HPV Vaccine: Lessons Learned in the Region of the Americas

In 2006, the human papillomavirus (HPV) vaccine was licensed and started to be introduced into national Expanded Programs on Immunizations (EPI) in the Region of the Americas. As of June 2018, this vaccine is included in the vaccination schedules of 34 countries and territories.

Monitoring and calculating HPV coverage rates is very important in immunization programs, since they indicate successes and identify problems, helping to analyze their causes and implement efficient measures to achieve desired outcomes. However, there are more challenges in monitoring and following up on HPV vaccination than in other vaccination schedules. Some of these problems are:

- Different vaccination strategies in schools or health services;
- Two- or three-dose schedules;
- Using doses in different calendar years; and
- Vaccinating only girls or children (gender-neutral).

Different target population: one or more cohorts of girls selected by age or by academic grade when vaccinating;

Data on the target population are not always available or up-to-date.

Vaccination Week in the Americas 2018 Launches in the Region

Vaccination Week in the Americas (VWA) was launched on 23 April in Havana, Cuba – a first-time launch location for the 16-year-old campaign. This year’s slogan was “Strengthen Your Defense! #GetVax #VaccinesWork” and had a football theme as the FIFA World Cup will be celebrated soon after.

“Vaccination is one of the most powerful tools we have to prevent disease and save lives,” said Carissa F. Etienne, PAHO director, at the opening ceremony, which took place at the Victoria de Giron Institute of Basic and Preclinical Sciences. Ministers and other high-level health authorities from Latin America, the Caribbean and other regions of the world participated in the launch.

Tedros Adhanom Ghebreyesus, Director General of the World Health Organization (WHO), also participated in the regional launch of VWA, which has served as the base for World Immunization Week since its start in 2012. “Not only does Cuba enjoy universal coverage for vaccines, [it is] also a producer and exporter of these life-saving products,” said Dr. Tedros. “World Immunization Week is an opportunity to remind all nations and all people of the incredible value of vaccines.”

During the opening ceremony, Cuban Deputy Health Minister, Jose Angel Portal Miranda, emphasized that in Cuba “vaccination is available to everyone, free of charge, and can be accessed from primary health care providers. As a result, vaccination coverage in Cuba for all vaccines currently stands at 98%, resulting in high population immunity.”

Portal Miranda also highlighted that an average of 4.8 million vaccines against 13 diseases are administered each year in Cuba, with eight of the eleven vaccines that are given being produced in the country itself. He also reminded the audience that the first polio prevention campaign in Cuba took place in 1962 with vaccinating 2.6 million children and adolescents under the age of 15. Thanks to this and other initiatives, the country was the first in the Region to eliminate polio.
At its meeting in July 2017 in Panama, PAHO’s Technical Advisory Group (TAG) on Vaccine-preventable Diseases made recommendations on HPV vaccination in the Region, including the following:

- TAG congratulated the PAHO Member States that have recently decided to introduce the HPV vaccine in their routine immunization programs. TAG reiterated the importance of prioritizing high coverage in the cohorts of nine to 14-year-old girls to ensure complete protection against HPV and achieve herd immunity among children. The currently available vaccines have comparable safety profiles and offer similar protection against cervical cancer.

- Considering the substantial health benefit of HPV vaccination, TAG encouraged the Member States that have not yet included the vaccine in their routine vaccination schedules to evaluate the feasibility, cost-effectiveness and other criteria relevant to making decisions at the national level and consider including this vaccine in national routine vaccination schedules.

- TAG urged Member States to carefully consider their approaches to communication on the HPV vaccine, to ensure the development of specifically targeted messages. Furthermore, TAG asked PAHO to support exchanges between countries on the lessons learned in communication about HPV vaccine safety and crisis management.

- TAG requested that PAHO support Member States in their efforts to better document HPV vaccination coverage at the sub-national and national level and how this data can be used to address strategies and achieve optimal coverage rates in the targeted groups for the complete vaccination series.

- Wherever possible, countries should monitor the impact of HPV vaccination.

In October 2017, PAHO held a workshop in the city of Antigua, Guatemala, with participation from 24 countries in the Region. The objective was to share experiences and lessons learned in the introduction of the HPV vaccine and communication strategies.

