Immunization Newsletter

Pan American Health Organization

Volume XXXVI Number 4 | Immunize and Protect Your Family | August 2014

PAHO's 2014 Technical Advisory Group Meeting

On 1-2 July 2014, the XXII Meeting of PAHO's Technical Advisory Group (TAG) on Vaccine-preventable Diseases took place in Washington, DC to review Regional progress on selected topics and issue recommendations to address pressing challenges faced by national immunizations programs in the Americas.

PAHO's Assistant Director, Dr. Francisco Becerra, welcomed the participants and gave a brief introduction to the TAG's charge as regional technical advisory group on vaccine-preventable diseases. This XXII TAG meeting was marked by the recent passing of Dr. Ciro de Quadros, TAG Chair since 2004. A minute of silence was observed in memory of Dr. de Quadros before starting the meeting, at the request of interim-Chair Dr. Peter Figueroa. Dr. Jon Andrus, PAHO Deputy Director, shared reflections to honor Dr. Ciro de Quadros.

In this issue of the Immunization Newsletter, we present the topics that were marked "For Decision" at the 2014 TAG Meeting:

- **Update on Pertussis Vaccination**
- **Status of Human Papilloma Virus Vaccination**
- **Vaccination with Pneumococcal Conjugate Vaccine in Adults**

We also present the following topics that were marked "For Information" at the 2014 TAG Meeting:

- **Update on the Regional Immunization Program of the Americas**
- **Update on the PAHO Revolving Fund**
- **Cholera Vaccination in the Americas**
- **Status of Influenza Vaccination in the Americas and Formation of the Network for Evaluation of Influenza Vaccine Effectiveness—REVELAC-i**

A complete list of topics can be seen in the 2014 TAG Report, accessible online at http://www.paho.org/immunization/TAG-Reports

PAHO's Technical Advisory Group Meeting, 2014.

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In This Issue

Cholera Vaccination in the Americas

In 2013, cholera transmission was reported in four countries of the Americas—Cuba, Haiti, Mexico, and the Dominican Republic. Although transmission in Haiti has declined significantly since cholera emerged in October 2010, the country is still reporting the greatest incidence in the Region. During the 12 months from June 2013 to May 2014, 44,867 cholera cases and 450 cholera-related deaths were recorded in Haiti. In contrast, during the 12 months from October 2010 to September 2011, 464,670 cases and 6,555 deaths were reported—10 and 15 times greater, respectively, than in the most-recent 12-month period.

Deployment of oral cholera vaccine (OCV) has been considered since October 2010. At that time, PAHO recommended focusing emergency efforts on time tested measures for cholera outbreak response. An expert consultation convened by PAHO in December 2010 recommended that the limited vaccine supply be used for demonstration projects and that efforts be taken to increase OCV availability. Between April and June 2012 two non governmental organizations, GHESKIO and Zanmi Lasante/Partners in Health, conducted separate but coordinated cholera vaccination of nearly 100,000 people in one urban and one rural area of Haiti. In July–August 2013, the Haitian Ministry of Health vaccinated an additional 120,000 people in two localities.

TAG discussed the use of the oral cholera vaccine (OCV) in October 2012 with a focus on the Island of Hispaniola. As part of a regional initiative for elimination of cholera transmission on the Island, TAG recommended deployment of OCV in Haiti to mitigate the cholera burden in the short and medium term, until significant and sustainable advances are achieved in infrastructure for drinking water supply and sanitation. TAG's recommendations were adopted in the "National Plan for the Elimination of Cholera in Haiti, 2013–2020," which the Haitian Government issued in February 2013.

