Immunization Newsletter

Pan American Health Organization

Evaluation of Ecuador's National Immunization Strategy

Participants from Ecuador's EPI evaluation, January-February 2017. Credit: PAHO

Since the 1980s, international evaluations of the Expanded Program on Immunization (EPI) have been conducted in the Region of the Americas under the technical coordination and guidance of the Comprehensive Family Immunization Unit of the Pan American Health Organization (PAHO). In the 1990s, these evaluations focused primarily on the epidemiological surveillance system for measles. Their scope was later expanded to include all components of the immunization programs.

In response to a request by Ecuador's Ministry of Health and National Secretariat for Planning and Development *(Senplades),* in 2017, PAHO sent a technical mission to conduct an international evaluation of the country's national immunization strategy (ENI)[1]. This evaluation resulted in a field diagnosis of the workings of each component of the immunization strategy, along with practical and feasible recommendations for the comprehensive improvement of immunization in Ecuador.

The evaluation team consisted of 20 international experts from Argentina, Brazil, Chile, Colombia, Peru, the United States, Switzerland and PAHO Headquarters in Washington, DC with extensive expertise in the field of immunization. National evaluators from the Ministry and *Senplades* also lent their support.

The evaluation mission was conducted from 20 January to 3 February 2017, visiting seven provinces in the country: Azuay, Chimborazo, Guayas, Manabí, Morona Santiago, Pichincha and Zamora Chinchipe. The sites evaluated were selected using a classification of high, medium and low risk, based on the behavior of programmatic, epidemiological, socioeconomic and demographic indicators of Ecuador. A total of 15 districts and 35 health centers were visited.

During the evaluation, 666 interviews of key people inside and outside the political, administrative and operational areas were conducted in all selected regions and districts and at the national level.

[1] This article was adapted from the Executive Summary of the Evaluation of National Immunization Strategy of Ecuador 2017, pp. 11-14.

IN THIS ISSUE

PAHO Holds ad hoc TAG Meeting to Discuss IPV Shortage

The Technical Advisory Group (TAG) on Vaccine-preventable Diseases held an ad hoc virtual meeting on 10 March 2017 to discuss the worsening of the supply situation of the inactivated poliovirus vaccine (IPV) at the global and regional level and the yellow fever outbreak in Brazil.[2] Previously, an ad hoc meeting of the TAG had been held in May 2016 to discuss the potential global IPV shortage.

Dr. Cuauhtémoc Ruiz Matus welcomed TAG members and staff from PAHO's Comprehensive Family Immunization Unit and then invited the TAG Chair, Dr. Peter Figueroa, to open the meeting. Dr. Figueroa expressed his grave concern about the deterioration of the global IPV supply, which was the key reason that this TAG meeting was called; following the May 2016 TAG recommendation. He also shared an update on the epidemiological situation of the polio endemic countries with the participants, as well as the perspective of global post-switch situation, through his role in the SAGE Polio Working Group.

The TAG thanked and recognized the contributions of Dr. Maria Cristina Pedreira, who is retiring at the end of March 2017, after a successful 17-year career working in immunization at PAHO/WHO. During this time, Dr. Pedreira supported immunization efforts in the Dominican Republic, Nicaragua and Colombia. Since December 2013, she has been a Regional Immunization Advisor in Washington, DC, with the main responsibility of coordinating IPV introduction and the successful completion of the switch from the trivalent oral polio vaccine (tOPV) to the bivalent oral polio vaccine (bOPV) in the Region.

The TAG also thanked the PAHO secretariat for the organization of this meeting. This was the second successful virtual meeting of the TAG.

[2] The topic of IPV shortage was excerpted from the 2017 ad hoc TAG meeting's Final Report and reprinted on page three of this issue of the Immunization Newsletter. The complete report is accessible online at www.paho.org/immunization/TAG-Reports.

Furthermore, 334 users were interviewed and 536,125 diagnoses were reviewed as part of active institutional case-finding of vaccine-preventable diseases (VPD).

From the analysis of the information gathered in the field, the team identified achievements and challenges in each of the 12 components evaluated and issued the respective recommendations. These components include:

1. Political priority and legal foundations
2. Planning and coordination
3. Biologicals and inputs
4. Cold chain
5. Training
6. Social mobilization
7. Operating expenses
8. Supervision and monitoring
9. Epidemiological and laboratory surveillance; safe vaccination
10. Information system
11. Evaluation
12. Research

The 5-year Plan of Action resulting from this evaluation is organized by the components of the evaluation. The major conclusions and recommendations of the evaluation team can be summarized as follows:

- The Integrated Intercultural Family and Community Health Care Model (MAIS/FIC), based on health promotion and disease prevention, offers an opportunity to improve public health in general and immunization in particular. Access to and achievements in immunization can be used as a tracer of the health model's implementation, demonstrating its effectiveness in reaching everyone. However, when transitioning from the EPI to the national immunization strategy, functions and responsibilities were disaggregated and assigned to different entities within the Ministry, among them: epidemiological surveillance, statistics, human talent, the first level of care, (maternity) hospital management, administration and drugs, promotion and communication. Despite this model's sound theoretical underpinnings, lack of coordination among the various entities was observed. Thus, coordination among all actors and levels involved in immunization activities must be strengthened.