During this workshop, the country data available in the PAHO/WHO/UNICEF Joint Reporting Form (JRF) for the year 2016 were analyzed to calculate the HPV vaccination coverage rate. Some of the conclusions of this analysis were:

- Some countries do not report the target population to the Ministry of Health; some do not report the target population; some do not report the doses used, only coverage; some do not report the target population; and some have considered the girls enrolled for vaccination as the target population to receive the first dose.

In addition, it was concluded that the countries have had difficulty in reaching the target population and that vaccination at school is the strategy that has proven to be the easiest way to enroll the target population. However, other complementary strategies must be found to vaccinate girls who do not attend school or who do attend but refuse the vaccine.

During this meeting, the subject of communication was widely discussed. It was emphasized that there was a need to have a comprehensive communications plan, including crisis response, to prepare messages targeted to each audience, and to have a permanent communications team. The ministries of health should maintain a budget line to carry out communication activities at least twice a year (or continuously, if possible).

The countries emphasized the importance of having an intersectoral communication, promotion, and social mobilization committee. They mentioned the need to devote more time to getting key partners involved, such as schools, parents and decision-makers, before introducing a vaccine and working more closely with doctors. They recognized the importance of identifying strategic partners in the news media and drawing media attention to vaccines. The influence of social networking should not be minimized.

The countries also consider it essential to quickly respond to rumors that appear in social networks, and feel it is extremely important to monitor the impact in the news media, so that adjustments can be made to vaccination strategies. It is also essential to monitor anti-vaccine movements and prepare to respond to them. The countries also felt they should pay attention to the situation in neighboring nations.

Even though the HPV vaccine is safe (with mild to moderate local and systemic adverse events), sociogenic rumors and events in the Region have led to concern among parents, which has negatively impacted coverage rates.

In the recommendations from the workshop, PAHO committed to help the countries with some of the gaps identified during the discussions of lessons learned, such as: developing a manual to standardize the calculation of HPV vaccination coverage rates in the Region, reviewing methodologies to assess the impact and effectiveness of the vaccine and inviting the countries to conduct impact assessments, and supporting the development of communication materials.
Schedules
Efforts to Complete Basic Vaccination
Sustaining Polio Elimination
Sustaining Measles Elimination
and social mobilization to community sensitization, throughout this year’s VWA, from communication Countries conducted a wide range of activities
Country Activities for VWA 2018
Countries conducted a wide range of activities throughout this year’s VWA, from communication and social mobilization to community sensitization, healthcare worker training and the vaccination of more than 70 million individuals.
Sustaining Measles Elimination
• Measles was declared as eliminated from the Americas in 2016 after the declaration of the elimination of rubella and congenital rubella syndrome (CRS) in 2015, culminating a 22-year mass vaccination effort against measles, mumps and rubella.
• Due to the risk of importation of measles and current outbreaks happening in our Region, more than 11 countries took WVA 2018 as an opportunity to intensify vaccination efforts against measles, with a goal of reaching approximately 6,000,000 people.
Sustaining Polio Elimination
• At least 14 countries vaccinated against polio as part of WVA 2018 activities: Brazil, British Virgin Islands, Colombia, Cuba, Grenada, Guatemala, Guyana, Honduras, Jamaica, Nicaragua, Panama, Paraguay, St. Lucia, St. Maarten, and Turks and Caicos.
• Cuba conducted their 57th annual polio vaccination campaign to sustain polio elimination; this campaign reached more than 480,000 children.
Efforts to Complete Basic Vaccination
Schedules
• At least 22 countries and territories used WVA 2018 to intensify activities for routine national immunization programs and administer multiple vaccines to improve coverage by starting, updating or completing childhood vaccination schedules.
Protecting Vulnerable Populations
• Every year, WVA is an opportunity to reach underserved populations. This year, 16 countries reached out to populations in vulnerable situations, including pregnant and postpartum women, health workers, older adults, indigenous populations, individuals with chronic disease, and prisoners and prison workers, among other occupational risk groups and vulnerable populations.
• Several countries focused efforts to protect occupational health workers against a range of diseases such as Hepatitis B, tetanus and influenza.
• As part of Brazil’s Month of Vaccination of Indigenous Peoples, a combined effort from the National Immunization Program and the Department of Indigenous Health was done to update the vaccination schedules of approximately 600,000 individuals in 1,373 indigenous communities, in addition to administering the annual dose of the influenza vaccine.
Communication Activities
• 27 countries carried out activities to improve public awareness regarding the importance of immunization for good health. Examples of these include health fairs, sensitization sessions, and other public awareness activities.
Integrated Health Activities
• The use of VWA for the integration of other public health activities together with vaccination has become systematized throughout much of the Region.
• 16 countries (Antigua and Barbuda, Barbados, Belize, Brazil, Colombia, Dominican Republic, Grenada, Guatemala, Guyana, Honduras, Jamaica, Nicaragua, Panama, Paraguay, St. Lucia, and Trinidad and Tobago) integrated other health interventions during VWA 2018.
• Examples of these health interventions include: Vitamin A distribution; deworming; prevention of mosquito borne diseases such as yellow fever, dengue, Zika, and chikungunya; health screenings for diabetes; vaccination of pets; promotion of healthy eating habits; domestic violence awareness; mental health screenings; and cancer awareness.
A Night of Vaccines is Celebrated in Argentina
Agustina receives the flu shot and runs to continue painting landscapes; Simon proves his dexterity with a ball made with socks and then responds to the call of his mother waiting in line for the measles dose; Elsa hurries with her cane while the vaccinator waits to give her the flu vaccine. In the background, a folkloric group plays on the stage, while around them children and adults try different sports and artistic games.
This scene corresponds to “The Night of Vaccines,” a vaccination initiative in the province of Córdoba, Argentina, held with support from PAHO/WHO to celebrate vaccination in the framework of Vaccination Week in the Americas, held from 21-28 April this year with a focus on football in the context of the 2018 World Cup.
Footballs, shirts and blue and white hats – colors of the Argentine flag – were present during the celebration, which lasted from 8 pm to 2 am. The Pediatric Hospital of the Jesus Child (Hospital Pediátrico Del Niño Jesús) opened its doors to the community to give the vaccines included in the national vaccination schedule for free and at the same time, offer various musical shows, games for children and soccer-tennis matches, among other forms of entertainment.
“It’s a vaccination party,” highlighted Hospital Director, Silvia Ferreyra, as she approached the tent where 50 vaccinators were present to apply doses. While waiting to receive the vaccine against hepatitis B, attendee Florencia Córdoba noted, “It’s a very good initiative in which we are all equal, regardless of whether we have social security.”
The Caribbean Immunization Technical Advisory Group (CiTAG) was launched during the 33rd Caribbean Immunization Managers’ meeting, held on 26-28 February 2018 in Port-of-Spain, Trinidad. The CiTAG, an independent group of experts in the fields of epidemiology, public health, microbiology, pediatrics and tropical medicine, is chaired by Dr. J. Peter Figueroa, Professor of Public Health, Epidemiology and HIV/AIDS at The University of the West Indies. They will advise ministers of health on immunization through the Council for Human and Social Development of CARICOM using evidence-based technical advice.