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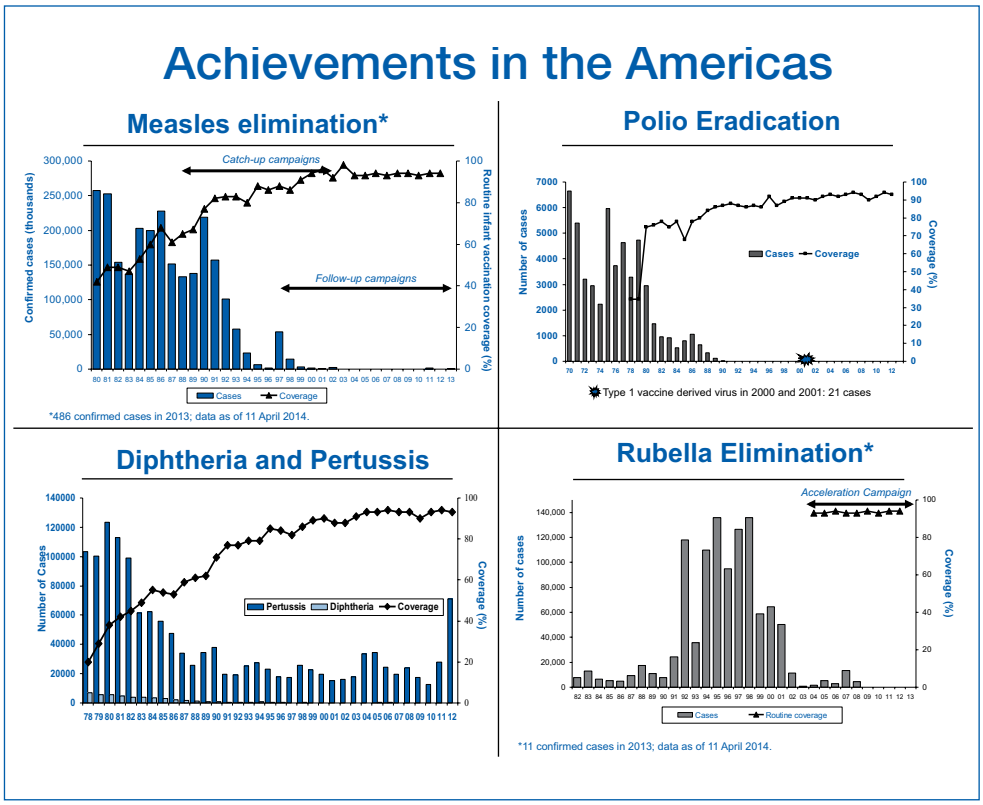
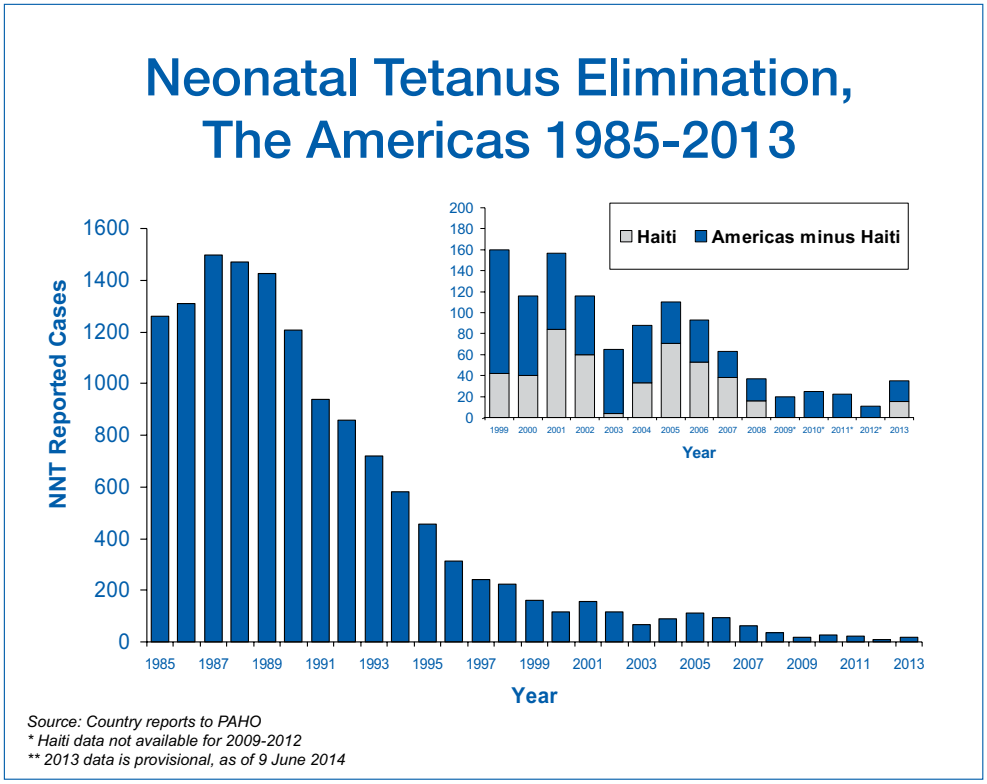
Update on the Regional Immunization Program of the Americas

The most recently available data on the situation of vaccine-preventable diseases (VPDs) and the immunization program of the Americas is presented under the framework of the Regional Immunization Vision and Strategy (RIVS).

The RIVS is the Global Immunization Vision and Strategy (GIVS) restructured to accommodate immunization needs and objectives at the regional level. Its goals are to maintain coverage achievements, complete the unfinished agenda and meet new challenges.





[1] NNT elimination is defined as <1 case of NNT per 1,000 live births in every municipality.

The Region is working to present the regional adaptation of the Global Vaccine Action Plan (GVAP) to PAHO's Directing Council in 2015.

Maintaining the Achievements

Coverage levels have remained over 90% throughout the Region and work is ongoing to maintain VPD control and elimination.

Available preliminary data for 2013, however, suggests that regional DTP3 and Polio3 coverage may have declined compared to previous years. This situation is being examined.

