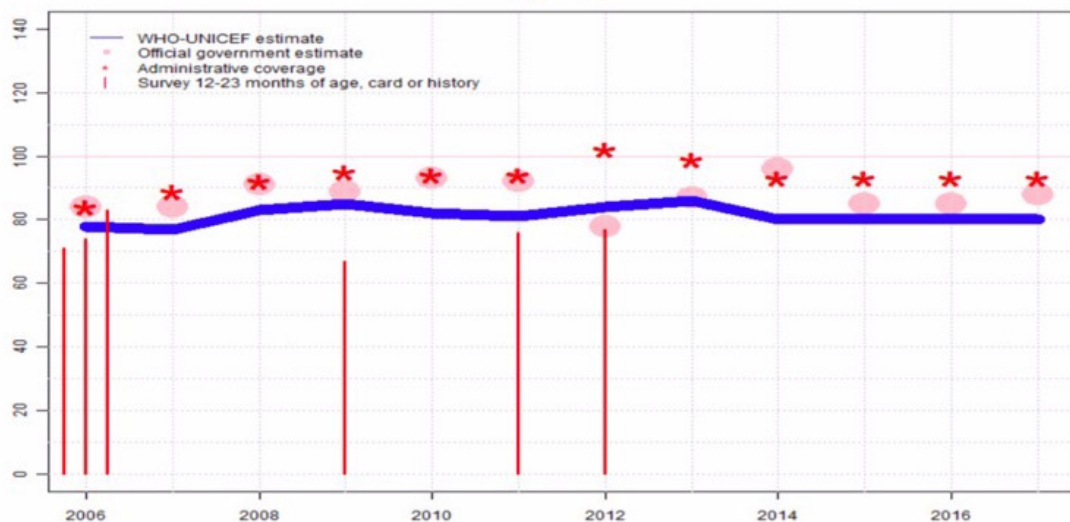
Therefore, booster immunization of DPT should be considered to initiate routinely in adults.¹³

Diphtheria vaccine is given as DTP (diphtheria-tetanus-pertussis) included in routine basic immunization program in Indonesia for



	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Estimate	86	87	92	94	97	98	97	96	95	95	95	96
Estimate GoC	•	•	•	•	•	•••	•••	•••	••	••	••	••
Official	93	93	86	89	94	93	88	93	98	90	90	90
Administrative	98	96	96	97	98	98	103	101	95	95	95	96
Survey	*	NA	NA	NA	NA	88	NA	NA	NA	NA	NA	NA

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	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Estimate	78	77	83	85	82	81	84	86	80	80	80	80
Estimate GoC	•	•	•	•	•	•	•	•	•	•	•	•
Official	84	84	91	89	93	92	78	87	96	85	85	88
Administrative	84	89	92	95	94	94	102	99	93	93	93	93
Survey	*	NA	NA	67	NA	76	77	NA	NA	NA	NA	NA

Figure 5. Diphtheria immunization coverage

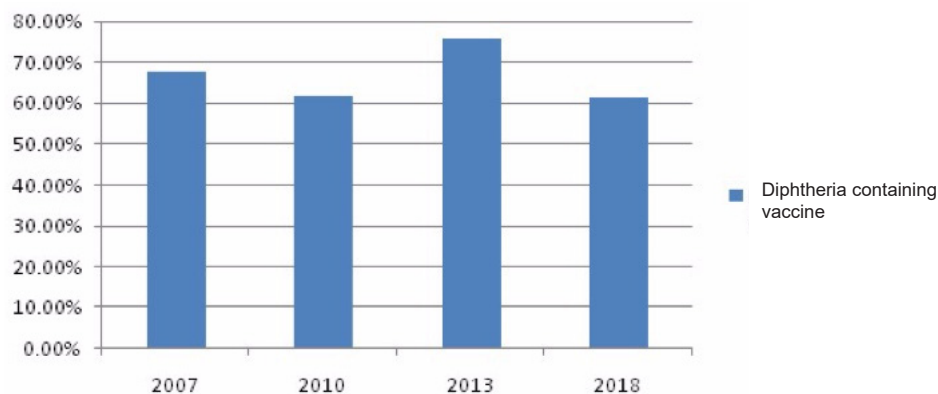


Figure 6. Diphtheria immunization coverage¹⁵

children endorsed by the government. It should be given at the age of 2, 4, and 6 month of age and given booster at 18 months old afterwards. Over the course of 2010-2017, the overall basic immunization coverage in Indonesia was over 95%.¹⁰⁻¹³ However, the immunization coverage for diphtheria itself still below the target accounting for 67.7% in 2007, 61.9% in 2010, 75.6% in 2013, and 61.3% in 2018.^{14,15} Ministry of Health regulated the effort to reduce and prevent diphtheria outbreak through several methods. First method was the study of epidemiology which included: 1) finding additional cases to be treated; 2) identifying and managing contacts through prophylaxis administration to eradicate the bacteria thus stopping the transmission; 3) identifying the risk factors and vulnerable groups to be managed according to evaluation.^{12,16} Second step is to stop the immunity gap through three rounds of Outbreak Response Immunization (ORI). The coverage target set was more than 90% for children administered with diphtheria containing vaccine with schedule at 0,1 and 6 months without reviewing the previous immunization status, especially in regions affected and had high risk of diphtheria. The subjects targeted for immunization was the age group of 1-18 years old. As the first step taken, twelve districts were chosen from three provinces which are Banten, DKI Jakarta and West Java considering the condensed population, high risk of transmission potential, and high level of mobilization.^{12,16}