With 22 countries/territories in the Caribbean, many of which are too small to support individual National Immunization Technical Advisory Groups (NITAGs) and given the history of Caribbean countries working successfully together in health, the health ministers took the wise decision in 2017 to establish the sub-regional CiTAG. This is an efficient mechanism to provide independent advice in keeping with the recommendations of the Global Vaccine Action Plan (GVAP) and PAHO’s Regional Immunization Action Plan (RIAP).

Recent hurricanes in the Caribbean and outbreaks of vaccine-preventable diseases (VPDs) in neighboring countries are a stark reminder that Expanded Programs on Immunization (EPIs) must be resilient and vigilant to maintain the polo, measles, CRS and rubella-free status of the Caribbean.

Priority areas for the CiTAG include sustaining confidence in immunization; promoting the strengthening/development of legislative frameworks to support vaccination; enhancing data quality through the implementation of electronic immunization registries (EIRs); VPD surveillance; strengthening laboratory capacities and linkages between EPI, surveillance, laboratory and the private sector and building EPI manager capacity.

The Caribbean Immunization Managers Meeting, where the CiTAG was launched, convened 70 persons from 29 countries/territories and was opened by Trinidad and Tobago’s Minister of Health, Honorable Terrence Devaluing, who gave the main address. The purpose of the meeting was to analyze achievements for 2017 and plan activities for 2018, while sharing country experiences on the immunization program.

Meeting presentations focused on specific VPDs, EPI programmatic areas and global and regional/sub-regional updates. Countries shared experiences with VPD surveillance, as well as sustainability plans for measles, introduction of new vaccines, Vaccination Week in the Americas, measles, yellow fever and diphtheria outbreaks and EIR implementation.