Addressing the Unfinished Immunization Agenda

Work in this area has revolved around targeting underperforming municipalities and other areas within countries. Latin American countries have identified risk areas based on coverage, VPD surveillance performance, and other socio-demographic and contextual factors. It is of concern that only about half of the ~15,000 municipalities in Latin America and the Caribbean (LAC) reach coverage rates ≥95%. Furthermore, it is also concerning that there are several municipalities, concentrated in a few countries, reporting coverage levels <50%.

Since its creation in 2003, Vaccination Week in the Americas (VWA) has served as a platform to target vulnerable populations every year. In 2014, VWA's slogan was "Vaccination: Your best shot" in acknowledgment of the FIFA World Cup of Football (Soccer) taking place in Brazil.

Finally, an important part of the unfinished agenda is the elimination of neonatal tetanus (NNT) as a public health problem in Haiti.[1] While cases have continued to decline over the years, elimination has proven challenging.

Meeting New Challenges

The introduction of new more expensive vaccines has been one of the main challenges immunization programs of the Americas have faced in recent years. About 90% of the birth cohort in the Region lives in countries that have introduced a pneumococcal conjugate vaccine in their regular program (~60% of the cohort of LAC); ~87% of cohort is living in countries that have introduced rotavirus vaccine (60% of the cohort of LAC), and ~75% of girls 10-14 years old live in countries that have introduced a human papilloma virus (HPV) vaccine.

Operational Activities

Of all the EPI components that the RIVS identifies as components requiring additional strengthening, cold chain and supply chain operations, syringe quality control program, economic evaluations (i.e. the ProVac Initiative), and vaccine effectiveness studies for rotavirus and conjugated pneumococcal vaccines were highlighted as a priority. The Revolving Fund for Vaccine Procurement is an important element of the program, as LAC countries finance >90% of national EPIs with national funds. ■

Update on Pertussis Vaccination

The TAG has made several recommendations regarding pertussis surveillance and vaccination in the last four years. One of these recommendations was that countries should not change the whole-cell vaccine from routine vaccination against pertussis to acellular vaccines, because of evidence suggesting the shorter duration of the immunity conferred by the acellular vaccine.

In November 2012, SAGE expressed concern about the apparent resurgence of pertussis in some industrialized countries despite high vaccine coverage with acellular pertussis (aP) vaccines, which in some settings was associated with an increase in infant pertussis deaths.

With the objective of reviewing the most recent evidence about aP vaccine effectiveness, SAGE established a working group that reviewed the data of 19 developing and industrialized countries from various regions around the world that showed high vaccination coverage with the whole-cell pertussis vaccine (wP) or the aP vaccine.

Given the natural periodicity of pertussis, disease resurgence was defined as a larger burden of disease than expected when compared to previous cycles in the same setting.

Main conclusions of SAGE pertussis working group:

- The vaccination against pertussis is highly effective in reducing disease caused by Bordetella pertussis, with a large decline in overall global incidence and mortality compared with the pre-vaccination era in both wP- and aP-using countries.
- To date, there is no evidence of a widespread global resurgence of pertussis. There is however evidence that resurgence has occurred in 5 of the 19 countries reviewed, 4 of which were exclusively using aP vaccines. The increased number of cases in 1 country using wP vaccine was considered to reflect factors other than the use of this vaccine, such as surveillance, laboratory methods, and low vaccine coverage in some areas.
- Recent modeling studies, as well as data from a baboon model, supported the hypothesis that wP to aP vaccine transition may be associated with disease resurgence.
- Although the reasons for the resurgence were found to be complex and varied by country, SAGE concluded that the shorter duration of protection and likely reduced impact on infection and transmission conferred by aP vaccines play critical roles.
- The influence of changes in circulating pertussis strains on the effectiveness of aP or wP vaccines was not found to contribute to observed country level resurgence.
- Licensed aP vaccines have lower initial efficacy, faster waning of immunity, and possibly a reduced impact on transmission relative to currently internationally available wP vaccines, as aP vaccines induce a different type of immune response, and are less effective in clearing mucosal infections.
- Surveillance and modeling data suggest that the use of aP vaccines may result in a resurgence of pertussis after a number of years and might lead to an increased risk of death in young infants compared with programs using wP. The magnitude and delay for this resurgence to occur are difficult to predict, given the many factors that intervene such as vaccine coverage, natural immunity, vaccine type, schedules, etc.
- Recent evidence suggests that maternal immunization with aP during pregnancy is safe and highly effective in protecting infants from pertussis and that it may have a high impact on morbidity and mortality in infants too young to have been immunized. This conclusion does not extend to wP vaccines, given the absence of immunogenicity and efficacy data in pregnant women and concerns regarding potential higher reactogenicity in adults.
- Vaccination of pregnant women is considered likely to be the most cost-effective complementary strategy to prevent pertussis-associated infant mortality.