- To take advantage of the moment and strengthen governance, the Ministry should put greater emphasis on:
  o improving the organizational structure to lend greater visibility to public health strategies such as immunization.
  o assigning stable human talent at all levels to ensure that the planning, training, supervision and evaluation of the strategy are properly conducted to guarantee that public health targets in immunization and epidemiological surveillance are met.
  o ensuring the creation of comprehensive health care teams and the training of primary health care technicians in keeping with the standards set in the MAIS regulations; this will make possible the extramural activities necessary for reaching the entire population, including the most vulnerable sectors.
  o finalizing the regulations governing the public health education program, which will improve evaluation of the stability and retention of personnel and their functions.
  o establishing intrainstitutional, interinstitutional and intersectoral coordination mechanisms.

- While investment in the national immunization strategy increased, in absolute terms, largely due to the introduction of new vaccines, the proportion of investment allocated to vaccination in the overall health budget decreased. Since 2015, only vaccine procurement has had a budget line, while the funding for critical operational activities, such as training, supervision/monitoring and epidemiological surveillance, has been cut. The recommendation is a budget line with the nation's current expenditures to guarantee the implementation of intra- and extramural vaccination, with emphasis on the search for remote populations in conditions of vulnerability.

- The mission observed a steady decline in vaccination coverage over the past four years, using the administered doses of penta3 and polio3 as a reference. Due to the substantial accumulation of susceptibles in the cohorts of recent years, it is essential to implement a contingency plan to increase vaccination coverage in the short term and reduce the risk of VPD transmission.

- With regard to the denominators, coherence between the 2010 census and the BCG doses administered in previous years was confirmed. The data from the National Statistics and Census Institute (INEC) on the population under 1 are adequate at both the national and provincial level.

- With regard to the Ministry's distribution of the population by district and institution, based on variables such as BCG, Td, and initial care coverage, there is evidence of inconsistencies in this distribution. This calls for a review of the methodology, with support from other actors such as INEC.

- The mission observed missed opportunities to forge interinstitutional and intersectoral strategic partnerships with stakeholders willing to collaborate with the Ministry: scientific societies, universities and the private sector. It is recommended that the Committee on Immunization Practices and the Committee on Interagency Cooperation be reactivated and that the committees that support VPD elimination be maintained.

- With regard to the supply chain, which is currently the responsibility of the administration and drug unit, it is recommended that a unified system for timely distribution of all vaccination supplies be implemented to reduce shortages at all levels.

- The cold chain needs to be strengthened and expanded at all levels and preventive and corrective maintenance ensured. This will require the preparation of a comprehensive plan with guaranteed funding.

- The mission observed weaknesses in the training and supervision processes of all entities at all levels. Thus, a training plan for all entities responsible for the various components of the evaluation should be prepared, implemented and evaluated.

- Likewise, the role of the National Public Health Research Institute (INSPI), as administrator of the national network of public health laboratories, should be strengthened.

- The epidemiological surveillance system is weak, especially at the local level, due to limited staffing, lack of trained staff, cutbacks in resources for extramural activities (including systematic case-finding) and insufficient analysis. It is therefore recommended that human talent be strengthened through training activities and that analysis and feedback units be created at all levels to detect, investigate and rapidly respond to VPD cases or outbreaks.

- With regard to the information system, the efficiency of the data entry process should be increased and procedures established for the collection, flow and dissemination of information. This includes ensuring that up-to-date paperwork is submitted at all levels. Furthermore, a formal working group should be created with INEC to review the methodology for assigning the population at the local level.

- Communication activities on the importance and benefits of vaccination should be conducted on a permanent basis, not only during vaccination campaigns, to promote a culture of prevention in the population and a demand for vaccination services. A social communications plan targeting both the internal and external public should be drafted and tailored to the context, especially the local level and native languages.

The current political, economic and social scenario in Ecuador is favorable for implementing a series of innovations to tackle its institutional challenges and commitments in order to improve the quality of life for its people.

The report from this evaluation and the 5-year Plan of Action will undoubtedly serve as management and negotiating tools that will help the country maintain VPD elimination and control and meet major public health targets in the 21st century. ∎

The following article was adapted from the Final Report of the 2017 ad hoc Meeting of PAHO's Technical Advisory Group (TAG) on Vaccine-preventable Diseases

How to Face the Global IPV Shortage

Background

In September 2015, the Global Commission for the Certification of Poliomyelitis Eradication declared that indigenous wild poliovirus type 2 had been eradicated worldwide. Considering that no cases of wild type 2 polio (WPV2) have been detected since 1999 and that the continued use of the type 2 component of tOPV in areas of low coverage contributed to the occurrence of paralytic polio due to vaccine-derived poliovirus type 2 (VDPV2), the WHO's Strategic Advisory Group of Experts on immunization (SAGE) recommended the phased withdrawal of the oral polio vaccine, starting with serotype 2, through the switch from the trivalent oral polio vaccine (tOPV) to the bivalent vaccine (bOPV).

To ensure that new birth cohorts have protection against the type 2 poliovirus, either wild due to any potential failures in containment or vaccine-derived, the SAGE recommended that all countries that were exclusively using OPV introduce at least one IPV dose in their routine vaccination schedule.

These recommendations were endorsed by the TAG and the TAG additionally recommended that countries in the Region of the Americas introduce a sequential vaccination schedule, ideally starting with two doses of IPV, followed by two or three doses of bOPV.

