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Diphtheria in the Dominican Republic: reduction of cases following a large outbreak

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ABSTRACT

Objective. *To describe the most recent outbreak of diphtheria in the Dominican Republic and the disease's occurrence and vaccination coverage in 2004–2013.*

Methods. *Clinical data of diphtheria cases that occurred in 2004 and that met the study's case definition were reviewed along with socioeconomic and epidemiological information from the cases' families. Univariate and multivariate analyses were performed to assess risk factors for fatal diphtheria. Routine surveillance and vaccination coverage data are presented.*

Results. *From January 2004–April 2005, a total of 145 diphtheria cases were reported; 80 (66%) of the 122 cases reported in 2004 met the case definition; 26 were fatal (case–fatality rate: 32.5%). Incidence was highest in the group 1–4 years of age at 5.3 per 100 000; 62.5% were male. Of the 80 cases, 61 (76%) where hospitalized in Hospital A, 17 in Hospital B, and 2 in two other hospitals. Earlier onset (first half of 2004), birth order, and tracheotomy were associated with fatal diphtheria* ($P < 0.05$); *cases in Hospital A were also more likely to be fatal* ($P = 0.066$). *The average annual diphtheria incidence was 4.91 cases/1 million people in 2000–2003, climbed to 8.8 cases per million in 2004–2005, and dropped to 0.38 in 2006–2014; no diphtheria cases have been reported since 2011. DTP3 vaccination coverage ranged from 72%–81% in 2000–2004 and from 81%–89% in 2005–2013.*

Conclusions. *The 2004–2005 diphtheria outbreak in the Dominican Republic resulted in important and avoidable morbidity and mortality. Annual cases declined and no cases have been reported in recent years. Maintaining high vaccination coverage and diligent surveillance are crucial to preventing diphtheria outbreaks and controlling the disease.*

Key words Diphtheria; vaccination; disease outbreaks; Dominican Republic.

Diphtheria is an acute bacterial disease caused by *Corynebacterium diphtheriae*, which can cause infection of the nasopharynx, result in obstruction of the airway, and lead to death. The toxin produced by the bacteria can also result in systemic complications of various organs. Though diphtheria anti-toxin (DAT) usage, improved treatment, and widespread immunization with diphtheria toxoid have dramatically reduced mortality and morbidity, vaccination continues to be essential to preventing the disease and avoiding large epidemics. Prompt recognition and treatment of diphtheria are very important, as the early use of DAT is associated with better outcomes (1–3).

Mass resurgence of diphtheria in countries of the former Soviet Union (4–6) and outbreaks in Latin America and the Caribbean (LAC) in the 1990s (7) highlighted diphtheria's morbidity and mortality impact and the importance of continuous surveillance—including laboratory confirmation of toxigenic *C. diphtheriae*, and vaccination activities that achieve high and homogenous coverage. Furthermore, in recent years, it has become very hard to find DAT or a manufacturer able to provide the licensed

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product in sufficient quantities on an emergency basis (8–9).

Diphtheria has been largely controlled in LAC following widespread vaccination with diphtheria toxoid-containing vaccines as part of the Expanded Program on Immunization (EPI) launched in the late 1970s (3, 10, 11). In 2000–2003, approximately 100 cases were reported in LAC each year, with the Dominican Republic reporting the highest count: an average of 43 cases annually during this period (10, 12). In 2004–2005, a large diphtheria outbreak occurred in the Dominican Republic and Haiti (453 cases) becoming the largest diphtheria outbreak in LAC in the 21st century (13, 14). Following that outbreak, diphtheria cases and deaths in Haiti have continued to occur, but in the Dominican Republic, they have dropped progressively (8, 12).

This report describes the 2004–2005 diphtheria outbreak in the Dominican Republic, highlighting the main risk factors for fatal diphtheria and the lessons learned regarding outbreak management, prevention and control. It also describes the occurrence of the disease and vaccination coverage in the country during the last decade.

MATERIALS AND METHODS

Outbreak investigation

All hospitalized cases reported to the Dominican Republic national vaccine-preventable disease surveillance system as diphtheria in January 2004–April 2005 were assessed; however, analysis was restricted to cases with disease onset in 2004, as explained below. A case was defined as clinically-confirmed if the patient had a history of a sore throat and a pharyngeal membrane, and a physician had diagnosed it as diphtheria. A case was defined as confirmed by a laboratory if the patient had catarrhal symptoms and a culture positive for *C. diphtheriae* or if the patient was epidemiologically linked to a case with a culture positive for *C. diphtheriae*.