SAGE Recommendations

- All children should be immunized against pertussis, with the goal of maintaining high coverage, as minor reductions can lead to an increase in incidence.
- The risk of resurgence associated with the use of aP vaccines for primary immunization, including increased disease in infants, compared with use of wP, indicates that countries where only a limited number of pertussis doses are used/affordable should continue to use wP vaccines for primary pertussis early infant vaccination. Thus the switch from wP to aP vaccines for primary infant immunization should only be considered if large numbers of doses (including several boosters) can be included in the national immunization schedules; this has substantial cost implications given the much higher cost of aP vaccines and higher number of doses required.
- Countries may consider the immunization of pregnant women with 1 dose of Tdap (in the 2nd or 3rd trimester) in addition to routine primary infant pertussis vaccination in countries or settings with high infant morbidity/mortality due to pertussis.
- SAGE emphasized the importance of efforts to improve surveillance of disease burden particularly in developing countries, and assessment of impact of infant immunization, with particular focus on fatalities in infants <1 year of age.

Recommendations:

- Although both available pertussis vaccines (aP and wP) elicit a good immune response, evidence suggests aP has a short-lived duration of protection. As such, countries should give preference to the use of wP containing vaccines. Countries using current vaccination schedules with whole-cell pertussis vaccines should continue to do so and countries using aP should actively monitor the risk that waning immunity poses to the population.
- PAHO should engage with partners, including WHO, in discussions with industry to advocate for the research and development of improved pertussis containing vaccines.
- Countries should ensure homogenous vaccination coverage ≥95% with 3 doses of pertussis containing vaccines in children aged <1 year; and encourage timely initiation and completion of the schedule. Coverage attained with the 4th dose of the DPT vaccine should be the object of careful recording, monitoring, reporting and evaluation.
- All countries should continue strengthening pertussis surveillance to better monitor the epidemiology of the disease. Also, countries should continue assessing the quality of their laboratory diagnostics and surveillance systems in order to evaluate the reliability of their data on incidence, case-fatality, age distribution, proportion of cases confirmed by different methods, and vaccine effectiveness.
- Every pertussis outbreak should be thoroughly investigated to improve the understanding of the current epidemiology of the disease in the Region of the Americas.
- The response to outbreaks of whooping cough should include lowering the age for initiating vaccination to 6 weeks and vaccinating pregnant women only in areas affected by the outbreaks. Currently, there is no evidence for TAG to recommend routine vaccination of pregnant women. ■

Vaccination with Pneumococcal Conjugate Vaccine in Adults

Pneumococcal pneumonia and other diseases caused by *Streptococcus pneumoniae* (*Spn*) continue to be a substantial cause of morbidity and mortality worldwide. Pneumonia is the most common manifestation in adults, and bacterial pneumonia is the most common form of invasive bacterial disease (IBD), accounting for 90% of the total number of cases. Mortality associated with pneumococcal pneumonia has hovered around 25% globally in recent decades.

The epidemiology of pneumococcal disease in adults in developing countries is not well described, but it is acknowledged that the burden of disease globally is significantly underestimated. The burden of pneumonia disease in adults is greater in adults ≥65 years of age as has been seen in the United States, Argentina, and Brazil. In addition, the burden of this disease has increased due to the number of individuals with chronic diseases or infected with human immunodeficiency virus (HIV), and the increased age of the population in many countries. Drug resistance, which is the greatest obstacle to the successful treatment of infections, has also been on the rise. In industrialized countries, fatality from pneumococcal bacteremia can reach 15-20% among adults and 30-40% in older adults, even when patients receive appropriate antibiotic therapy and intensive care.

The 13-valent pneumococcal conjugate vaccine (PCV) is prequalified by the WHO and licensed for ages ≥50 years in several countries. Preliminary results of placebo-controlled double-blind clinical trials of PCV13 vaccine, carried out in over 85,000 people aged ≥65 years, showed efficacy in pneumonia reduction (CAPiTA study). However, to date, the final results have not been published.

As demonstrated with PCV7 vaccine, recently published studies demonstrate a reduction in invasive pneumococcal disease (IPD) and pneumonias in adults in the United States with the introduction of PCV13 in the vaccination schedule for children. In other industrialized countries, the incidence of IPD has decreased sharply with the introduction of pneumococcal conjugate vaccines, including other age groups that are not the primary vaccination target group, due to the herd immunity effect these vaccines provide.

Given that data on the herd effect is limited in low and medium income countries, it is difficult to predict the impact of pneumococcal conjugate vaccines introduced into the childhood vaccination schedule on the reduction of pneumonia, IPD, and serotype replacement in LAC. However, a study in Brazil demonstrates the effect of PCV10 on the reduction of child carriers. Several issues need to be considered in evaluation of the herd effect:

- Availability of surveillance data in the adult population (most LAC countries do not have this information).
- At least three years since the introduction of PCV in children.
- Data on colonization rates in children. In LAC, rates are around 45%.
- Strength of pneumococcal infection transmission. Socio-demographic factors such as overcrowding may facilitate pneumococcus transmission from a colonized person to others.
- Individual immunological response to the vaccine may be influenced by factors such as malnutrition, immunological status, and others.
- PCV vaccination coverage in children. PCV vaccine coverage in LAC is high in general.
- Vaccination schedules adopted by the countries (3+1; 3+0; 2+1).

