Seroprevalence of Measles, Rubella, Tetanus, and Diphtheria Antibodies among Children in Haiti, 2017

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Abstract. In Haiti, measles, rubella, and maternal and neonatal tetanus have been eliminated, but a diphtheria outbreak is ongoing as of 2019. We conducted a nationally representative, household-based, two-stage cluster survey among children aged 5–7 years in 2017 to assess progress toward maintenance of control and elimination of selected vaccine-preventable diseases (VPDs). We stratified Haiti into West region (West department, including the capital city) and non-West region (all other departments). We obtained vaccination history and dried blood spots, and measured antibody concentrations to VPDs on a multiplex bead assay. Among 1,146 children, national seropositivity was 83% (95% CI: 80–86%) for tetanus, 83% (95% CI: 81–85%) for diphtheria, 87% (95% CI: 85–89%) for measles, and 84% (95% CI: 81–87%) for rubella. None of the children had long-term immunity to tetanus or diphtheria (IgG concentration ≥ 1 international unit/mL). Seropositivity in the West region was lower than that in the non-West region. Vaccination coverage was 68% (95% CI: 61–74%) for ≥3 doses of tetanus- and diphtheria-containing vaccine (DTP3), 84% (95% CI: 80–87%) for one dose of measles-rubella vaccine (MR1), and 20% (95% CI: 16–24%) for MR2. The seroprevalence of measles, rubella, and diphtheria antibodies is lower than population immunity levels needed to prevent disease transmission, particularly in the West region; reintroduction of these diseases could lead to an outbreak. To maintain VPD control and elimination, Haiti should achieve DTP3 and MR2 coverage ≥95%, and include tetanus and diphtheria booster doses in the routine immunization schedule.

INTRODUCTION

An essential function of national immunization programs is to routinely estimate vaccination coverage to evaluate performance and assess progress toward maintenance of vaccine-preventable disease (VPD) control and elimination. Serosurveys measuring antibody responses to VPDs offer an objective measure of population immunity that can be useful to identify immunity gaps, monitor progress toward VPD elimination, investigate causes of disease resurgence, and, in certain settings, estimate vaccination coverage.1-3 The immune response to vaccination depends on several factors, including the individual’s humoral and cellular immune system, age at vaccination, type of vaccine (live versus inactivated), and number of doses received.1,4,5

Haiti’s national immunization program has made significant progress toward the Pan American Health Organization (PAHO) regional VPD elimination goals. The last confirmed measles and rubella cases occurred in 2001 and 2006, respectively,5 and measles and rubella/congenital rubella syndromes were verified to be eliminated in 2014.6 Maternal and neonatal tetanus were verified to be eliminated in 2017.7,8 However, a diphtheria outbreak started in Haiti in 20144 and continues as of December 2019.10,11 In addition, Haiti has not reached the vaccination coverage targets recommended by the PAHO.12,13

Three doses of diphtheria–tetanus–pertussis containing vaccine (DTP) at 6, 10, and 14 weeks, and one dose of measles–rubella vaccine (MR) at 9 months are recommended in the routine vaccination schedule. Diphtheria toxoid and tetanus toxoid are the antigens of interest in this survey. Measles–rubella vaccination campaigns targeting children aged 9 months to 9 years and 9–59 months were conducted in 2012 and 2016, respectively.5 A second dose of MR at 13 months of age was introduced in 2016.14 A booster dose of DTP has been recommended for children aged 15 months since the 1980s, except 2012–2015 because of financial constraints.

Data on measles, rubella, diphtheria, and tetanus immunity among children in Haiti are unknown and are needed to evaluate progress toward maintaining elimination and preventing epidemics. We conducted this survey to estimate immunity to these VPDs among children aged 5–7 years at the time of the survey. We compared serologic results with survey estimates of DTP and MR coverage.