To describe the characteristics of the cases and determine risk factors for fatal diphtheria, parents or guardians of the reported cases were interviewed using a standard questionnaire that was a revised version of the routine case-investigation form for diphtheria surveillance, collecting demographical, clinical, and epidemiological information. A medical epidemiologist abstracted clinical data from hospital charts. Variables recorded included age at disease onset; sex; municipality of residency; locality (rural or urban/peri-urban); vaccination history; monthly family income (in 2004, US$ 1 = 39.24 Dominican pesos); education of the mother or guardian; number of persons living in the household and number of rooms in the residence; date of symptoms onset; hospital of admission and date of hospitalization; main symptoms and signs; use, dosage, and start date for DAT treatment; use of antibiotics and corticosteroids; laboratory test results; complications; subjective evaluation of severity; neck edema; tracheotomy; and outcome (death or recovery).

For this study, a case was defined as adequately vaccinated if: a vaccination card or health center record showed that the person had received three doses if he/she was less than 18 months of age or three doses plus at least one booster if older. Information regarding the follow-up of household contacts was also recorded, including the occurrence of cases among them, use of prophylactic antibiotics, and vaccination. The main analysis was limited to cases reported in 2004 because these had more complete information. Few of the cases reported in 2005 had the revised case-investigation form completed and their hospitalization chart reviewed.

Nasopharyngeal specimens were cultured using tellurite-containing media at the bacteriological laboratory in the infectious disease department at the national children's reference hospital in Santo Domingo (Hospital A) and, starting in mid-July 2004, also at the bacteriological laboratory in the provincial hospital of the second largest city in the Dominican Republic (Hospital B). In order to confirm the etiology of the outbreak as diphtheria, and because the Dominican Republic does not have toxigenicity testing capability, 16 isolates were sent to the diphtheria laboratory at the Centers for Disease Control and Prevention (CDC; Atlanta, Georgia, United States) for real-time polymerase chain reaction (RT-PCR) confirmation.

Cases and vaccination coverage rates

The numbers of diphtheria cases in the Dominican Republic for 2000–2003 and 2005–2014 were obtained from the national vaccine-preventable disease surveillance system. Population estimates to calculate diphtheria incidence rates were obtained from the Population Division of the Economic Commission for Latin America and the Caribbean (ECLAC) (15).

For data on coverage with the third dose of a diphtheria-tetanus-pertussis vaccine (DTP3) in children less than 1 year of age, in relation to the outbreak, the study used 2003 DTP3 coverage rates by province (31 provinces) and health region (9 regions) as reported to EPI. For the remaining years, national coverage rates reported from the Dominican Republic to PAHO/WHO were used (12).

Statistical analyses

Outbreak data were entered into Microsoft Excel™ (Microsoft Corporation, Redmond, Washington, United States) and analyzed using its functions and Epi Info™ version 3.5 (CDC, Atlanta, Georgia, United States). A Poisson regression was used to compare the number of diphtheria cases in 2004 and 2005 with the average occurrence of cases by epidemiological week in 2000–2003, in order to assess the occurrence of a higher than expected number of cases. Linear regression was used to evaluate whether diphtheria incidence by province and health region was associated with reported DTP3 coverage. To determine risk factors for fatal diphtheria, the analyses used chi-square test and Fischer's exact test for discrete variables, as well as Wilcoxon for continuous variables (bivariate). Finally, a logistic regression (multivariate) was employed to control for clinical and demographic and socioeconomic factors. The results present adjusted odds ratios (OR) with 95% confidence intervals (95%CI) and consider $P < 0.05$ to be statistically significant.

This article evaluates an outbreak investigation using existing data; therefore, ethical review was not sought.