In light of the limited IPV supply and in order to ensure that all countries in the Region had access to IPV prior to the switch, PAHO agreed with the countries that purchase the vaccine through the Revolving Fund (RF), to only introduce one dose of IPV in their routine schedule until there is sufficient supply to introduce a second dose.

Initial response to the limited IPV supply

In May 2016, the TAG held an ad hoc virtual meeting to discuss the global IPV shortage and the supply situation in the Region and reviewed the scientific evidence about the safety and immunogenicity of the administration of two fractional doses of IPV (fIPV), 0.1 ml or 1/5 of the complete dose, administered intradermally (ID). With the situation presented at that time, the TAG recommended that countries reduce IPV wastage, prepare to respond to a possible shortage of IPV, strengthen outbreak response, evaluate the capacity for the use of ID fIPV in the routine program and strengthen epidemiological surveillance.

During 2016, in order to avoid IPV stock-outs in the Region, the Revolving Fund and PAHO's Comprehensive Family Immunization Unit maintained contact with the vaccine producers and closely monitored and adjusted the vaccine delivery schedule. These actions enabled the Region to avoid IPV stock-outs, to date.

Current IPV supply situation

The two global IPV producers have faced production problems and consequently have communicated several reductions in the global IPV offers. At this time, it is anticipated that the global IPV supply situation will continue to worsen and will remain low until at least the end of 2018.

The only provider through the Revolving Fund that offers the vaccine in vials is Bilthoven Biologicals, at a cost of US$1.90 per dose. The other IPV producer, Sanofi, that did not accept the RF conditions, has offered a limited quantity of IPV doses in pre-filled syringes, at a cost of US$5.30 per dose. This offer has helped reduce supply gaps in the Region, but is not sufficient to respond to the total demand.

To date, as a result of the combined efforts among the countries, the Revolving Fund and the Immunization Unit, which has included monitoring of IPV stocks in countries, adjustments to the vaccine delivery schedule and permanent discussions with the providers, the countries have received sufficient vaccine supply to complete their polio vaccination schedule in the target population. However, even whilst maintaining these collaborative efforts, according to information received from countries about their current IPV stocks, it is estimated that as of July 2017, the countries of the Region will begin to face IPV stock-outs.

Scientific evidence on the use of fIPV

The available scientific evidence has shown that two doses of ID fIPV present a higher seroconversion for all serotypes than one full dose of IPV administered intramuscularly (IM). The maternal antibodies interfere with the immunological response, mainly for serotype 2, but there is less interference when the first dose is administered after 2 months of age. Also, the studies showed that the longer the interval between fractional doses, the better the immunological response. Adverse events occur more frequently with ID administration than with IM; however, they are generally mild local reactions such as erythema and induration.

Programmatic and operational considerations for the use of fIPV

In general, the ID administration of vaccines is more difficult than IM; for that reason, it is important that all health workers are adequately trained in order to guarantee safe administration of the vaccine. Additionally, the timely supervision of fIPV introduction is critical to ensure the safe and effective implementation of this schedule.

According to the WHO open-vial policy[3], IPV in multi-dose vials can be used for up to 28 days. For the application of fractional doses, a 0.1 ml 27 G 3/8 syringe should be used – which is the same one that is used for BCG in some countries. There are countries that administer BCG in a 0.05ml syringe and therefore do not have any stock of 0.1 ml syringes. According to information from the RF, it is likely that the 0.1 ml BCG syringe is not available in the majority of countries.

To introduce a fIPV schedule, updates to the registration systems need to be taken into consideration during the planning, training and supervision processes.

The use of fIPV ID is based on independent scientific evidence and is not specified on the label, which means that it is necessary for countries to follow the procedure of their respective National Regulatory Authority (NRA) to use this vaccine off-label.

TAG Recommendations

After reviewing the projections of production and the delivery schedule for IPV purchased through the RF and considering the potential threat of IPV stock-outs in the Region, as well as the scientific evidence on the immunogenicity of fIPV, the TAG recommends:

- Countries that administer more than 100,000 doses of IPV each year and have the capacity to adequately train health care workers and supervise implementation should immediately begin to prepare to implement a fractional dose IPV schedule. These countries include: Argentina, Bolivia, Brasil, Chile, Colombia, Cuba, Ecuador, El Salvador, Honduras, Nicaragua, Paraguay, Peru, Uruguay and Venezuela.

- The administration of a sequential schedule of two fractional doses followed by two or three doses of bOPV, with the first dose at two months of age and with intervals of 8 weeks between each dose of the basic vaccination schedule during the first year of life.

IPV continued from page 3

Vaccination Schedule	Basic			Booster	
	1st	2nd	3rd	4th	5th
	fIPV	fIPV	bOPV	bOPV	bOPV

- Brazil and Uruguay, countries that introduced IPV prior to 2015 and use a schedule of three doses of IPV, should review their vaccination schedules based on the current availability of the vaccine.

- Guatemala, Haiti and the Dominican Republic should carefully consider their capacity to introduce a schedule with two fractional IPV doses, weighing the training and supervision requirements and the need to achieve high coverage, with the risk of facing a stock-out. The TAG assesses that it may be best if these countries do not introduce the fractional dose schedule at this time.

- Countries that use less than 100,000 doses of IPV each year will likely face higher wastage of the vaccine if they are not able to effectively use the quantity of fractional doses in each vial within the timeframe of the open-vial policy. For that reason, these countries should carefully assess their situation because it may not be appropriate for them to introduce a fractional dose schedule.