MATERIALS AND METHODS

Design and sampling. The survey was a nationally representative, household-based, stratified, two-stage cluster survey conducted in November 2017. The survey was designed to estimate chronic hepatitis B virus (HBV) infection and immunity to diphtheria, tetanus, measles, and rubella. Haiti was stratified into West region, which contains the West department (including the urban metropolitan Port-au-Prince, where 1/3 of Haiti’s population lives),15 and non-West region (all other departments). The primary and secondary sampling units were 78 enumeration areas (EAs) per region, selected by
probability proportional to size, and 62 households per EA, selected by simple random sampling. A total of 4,836 households were targeted with the goal to recruit at least 455 children aged 5–7 years per region. For EAs containing 62 or fewer households, all households were included in the survey. During the survey, the teams conducted two revisits to a household before determining that a household was unoccupied or that an eligible child did not live in the household. If more than one eligible child was present, then one child was selected by simple random sampling. Children were included in the survey if the caregiver gave consent for the child’s participation. Further details of age selection, sampling, and the sample size calculation, which were based on the estimated HBV infection prevalence, are reported elsewhere.16

Data collection. A questionnaire was administered to caregivers, which included questions about household composition, caregiver’s demographics and socioeconomic characteristics, child’s demographics and education level, and child’s vaccination status. Caregivers were asked to present all cards from routine vaccination visits and campaigns.

At least three drops of blood were collected by finger prick onto TropBio filter wheels (Cellabs, Sydney, Australia). The blood spots were dried in the field (creating dried blood spots [DBS]), and then transported to the National Public Health Laboratory in Port-au-Prince, where they were stored in the freezer at −40°C. Dried blood spots were analyzed at the CDC Atlanta.

Laboratory methods and analysis. Corynebacterium diphtheriae toxoid (List Biological Laboratories, Campbell, CA), tetanus toxoid (Massachusetts Biological Laboratories, Boston, MA), and recombinant measles virus N (MVN) protein (Meridian Life Sciences, Memphis, TN) were purchased from the indicated sources. Recombinant MVN protein from insect cell expression was partially purified by MonoQ HR5/5 column chromatography (GE Healthcare, Piscataway, NJ) in buffer containing 25 mM Tris at pH 8.0. Measles virus N protein was dialyzed (Spectra Por-3 tubing, Spectrum Laboratories, Rancho Dominguez, CA) into buffer containing 10 mM NaCl and was dialyzed (Spectra Por-3 tubing, Spectrum Laboratories, Rancho Dominguez, CA) into buffer containing 10 mM NaHPO₄ at pH 7.2 with 0.85% NaCl (phosphate-buffered saline [PBS]). Bead coupling conditions have been described elsewhere.17,18 Because the magnetic beads are larger than the previously used SeroMap beads, the protein amounts were increased by 15%; 14.4 μg of tetanus toxoid, 69 μg of diphtheria toxoid, and 69 μg of measles virus N protein were used to couple 12.5 × 10⁶ magnetic beads in a 1-mL final volume. Inactivated whole rubella virus (Meridian Life Sciences, grade 4) was coupled using 34.5 μg for 12.5 × 10⁶ magnetic beads in 1 mL of buffer containing 50 mM 2-(N-morpholino)ethanesulfonic acid at pH 5.0% and 0.85% NaCl.

For each specimen, a single 6-mm punch of DBS was eluted in buffer B (PBS containing 0.5% bovine serum albumin [BSA], 0.3% Tween-20, 0.1% casein, 0.02% sodium azide, 0.5% polyvinyl alcohol, 0.8% polyvinylpyrrolidone, and 3 μg/mL E. coli extract) by incubation overnight at 4°C. A final dilution of 1:200 whole blood (equivalent to 1:400 serum dilution with 50% hematocrit assumption in whole blood) was prepared in buffer B, and specimens were stored at 4°C until analysis.

