Immunization in the Americas:
Prioritizing Vulnerable Populations

In September of 2003, the Directing Council of the Pan American Health Organization (PAHO) called for the elimination of rubella and congenital rubella syndrome (CRS) from the Americas by the year 2010. This and other Directing Council resolutions leading to the successful eradication of polio and measles are grounded in the guiding principle of reaching the poorest of the poor in our Region. Today, as we stand on the brink of the elimination of rubella and CRS, we should feel proud that we have successfully secured the protection of our most vulnerable populations against these killer diseases. This success represents an extraordinary national commitment to eliminate rubella, while also sustaining the gains of polio eradication and measles elimination, and to provide universal access to vaccines in the Region.

The need to reach underserved communities with life-saving vaccines will persist beyond rubella elimination: this will remain a universal challenge that will never go away. Vaccination Week in the Americas has been successful in helping to maintain the commitment necessary to protect children and their families living in the most underserved communities. Since 2003, with the launch of the first Vaccination Week in the Americas, more than 250 million people, many of them living in the poorest areas, have been vaccinated through this initiative. The initiative also reaches indigenous and Afro-descendant populations who, in our Region, still endure widespread inequities in living conditions, health status, and health services coverage when compared to the rest of the population.

Reducing inequities in access to health services has long been a priority in PAHO’s approach to providing immunization technical cooperation to PAHO Member States. Prioritizing and targeting underserved communities with low immunization coverage was an essential strategy for sustaining measles elimination in the Americas, eliminating rubella and CRS, improving quality of routine services, and strengthening national capacity to make evidenced-based decisions for introduction of new and underutilized vaccines. The Organization places great emphasis on achieving the Millennium Development Goals and recognizes the benefit of immunization and its potential impact in reaching these targets.

Working together, we will continue to build on this foundation of success in addressing the current influenza pandemic crisis. We must ensure that vulnerable populations are the centerpiece of our response. The PAHO Revolving Fund for vaccine procurement will continue to play a critical role in ensuring equity and access to pandemic vaccines when they become available.

Our immunization team is highly committed to assisting countries in providing the best immunization services possible to all children and families of the Americas. We feel honored to work hand in hand with our colleagues in every Ministry towards achieving common goals and working in areas of mutual interest. I am proud to once again assure you of PAHO’s commitment to provide excellence in technical cooperation. Working together, we will continue to improve the health of children and their families in the Americas!

I wish you all the best, and I sincerely hope you have a highly productive 28th Meeting of PAHO’s Technical Advisory Group on Vaccine-preventable Diseases.

Mirta Roses Periago
Director, Pan American Health Organization
Washington, D.C.
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Preface

Regional Immunization Vision and Strategy

The countries of the Hemisphere, with technical cooperation from the Pan American Health Organization (PAHO), have made extraordinary advances in public health, providing children with protection against basic vaccine-preventable diseases. The Expanded Program on Immunization, created in 1977 by resolution of the PAHO Directing Council, laid the foundation for the creation of a program that was technically, financially, and socially sound. National infrastructure and human resource capabilities were extensively buttressed, and the Revolving Fund for the procurement of vaccines, syringes, and supplies was created. During its 30-year existence, the Fund has been among the most successful of the technical cooperation mechanisms that have permitted equitable access to affordable, quality vaccines in sufficient quantities.

In our Region, immunization has been responsible for nearly one-quarter of the reduction in mortality in children under 5 years between 1990 and 2002, making a significant contribution to the achievement of the Millennium Development Goals (MDGs) and the goal of the World Health Organization’s Global Immunization Vision and Strategy (GIVS).

The Region still faces substantial epidemiological, demographic, and social challenges. New vaccines and new ways of organizing and delivering services have provided hope for addressing those challenges. PAHO, through the Regional Immunization Vision and Strategy (RIVS), has developed a road map to offer all of the Region’s inhabitants the opportunity to receive the vaccines capable of protecting them against the greatest possible number of diseases, using an integrated approach in the context of family and community health, and also based on PAHO’s principles of equity, quality, access, and Pan-Americanism.

The RIVS has three strategic lines of work, each with several goals:

1. **Maintaining the achievements.** The historical advances that have made it possible to eliminate and control diseases and reduce risks must be maintained:
   - Keeping the Region polio-free;
   - Keeping the Region free of endemic measles transmission;
   - Maintaining diphtheria control;
   - Maintaining pertussis control; and
   - Maintaining and increasing the gains made in the control of *Haemophilus influenzae* type b.