To date, 27 countries and territories in the Region have introduced pneumococcal conjugate vaccines (PCV10 or PCV13); however, there is still no evidence of herd effect in LAC countries.

More recently, PCV13 immunogenicity studies have been conducted in adults. These studies have demonstrated good immunogenicity, especially for the serogroups included in the vaccine, both in healthy adults and in high-risk patients. The available data indicate that the high-risk population has a greater probability of developing pneumococcal disease and death.

In regard to cost-effectiveness, there are few studies on the cost-effectiveness of PCV13 vaccine in adults in LAC. Cost-effectiveness analyses in LAC will depend on future studies based on data on the adult disease burden, direct local medical costs, vaccine costs, herd effect, and data on efficacy of PCV13 in adults.

Countries should consider programming and logistical aspects of the introduction of a new vaccine in the immunization program, considering recent prior experiences with the introduction of other new vaccines.

PAHO organized a working group in WDC, on 2-3 June 2014 in order to discuss the topic of adult vaccination with the 13-valent pneumococcal conjugate vaccine (PCV13) as a public health policy in Latin American and Caribbean countries (LAC). The conclusions of the group discussion were presented to the TAG.

Recommendations

- TAG endorses the recommendations of the working group, including:
  - The introduction of pneumococcal conjugate vaccines in children continues to be the priority for reduction of pneumococcal disease.
  - Introduction of PCV13 vaccination for healthy adults into immunization programs will depend on the results of studies of efficacy, cost-effectiveness, and herd effect.
  - Countries that have already introduced the 23-valent polysaccharide vaccine for use in adults could use the sequential schedule (conjugate-polysaccharide) for high-risk adults*.
  - Countries that do not use pneumococcus vaccine in high-risk adults* and consider vaccination of this population a priority could include PCV13 in their vaccination schedules, based on immunogenicity studies.
  - Implementation or strengthening of epidemiological surveillance of pneumonias and IPD in adults is a priority for countries.
  - Countries that have already introduced PCV vaccines for children should spell out mechanisms to measure the impact of vaccination on other age groups (herd effect).
- TAG encourages innovative surveillance and assessment approaches to better understand the preventable burden of pneumococcal disease in adults. Interaction with influenza surveillance networks should be further explored.
- Countries should seek to improve PCV vaccination coverage rates in children.

* Adults in high risk groups are adults ≥50 years of age, with the follow conditions: cerebrospinal fluid leak, cochlear implant, sickle cell disease/other hemoglobinopathy, congenital or acquired asplenia, immunocompromised persons, congenital or acquired immunodeficiency, human immunodeficiency virus infection, chronic renal failure, nephrotic syndrome, leukemia, lymphoma , Hodgkin's disease, generalized malignancy, iatrogenic immunosuppression, solid organ transplant, and multiple myeloma. This is a special recommendation for individual clinical decision-making. ■

Status of Human Papilloma Virus Vaccination

As of June 2014, 21 countries and territories in the Americas have introduced the vaccine against human papillomavirus (HPV) in their publicly funded immunization programs. Notably, Brazil introduced the HPV vaccine in March 2014 and 4.2 million Brazilian girls aged 11–13 years (85.3% of the target population) received the first vaccine dose by the end of June. Compared to the Sub regions of North America, the Southern Cone and the Andes, fewer countries in Central America and the Caribbean have introduced the HPV vaccine. Overall, an estimated 83% of a typical birth cohort of adolescent girls (6.3 million girls) has in principle access to HPV immunization in the Americas.

However, data on HPV vaccination coverage are limited. Only one country publishes coverage data each year, which are estimated through nation-wide surveys. For 2012—the sixth year of vaccination in this country—the estimated first-dose coverage in girls aged 13 years was 47%; drop-out between the first dose and the dose given after six months was 57%. For the same year, nine countries reported the number of administered HPV vaccine doses in their UNICEF/WHO Joint Reporting Forms (JRF); overall, 8.7 million doses were administered. For the four countries with adequate data for analysis (4.7 million doses administered), first-dose coverage ranged from 51% to 81%. Drop-out between the first dose and the dose given after six months ranged from 14% to 41% for the three countries with a classical 3-dose immunization schedule and was 48% for the country with an extended 3-dose immunization schedule. Although limited, these coverage data indicate that real access to and/or acceptability of the HPV vaccine and the monitoring of vaccinated cohorts remain deficient.