For the detection of IgG antibodies against the antigens coupled to microbeads, the multiplex bead assay (MBA) was performed as described previously19 in flat bottom Bio-Plex Pro 96-well plates (Bio-Rad, Hercules, CA), with specimens run in duplicate. Washes between incubation steps used a handheld magnet (Luminex Corp, Austin, TX). Beads (250,000 beads/antigen/plate) were suspended in buffer A (PBS, 0.5% BSA, 0.05% Tween-20, and 0.02% NaN₃), and 50 μL of bead mastermix was added to each well. After addition of 200 μL wash buffer (PBS, 0.05% Tween-20; [PBS]) to each well, wash buffer was left in each well for one minute to allow bead magnetization before inverting the plate to evacuate the wells of liquid. Plates were washed twice with PBS, and 50 μL of specimen (at 1:200 whole blood dilution) was added to each well and incubated with shaking at room temperature for 90 minutes. After three washes with PBS, beads were incubated with biotinylated antihuman IgG (1:500, Southern Biotech, Birmingham, AL) and biotinylated antihuman IgG₅ (1:625, Southern Biotech). Then, plates were incubated for 45 minutes and washed three times with PBS and biotinylated antihuman IgG₅ conjugated to phycoerythrin (PE) (1:200, Invitrogen, Waltham, MA) was added to detect bound secondary antibody. After a 30-minute incubation, wells were washed three times with PBS and incubated in buffer A for 30 minutes under light shaking to remove any loosely bound antibodies. Specimens were resuspended in 100 μL PBS, and fluorescence data were collected immediately on the MAGPIX with Bio-Plex Manager™ software 6.1 (Bio-Rad, Hercules, CA) with a target of 50 beads per region per well. Median fluorescence intensity (MFI) signal was generated for a minimum of 50 beads/region, and background MFI from wells incubated with buffer B was subtracted from each specimen to give a final value of MFI minus background (MFI-bg) for analysis.

Serial dilutions of reference serum standards from the WHO International Laboratory for Biological Standards were made for tetanus (TE-3; 120 international units/mL [IU/mL]), rubella (67/182; 80 IU/mL), and diphtheria (10/262; 2 IU/mL). These dilution series were run under the same assay conditions listed earlier and on the same MAGPIX machine as the unknown specimens. Regression curves for each standard were produced to translate an unknown specimen’s MFI-bg assay signal value to an IgG concentration of IU/mL serum. A reference standard for the measles virus plaque reduction neutralization test (PRNT)20, 3 IU/mL is available for the quantitation of total virus-neutralizing antibody responses, but the standard has not been calibrated for use in ELISA format. Because only IgG antibodies to the MVN protein are detected in our multiplex assay, a ROC-optimized MFI-bg cutoff value that provided good sensitivity and specificity compared with the "gold standard" PRNT was determined (Coughlin et al., unpublished).18 This value was translated to the magnetic bead set used in this work and was determined to be 314 MFI-bg units.

Seropositivity for tetanus, diphtheria, and rubella antibodies was defined by extrapolated IU/mL antibody concentration. Tetanus and diphtheria antibody seropositivities were defined using the standard cutoff of 0.01 IU/mL.21–24 Tetanus and diphtheria antibody seropositivity cutoffs were further categorized as IgG < 0.01 IU/mL, 0.01 to < 0.1 IU/mL, 0.10 to < 1 IU/mL, and 1 IU/mL.17,23 These categories are associated with a lack of protection, minimal protection, full protection, and long-term protection against diphtheria.21 Increasing antibody concentrations against tetanus are associated with a decreased risk of infection and longer term protection.22,25,26 Rubella antibody seropositivity was defined
as ≥ 10 IU/mL. Measles antibody seropositivity was defined as 314 MFI-bg units, as described previously.

**Statistical analysis.** Data from the questionnaires were entered into a Microsoft Access (Microsoft Corp., Redmond, WA) database and analyzed using SAS 9.4 (The SAS Institute, Cary, NC). Descriptive analyses of demographic and socioeconomic characteristics were calculated. Seroprevalence and vaccination coverage estimates, both nationally and for the West and non-West regions, were calculated, accounting for survey design, which included strata, cluster, and weight statements. The SAS statements and survey weight calculations used in this survey are described elsewhere. The number of card-documented doses and dates of vaccination (if noted on card) with any diphtheria-tetanus-pertussis containing vaccine (DTP) and MR was noted. Diphtheria–tetanus–pertussis containing vaccine was recorded as DTP1–4+ (DTP doses 1–4 or more), and MR coverage from routine or campaign cards was combined and recorded as MR1 and MR2+. For children without a card, caregiver recall was used to determine vaccination status. If the caregiver answered “I don’t know” to whether the child received any doses or to the number of doses, the child was coded as missing vaccination data. Vaccination coverage estimates by card documentation and caregiver recall were combined to determine coverage by either source.

Diphtheria–tetanus–pertussis containing vaccine 3+ and MR2+ were considered fully vaccinated because the children had been eligible for three doses of DTP through the routine system and two doses of MR through the routine system plus campaigns. The median time to vaccination was assessed using survival analysis among children with dates on their routine vaccination card, and results were displayed with Kaplan–Meier curves, highlighting timely vaccination (within 2 weeks for DTP1 and DTP3 and 1 month for MR1). Measles–rubella vaccine 2 timeliness was not calculated because MR2 was introduced into the routine immunization program in 2016.