- The TAG emphasizes the importance of reaching and maintaining vaccination coverage equal to or greater than 95% in each district or municipality.

- The TAG reiterates its recommendations made in May 2016. ∎

Estimating the Contagiousness of a Disease with the Basic Reproduction Number

The basic reproduction number **(R₀)** is a parameter for estimating or quantifying the contagiousness of a disease. It represents the average number of cases caused directly by an infectious case during its communicable period when introduced into a completely susceptible population. For example, an R_0 of 17 for measles in a completely susceptible population (in this case, without any vaccination) indicates that one case of measles would result in an average of 17 secondary (new) cases during its communicable period. An infection will persist in the community as long as each infected case transmits the infection to at least one individual (state of equilibrium or endemicity). If the R_0 is < 1, the infection will tend to decline until its eventual disappearance. The higher the R_0 value, the harder it will be to control, eliminate or eradicate a communicable disease.

Utility of the R_0

It makes it possible to:

1) quantify an infection's communicability—that is, to have an idea of how successful a disease will be in spreading.

2) estimate the percentage of vaccination coverage necessary for blocking transmission of the infection.

3) estimate the proportion of susceptibles that would remain when the infection is endemic.

Calculating the R_0 number:

The R_0 number has three components, expressed as:

b: the case rate or probability that an infectious case will transmit the infection to its contacts during the communicable period or the strength of the infection;

c: the number of potentially infectious contacts of a typical case per unit of time;

and

d: the length of the case's communicability, expressed in an identical unit of time.

The R_0 formula is:

$$R_O = b * c * d$$

The average number of contacts produced by effective contact with an infectious case during its communicable period is the product of c times d. The R_0 number is the product of the probability of transmission per contact times the average number of contacts in the communicable period.

Example: If the measles case rate is 0.80 **(b)** and the number of close contacts during the communicable period is estimated at 20 per week **(c)** and the length of the period is one week **(d)**, then R_0 = b · c · d = 0.80 · 20 · 1 = 16; thus, according to these estimates, every case of measles will produce 16 cases per week.

Effective reproduction number (R_e): Using the R_0, we can obtain the effective reproduction number, which is the average number of secondary cases produced by an infectious case when the population is partially immune as a result of prevention and control measures, such as vaccination.

The R_e formula (where P = vaccination coverage) is:

$$R_e = (R_0 - (P * R_0))$$

Critical vaccination proportion and community, or herd immunity

The critical vaccination proportion (P_c) is the percentage of the population that must be immune to achieve herd immunity (that is, for the R_0 to be reduced to an R_e of one, meaning that one new case would produce an average of one secondary case). The value of the critical vaccination proportion (P_c) depends on the infectious agent involved. All of this assumes homogeneous mixing.

Figure 1: Relationship between the basic reproduction number and the critical vaccination proportion.
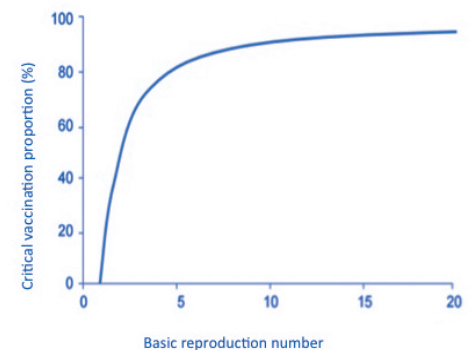
Herd immunity is the resistance in a community or group of individuals to the spread of an infectious disease and is directly dependent on the proportion of people in that population who are immune to the causative agent of the disease.

Identification of the P_c is critical to determine the value that vaccination coverage against an agent should reach to achieve its control, elimination or eradication. Control of an agent's transmission is achieved when the value of the effective reproduction number (R_e) is less than 1 (R_e <1) – that is, when each infectious case results in less than one new case: if the R_e is reduced to less than 1, the simultaneous introduction of two or more infectious cases in that population would be required to produce a secondary case. For example, if the R_e is reduced to 0.5, two infectious cases would be needed to produce a secondary case (calculated as follows: 1/0.5 = 2; likewise, if the R_e is reduced to 0.25, four infectious cases would have to be introduced to produce a secondary case: 1/0.25 = 4). This does not mean that new cases will not occur, but rather, that transmission of the disease will not be sustained

BASIC REPRODUCTION NUMBER continued from page 4

and that the transmission period will be brief, due to the presence of many immune individuals and few susceptibles in the population or an increase in control measures. In other words, getting the R_e below 1 is what it would take to interrupt transmission of the disease, gradually reducing the probability that the introduction of infectious cases would produce secondary cases until, in the best-case scenario, indigenous cases are eliminated.

These concepts are extremely important in systematic immunization programs, since vaccination coverage must be greater than this critical vaccination proportion to prevent epidemics or achieve the elimination of the diseases. Maintaining high uniform coverage makes it possible to obtain the maximum protective effect from vaccination in the general population. Being vaccinated not only implies individual protection, but a contribution through solidarity and equity to the protection of the population as a whole, especially people who, for one reason or another, have been unable to receive the vaccines or have not obtained adequate protection. An example of this is the fact that the countries of the Americas have sought to achieve 95% or more coverage with all vaccines in their immunization schedules, which has enabled them to advance rapidly toward the eradication, elimination and control of vaccine-preventable diseases (VPDs).