In July 2013, TAG recommended extended HPV immunization schedules for adolescents aged <14 years. TAG considered that these schedules could offer immunological, programmatic and financial advantages. In April 2014, WHO's Strategic Advisory Group of Experts on Immunization (SAGE) discussed the same issue. Specifically, SAGE considered that vaccine-induced antibodies mediate HPV vaccine efficacy and that, as immunobridging studies show, adolescent women had similar or higher antibody titers than adult women. SAGE also considered a systematic review of randomized and non-randomized studies and a descriptive review of observational studies, as well as the findings of an ad-hoc expert consultation on HPV immunization schedules. SAGE concluded that, based on immunologic evidence, a 2-dose extended schedule with a minimum interval of six months administered to adolescent women was non-inferior to a 3-dose classical schedule administered to adolescent and adult women. SAGE recognized that the potential of reducing the dose schedule from 3 to 2 and the flexibility in intervals between doses may lead to improvement in vaccination coverage.

Despite concerns by the public and some health professionals, the HPV vaccine is safe. In 2013–2014, WHO's Global Advisory Committee on Vaccine Safety (GACVS) reviewed the occurrence of events supposedly attributed to HPV vaccine and immunization at three occasions, namely in June and December 2013, and March 2014. At the last occasion, GACVS stated that "it is important to highlight and reiterate [these reviews] because a number of national immunization programs have been facing real and potential public losses of confidence in their programs as a result of increased negative publicity, even from safety issues that have been addressed." The efforts made by immunization programs to guarantee safe vaccine development and administration, the characteristics of today's HPV vaccines, the data generated in the controlled clinical trials, and the data emerging from post-marketing active surveillance and large and lengthy studies are the four elements that underpin HPV vaccine safety.

Emerging evidence shows the effectiveness of HPV immunization programs in reducing HPV infections and precancerous cervical lesions among young women. HPV immunization has a real potential to curb the burden of HPV-related cancers within a generation. However, the realization of this potential depends on a greater uptake and acceptability of the HPV vaccine by the public and health professionals alike.

Recommendations:

- TAG affirms the sound and robust evidence base that demonstrates the safety and efficacy of HPV vaccines among adolescent and young women. TAG also endorses the March 2014 and prior GACVS statements related to HPV vaccine safety. As such, TAG continues to encourage countries to adopt HPV vaccines in the routine national immunization schedule to prevent cervical cancer. To harmonize regional and global recommendations on HPV immunization schedules, TAG endorses the April 2014 SAGE recommendations. Specifically,
  - A 2-dose schedule with an interval of at least six months between doses is recommended for girls aged <15 years of age. This also applies to girls aged ≥15 years at the time of the second dose. If for any reason the interval between the first and second dose is shorter than 5 full months, a third dose should then be given ≥6 months after the first dose.
  - The 3-dose schedule (0, 1/2, 6 months) remains recommended for girls aged >15 years (when immunization is initiated) and for immunocompromised individuals of all ages, including those known to be HIV-positive;
  - These schedule recommendations apply to both the bivalent and tetravalent vaccines.
- Manufacturers and countries should work towards the harmonization of licensure information with recommended schedules at national level.
- TAG reaffirms that it is important for countries that are considering the introduction of the HPV vaccine, to carefully plan information systems to collect and analyze coverage data at all levels. Countries that have already introduced an HPV vaccine should strengthen their efforts to characterize vaccination coverage at subnational and national levels.
- TAG expresses concerns about the estimated low HPV vaccine coverage and high drop-out rate, which may indicate significant barriers, from parents and/or health workers, to access or lack of follow-up. TAG recommends that countries gather data to characterize these issues and to develop communication strategies to address them. ■

Update on the PAHO Revolving Fund

For 35 years, the PAHO Revolving Fund (RF) has been one of the cornerstones of success of the immunization programs in the Region, in terms of the elimination and control of vaccine-preventable diseases and the rapid and sustainable introduction of new vaccines. In 2013, on behalf of 41 countries and territories, the RF acquired 46 different vaccine presentations, as well as syringes and cold chain equipment. A total of 1,335 purchase orders, with a consolidated value of $495 million, were also placed, with more than 95% of funds from coming national budgets.

The RF is faced with situations of limited or sensitive supply for four vaccines: yellow fever, Tdap, varicella and MMR. The global production capacity of the yellow fever vaccine continues to be insufficient. Because of this, a WHO/UNICEF/PAHO working group was established to prioritize the allocation of the limited supply.

The global demand for Tdap and varicella vaccines is increasing faster than production capacity, creating conditions of scarcity. In addition, reducing inventories in progress and long production cycles for these vaccines affect the availability to meet demands from countries that are not planned in advance.

With regard to measles-containing vaccines (MR and MMR), the global supply is inconsistent. Of the four prequalified producers, one has 80% of global production capacity, two have production difficulties and high prices, and one is stopping. The growing global demand for these vaccines can affect the timely supply, if countries in the Region do not plan their needs precisely and in advance.

To address these challenges, the RF has made improvements to its tools for supporting countries in their timely, long-term demand planning, as well as in their plans for vaccine introduction.