2. **Addressing the unfinished agenda.** Considering the progress made, appropriate action must be taken to meet the desired goals:
   - Improving immunization coverage and services at the local level, such as municipalities with coverage below 80%;
   - Eliminating rubella and congenital rubella syndrome;
   - Eliminating neonatal tetanus as a public health problem in all countries;
   - Achieving epidemiological control of hepatitis B; and
   - Increasing the use of “underutilized” vaccines such as those for seasonal influenza and yellow fever (in enzootic countries).

3. **Meeting new challenges.** To meet the challenges created by the availability of new vaccines and new approaches to health service delivery and financing mechanisms, guidance should be directed to strengthen the immunization program, with a view to:
   - Introducing new vaccines that will facilitate attainment of the MDGs (rotavirus, conjugated pneumococcus, human papillomavirus) when countries can do so sustainably;
   - Strengthening national capacity for evidence-based decision-making (ProVac Initiative);
   - Promoting the financial sustainability of the program;
   - Increasing technical expertise at all levels of the program; and
   - Ensuring equitable access to quality vaccines, syringes, and supplies through the Revolving Fund as a cooperation mechanism for the procurement of these inputs.

These strategies are part of primary health care and will require continuous sustainable reinforcement in the following areas:

- Infrastructure;
- Operational capacity;
- Management and logistics;
- Technical expertise of human resources;
- Proper management and modernization of the cold chain;
- Cost-effectiveness analysis;
• Integrated information system;
• Epidemiological surveillance;
• Laboratory network; and
• Supervision and operational evaluation.

Vaccination has proven to be among the most cost-effective public health intervention medical science has to offer. Certainly vaccination is one of the most socially and politically acceptable public health strategies that we have. In our Region, it is estimated to have contributed to the reduction of the mortality in children under 5 years by nearly 25% since 1990, putting us on the path toward achievement of MDG 4. It is also making considerable contributions to MDGs 5 and 6. However, these achievements must be maintained. Efforts need to be made to responsibly promote the use of new vaccines and tools that will enable us to make accelerated progress toward reducing the disease burden of vaccine-preventable diseases in all our populations, as established in the RIVS.
Session 1: Protecting the Achievements

Measles, Rubella, and CRS Elimination

Poliomyelitis Eradication
Introduction
The Region of the Americas interrupted endemic measles virus circulation in 2002 and has limited endemic rubella virus transmission to only one country since 2009 by pioneering and successfully implementing the current measles/rubella vaccination strategies. By the end of 2008, all countries had introduced measles-rubella (MR) containing vaccine into their routine immunization program, an estimated 440 million people had been protected against measles and rubella through catch-up, follow-up, and speed-up interventions, and countries have continued their efforts to maintain high coverage in the routine program and to strengthen integrated measles/rubella surveillance and congenital rubella syndrome (CRS) surveillance. However, many challenges remain, including the ongoing risk of importations, secondary spread, preventing and responding to outbreaks, and ensuring quality surveillance and laboratory capacity to provide evidence for elimination.

Methods
Measles, rubella, and CRS cases reported to the Immunization Project of the Pan American Health Organization (PAHO) through weekly epidemiologic surveillance tables and country reports were reviewed and analyzed to identify trends in incidence and case characteristics, and to assess regional challenges in this stage of elimination.

Results
During 1998–2008, confirmed rubella cases decreased 97%, from 135,947 to 3,903. A shift in distribution and increase in cases in 2007 resulted from outbreaks, particularly among males, in Argentina (N=90), Brazil (N=8,739), and Chile (N=4,263), countries that initially vaccinated only females in rubella mass vaccination activities. During 2008, these three countries accounted for 98% (N=3,810) of confirmed rubella cases and reported 100% (N=28) of confirmed CRS cases (25 in Brazil, 2 in Chile, and 1 in Argentina). In response to these outbreaks, countries intensified surveillance activities and vaccination interventions. Countries that had completed the recommended measles/rubella vaccination interventions had not reported any endemic rubella cases.