RESULTS

Outbreak description

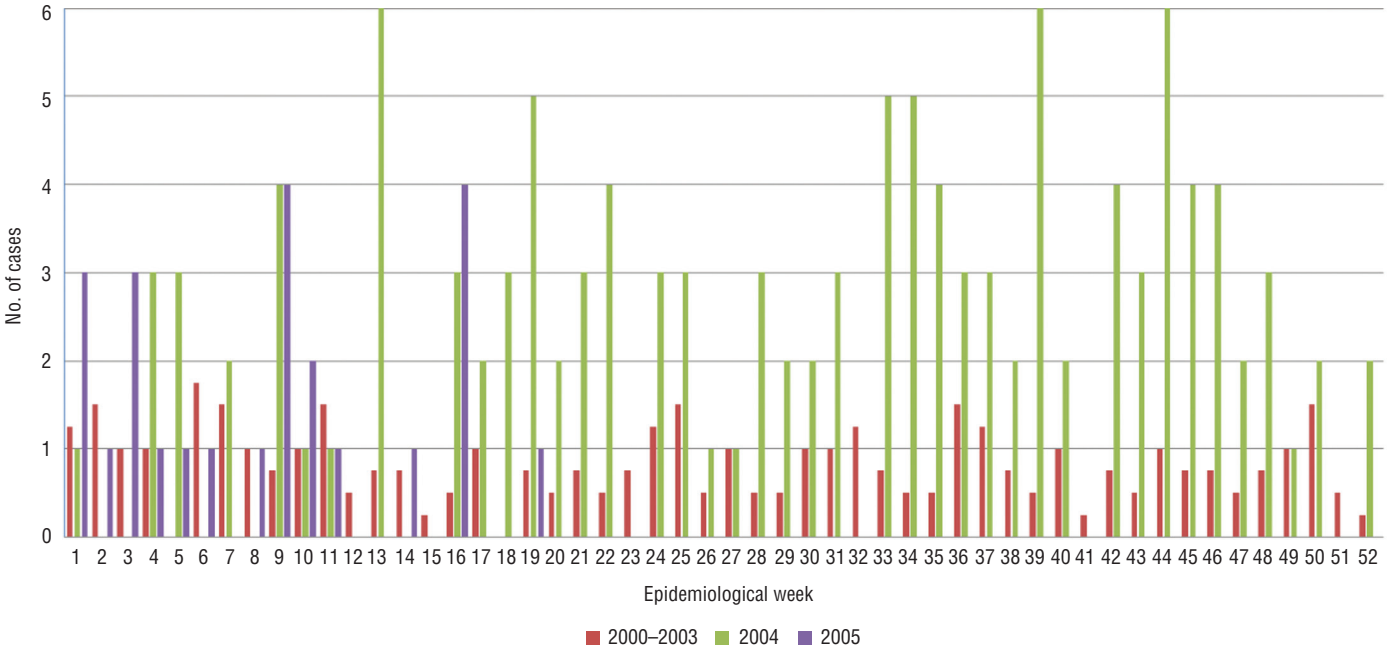
Using 2-week intervals, the number of diphtheria cases reported in 2004 and 2005 were compared to the average number reported in 2000–2003. This showed a statistically significant increase, with the first higher than expected number of cases appearing in week 9, 2004, and the last, in week 16, 2005 ($P < 0.001$) (Figure 1). No cutaneous diphtheria was reported.

Of the 145 cases reported in January 2004–April 2005 (week 16), 122 were reported in 2004 and 80 of these (66%) met

the case definition, either as clinically confirmed diphtheria (38 cases) or diphtheria confirmed by laboratory (42 cases, of which 3 were epidemiologically linked). All 16 isolated *C. diphtheriae* tested with RT-PCR and ribotyping were *Corynebacterium diphtheriae* biovar mitis.

The median age of the cases was 3 years, and ranged from 3 months–13 years. Incidence was highest in the 1–4 year age group at 5.3 per 100 000; 62.5% were male. The median income per family was approximately US$ 89, ranging from $18–$1 019 per month. Education level was primary school or less for 53 of the 71 guardians (75%) with this data; 14 had no formal education. Regarding households, 72% of the cases lived with at least three children less than 15 years of age. Of the 80 total cases, 61 were hospitalized in Hospital A; 17 in Hospital B; and 2 in two other hospitals. Cases in Hospital A were different from

FIGURE 1. Cases of diphtheria by epidemiological week, Dominican Republic, 2000–2005[a]



[a] Case average for years 2000–2003.

TABLE 1. Selected characteristics of diphtheria cases by hospital, Dominican Republic, 2004

Characteristic	Hospital A	Other hospitals	*P*	Laboratory-confirmed cases	Clinically confirmed cases	*P*
Confirmation criteria						
Lab	38	4	0.002			
Clinical	23	15				
Area						
Urban and peri-urban	39	12	0.910	27	24	0.313
Rural	14	4		12	6	
Sex						
Female	21	9	0.308	11	19	0.028
Male	40	10		31	19	
Vaccination status						
Up-to-date for age	4	6	0.011	0	10	0.000
Unvaccinated or undervaccinated	55	13		41	27	
Parental education						
No education	13	1		11	3	
1–8 years	31	8	0.242	18	21	0.036
9–12 years	8	4	0.117	4	8	0.019
> 12 years	2	4	0.005	1	5	0.018
Tracheotomy						
Yes	17	3	0.258	15	5	0.014
No	42	16		25	33	
Contact vaccination						
Yes	55	22	0.032	36	31	0.053
No	2	5		1	6	
Contact antibiotic use						
Yes	36	6	0.034	19	23	0.278
No	20	11		18	13	

cases in other hospitals in terms of confirmation criteria, vaccination history, case-fatality rate, guardian education, and contact management (Table 1). The difference between the confirmation criteria in the two hospital groups is lost after week 24, when Hospital B started doing culture for *C. diphtheriae*.