Example: In the case of diseases like measles, characterized by a single host, a primarily direct transmission mechanism, long-lasting immunity, and assuming a random pattern of contact between susceptibles and infectious cases, the reduction in the initial R_o in a partially immune population can be calculated multiplying the R_o by the fraction or percentage of susceptibles. Take an infection with an R_o of 8 that penetrates a susceptible population: in a natural situation — that is, without a vaccinated population — a primary case will produce 8 secondary cases. If the proportion of the population vaccinated against the infection is 25% (critical vaccination proportion: $P_c = 0.25$), then 2 out of every 8 individuals will escape the infection; that is, the effective reproduction number, R_e, will be 6 (75% will be infected). If 75% are vaccinated, the R_e would be equal to 2; that is, 6 out of 8 individuals would escape the infection.

In a vaccinated population, the number of individuals that escape the infection is: $(P_c \cdot R_o)$. Applying these formulas to the last situation in the previous example (75% of the population vaccinated), we have: no. of individuals protected $= P_c \cdot R_o = 0.75 \cdot 8 = 6$, and no. of secondary cases per case or $R_e = R_o - (P \cdot R_o) = 8-(0.75 \cdot 8) = 8-6 = 2$.

Over the past 20 years, the concept of herd immunity has become key in defining immunization program objectives and strategies, since it makes it possible to determine the intensity of the action needed to prevent epidemic outbreaks and control and eliminate infectious diseases.

For herd immunity to block the transmission of an infectious agent, immunization programs must bring the R_o value to below 1. To prevent a primary case from causing an epidemic, the number of secondary cases $(R_o-(P \cdot R_o))$ should be <1. This equation is used to obtain the critical vaccination proportion (P_c), or vaccination threshold level, for blocking transmission of the infection: $P_c (R_o-1)/R_o$; that is, P_c 1-$(1/R_o)$.

Example: If we assume that measles has an R_o of 18, the P_c should be at least: 1-(1/18) = 0.94, or 94%. In short, to prevent an epidemic, the P_c for the population to be vaccinated must be greater than 1 minus the inverse of R_o. With this level of vaccination, there can still be secondary and even tertiary cases. However, the possibility of epidemics has been minimized. **Table 1** shows the P_c value for several infectious VPDs and **Figure 1**, the relationship between the R_o and the P_c: note that when the R_o is above 10, the P_c necessary for producing a substantial indirect protective effect is very high—that is, high vaccination coverage is required.

Table 1: Basic case reproduction number (R_o) and critical vaccination proportion (P_c) for certain vaccine-preventable childhood diseases

Infectious disease	Basic reproduction number (R_o)	Cricitcal vaccination proportion of (P_c)	Location and date	Reference
Measles	18	94%	Senegal, 1964	Blue (1964)
Smallpox	2.3	57%	West Africa, 1960s	Forge, et al. (1975)
Mumps	8	87%	United Kingdom, 1987	Farrington (1990)
Rubella	6	83-85%	United States, 1967	Hayden, et al. (1977)

Source: Almut Scherer and Angela McLean. Mathematical models of vaccination. British Medical Bulletin, 2002;62.

In general, the reproduction number of a contagious disease depends mainly on its potential for contagion, which is a characteristic of the agent, the length of the communicable period related to the characteristics of the disease and the conditions of the host and the number of susceptibles in effective contact with the infectious case during the communicable period. Considering the latter two conditions, we can identify actions that diminish or interrupt the speed or extent of the transmission. In this regard, while it is not always possible to reduce the communicable period, the number of contacts with susceptible people can be reduced by isolating the case, though this is not always effective. Another way of reducing the probability of effective contacts is to reduce the number of susceptibles in the population and this is precisely where immunization's potential is greatest.

However, when estimating vaccination coverage, it is necessary to consider the effectiveness of the vaccine employed, because vaccines are not 100% effective. This means that to protect the necessary percentage of the population, a higher percentage must be vaccinated. Thus, as long as there are regions of the world where the measles virus is circulating, the regions where cases of this disease no longer occur are at risk of secondary cases caused by the introduction of an imported case, even with 99% vaccination coverage.

In a world where measles is still endemic in other regions and where people travel, and given the high contagiousness of measles, 99% coverage will be best to reduce a maximum estimated measles R_o of 18 to an R_e of 1. To achieve this, it is recommended that high coverage is not only achieved for the first dose of the measles-containing vaccine (MCV1), but also for the second dose (MCV2). Surveillance must also be in place to rapidly detect importations and transmission, in order to implement outbreak control measures as soon as possible.

Routine vaccination programs must reach at least the upper threshold of the critical vaccination indicator. However, given the assumptions, these numbers are conservative estimates, since the models used to calculate them assume that populations behave in an ideal manner. For example, they assume that vaccinated people are homogeneously distributed throughout the population, they do not consider the presence of pockets of susceptibles, or they assume that infectious cases interact randomly with the susceptible population. These types of assumptions lead to underestimation of the vaccination coverage needed to achieve herd immunity under real conditions. Furthermore, reaching the critical vaccination level protects against outbreaks but is probably not enough to eliminate the transmission of an infectious agent. Thus, the P_c should be increased to ensure herd immunity under real conditions for VPDs in the process of elimination. ■

Vaccination against Yellow Fever in Paraguay

Background

In South America, the endemic area of the yellow fever virus (YF) has historically included the tropics and sub-tropics of Bolivia, Brazil, Colombia, Ecuador, Guyana, French Guiana, Peru, Suriname and Venezuela. At the end of 2007, an extensive epizootic developed, including a large ecological area shared by Brazil, Paraguay and the Province of Misiones in northern Argentina, which redefined the YF enzootic area in South America.