Recommendations:

- TAG reaffirms its recognition of the RF as a pillar in the progress and success of country immunization programs in the Americas. In turn, the TAG acknowledges the support that countries and territories provide to the RF.
- The TAG continues to recommend that countries ensure the development of increasingly accurate demand forecasts and with greater long-term visibility. The PAHO RF should support countries in the process of planning and monitoring.
- TAG continues to support other regional pooled procurement initiatives, such as the ongoing discussion in the Eastern Mediterranean Region of the World Health Organization. ■

Status of Influenza Vaccination in the Americas and Formation of the Network for Evaluation of Influenza Vaccine Effectiveness—REVELAC-i

The Region of the Americas has made considerable strides in the introduction of the seasonal influenza vaccine. By 2013, 40 of the 45 countries and territories of the Americas were using the seasonal influenza vaccine in the public sector to protect one or more risk groups. This includes 40 countries and territories that vaccinate the elderly, 39 that vaccinate health workers, 30 that vaccinate children (5 of them only children with chronic diseases), and 36 that vaccinate adults with chronic diseases. Great progress has been made in the vaccination of pregnant women, growing from 7 countries in 2008 to 26 countries in 2013.

To guide vaccine policy, especially during the last decade, countries located in tropical areas, especially in Central America, have worked to improve surveillance systems for the influenza virus in the sub-region. However, there are still uncertainties about the most appropriate timing and formulation for vaccination in this sub-region. A similar situation is observed in countries such as Peru with two influenza circulation patterns during the year.

During 2012, a pilot was carried out in four Central American countries to evaluate the effectiveness of the influenza vaccine, using the existing severe acute respiratory infection (SARI) surveillance platforms already in these countries. This was a collaborative project among the United States Centers for Disease Control and Prevention (CDC), Training Programs in Epidemiology and Public Health Interventions Network (TEPHINET), and PAHO. The project took advantage of the lessons learned from the pilot and the official creation of the Network for Evaluation of Influenza Vaccine Effectiveness in Latin America and the Caribbean (REVELAC-i) in February 2013. That same year, the project was implemented in Argentina, Brazil, Chile, Colombia, Costa Rica, El Salvador, Honduras, Panama, and Paraguay during the 2013 influenza season.

The objective was to estimate effectiveness of the trivalent seasonal influenza vaccine in preventing SARI from influenza in the target vaccination groups (children and the elderly) that go to sentinel hospitals for SARI, using a test-negative case-control design.

The nine countries participated with 71 sentinel hospitals.

The REVELAC-i platform offers the opportunity to:

- Systematically evaluate VE using the existing sentinel hospital platform in countries.
- Continue integration of epidemiological surveillance, laboratory, and immunization programs to produce evidence for decision-making on influenza virus prevention and control.
- Explore the integration of sentinel surveillance for viral respiratory diseases with bacterial respiratory diseases using the REVELAC-i platform.
- Develop mechanisms to share experiences, lessons learned, and common methods among countries and research centers on influenza vaccine effectiveness, as well as for learning the impact of influenza vaccination.
- Conduct other evaluations, such as the effect of influenza vaccination on newborns in cohorts of pregnant women.
- Conduct knowledge, attitudes, and practices surveys on influenza vaccination, among others.

See REVELAC-i on page 7

REVELAC-i cont. from page 6

Recommendations:

- TAG notes the progress made in influenza vaccine use and urges countries to expand the use of this vaccine and achieve higher coverage rates, in line with previous TAG and SAGE recommendations with an emphasis on pregnant women and health care workers.
- The TAG applauds the formation and progress of the Network for Evaluation of Influenza Vaccine Effectiveness (REVELAC-i) and encourages Latin American and Caribbean countries to continue to produce evidence on the performance and impact of the influenza vaccine; and to strengthen the integration among immunization, epidemiology, and laboratory.
- PAHO should support the continued strengthening of influenza surveillance and should analyze and present the data by geographical areas within countries, particularly in larger countries where the influenza epidemiology and seasonality varies by region.
- PAHO should continue to provide guidance to countries on choosing the most adequate vaccine for their epidemiological and contextual situation. ■

Multicenter Evaluation of Influenza Vaccine Effectiveness in Latin America*

2012 Pilot phase

COUNTRY	TARGET GROUPS	
	Children	Elderly
Costa Rica	6 months – 10 years with chronic diseases	≥65 years
El Salvador	6 – 59 months	≥60 years
Honduras	6 – 35 months with chronic diseases	≥60 years
Panama	6 – 59 months	≥60 years

CDC, Influenza Division
CDC-CAR, Influenza Program
Pan American Health Organization

Protocol piloted in 18 sites

*Case-control (test-negative design) based on hospital sentinel surveillance of severe acute respiratory infection (SARI)

2013 Implementation

REVELAC-i

Influenza Vaccine Effectiveness Evaluation Network for Latin America and the Caribbean