Vaccination coverage in the Caribbean remains higher than the regional and global average with DTP3 being 95% in 2016 compared to 91% in the Americas and 86% globally. Despite plans to sustain measles, rubella, CRS and polio elimination, countries need to improve the quality of surveillance systems for timely detection and management of importations.

The Caribbean has been validated for the containment of WPV2, VDPV2 and OPV2/Sabin 2 infectious and potentially infectious materials. The CiTAG convened the 70 countries working successfully together in health, the health ministers took the wise decision in 2017 to establish the sub-regional CiTAG. This is an efficient mechanism to provide independent advice in keeping with the recommendations of the Global Vaccine Action Plan (GVAP) and PAHO’s Regional Immunization Action Plan (RIAP).

A risk communication training workshop was held in conjunction with the meeting. The workshop’s objective was to train EPI managers in the principles of risk communication to encourage positive behavior change in support of vaccination, strengthen the capacity of EPI managers to develop immunization messages targeting various audiences (parents, children, anti-vaccine groups) and to effectively communicate with the media and the public.

The workshop focused on the Single Overarching Communication Outcome (SOCO), how to develop messages and the principles of effective communication using various media. Participants worked in groups to develop SOCOs and messages using examples of myths/beliefs and challenges with the uptake of the influenza and MMR vaccines while sharing and exploring strategies to address these through effective communication.

Overall, the Caribbean EPI Managers’ meeting and risk communication training workshop were successful, and participants benefitted greatly. A final report detailing the topics discussed in this meeting can be found at http://bit.ly/carmeeting.
Haiti Eliminates Neonatal Tetanus

Objective 2.1 of the Regional Immunization Action Plan (RIAP) is the elimination of neonatal tetanus as a public health problem in the Region. Elimination of neonatal tetanus is defined as a country having fewer than one case per 1000 live births in each district. If neonatal tetanus is eliminated, maternal tetanus is also eliminated.

Haiti was the only country in the Region that had not achieved this goal despite the implementation, since 2003, of the recommended strategies for the elimination of maternal and neonatal tetanus. A literature review and field visits conducted in June 2016 concluded that there is a likelihood of elimination of maternal and neonatal tetanus in Haiti. To confirm the elimination of the maternal and neonatal tetanus in Haiti, a neonatal tetanus mortality survey was conducted in the Southern Department, which posed the highest risk for maternal and neonatal tetanus in the country after the pre-validation stage. The assumption was that if the most at-risk department had eliminated maternal and neonatal tetanus, the disease could be considered eliminated in all other districts and therefore, throughout the country.

A household survey of neonatal mortality was conducted; sampling for batch quality control was coupled with a cluster survey. The survey included all live births in the homes of resident mothers visited from 1 April 2016 to 30 April 2017. The survey was designed to identify neonatal deaths and, through verbal autopsy, diagnose whether deaths were caused by tetanus. The elimination of maternal and neonatal tetanus should be validated if less than two neonatal deaths due to tetanus were identified. The survey was carried out 12-25 June 2017.

A total of 10,516 households were surveyed and 2,302 live births were examined. Td2 coverage was 53% among mothers (card + case history); 45% of deliveries were in a health facility; and 31% of mothers applied substances to the umbilical cord. Since no tetanus cases were identified among the 44 neonatal deaths recorded in a good-quality survey, neonatal tetanus was considered eliminated in the Southern Department for the period from 1 May 2016 to 30 April 2017. Therefore, maternal and neonatal tetanus was considered eliminated in Haiti for the same period.

To maintain maternal and neonatal tetanus elimination, Haiti will have to:
1. Achieve and maintain T2+ coverage >80% during routine immunization in each department;
2. Organize routine immunization activities with the DT vaccine in women of childbearing age in high-risk departments;
3. Adopt and implement a policy of administering additional doses of DT (children 4-6 years old and adolescents 13-17 years old);
4. Improve the accessibility and quality of deliveries assisted by qualified personnel;
5. Strengthen the education of mothers and the community about umbilical cord care;
6. Strengthen case-based surveillance;
7. Institute periodic analysis of the risk of maternal and neonatal tetanus in each municipality/district.