In 2008, 34 years after the last case of YF was reported in 1974, Paraguay reported an epidemic outbreak of YF in the district of San Estanislao, located in the Second Department (San Pedro). By epidemiological week 22 of 2008, a total of 28 cases were confirmed. The outbreak spread to three departments, including the Asunción metropolitan area. The outbreak in the urban area was the first one reported in the Americas in the last 50 years.

In the urban outbreak in the Asunción metropolitan area, nine cases were clustered in the Laurelty neighborhood of the San Lorenzo municipality. This area presented high levels of *Aedes aegypti* infestation, which contributed, among other factors, to effective urban transmission. Five of the cases (56%) were women; the average age was 25 years, with a range from 11 to 39 years old. Three of the nine cases died from the disease (33% case fatality). With respect to occupation, none was an agricultural worker, the cases were not linked and none had traveled outside the department.

Paraguay introduced the YF vaccine into the routine immunization program in 2006, the target population being 1-year-old children. The country redefined risk areas and adjusted the vaccination plan to maintain high coverage in enzootic areas, continued travel to these areas and routine vaccination. After the outbreak, Paraguay was included in the World Health Organization (WHO) list of YF endemic areas.

In 2012, after the pneumococcal vaccine was introduced into the national vaccination schedule, the age of administration for the YF vaccine was changed from 12 to 18 months for operational reasons. After this change, coverage decreased. In light of this situation and considering recommendations made by the Technical Advisory Group (TAG) on Vaccine-preventable Diseases in 2009, vaccine administration to 12-month-olds was reinstated. This included vaccinating the population from 2 to 59 years old not previously vaccinated, in accordance with the recommendation detailed in the WHO position paper[4] (June 2013).

In January 2017, based on the epidemiological alert issued by the Pan American Health Organization/World Health Organization (PAHO/WHO) in reference to a YF outbreak in Brazil, the Ministry of Public Health and Social Welfare *(MSPyBS)* implemented a plan that included several strategic components. Actions taken and results obtained up to March 2017 are described below:

Comprehensive approach

The Integrated Management Strategy for vector-borne disease prevention and control (IMS-vectors) was the entity responsible for coordinating and identifying activities aimed at preparedness and response to the YF situation. It was chaired by the Vice-Minister of Health and convened several *MSPyBS* directors and programs and included participation by the National Immunization Technical Advisory Group, the Paraguayan Pediatric Society and the Paraguayan Society for Infectious Diseases. Before establishing the action plan and IMS-vectors strategy, a review was conducted of lessons learned during the outbreak of 2008.

The comprehensive action plan included six components: 1) vector control; 2) vaccination; 3) epidemiological surveillance; 4) epizootic surveillance; 5) clinical management and; 6) risk communication.

Analytic work was done weekly to evaluate the progress in the different components, assess the epidemiological situation of YF and determine the required approach.

Risk analysis

In order to target interventions, a risk analysis was conducted considering the reported epizootics and the YF situation in Brazilian departments that share a border with Paraguay, specifically Mato Grosso do Sul and Paraná.

The variables considered in the evaluation of epizootic risk were: 1) forest areas with a probable presence of nonhuman primates; 2) settlements near jungle areas; 3) migration to areas at risk of epizootics and/or importation. In turn, the following variables were considered in order to evaluate the risk of the disease spreading: 1) vaccination coverage in the population aged 1 to 59 years old; 2) population density and 3) urbanization. On the basis of these variables, a point system was established and the following risk levels were determined: low (0 to 4 points), medium (5 to 7 points) and high (8 to 12 points).

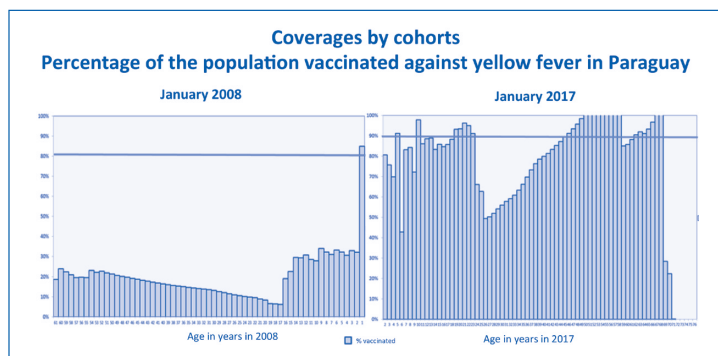### Categorization of YF risk in Paraguay

Department	Epizootic			Spread of the outbreak				Risk	Level of risk
	Forest areas with a probable presence of nonhuman primates	Presence of settlements near jungle areas	Migration to areas at risk of epizootics and/or importation	Vaccination coverage of the population aged 1-59 years old		Population density	Urbanization		
	Yes= 1, No=0	Yes= 1, No=0	Yes= 1, No=0	Percentage	Value	Yes= 1, No=0	Yes= 1, No=0	Value (0-12)	
San Pedro Norte	1	1	1	86%	2	0	0	5	Medium
San Pedro Sur	1	1	0	77%	2	0	0	4	Low
Central	0	0	1	80%	2	1	1	5	Medium
High Paraguay	1	0	0	59%	3	0	0	4	Low
Concepción	1	1	1	79%	3	0	0	6	Medium
Amambay	1	1	1	68%	3	0	0	6	Medium
Canindeyú	1	1	1	50%	3	0	0	6	Medium
High Paraná	1	1	1	67%	3	1	1	8	High
Asunción	0	0	1	93%	1	1	1	4	Medium
Cordillera	0	0	1	60%	3	0	1	5	Medium