Rao–Scott chi-square tests were used to determine associations between demographic and socioeconomic factors with antibody seropositivity and vaccination coverage, and to compare vaccination coverage to antibody seropositivity. A P-value of < 0.05 was considered statistically significant for all tests.

**Ethics/human subjects.** The National Bioethics Committee in Haiti and the PAHO Ethics Review Committee reviewed and approved the protocol. The Human Subjects Protection Office at the CDC reviewed the protocol, and the protocol did not require review by the Institutional Review Board.

**RESULTS**

**General characteristics.** During the household enumeration, some EAs contained fewer than 62 households, so a total of 4,736 households were included for inclusion in the survey. Of 4,736 households, contact was made at 4,587 (97%) households during the survey, and 1,181 households (26%) of the 4,587 households included at least one child aged 5–7 years. Among 1,181 children identified for potential enrollment, 1,152 (98%) caregivers provided consent. Of the 1,152 children included in the survey, 1,146 (99%) had enough DBS specimen to be included in the analyses. Of the 1,146 children included in the survey, 524 (46%) lived in the West region and 622 (54%) lived in the non-West region. Among children, 50% were male and 62% were in primary school. Among the children’s caregivers, 75% had a job and 33% had at least some secondary school education (Table 1). Characteristics of the children and their caregivers were similar by region, except that caregivers in the West region had a higher education level than caregivers in the non-West region (P = 0.01).

**Seropositivity.** Nationally, the weighted seropositivity among children aged 5–7 years in Haiti in 2017 was 83% (95% CI: 81–85%) for diphtheria antibody, 83% (95% CI: 80–86%) for tetanus antibody, 84% (95% CI: 81–87%) for rubella antibody, and 87% (95% CI: 85–89%) for measles antibody (Table 2). Seropositivity for diphtheria, tetanus, and measles antibodies was significantly lower in the West region than in the non-West Region. Seropositivity against rubella was lower in the West region, but the difference was not statistically significant (Table 2). None of the enrolled children had tetanus or diphtheria IgG concentrations ≥ 1.0 IU/mL (Table 2). When comparing antibody seropositivity with each component of the combination vaccines, 8% (95% CI: 6–11%) of children were immune to tetanus only, 9% (95% CI: 7–11%) were immune to diphtheria only, 75% (95% CI: 71–77%) were immune to both, and 9% (95% CI: 7–11%) were susceptible to both. Furthermore, 6% (95% CI: 5–9%) of children were immune to measles only, 3% (95% CI: 2–4%) were immune to rubella only, 81% (95% CI: 78–84%) were immune to both, and 10% (95% CI: 8–12%) were susceptible to both.

**Vaccination coverage.** Of 1,146 enrolled children, 552 (49%) had a routine vaccination card available, 145 (13%) had a campaign card from the 2012 and/or 2016 campaigns, and 603 (54%) had either a routine or campaign card. There was no difference among children from the West and non-West regions regarding card availability (P = 0.8). Few children had both routine and campaign cards (94/1,146, 8%). For children without vaccination cards, the caregivers were most likely to report that the card was in another location (48%) or that the caregiver lost the card (43%). Diphtheria–tetanus–pertussis containing vaccine or MR status was unknown for 186 (16%) and 177 (15%) participants, respectively. Diphtheria–tetanus–pertussis vaccine coverage by card or recall was as follows: DTP1 91% (95% CI: 87–94%), DTP2 84% (95% CI: 78–88%), DTP3 68% (95% CI: 61–74%), and DTP4+ 34% (95% CI: 30–39%). Measles–rubella vaccine 1 coverage by card or recall was 84% (95% CI: 80–87%), and MR2+ coverage was 20% (95% CI: 16–24%). There was no difference in vaccination coverage between the West and non-West regions (Table 3). Of 552 children with cards, vaccination dates were available for 515 (93%) for DTP1, 465 (84%) for DTP3, and 451 (82%) for MR1. The median time to receipt of DTP1 was 10 weeks, DTP3 was 515 (93%) for DTP1, 465 (84%) for DTP3, and 451 (82%) for MR1. The median time to receipt of DTP1 was 10 weeks, DTP3 was 515 (93%) for DTP1, 465 (84%) for DTP3, and 451 (82%) for MR1. The median time to receipt of DTP1 was 10 weeks, DTP3 was 515 (93%) for DTP1, 465 (84%) for DTP3, and 451 (82%) for MR1. The median time to receipt of DTP1 was 10 weeks, DTP3 was 515 (93%) for DTP1, 465 (84%) for DTP3, and 451 (82%) for MR1.
A sensitivity analysis was performed among children with cards to investigate whether card coverage would more accurately reflect immunity than recall. Immunity by vaccination status was similar for all antigens whether measured by card only or card and recall. For tetanus immunity, there were only 16 children with cards who had no documentation of tetanus vaccination, and, of these children, 54% (95% CI: 30–76%) were immune to tetanus (Table 4).