The Elephant in the Room: Vaccine Hesitancy vs. Moral Obligation to Get Vaccinated

As of 30 June 2018, eleven countries in the Region of the Americas (Antigua, Argentina, Brazil, Canada, Colombia, Ecuador, Guatemala, Mexico, Peru, United States and Venezuela) are experiencing measles outbreaks. Despite significant media coverage, there is still not enough public discussion about a key issue: Why are we struggling against this serious and highly contagious disease, given that we have a highly effective vaccine capable of entirely avoiding it? Why are we allowing our populations, children included, under the risks of serious complications resulting from measles, including death — given that the disease is entirely preventable?

Something does not make sense, Public health authorities across the Region have shown low immunization rates in the affected areas. Immunization rates have been decreasing as vaccine hesitancy has become more popular. Anti-vaccination views originated in the developed world in response to a fraudulent publication advancing a fake link between vaccines and autism. They have now reached new areas in our Region and are being spread rapidly through social media.

Yet the elephant in the room is not only the anti-vaccination ideology, but also the justifications being provided to support it. Anti-vaccination supporters make claims about facts and about what is morally right. Some of the fact-related claims are that vaccines are unsafe and that they are not efficacious in preventing disease. These claims are disproven when showing the facts as captured by the overwhelming available evidence. Immunization experts are well positioned to show anti-vaccination supporters and the public that these claims are wrong. To prevent the spread of false claims, national immunization programs should consider being more proactive about sharing the evidence on the remarkable safety and efficacy of vaccines with the public in ways they can easily understand.

Moral claims often invoke people’s individual rights, such as the right to decide what goes into their own body and thus refuse vaccination. Unlike claims about facts, moral claims do not get refuted with evidence. Conversations are likely to end there, because public health and medical care professionals often feel “out of their comfort zone” when discussions veer to moral arguments. Indeed, disproving the moral claims made against vaccination seems to imply challenging individual rights, and that is a territory that health care professionals would as a rule try to avoid.

However, something too important is at stake for the conversations to stop there. In order to advance health and ensure that our populations are not susceptible to serious yet preventable diseases, it is imperative that immunization professionals acquire an “ethics vocabulary” to effectively rebut moral claims against vaccination and to decidedly advance the arguments supporting our moral duty to vaccinate.

Those invoking individual rights to argue against vaccination miss a key point — that what is at stake is not just one’s own health but the health of other people. Certainly, an argument based on individual rights would suffice to justify refusing dialysis, for example, which is an intervention that would only impact on one’s individual health. Yet it cannot possibly suffice for a discussion about vaccination, where one may be harming others by spreading an infectious disease, like measles.

Refusal to be vaccinated against infectious diseases can lead to harming others and whatever harm we may think is acceptable to impose upon ourselves, it is ethically unacceptable to bring about harm to others. Indeed, we argue that we have a moral duty not to cause harm to others. So, if we can reduce the risk of causing harm to others through vaccination against contagious diseases, we have the moral duty to do so. That means that we have the moral obligation to be vaccinated against contagious diseases.1

One could argue that this argument only applies to voluntary actions. We may unintentionally cause harm to others, for example, if I fall while holding a candle and burn you. We would— and reasonably so— refuse to say that in such circumstance I did something morally wrong towards you. Likewise, in situations where vaccines are not available, it would not be reasonable to argue that people are not fulfilling their moral obligations, but refusing an available vaccine is a voluntary action and therefore it can be argued that those who opt out of vaccination

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are morally responsible for the harms caused to others, including their deaths.  

Public health ethics provide the framework for these ethical arguments about vaccination. As such, the arguments take salient characteristics of public health into account—that we are concerned with the health of populations and not only of isolated individuals; that we are dealing with public goods, like herd immunity, that no individual can possibly decide to forego; and that collective action and social cooperation are crucial.

There are many other important public health ethics arguments about vaccination that consider other key public health features, such as the mandate of the public health authority to advance the population’s health, which implies the capacity to impose interventions along with the responsibility to be accountable for the work. Public health ethics provide a powerful vocabulary to argue for vaccination. We must embrace it to advance the health of our populations in a morally sound and effective way.

Contributed by: Dr. Carla Saenz, Regional Program on Bioethics, Department of Health Systems and Services, PAHO/WHO.

Characteristics of the Recent Diphtheria Outbreaks in the Americas

In the Americas, diphtheria has been under control for decades. However, two major outbreaks have been reported in Haiti and Venezuela in recent years, and other related outbreaks to Venezuela have occurred in Colombia, Brazil and the Dominican Republic.