The median period between symptom onset and hospitalization was 3 days, ranging from 0–11 days. The length of hospitalization for those who recovered was 7.5 days (median), ranging from 2–37 days. Regarding treatment, of the 70 cases with information available on the use of DAT, only two cases did not receive it; one died upon arrival at the hospital. In Hospital A, 86% of the cases received high doses of DAT (≥ 80 000 units), compared to 39% in other hospitals ($P < 0.001$). All cases were given antibiotics in the hospital, except the case that died upon arrival. Of the 54 cases for which the antibiotic administered was recorded, 53 (98%) received penicillin and 1 received a cephalosporin. Twenty-six cases (48%) also received chloramphenicol (all in Hospital A). For 36 cases, the use of corticosteroids was also registered, not varying by hospital. Vaccination with diphtheria toxoid-containing vaccines upon hospitalization was not systematically recorded.

Most cases occurred in the National District, where the capital city of Santo Domingo is located, and in Santiago, with 29 and 10 cases, respectively. These two provinces concentrated approximately 48% of the 2004 country's population. The remaining 39 cases were distributed in 18 of the 31 provinces of the country (in 8 of the country's 9 health regions), with variable incidence rates.

Of the 78 cases with vaccination data recorded, 10 (13%) were considered to be adequately vaccinated for their age; all but one of these children recovered. The exception was a 15-month old child who had received three diphtheria toxoid-containing vaccine doses. No adequately vaccinated child had laboratory-confirmed diphtheria. The national 2003 DTP3 coverage reported in the country was 75% (range: 57%–155% by province and 64%–95% by health region). No correlation between diphtheria incidence and routine DTP3 coverage rates by province or health region was found ($R^2 = 0.02$; $P > 0.438$).

Contacts

Vaccination was indicated for household contacts of 67 (91%) of the 74 cases with this information recorded. However, vaccination follow-up to complete series was not recorded. The investigation also noted the frequent indiscriminate vaccination of neighbors, but the magnitude of this occurrence was not quantified. Antibiotic prophylaxis was indicated for the contacts of 41 (57%) of 72 cases with this information available; however, it was not indicated for all household members in 13 of them. The proportion of cases whose contacts were given antibiotics changed from 35.3% between epidemiological weeks 1–24 to 76.3% after week 24 ($P = 0.001$), when contact management guidelines were issued.

Fatal diphtheria

Of the 80 cases, 26 died, resulting in a case-fatality rate (CFR) of 32.5%. CFR was highest (41%) at Hospital A (Table 1). The median age of children with fatal diphtheria was 24 months of age (range: 13 months–8 years). Of the fatal cases, 24 were reported as having complications: 22 respiratory, 1 cardiovascular, and 1 both. The median number of days between symptom onset and death was 4 days (range: 1–12 days), and between hospitalization and death was 1 day (range: 0–4 days). The cause of death was recorded in the medical chart for 21 cases: "cardiorespiratory arrest" for 10 (47.6%); "respiratory insufficiency" for 8 (38.1%); and "septic shock," "toxigenic shock," and "possible myocarditis" for 1 (4.8%) each.

After the bivariate analysis, the multivariate model included the period of occurrence of the case, tracheotomy, days between onset and hospitalization, presence of cervical edema, presence of complications, hospital, and child's birth order in the family. Period of onset, birth order, and tracheotomy were associated with fatal diphtheria at $P < 0.05$; hospital was associated with a $P = 0.066$ (Table 2).

Diphtheria incidence and vaccination coverage

The average annual incidence of diphtheria in 2000–2003 was 4.91 cases per 1 million. In 2004–2005, it reached 8.8 / 1 million. For the period 2006–2014, it was reduced to 0.38 / 1 million. Figure 2 shows the number of reported diphtheria cases by year.

In the Dominican Republic, the routine immunization schedule recommends three primary doses of diphtheria toxoid-containing vaccines at 2, 4, and 6 months, and two booster doses at 18 months and 4 years of age. Reported coverage levels with three doses of DTP-containing vaccines (DTP3) among children less than 1 year of age fluctuated from 72%–83% between 1994 and 2003, with marked disparities within the country. Coverage of booster DTP is not routinely monitored. DTP3 coverage rates have shown some increase since 2004, but until 2013 remained below 90% (Figure 2).