Coverage ranges	Value
95% to 100%	1
80% to 94%	2
50% to 79%	3
Below 50%	4

Level of risk	
Value	Category
0 to 4	Low
5 to 7	Medium
8 to 12	High

Analysis of the vaccination coverage situation

The Expanded Program on Immunization (EPI), with PAHO's technical support, conducted a detailed analysis of the vaccinated cohorts by district. Paraguay has an estimated population of 7,639,000, of which 5,700,000 have been vaccinated. This analysis noted significant progress in YF vaccination coverage and identified areas with the greatest gaps in vaccination coverage, where vaccination and monitoring actions should be stepped up. Vaccination was monitored in districts bordering Brazil, including 100% of settlements and communities near forest areas. The risk analysis and the analysis of vaccination coverage by cohort were used to guide vaccination efforts and vector control in high-risk epizootic areas.

Coverages by cohorts
Percentage of the population vaccinated against yellow fever in Paraguay

January 2008 — Age in years in 2008
January 2017 — Age in years in 2017
□ % vaccinated

An active institutional search was implemented for Events Supposedly Attributable to Vaccination or Immunization (ESAVI). As of March 31 2017, no severe ESAVI case associated with the yellow fever vaccine had been reported.

Conclusions

The comprehensive approach has strengthened implementation and above all, monitoring of comprehensive interventions including vaccination, vector control, epizootic surveillance and ESAVI surveillance. Paraguay's progress in vaccination against yellow fever has allowed the country to remain disease-free and decrease its risk of urban transmission. The lessons learned during the outbreak of 2008 are reflected in the country's progress in yellow fever prevention and control. ∎

Table 1. Prices for Vaccines Purchased through the PAHO Revolving Fund, 2017 (prices in US$)

Vaccine		Doses per vial	Average cost per dose
BCG		10	0.1406
Bivalent Oral Polio (bOPV)		10	0.1600
		20	0.1333
Cholera		1	1.8500
DPT		10	0.2048
DT	Pediatric	10	0.1670
DTaP Triple Acellular	Pediatric	1	15.0000
DTaP-IPV	Tetravalent Acellular	1	11.0000
DTaP-IPV-Hib	Pentavalent Acellular (pre-filled syringe)	1	13.6000
DTaP-IPV-Hep B-Hib	Hexavalent Acellular	1	19.8000
DTP	Hib Lyophilized	1	2.6500
DTP Hepatitis B Hib Pentavalent	Liquid	1	1.0640
Hepatitis A	Pediatric	1	8.0562
	Adult	1	13.2000
Hepatitis B (Recombinant)	Adult	10	0.1815
	Adult	1	0.3264
	Pediatric	1	0.2165
Hib	Lyophilized	1	2.0500
Human Papiloma Virus (HPV)	Bivalent	1	8.5000
	Quadrivalent	5	9.8000
Inactivated Polio (IPV)		1	5.3000
		5	1.9000
Measles-Rubella		1	2.2500
		10	0.6060
Measles/Mumps (Jeryl-Lynn Strain)/Rubella		1	6.0000
Measles/Mumps (Urabe Strain)/Rubella		1	4.5000
Measles/Mumps (Zagreb Strain)/Rubella		1	2.4900
		5	1.3000
Meningococcal ACYW135		1	20.3000
Pneumococcal Conjugated Pediatric	10-valent (PCV-10)	1	12.8500
	13-valent (PCV-13)	1	14.5000

Vaccine		Doses per vial	Average cost per dose
Pneumococcal Unconjugated	Adult 23-valent	1	6.8100
Rabies Human Use (Vero Cells)			12.2000
Rotavirus, Liquid	2-dose immunization schedule	1	6.5000
Seasonal Influenza Trivalent Southern Hemisphere 2016	Adult	1	4.3000
	Adult Korean Origin	10	2.7000
	Adult French Origin	10	3.4000
	Pediatric Korean Origin	20	1.3500
	Pediatric French Origin	20	1.7000
Seasonal Influenza Quadrivalent Southern Hemisphere 2017	Adult	10	5.1400
Td	Adult	10	0.1103
Tdap Triple Acellular	Adolescent/Adult	1	11.3943
Typhoid Polysaccharide		20	9.0000
Varicella		1	14.8502
Yellow Fever		10	1.1747

2017 Vaccine Prices Amendment I

Member States will be billed according to these prices, unless otherwise stipulated in country agreements. PAHO invoices will include the cost of the vaccine, a 4.25% service charge (applicable only to the cost of the biological product) and actual charges for packing, freight and insurance.

PAHO/WHO Representatives are encouraged to issue proforma invoices based on the "FCA" average prices (indicated in the price list). For estimating the cost of packaging, insurance and freight, use 15% of the value of the biological products for budgetary purposes. This is due, in part, to the origin of the product. The actual cost of these services may vary and will be reflected in the PAHO invoice, which is issued approximately 30 days after the order has been delivered. Delivery lead time is approximately 60 days after the requisition is received by the Procurement and Supply Management Department.