Other measurements taken by the health policy makers in Indonesia were community

education and logistics provision for diphtheria cases management, laboratory examination, and ORI implementation while private sectors focused on the administering booster of DPT vaccine for adults.¹⁷ The content on community education were about healthy and hygienic life style as prevention of diphtheria transmission as well as the importance of completing routine immunization or ORI.^{12,16}

DISCUSSION

Diphtheria is an infection of the upper respiratory tract caused by *Corynebacterium diphtheria*. Generally, it affects children aged 1-10 years old although it can also occur in adults.¹² Risk factors increasing the possibility of diphtheria infection including nutritional status, incomplete immunization history, and previous contact with those infected.¹⁸ Additionally, other factors may also include availability of bacterial transmission, poor condition of the house and its surroundings, and population density. Most problems of diphtheria epidemiology originate from lack of immunization coverage, socioeconomic problems, handling incomplete carriers, and high migrations the community.¹⁵

Diphtheria remains a public health problem in Indonesia. Over the course 2010-2017, Indonesia's incidence of diphtheria reached its peaked in 2012 and 2017, accounting for 1,192 cases and 954 cases, respectively.^{11,12} The amount of diphtheria cases in 2017 were twice the case number in previous year, leading to declaration of diphtheria outbreak from Indonesian government. Thus, Indonesian

Ministry of Health established the Outbreak Response Immunization (ORI) adapted from WHO recommendation to be implemented across the nation as an effort to reduce diphtheria case in Indonesia.¹²

East Java was the most severely affected area contributing approximately 80% of total cases in Indonesia.¹⁹ One of the dominant risk factors was incomplete immunization history (p value = 0.0037; OR = 4.667) as described in the study by Arifin et al¹⁸, contributing to the rate of diphtheria cases in Bangkalan Primary Health Care, Surabaya. It was found that there was 18% of diphtheria cases with incomplete history of DPT immunization and 82% of those without any DPT immunization at all.¹⁷ A similar study in East Java also found that the rate of achievement in DPT immunization program was a risk factor in diphtheria transmission. Moreover, the DPT immunization coverage itself in Indonesia has yet to reach 100%.¹⁶

The low immunization coverage in Indonesia may be due to several reasons as reported by Ministry of Health Republic of Indonesia, such as rejection towards immunization by certain group/community which results in incomplete immunization status.²⁰ Low level of education was an important factor contributing to immunity gap in many regions while some parents also refuse to deal with the side effect of DPT immunization such as the fever. There was also belief that vaccines are prohibited under Islamic law. However, the Indonesian Ulama Council (MUI) has created a countermeasure that vaccines were not prohibited by religion.²¹ Lack of healthy lifestyle education in schools also leads to students' vulnerability towards diphtheria.

The spread of diphtheria from one province to others, such as occurred in Jakarta, West Java, and Banten may be due to antibiotic resistance aside from the dense population and incomplete immunization status. Penicillin and erythromycin are antibiotics given to treat diphtheria, as a study by Rockhill et al²² (1982) found that there was 100% susceptibility of ampicillin and erythromycin towards diphtheria pathogen in Cipto Mangunkusumo Hospital, Jakarta. However, another study conducted in 2015 found that there was 84% susceptibility pattern against

the bacteria in penicillin and 91.2% susceptibility in erythromycin, thus showing an increase resistance towards the antibiotics.²³ Therefore, Indonesia requires more research to improve the management of diphtheria.

The WHO recommended Outbreak Response Immunization as an effort made immediately to end the transmission, reduce the number of cases of diphtheria and prevent the disease from expanding. This recommendation was adapted in Indonesian immunization guideline by the Ministry of Health in which three rounds of diphtheria immunization was conducted, covering age 1 year to less than 19 years of age, which was carried out in schools, posyandu, primary health care's and other health-care facilities. The initial week of vaccination implementation was prioritized in school-based. The vaccines used were DPwT-HB-Hib for ages 1 year to <5 years; DT vaccine for ages less than 7 years and Td vaccine for ages 7 years and over.^{13,16}

This activity involved professional organizations such as the Indonesian Pediatricians Society (IPS), Association of Indonesian Internal Medicine Specialists (PAPDI), the Indonesian Medical Association (IDI), the Indonesian Midwives Association (IBI) and the Indonesian National Nurses Association (PPNI) to assist in the implementation of ORI and primary health care's, District or City Health Offices and Provincial Health Offices related were responsible for reporting the daily ORI coverage to the Ministry of Health's Immunization Sub Directorate.^{13,16} The success of controlling diphtheria was influenced by public awareness in obtaining and completing immunizations. Additionally, the role of health-care workers in maintaining the quality of cold-chain vaccine management and immunization services were important. There will be an immunity gap in the population and will lead to the increasing of diphtheria incidence, if immunization coverage did not increase.¹³ Three important strategies for tackling diphtheria were firstly to immunize immediately children aged 1-19 years, early detection and proper handling of diphtheria cases, and identify appropriate diphtheria contact or carrier management procedures. Diphtheria

surveillance supported by the national laboratory surveillance must be reinforced in order to detect early outbreak in the community, treat the diphtheria case and detect diphtheria contacts or carriers appropriately. These efforts require the support of policy makers, the community and the provision of adequate healthcare resources from the local government and the commitment of health workers to carry out all these efforts with full responsibility.¹³

CONCLUSION

There were increased number of diphtheria cases in Indonesia over the course of 2010-2017. One of the important lessons that diphtheria cases remain a problem was that immunization coverage was not as expected on target and no booster vaccination for adult routinely implemented. The ORI program was an effort to end transmission, reduce the number of cases of diphtheria and prevent the disease from spreading. The ORI program was performed at 0, 1 and 6 months, represented good indicator of all efforts from multi-sectoral departments, health workers, community, leaders and government.

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