DISCUSSION

The largest outbreak of diphtheria in the Western Hemisphere this century occurred in 2004–2005 in the Dominican Republic and in neighboring Haiti. Following this outbreak, diphtheria incidence in the Dominican Republic progressively declined until 2012, when for the first time ever, no diphtheria case was reported in the country.

The outbreak in the Dominican Republic was likely the result of several factors, but mainly due to the existence of pockets of unvaccinated children. Most cases lived in low-income urban areas with difficult access to vaccination posts. Unlike the resurgence of diphtheria that occurred in the former Soviet Union (4, 5) and in Ecuador in 1994 (7), which affected mostly young adults, in the Dominican Republic, children 1–4 years of age were most at-risk, suggesting that recent low coverage levels were the main factor responsible for this outbreak. Failures in the cold chain, notably freezing of diphtheria-containing vaccines, may not be ruled-out as a contributing factor, but the cold chain was not assessed. Observation also suggested that urban cases came from new settlements in the outskirts of cities, where access to health services is limited.

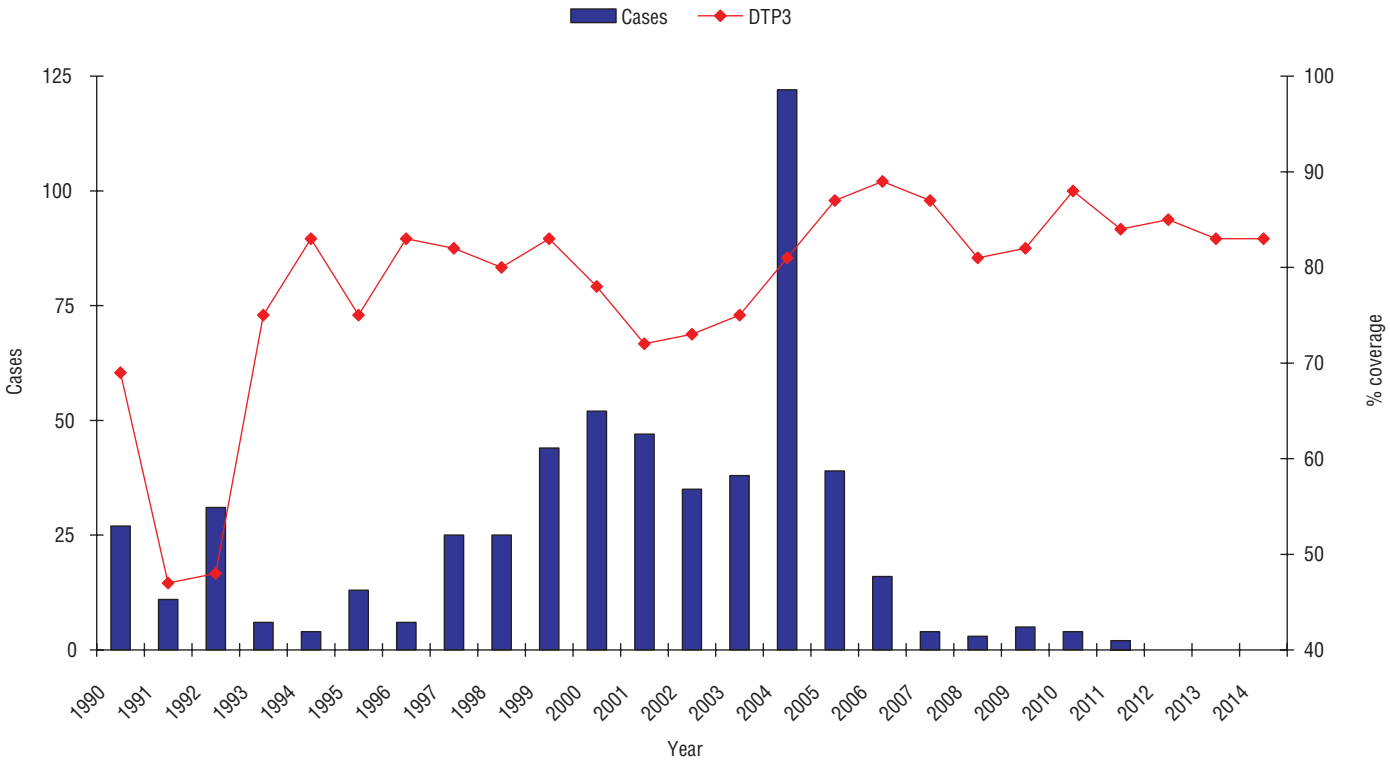
Even though diphtheria was endemic in the Dominican Republic and case investigation and follow-up guidelines existed at the beginning of the outbreak, it was difficult to implement outbreak control vaccination activities and to manage household contacts. Also, the initial access to DAT was not smooth.