Please continue to work closely with the Revolving Fund for Vaccine Procurement in updating quarterly vaccine requirements from Member States. The accuracy and availability of this information is critical to PAHO's work with suppliers to ensure the timely manufacturing and availability of the products.

Table 2. Prices for Syringes Purchased through the PAHO Revolving Fund, 2016-2017 (prices in US$)

DISPOSABLE SYRINGES, PLASTIC WITH ATTACHED NEEDLE		
SIZE	PACKED PER CASE	PRICE PER UNIT*
1cc 22G x 1 1/2"	3600	$0.0320
	2000	$0.0318
	3000	$0.0241
	1400	$0.0293
1cc 23G x 1"	3600	$0.0315
	2000	$0.0318
	3200	$0.0219
	1400	$0.0293
1cc 25G x 5/8"	3600	$0.0320
	1400	$0.0293
	3200	$0.0219
1cc 26G x 3/8"	1400	$0.0293
3cc 23g x 1"	1000	$0.0398
5cc 22G x 1 1/2"**	1800	$0.0330
	1800	$0.0259

AUTO-DISABLE SYRINGES, PLASTIC WITH ATTACHED NEEDLE		
SIZE	PACKED PER CASE	PRICE PER UNIT *
0.5cc 22G x 1 1/2"	3000	$0.0660
0.5cc 23G x 1"	3000	$0.0395
	1400	$0.0340
0.5cc 25G x 5/8"	1400	$0.0390
	3000	$0.0510
0.5cc 26G x 3/8"	1400	$0.0420
0.1cc 27G x 3/8"	3000	$0.0656
	1400	$0.0420

* Prices FCA (Free Carrier) for each syringe.
** Different suppliers are used when syringe size and packaging are the same, but have different prices.

2016-2017 Syringe Prices Amendment I

Member States will be billed according to these prices, unless otherwise stipulated in country agreements. PAHO invoices will include the cost of the syringes, a 4.25% service charge (applicable only to the cost of the syringes), and actual charges for packing, freight and insurance.

PAHO/WHO Representatives are encouraged to issue proforma invoices based on the "FCA" prices. For estimating the cost of packing, insurance and freight, use 25% of the value of the syringes for ocean shipments and use 110% of the value of the syringes for air shipments. This is due, in part, to the origin of the product, the weight and the shipping mode — air or sea. The actual cost of these services may vary, and will be reflected in the PAHO invoice, which is issued approximately 30 days after the order has been delivered. Delivery lead time is approximately 30 days by air and 60 days by ocean after the requisition has been received by the Procurement and Supply Management Department.

Please continue to work closely with the Revolving Fund for Vaccine Procurement in updating quarterly syringes requirements from Member States. The accuracy and availability of this information is critical to the work with suppliers done by PAHO's Department of Procurement and Supply Management, to ensure the timely manufacturing and availability of syringes.

Source: For up-to-date vaccines prices, please visit: www.paho.org/revolvingfund (click on "Vaccine Prices, 2017" - under the 'Revolving Fund Related Documents' column). ∎

Comprehensive Family Immunization Unit

Pan American Health Organization

World Health Organization

REGIONAL OFFICE FOR THE **Americas**

COLUMN: What I Have Learned…

By Dr. Papa Coumba Faye, former PAHO/WHO immunization advisor for Haiti

Dr. Papa Coumba Faye.

Five years ago, I joined the PAHO office in Haiti after 12 years in the field of vaccination in Africa, first as program manager in Senegal and then as coordinator of a project to support the establishment and operation of the Technical Advisory Groups (TAG) on Vaccine-preventable Diseases.

Since joining the PAHO immunization program, I have had the opportunity to work with talented and committed professionals who have made the Region of the Americas a global leader in immunization. PAHO/WHO has successfully developed and implemented strategies for the elimination and eradication of vaccine-preventable diseases, most recently with the declaration of the Region of the Americas as the first WHO region free of measles and rubella.

At PAHO, I have had the opportunity to participate and above all, learn from the implementation of original initiatives and strategies such as Vaccination Week in the Americas, whose success led to World Immunization Week, held since 2012.

The five years I have spent in this country – so far, yet so near to Africa – have given me a great opportunity to collaborate and spend time with men and women whose passion, courage and commitment command admiration. Among the professionals who have left a strong impression on me, I would particularly like to mention Ms. Marie-Nicole Noël—one of the pillars of the Expanded Program on Immunization (EPI) in Haiti. I have often told her she reminds me of a certain Bernadette Ndiaye, who guided my first steps in the EPI in Senegal.

I would also like to pay tribute to the health workers who work at the margins of the health system, often in very difficult conditions, walking long hours on arduous paths to reach children and mothers who need vaccination.

In Haiti—a priority country for PAHO/WHO—although real progress has been made in recent years, challenges remain in terms of health in general and immunization in particular. The EPI still needs the support of all technical and financial partners to strengthen itself on a sustainable basis. PAHO/WHO will therefore need to continue its efforts to gain strong political commitment and increased support for immunization and to strengthen the leadership and management capacities of national immunization program managers at all levels.

Finally, I would like to express my gratitude and appreciation to those who have trusted and supported me through all these years, in particular Drs. Gina Tambini, Cuauhtémoc Ruiz Matus, Léa Guido, Jean-Luc Poncelet and Luis Codina.

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. ■