DISCUSSION

This survey is the first to estimate immunity against diphtheria, tetanus, measles, and rubella among children in Haiti and provides important data for Haiti’s immunization program. None of the children showed evidence of long-term protection against tetanus or diphtheria, which supports the biologic finding that immunity wanes over time in the absence of tetanus and diphtheria booster doses. Maternal and neonatal tetanus elimination has been achieved in Haiti, but long-term immunity is needed to sustain elimination. The lack of long-term protection is concerning because, according to national coverage surveys, DTP3 coverage in Haiti has fallen from 63% to 55% from 2012 to 2017. According to the World Health Organization-United Nations Children’s Fund (WHO-UNICEF) vaccination coverage estimates, DTP3 coverage was only 64% in 2018. In addition, the vaccination coverage estimates for all antigens in Haiti, such as third-dose polio vaccine (64% in 2018), are low, which raises concerns for control and elimination of other VPDs.

### Table 1
Demographic and socioeconomic characteristics of surveyed children aged 5–7 years and their caregivers—Haiti, 2017

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total, N = 1,146</th>
<th>West region, N = 524</th>
<th>Non-west region, N = 622</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender of child</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>570 (49.8)</td>
<td>269 (51.4)</td>
<td>301 (48.4)</td>
</tr>
<tr>
<td>Female</td>
<td>575 (50.2)</td>
<td>254 (48.6)</td>
<td>321 (51.6)</td>
</tr>
<tr>
<td><strong>Age of child (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>353 (30.8)</td>
<td>150 (28.6)</td>
<td>203 (32.6)</td>
</tr>
<tr>
<td>6</td>
<td>410 (35.8)</td>
<td>207 (39.5)</td>
<td>203 (32.6)</td>
</tr>
<tr>
<td>7</td>
<td>383 (33.4)</td>
<td>167 (31.9)</td>
<td>216 (34.7)</td>
</tr>
<tr>
<td><strong>Education level of child</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>42 (3.7)</td>
<td>22 (4.2)</td>
<td>20 (3.2)</td>
</tr>
<tr>
<td>Kindergarten/preschool</td>
<td>390 (34.1)</td>
<td>188 (36.0)</td>
<td>202 (32.5)</td>
</tr>
<tr>
<td>Primary</td>
<td>712 (62.2)</td>
<td>312 (59.8)</td>
<td>400 (64.3)</td>
</tr>
<tr>
<td><strong>Age of caregiver (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 30</td>
<td>316 (27.6)</td>
<td>135 (25.8)</td>
<td>181 (29.1)</td>
</tr>
<tr>
<td>30–39</td>
<td>463 (40.4)</td>
<td>233 (44.6)</td>
<td>230 (37.0)</td>
</tr>
<tr>
<td>≥ 40</td>
<td>366 (32.0)</td>
<td>155 (29.6)</td>
<td>211 (33.9)</td>
</tr>
<tr>
<td><strong>Caregiver has a job</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>219 (19.1)</td>
<td>78 (14.9)</td>
<td>141 (22.7)</td>
</tr>
<tr>
<td>Some or completed primary</td>
<td>451 (39.4)</td>
<td>164 (31.3)</td>
<td>287 (46.1)</td>
</tr>
<tr>
<td>Some secondary</td>
<td>372 (32.5)</td>
<td>207 (40.0)</td>
<td>165 (26.5)</td>
</tr>
<tr>
<td>Completed secondary or higher</td>
<td>104 (9.1)</td>
<td>75 (14.3)</td>
<td>29 (4.7)</td>
</tr>
</tbody>
</table>

* Data missing from some questionnaires.