In both Haiti and Venezuela, routine immunization coverage with DPT3 and DPT4 has been recurrently below 95%, when the required standard level defined for the Americas is to have vaccination coverage above 95% (Figure 1). These low coverages have therefore resulted in an increase of the susceptible population among children and adults.

In Haiti, the disease reemerged at the end of 2014 and on epidemiological week (EW) 6 of 2018, 410 probable cases were notified, including 75 deaths. The case fatality rate was 22.3% in 2015, 27% in 2016 and 10.7% in 2017 and 2018. In 2015 and 2017, children under ten years old were more affected.

As part of the outbreak control measures, the Ministry of Health planned three rounds of vaccination campaigns, targeting children 1-14 years of age in 44 communes of nine departments. The pentavalent vaccine was used to vaccinate children aged 1-6 years, and the Td vaccine was used to vaccinate children aged 7-15 years. The first phase of the first round of the campaign was conducted from 11 to 15 March 2018 in eight states (29 communes); and the second phase was conducted from 8 to 12 April 2018, in 15 communes of the West Department. Administrative coverage reached 98% in the first eight departments and 81% in the West Department. Since the end of the first phase of the campaign, a reduced number of diphtheria cases and deaths have been notified. The dates for the implementation of the two remaining rounds have not been confirmed.

In Venezuela, from the beginning of the outbreak in EW 26 2016 to EW 5 2018, a total of 969 probable diphtheria cases were reported (324 cases in 2016, 609 in 2017 and 36 in 2018), 726 of which were confirmed by laboratory or clinically and 113 died (17 in 2016 and 96 in 2017), with a case fatality rate of 15.5%. In 2016, cases were reported in five states (Anzoátegui, Bolívar, Delta Amacuro, Monagas and Sucre), while in 2017, confirmed cases were reported in 22 states and the Capital District. In 2018, nine federal entities have reported confirmed cases. Cases have been reported among all age groups; however, the highest incidence rate occurred among children aged 5-15 years.

As part of the control measures, routine vaccination was intensified with the pentavalent vaccine among children aged two months-six years and a vaccination campaign was implemented with the Td vaccine, aimed at children aged seven to 15 years. The first phase of this campaign is being implemented in nine states and the second phase in 15 states.

In Colombia, two confirmed cases of diphtheria imported from Venezuelan citizens were reported in 2018. The cases include a three and 14-year-old, both without vaccination history, with onset of symptoms on 2 January and 23 March, respectively. The two cases were reported by the La Guajira Department and were confirmed based on clinical, epidemiological and laboratory criteria.

In Brazil in 2017, there were 42 suspected cases reported in 14 states. Of the reported cases, five were confirmed in four states: Acre (1), Minas Gerais (2), Roraima (1 fatal case, imported from Venezuela), and São Paulo (1). The remaining 37 cases were ruled out. Three of the five confirmed cases (two in Minas Gerais and one in São Paulo) had received the full vaccination schedule. The age of the confirmed cases ranges from four to 66 years (median 19 years), four are male and one is female. Additionally, in EW 14 of 2018, six suspected cases were reported in six states; the case reported in the state of Roraima (imported from Venezuela) is currently under investigation. As of EW 14, none of the cases have been confirmed.

In the Dominican Republic, there were three suspected diphtheria cases reported in 2017, but only one was confirmed for diphtheria. The other two cases were discarded by clinical criteria (1) and by laboratory (1). No fatalities were reported.

Health authorities from Haiti, Venezuela and from their neighboring countries (Colombia, Brazil and the Dominican Republic), are intensifying epidemiological surveillance, investigations, medical care and vaccination.

Figure 1 Penta-3 and DPT-4 Routine Immunization Coverage in Haiti and Venezuela, 1981-2016


PAHO Recommendations

• The countries of the Americas should be aware that epidemic diphtheria outbreaks may occur when there are pockets of low vaccination coverage. The risk is also present when the cold chain cannot guarantee adequate temperatures for the preservation of pentavalent/DPT vaccine until the time of administration, especially when freezing of these vaccines occurs.

• Countries should ensure homogenous vaccination coverage of more than 95% with DPT3 and boosters.

• Epidemiological surveillance of diphtheria should be maintained and reinforced to detect a case in a timely manner.

• Early recognition and treatment of cases is very important, since the complications of diphtheria are directly proportional to the number of days between the onset of the disease and the administration of the antitoxin, and the early use of the diphtheria antitoxin is associated with better outcomes.

• Health care providers should receive training in diagnosis and reporting, as well as on case and contact management.