CFRs were higher than reported in other settings (1–3, 6), particularly in Hospital A. Mild cases may not have been recognized and reported. Also, Hospital A, being the national children's

TABLE 2. Factors associated with diphtheria fatal outcome, Dominican Republic, 2004

Variable		Overall		Deceased		Recovered		Univariate			Multivariate		
		No.	%	No.	%	No.	%	Risk ratio	95% Confidence interval	*P* value	Odds ratio	95% Confidence interval	*P* value
Age in months (m) or years (y) (*n* = 80)	Median (range)	3 years (3m–13y)		24 months (13m–8y)		42 months (3m–13y)				0.145			
	< 2 years	21	26.3	10	38.5	11	20.4	1.7	0.79–3.68	0.17			
	2–4 years	34	42.5	9	34.6	25	46.3	0.95	0.41–2.19	0.896			
	5–14 years	25	31.3	7	26.9	18	33.3	Ref					
Sex (*n* = 80)	Male	50	62.5	19	73.1	31	57.4	1.63	0.78–3.41	0.175			
	Female	30	37.5	7	26.9	23	42.6	Ref					
Zone (*n* = 69)	Rural	18	26.1	6	28.6	12	25.0	Ref					
	Urban	51	73.9	15	71.4	36	75.0	0.88	0.40–1.92	0.756			
Period of onset (*n* = 80)	EPI weeks 1–24	34	42.5	14	53.8	20	37.0	1.58	0.84–2.97	0.154	5.29	1.18–23.71	0.3
	EPI weeks 25–52	46	57.5	12	46.2	34	63.0	Ref					
Vaccination (*n* = 78)	Adequate	10	12.8	1	4.0	9	17.0	Ref					
	Inadequate	68	87.2	24	96.0	44	83.0	3.53	0.53–23.29	0.015			
Hospital (*n* = 80)	A	61	76.3	24	92.3	37	68.5	3.74	0.97–14.38	0.019			
	B or other	19	23.8	2	7.7	17	31.5	Ref					
Maternal (or guardian) education (*n* =71)	None	14	19.7	5	25.0	9	17.6	2.14	0.61–7.41	0.217			
	Grade 1–8	39	54.9	12	60.0	27	52.9	1.85	0.59–5.75	0.261			
	Grade 9+	18	25.4	3	15.0	15	29.4	Ref					
Crowding (*n* = 76)	Median (range)	3.2 (1.3–20)		3.7 (1.5–9.0)		3 (1.3–20)				0.75			
	1–<3 persons/ room	26	34.2	7	30.4	19	35.8	Ref					
	3–<5 persons/ room	29	38.2	9	39.1	20	37.7	1.15	0.50–2.65	0.734			
	5+ persons/room	21	27.6	7	30.4	14	26.4	1.24	0.52–2.97	0.633			
Household income (US$) (*n* = 68)	Median (range)	89.2 (17.8–1019.4)		89.2 (17.8–203.9)		82.8 (19.1–1019.4)				0.661			
	≤50	20	29.4	5	25.0	15	31.3	0.83	0.33–2.12	0.7			
	51–100	18	26.5	6	30.0	12	25.0	1.11	0.47–2.60	0.89			
	>100	30	44.1	9	45.0	21	43.8	Ref					
Number of children (*n* = 76)	Median (range)	3 (1–8)		4 (2–6)		3 (1–8)				0.105			
	1–3 children	45	59.2	10	43.5	35	66.0	Ref					
	4–5 children	23	30.3	9	39.1	14	26.4	1.76	0.83–3.72	0.141			
	6+ children	8	10.5	4	17.4	4	7.5	2.25	0.93–5.44	0.186			
Birth order (*n* = 75)	Median (range)	2 (1–8)		3 (1–8)		2 (1–8)				0.025			
	1st or 2nd	39	52.0	6	27.3	33	62.3	Ref					
	3rd or more	36	48.0	16	72.7	20	37.7	2.89	1.27–6.57	0.006	1.24	0.99–1.54	0.53
Contact with other case (*n* = 42)	Yes	16	38.1	6	50.0	10	33.3	1.63	0.63–4.18	0.315			
	No	26	61.9	6	50.0	20	66.7	Ref					
Days between symptoms onset and hospitalization (*n* =78)	Median (range)	3 (0–11)		2 (0–10)		3 (0–11)				0.24			
	0–1 days	14	17.9	5	20.8	9	16.7	1.53	0.64–3.65	0.358			
	2 days	17	21.8	8	33.3	9	16.7	2.01	0.98–4.14	0.067			
	3+ days	47	60.3	11	45.8	36	66.7	Ref					
Use of antitoxin (*n* = 70)	Yes	68	97.1	19	90.5	49	100.0	Ref					
	No	2	2.9	2	9.5	0	0.0	3.58	2.44–5.24	0.087			
Dose of antitoxin (*n* = 62)	<80 000 U	18	29.0	3	16.7	14	31.8	0.53	0.18–1.60	0.185			
	80 000+ U	44	71.0	15	83.3	30	68.2	Ref					
Days between symptoms onset and use of antitoxin (*n* = 55)	Median (range)	3 (0–11)		2 (1–10)		3 (0–11)				0.136			
	0–1 days	6	10.9	3	16.7	3	8.1	1.94	0.71–5.26	0.235			
	2 days	18	32.7	7	38.9	11	29.7	1.51	0.66–3.46	0.338			
	>=3 days	31	56.4	8	44.4	23	62.2	Ref					
Tracheotomy (*n* = 78)	Yes	20	25.6	14	58.3	6	11.1	4.06	2.16–7.64	<0.001	9.3	1.81–47.63	0.007
	No	58	74.4	10	41.7	48	88.9	Ref					
General situation (*n* = 71)	Not compromised	20	28.2	1	4.3	19	39.6	Ref					
	Compromised	38	53.5	15	65.2	23	47.9	7.89	1.12–55.52	0.005			
	Toxic	13	18.3	7	30.4	6	12.5	10.77	1.49–77.65	0.001			
Cervical edema (*n* = 77)	Yes	20	26.0	7	30.4	13	24.1	1.25	0.60–2.58	0.56			
	No	57	74.0	16	69.6	41	75.9	Ref					
Complications (*n* = 76)	Yes	59	77.6	24	100.0	35	67.3	Undef		0.001			
	No	17	22.4	0	0.0	17	32.7	Ref					
Corticosteroids (*n* = 50)	Yes	36	72.0	12	75.0	24	70.6	1.17	0.45–3.01	1			
	No	14	28.0	4	25.0	10	29.4	Ref					
Antibiotic prior to hospitalization (*n* = 66)	Yes	32	57.1	8	47.1	24	61.5	0.67	0.30–1.47	0.314			
	No	24	42.9	9	52.9	15	38.5	Ref					