### Table 2
Seropositivity for diphtheria, tetanus, measles, and rubella among children aged 5–7 years—Haiti, 2017

<table>
<thead>
<tr>
<th>Disease (immunity threshold)</th>
<th>Total, N = 1,146</th>
<th>West region, N = 524</th>
<th>Non-west region, N = 622</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria (≥ 0.01 IU/mL)</td>
<td>934 (83.1 [80.7–85.4])</td>
<td>390 (75.1 [70.5–79.1])</td>
<td>544 (87.5 [84.5–90.0])</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Tetanus (≥ 0.01 IU/mL)</td>
<td>930 (82.7 [79.5–85.5])</td>
<td>396 (75.7 [69.0–81.3])</td>
<td>534 (86.5 [83.1–89.4])</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Rubella (≥ 10 IU/mL)</td>
<td>943 (84.0 [80.5–86.9])</td>
<td>411 (79.9 [73.8–84.9])</td>
<td>532 (86.1 [81.9–89.4])</td>
<td>0.07</td>
</tr>
<tr>
<td>Measles (≥ 314 Median fluorescence intensity minus background)</td>
<td>975 (87.4 [85.1–89.3])</td>
<td>410 (80.2 [75.1–84.5])</td>
<td>565 (91.2 [88.7–93.2])</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Diphtheria immunity categories (IU/mL)†

| < 0.01 | 212 (16.9 [14.6–19.3]) | 134 (24.9 [20.9–29.5]) | 78 (12.5 [10.0–15.5]) | < 0.001 |
| 0.01 to < 0.1 | 559 (48.4 [43.8–52.9]) | 257 (48.4 [42.5–54.4]) | 302 (48.3 [42.3–54.4]) | – |
| 0.1 to < 1 | 375 (34.8 [30.4–39.4]) | 133 (26.6 [21.6–32.4]) | 242 (39.2 [33.3–45.4]) | – |
| ≥ 1 | 0 0 0 0 | 0 0 0 0 | 0 0 0 0 | – |

Tetanus immunity categories (IU/mL)†

| < 0.01 | 216 (17.3 [14.5–20.5]) | 128 (24.3 [18.7–31.0]) | 88 (13.5 [10.6–16.9]) | < 0.01 |
| 0.01 to < 0.1 | 373 (32.6 [29.2–36.3]) | 160 (31.6 [26.8–36.7]) | 213 (33.2 [28.6–38.2]) | – |
| ≥ 0.1 to < 1 | 557 (50.1 [45.8–54.4]) | 236 (44.1 [38.4–50.0]) | 321 (53.3 [47.7–58.9]) | – |
| ≥ 1 | 0 0 0 0 | 0 0 0 0 | 0 0 0 0 | – |

* Percentages account for strata, cluster, and weight.
† This section compares the proportion of children in each immunity category between the West and non-West regions.
In this survey, diphtheria immunity among children aged 5–7 years was 83% overall and 75% in the West region, which may not have reached the level needed for herd protection (80–85%). Reviews of diphtheria cases in Haiti found that most cases were unvaccinated or incompletely vaccinated, and school-aged children have been disproportionally affected. In the current survey, 9% of children were immune to diphtheria and not tetanus, which could mean that they were exposed to the diphtheria toxin through natural infection. In response to the epidemic, the Ministry of Public Health and Population launched a vaccination campaign during March–April 2018, and, 1 month after the campaign, the number of diphtheria cases and deaths declined from 65% in 2012 to 61% in 2017, according to national vaccination coverage surveys. In 2018, MR2 coverage was only 38% according to WHO–UNICEF vaccination coverage estimates. The measles and rubella immunity data from this survey support the PAHO and WHO recommendations that countries should achieve ≥95% coverage with two doses of MR vaccine through the routine immunization system, and that measles-containing vaccine immunization campaigns may be indicated if the routine system has not reached high coverage. Considering the findings of this survey, it may be useful to conduct an immunization campaign with MR and age-appropriate tetanus- and diphtheria toxoid-containing vaccine.