• A strategic stock of Diphtheria Antitoxin (DAT) is available. DAT can be purchased through PAHO’s Revolving Fund.

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The Seven Most Frequently Asked Questions about Diphtheria

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<th>QUESTION</th>
<th>ANSWER</th>
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<tbody>
<tr>
<td>1. What is diphtheria?</td>
<td>Diphtheria is an acute disease of bacterial origin that can affect the nasopharynx and may lead to obstruction of the airways and potentially, death. The most frequent symptoms are sore throat, fever (generally mild, rarely exceeding 38.5°C), difficulty when swallowing and breathing. The severity of the signs and symptoms is usually proportional to the extent of the local disorder since it is related to production of the toxin in the diphtheria membrane. When a sufficient amount of the toxin is absorbed, the patient may be pale, have a rapid pulse, and present extreme weakness. Symptoms appear in 2 to 5 days (ranging from 1 to 10) after exposure to the agent.</td>
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<td>2. What is the causative agent?</td>
<td>The causative agent is Corynebacterium diphtheriae, a gram-positive bacillus, which has four biotypes: mitis, intermedius, gravis, and belfanti. The most significant virulence factor of C. diphtheriae is the exotoxin that produces local and systemic cellular necrosis. C. diphtheriae is transmitted from one person to another through direct contact with the mucous membranes of the airways of a sick individual or carrier. Transmission rarely occurs through contact with skin lesions or fomites.</td>
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<td>3. What is the definition of a suspected case of diphtheria recommended by the WHO?</td>
<td>Upper respiratory tract illness characterized by nasopharyngitis, pharyngitis, tonsillitis or laryngitis, and presence of adherent pseudo membrane of the tonsils, pharynx, larynx and/or nose. Note: Some countries may consider expanding the definition of a suspected case to include mild cases with no pseudo membrane or non-scarring ulcers in a person with a history of travel to endemic countries or countries with diphtheria outbreaks.</td>
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<tr>
<td>4. How is the diagnosis of diphtheria confirmed?</td>
<td>Through a C. diphtheriae culture and demonstration of secretion of the exotoxin using an immunoprecipitation reaction (e.g. modified Elek Test). Polymerase chain reaction (PCR) is useful for detection of the diphtheria toxin gene, which provides a rapid diagnosis when the culture is not positive. In these cases, the epidemiological context should be considered and each case evaluated.</td>
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<td>5. How should the sample be obtained for laboratory diagnosis?</td>
<td>Two samples should be collected after initial contact with the suspected case: a pharyngeal swab and nasal swab. Both samples should be obtained using cotton-tip swabs. These samples should ideally be obtained before initiating antibiotic treatment. The pharyngeal swab should be obtained under direct visualization, preferably from the edge or directly beneath the pseudo membrane, twirling the swab, then removing and placing it in the transport medium. To take the nasal swab, gently insert the swab into the nostril until the anterior wall of the pharynx is reached and rub gently. The swabs should be appropriately labeled with a unique identifier and the source of the sample and placed in the appropriate transport media (Amies or Stuart transport media). If possible, a sample of the pseudo membrane should also be obtained and placed in saline solution (not formalin).</td>
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<td>6. What is the recommended management of diphtheria cases?</td>
<td>Diphtheria antitoxin (DAT): Should be administered as soon as the disease is suspected. The antitoxin neutralizes the circulating (unbound) toxin, but not the toxin fixed to the tissues. Antibiotics: Antibiotics eliminate the bacteria and thus reduce the duration of communicability and carriage. The recommended antibiotics are penicillin and erythromycin for 14 days. Other measures: Healthcare-associated infection prevention and control (HAIPC), monitoring (respiratory, cardiac, renal), support measures, strict rest (two weeks), and vaccination during the convalescence period.</td>
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<td>7. What is the recommended DAT dose and how is it administered?</td>
<td>The recommended dose is the same for children and adults, and ranges between 20,000 and 100,000 units depending on the location and extent of the pseudo membrane, the interval since the time of onset of symptoms, and the severity of the infection (Table 1). Table 1. Suggested dose ranges for use of DAT</td>
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<thead>
<tr>
<th>Indication</th>
<th>Dose (units)</th>
<th>Form of administration</th>
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<tbody>
<tr>
<td>Nasopharyngeal lesions</td>
<td>40,000 to 60,000 IU</td>
<td>Intramuscular (IM)</td>
</tr>
<tr>
<td>Nasopharyngeal lesions (48 hours or less)</td>
<td>20,000 to 40,000 IU</td>
<td>Intramuscular (IM)</td>
</tr>
<tr>
<td>Extensive disease (three days or longer) or diffuse swelling of the neck</td>
<td>80,000 to 100,000 IU</td>
<td>Intravenous (IV)</td>
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Once the dose and form of administration are determined, a single dose of antitoxin should be administered. The DAT is mixed with 250-500 ml of normal saline solution and is slowly administered over 2-4 hours, closely monitoring the patient for anaphylaxis. The dose should not be repeated. IV is the preferred form in severe cases, with IM used in mild to moderate cases. Staff who administer DAT should be trained and should have the experience, equipment and drugs required to treat the patient in the event of anaphylaxis symptoms. Use of DAT in pregnant women should be based on a risk-benefit analysis. It is important to always read the brochure on the available product to confirm doses and the manufacturer’s recommendations regarding susceptibility testing, administration, adverse events, etc. |