FIGURE 2. Reported diphtheria cases and DTP3 coverage rates, the Dominican Republic, 1990–2014[a]



[a] Data for 2014 are preliminary, as of 26 December 2014.

referral hospital, likely received the more dire cases. The inverse relation observed between symptoms onset and hospitalization, and therefore the earlier use of DAT, may reflect that only children with severe diphtheria were diagnosed or that symptom onset may have occurred earlier than reported, but that the guardian only reported the symptoms when they became severe. Also, the decline in CFR during the second semester of 2004 may reflect an improvement in case recognition and management following meetings and the development and circulation of clinical management protocols. Interestingly, myocarditis, one of the most common causes of death due to diphtheria described in the literature (1–3), was only reported as the cause of death in one case. This suggests limited recognition of this condition, confusion with respiratory complications, limitations in diagnosing myocarditis (by electrocardiogram), lack of proper cause of death registration, or a mix of these factors.

Outbreak investigation and control measures seemed to have had an important impact on the course of the outbreak and on diphtheria occurrence in the Dominican Republic. The outbreak resulted in the revision of diphtheria case definitions and the epidemiological case-investigation form; the development and update of protocols for clinical management, specimen collection and processing; enhanced laboratory diagnosis capabilities; improved management of DAT stocks for prompt availability; and improved procedures for epidemiological surveillance, case investigation, and contact management (16). The release and wide dissemination of revised guidelines for case and contact management likely had a significant impact on case outcome. Finally, the thorough investigation of this outbreak allowed for more focused vaccination interventions.

To control the outbreak, the Dominican Republic focused the 2005 Vaccination Week in the Americas (VWA) activities on completing immunization schedules nationwide. VWA, which ran during the last days of April–start of May, coincided with the end of the outbreak. Countries of the Americas have continued using VWA as an opportunity to update vaccination schedules (17, 18).