The antibody seroprevalence against all four VPDs was lower in the West region than in the non-West region. Vaccination coverage surveys have shown lower coverage from routine immunization services and campaigns in the West department/Port-au-Prince area, which could be due to difficulties reaching children in urban areas. Before measles elimination, an international measles importation led to an outbreak in Haiti, particularly in Port-au-Prince, which is further evidence that the West department is at risk of an epidemic. The immunity gap in the West region suggests that additional interventions should take place to improve vaccination coverage in Port-au-Prince.

This serosurvey highlighted benefits of using serosurvey data in addition to vaccination coverage data. Diphtheria–tetanus–pertussis containing vaccine 3 coverage by card or recall underestimated seropositivity (83%) for diphtheria and tetanus antibodies. Some children who did not receive any doses of DTP based on card documentation were immune to tetanus, which could only occur after vaccination. Surveys
using card documentation or recall to assess vaccination coverage are at risk of information and recall bias, and both card documentation and recall have been found to underestimate actual DTP coverage or immunity.\textsuperscript{17,41,42} In addition, almost 20% of children were excluded from the vaccination coverage estimates because they were missing vaccination cards, and their caregiver did not remember whether the child had been vaccinated. Many of these children might have been vaccinated, leading to higher seroprevalence than vaccination coverage. In this survey, 8% of children were immune to tetanus and not diphtheria, which indicates that the children were most likely vaccinated against diphtheria and tetanus, but their diphtheria immunity had already waned by the time of the survey. Measles–rubella vaccine 2+ coverage was likely underestimated in the current survey because all children were eligible for at least two MR doses through the routine system and at least one of the campaigns. An MR vaccination coverage survey conducted after the 2012 MR campaign estimated
### TABLE 4: Seropositivity for diphtheria, tetanus, measles, and rubella by vaccination status among children aged 5–7 years—Haiti, 2017*

<table>
<thead>
<tr>
<th>Seropositivity</th>
<th>Diphtheria immune (0.01 IU/mL)</th>
<th>Tetanus immune (0.01 IU/mL)</th>
<th>Measles immune (10 IU/mL)</th>
<th>Rubella immune (1 IU/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (IQR)</td>
<td>Median (IQR)</td>
<td>Median (IQR)</td>
<td>Median (IQR)</td>
</tr>
<tr>
<td>Unvaccinated</td>
<td>74.2 (72.5–76.8)</td>
<td>72.5 (70.7–74.6)</td>
<td>56.7 (55.5–58.2)</td>
<td>79.3 (77.8–80.8)</td>
</tr>
<tr>
<td>Partial</td>
<td>76.8 (75.0–78.6)</td>
<td>74.9 (73.1–76.6)</td>
<td>60.0 (58.6–61.5)</td>
<td>83.1 (81.6–84.6)</td>
</tr>
<tr>
<td>Complete</td>
<td>81.0 (79.3–82.7)</td>
<td>81.1 (79.3–82.7)</td>
<td>72.7 (71.1–74.2)</td>
<td>84.1 (82.6–85.7)</td>
</tr>
</tbody>
</table>

*Percentages account for strata, cluster, and weight.

**Median** serum neutralizing antibodies to diphtheria; however, studies have shown that the MFA performs well compared with the gold standard Vero cell test.45,46

This survey provides the first estimates of immunity to diphtheria, tetanus, measles, and rubella among children in Haiti. The findings highlight the need to attain ≥95% DTP3 and MR2 coverage nationally, particularly in the metropolitan Port-au-Prince area, and to introduce tetanus- and diphtheria toxoid-containing booster doses for children aged 4–7 years and 9–15 years and sustain high coverage of booster doses. The survey results also highlight the benefit of supplementing vaccination coverage data with seroprevalence data to provide a better assessment of the vaccination program and identify immunity gaps. Without achieving high vaccination coverage and adequate booster doses as per the WHO-recommended schedule, Haiti risks reestablishment of measles or rubella, an increase in maternal and neonatal tetanus cases, and ongoing diphtheria epidemics.
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Financial support: This survey was supported by a cooperative agreement between the CDC and the Haiti Ministry of Public Health and Population and a cooperative agreement between the CDC and PAHO.

Disclosures: Valery Blot works for Institut Haitien de l’Enfance, the institution that was funded through a cooperative agreement between CDC and the Haiti Ministry of Health and Population to implement the survey. The findings of this survey were presented in part at the IDWeek 2019 conference October 2–6, 2019, Washington, DC.


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