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What I Have Learned about Introducing the HPV Vaccine in Colombia...

By Diego Alejandro García, Manager of the Expanded Program on Immunization in Colombia

On 17 August 2012, after numerous analyses, considerations, and a recommendation from our vaccine advisory committee, we began vaccinating against human papillomavirus (HPV), given the clear benefit it would have for Colombian women and girls and the fact that nearly 2,300 women die of cervical cancer each year in this country.

We were aware of the news that was circulating on the Internet regarding the HPV vaccine, and therefore felt that before starting to vaccinate, it would be necessary for the country’s scientific and academic institutions to lead coordinated local efforts to build the HPV vaccination capabilities of pediatricians, gynecologists, and general practitioners so that they could support vaccination activities in their respective locations.

Furthermore, in conjunction with the education sector, we designed a vaccination strategy in public and private educational institutions to ensure a high rate of vaccination coverage, taking advantage of the concentrated population.

Because of this work, in 2012 we achieved 97% coverage with the first dose (conventional 0-2-6-month schedule), 96% coverage with the second dose and 89% coverage with the third dose in a cohort of fourth-grade girls in elementary school, aged nine or older. Thanks to these high coverage rates, we were able to mobilize resources to conduct a catch-up campaign in 2013 for all fourth-grade elementary school girls up to eleventh grade in high school, achieving a first-dose coverage rate of 95% and a second-dose coverage rate of 85% with an extended 0-6-60-month schedule.

Unfortunately, in 2014, several alleged vaccine-related events occurred, initially in a small concentrated group of people including an unvaccinated child. These events gradually increased as the presence of a nonspecific symptomatology was associated with the HPV vaccine. The event of public health interest occurred in a municipality in the northern part of the country, in a community with significant social problems. A huge amount of sensationalist coverage by the news media exacerbated the problem, with increased reporting of alleged adverse events in national news broadcasts. This was compounded by political opportunism and a few lawyers who were promising million-dollar compensations from suing the government.

In addition, one or two Colombian doctors informed the families of these girls that their symptoms could be attributed to the HPV vaccine, despite statements regarding the safety of the vaccine issued by many scientific and academic institutions in Colombia and around the world, as well as PAHO and WHO.

Given this, we went from a first-dose coverage rate of 97% in 2012 to 6% in 2016, which slightly increased to 15% in 2017. As a result, we lost the opportunity to protect our girls from a disease in adulthood that could have been prevented through vaccination. In 2017, we considered stepping up local actions because when we conducted campaigns at the national level, the anti-vaccine groups immediately mobilized. This strategy made it possible to increase the number of doses given, from 79,000 in 2016 to 214,000 in 2017. Of these, 50,000 and 143,000, respectively, were among girls aged ten-17 who had been keeping their vaccination schedules up to date; the remainder were among the cohort of nine-year-old girls.

Colombia has continued to step up its efforts to promote HPV vaccination, as we are convinced of the great benefit that it brings to the health of our people, which is why we are working closely with the entire medical community. We continue to fight against the false beliefs surrounding this vaccine and the strong anti-HPV vaccine movement that has intensified in our country. Although it has not been easy, we will not give up.

The objective of the “What I Have Learned” column is to provide a space for immunization professionals from across the Americas to share their unique experiences and lessons learned. Individuals who are interested in authoring a column are encouraged to contact Octavia Silva at silvao@paho.org.