The reduction of diphtheria incidence in the Dominican Republic following the outbreak is encouraging, but without sustained high vaccination coverage rates, the risk of resurgence remains. Neighboring Haiti continues to report diphtheria cases and deaths (12). In the Dominican Republic, reported coverage rates with DTP3 among children less than 1 year of age following the outbreak are slightly higher than in years prior, but they remain < 90%. Catch-up of older children may be occurring, but this is not routinely quantified.

Limitations

This outbreak investigation has several limitations. It is based on the analysis of surveillance data in the context of an outbreak. Even though routine case investigation was enhanced by interviews and chart reviews, this was not a "study" with dedicated personnel. Underdiagnosis and underreporting was likely widespread, as case ascertainment was based on passive surveillance, starting with those cases that were physician-diagnosed and reported. Furthermore, our analysis focused only on hospitalized cases in 2004 and had to meet a more specific case definition than the one used regularly in the country.

Also, at the beginning of the outbreak, laboratory confirmation was only available in Hospital A. Determining risk factors for diphtheria occurrence was limited due to the lack of a comparison group. Regarding vaccination status of cases, even though local health centers were visited to check vaccination registries, particularly for preschool children, we considered only documented vaccination history, which may have led to misclassification since some vaccinated persons may not have been recorded as such. It's also likely that there was some degree of recall bias depending on outcome and interval between disease and interview. Finally, for clinical features, we relied on the attending physician's diagnosis using non-standardized procedures for recording signs, complications (including confirmatory tests, e.g., electrocardiograms and x-rays), and cause of death, and medical charts of varying quality for clinical variables. In spite of these limitations, we believe that the main findings stand: the outbreak affected mainly inadequately-vaccinated persons living in poverty.

Conclusions

The current limited availability of DAT in the world makes diphtheria occurrence extremely worrisome at this time (8, 9). In the Americas, only the United States currently has ready access to DAT, but it is through a new investigational drug protocol and the stock is very limited (19).

This last outbreak in the Dominican Republic serves as a reminder that diphtheria can result in unnecessary morbidity and mortality. To prevent diphtheria outbreaks, it is important to ensure high and homogeneous vaccination coverage and epidemiological surveillance systems that are able to detect diphtheria cases early, allowing for prompt and aggressive control measures.

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Difteria en la República Dominicana: reducción de casos tras un extenso brote epidémico

RESUMEN

Objetivo. Describir el brote epidémico más reciente de difteria en la República Dominicana, la incidencia de la enfermedad y la cobertura de la vacunación del 2004 al 2013.

Métodos. Se analizaron los datos clínicos de los casos de difteria acaecidos en el 2004 y que cumplieron con la definición de caso del estudio, junto con la información socioeconómica y epidemiológica de las familias en las que aparecieron los casos. Se llevaron a cabo análisis de una sola variable y de múltiples variables para evaluar los factores de riesgo de difteria mortal. Se presentan los datos de vigilancia ordinaria y cobertura vacunal.

Resultados. De enero del 2004 a abril del 2005, se notificaron un total de 145 casos de difteria; 80 (66%) de los 122 casos notificados en el 2004 cumplieron con la definición de caso; 26 fueron mortales (tasa de letalidad por caso: 32,5%). La incidencia más alta (5,3 por 100 000) se produjo en el grupo de 1 a 4 años de edad; 62,5% fueron varones. De los 80 casos, 61 (76%) se hospitalizaron en el Hospital A, 17 en el Hospital B, y 2 en otros dos hospitales. La aparición más temprana (primera mitad del 2004), el orden de nacimiento y la traqueotomía se asociaron con difteria mortal ($P < 0$,05); la probabilidad de evolución mortal fue mayor en los casos ingresados en el Hospital A ($P = 0,066$). La incidencia promedio anual de difteria fue de 4,91 casos por millón de personas del 2000 al 2003, ascendió a 8,8 casos por millón durante los años 2004 y 2005, y descendió a 0,38 del 2006 al 2014; no se han notificado casos de difteria desde el 2011. La cobertura de la vacunación con DTP3 varió de 72 a 81% del 2000 al 2004 y de 81 a 89% del 2005 al 2013.

Conclusiones. El brote epidémico de difteria de los años 2004 y 2005 en la República Dominicana ocasionó una importante morbimortalidad prevenible. Se produjo un descenso en la incidencia de casos y no se han notificado nuevos casos en los últimos años. El mantenimiento de una alta cobertura vacunal y de una vigilancia eficiente es crucial para la prevención de los brotes epidémicos de difteria y el control de la enfermedad.

Palabras clave Difteria; vacunacion; brotes de enfermedades; República Dominicana.