Argentina
Brazil
Chile
Colombia
Costa Rica
Cuba
El Salvador
Honduras
Mexico
Panama
Paraguay
Uruguay
Nicaragua

Population of REVELAC-i Study

COUNTRY	TARGET GROUPS		NUMBER OF HOSPITALS
	Children	Elderly	117
Argentina	6–24 months	≥65 years	4
Brazil	6–23 months	≥60 years	29
Chile	6–23 months	≥65 years	6*
Colombia	6–23 months	≥60 years	7
Costa Rica	6 months–10 years **with chronic diseases**	≥65 years	6*
Cuba	6–23 months	≥65 years	TBD
El Salvador	6–59 months	≥60 years	4*
Ecuador	6–23 months	≥65 years	TBD
Honduras	6–35 months **with chronic diseases**	≥60 years	3*
Mexico	6–59 months; 3–9 years **with chronic diseases**	≥65 years	46
Panama	6–59 months	≥60 years	10*
Paraguay	6–35 months	≥60 years	2

*All SARI surveillance sentinel sites included.
Sentinel hospitals selected based on: surveillance quality, SARI patients volume among target groups, reporting of PCR results for influenza, representativeness, availability of vaccination records at local level etc.

The *Immunization Newsletter* is published every two months, in English, Spanish, and French by the Comprehensive Family Immunization Project of the Pan American Health Organization (PAHO), Regional Office for the Americas of the World Health Organization (WHO). The purpose of the *Immunization Newsletter* is to facilitate the exchange of ideas and information concerning immunization programs in the Region, in order to promote greater knowledge of the problems faced and possible solutions to those problems.

An electronic compilation of the *Newsletter,* "Thirty years of *Immunization Newsletter:* the History of the EPI in the Americas", is now available at: www.paho.org/inb.

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ISSN 1814-6244
Volume XXXVI Number 4 • August 2014

Editor: Carolina Danovaro
Associate Editors: Cuauhtémoc Ruiz Matus and Octavia Silva

Pan American Health Organization
World Health Organization
REGIONAL OFFICE FOR THE Americas

Comprehensive Family Immunization Unit

525 Twenty-third Street, N.W.
Washington, D.C. 20037 U.S.A.
http://www.paho.org/immunization

CHOLERA VACCINATION continued from page 1

In Haiti, approximately 200,000 people received at least one dose of OCV in 2012–2013. These experiences demonstrate the feasibility of vaccination against cholera; second-dose coverage, measured with surveys, ranged from 63% to 77%. There are plans to vaccinate an additional 200,000 people in July and August 2014. The results of a clinical trial in an endemic area of Calcutta, India, show that OCV can have an effectiveness of 65% in the five years after vaccination.

The occurrence of cholera in Cuba and Mexico not only underscores the risk of importations, but also that indigenous transmission can occur after an importation. Although the cholera epidemic of the 1990s, which affected 21 countries of the Region, finally caused improvements in access to drinking water and sanitation, conditions that enable cholera transmission persist to different extents in some areas of all of the countries of the Region. For example, in 2010 in Central America, an estimated 12.7 million people (6% of the population) were living without access to drinking water and 35.7 million people (17%) without improved sanitation.

The emergency of cholera in Haiti has renewed the global debate on the role of reactive vaccination. Since 2012, OCV has been deployed in several African countries that experienced a cholera outbreak. The effectiveness of two doses of OCV was 87% in an outbreak in Guinea. Simulations suggest that reactive vaccination of people at high risk of exposure would be the most effective use of a limited vaccine stock. As part of contingency plans for Vibrio cholerae importations, a tactical use of OCV should be considered as part of an integrated response in specific geographical areas that have a high proportion of people who live in vulnerable conditions, such as rural populations with difficult access to health services (including indigenous people) and urban and peri-urban populations with vulnerability in access to drinking water and sanitation.

Jointly with partners, WHO launched in the second semester of 2013 a global OCV stockpile. This mechanism is managed as a rotating fund by the International Coordinating Group, which already manages similar stockpiles of meningococcal meningitis and yellow fever vaccines for outbreak response. Until June 2014, the International Coordination Group (ICG) accepted 5 country requests for a total 1.4 million doses. The global stockpile thus promises to be a great contribution to the timely deployment of OCV in outbreak settings.

Recommendations:

- TAG supports PAHO's efforts towards cholera transmission elimination in the Region of the Americas through the integrated action and contingency plans, including the use of OCV where indicated. To this end, efforts to mobilize sufficient resources for maintaining the role of the PAHO Secretariat in the Regional Coalition for Water and Sanitation to Eliminate Cholera in Hispaniola should be pursued.
- TAG reinforces previous recommendations to maintain WASH Advocates as a fundamental pillar to the comprehensive approach towards an overarching goal to eliminate cholera transmission. TAG also reaffirms that vaccination is one of possible short-term actions toward the achievement of the long-term elimination goal.
- Countries should continue cholera surveillance and assess the impact of OCV where used. ■