Effective interventions, including strengthening of measles elimination through the rubella initiative, have resulted in historically low numbers of annually reported measles cases (ranging from 85 to 207 cases each year between 2003 and 2008) following international importations. The highest incidence rate (0.26 per million people) was reported in 2006 due to outbreaks. Recent outbreaks indicate that 64% of importations to the Americas came from Europe, resulting in a collective estimated cost of around US $21,000 in Ecuador and Chile alone to contain outbreaks and limit secondary cases. From 2008-2009, 75% of cases reported in Latin America and the Caribbean were detected through the private sector.

The programmatic and financial impacts that importations have had in the Americas highlight regional challenges related to ongoing virus transmission in other parts of the world, such as limiting cases secondary to importations; preventing and responding to outbreaks; reaching unreached populations with interventions; improving integrated measles/rubella and CRS surveillance, including strengthening the role of the private sector and confronting laboratory challenges in case classification; and virus detection and isolation during the elimination stage.

Conclusions
High coverage attained through measles and rubella vaccination strategies have led to the rapid reduction of susceptibles and have provided an additional opportunity to maintain measles elimination and achieve rubella elimination in the Region. Given that measles and rubella remain endemic in other regions of the world, countries of the Americas should maintain high quality elimination strategies to ensure the required level of population immunity to prevent the reestablishment of virus transmission following importations. In addition, countries should maintain a high level of preparedness through improved surveillance, advanced planning, and laboratory readiness to quickly detect and respond to importations and prevent cases secondary to importations.

(a) Preliminary data; (b) Data reported up to 1 March 2009 for Argentina, Brazil, and Chile; (c) Until Epidemiological Week 11/2009.

1 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
**Introduction**

Accelerated measles control activities have resulted in a reduction in global measles mortality of nearly three-quarters over the period 2000 to 2007. Worldwide between 1996 and 2007, 45 countries added rubella vaccine to their national childhood immunization schedule. Despite this progress both measles and rubella remain endemic in all Regions of the World Health Organization outside of the Americas. Because of the large numbers of international travelers visiting the Americas each year and the ease of transmission of both measles and rubella via the respiratory route, the risk of importations of measles and rubella into the Americas remains high. In the first 3 months of 2009, 11 new measles outbreaks were reported worldwide including 4 in countries in the Americas as a result of importations.

**Methods**

Strategies for reducing the number of importations of measles and rubella into the Americas include 1) improved control and eventual elimination in other regions; 2) ensuring international travelers are appropriately vaccinated; and 3) enhanced disease and virus surveillance.

**Results**

Progress is being made towards elimination goals in the European, Eastern Mediterranean and Western Pacific Regions and a recent request by the Executive Board of the World Health Assembly to assess the feasibility of global elimination of measles is providing the opportunity to evaluate this as the next global goal for measles control. While the 2007 International Health Regulations provide the framework for recommendations for travelers to be vaccinated against both measles and rubella before departure, they stop short of making vaccination an absolute requirement because of the logistic difficulties involved in implementing such a requirement and its impact on free trade and travel. Enhanced surveillance that includes contact tracing and real-time sharing of case and genotype information is a powerful public health tool for controlling and preventing importations. An recent example of this is documentation of the spread of D4 measles virus (Enfield strain) by the Global Measles/Rubella Laboratory Network.

**Conclusions**

Increased political commitment and financial support is needed to accelerate efforts to reduce international spread of both measles and rubella and ultimately interrupt transmission of both viruses worldwide.

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2 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
Prioritizing Vulnerable Populations

Current Status of Measles and Rubella Elimination in the United States
Armstrong G1

Introduction
In 2000 and 2004, expert committees, after reviewing data on measles, rubella, and congenital rubella syndrome (CRS) epidemiology, population immunity, adequacy of surveillance and molecular epidemiology, declared that measles and rubella had been eliminated (absence of endemic disease transmission) from the United States. Since both declarations, there have been historically low rates of these diseases. However, with an estimated 20 million measles cases occurring around the world each year, a presumably much higher number of rubella cases, and over 400 million arrivals into the United States each year, importations of measles and rubella are inevitable.

Methods
Cases of measles and rubella are reported to the Centers for Disease Control and Surveillance by state health departments by the National Notifiable Diseases Surveillance System using standardized case definitions.

Results
Between 1998 and 2007, 37-116 cases (yearly incidence: <1 reported case/million population) of measles were reported each year in the United States, of which 18-54 were among individuals who had acquired the disease abroad. In 2008, there were provisionally 140 cases of measles, including 7 outbreaks. Seventeen (12%) case-patients were hospitalized. Twenty four cases were importations (the majority from Western Europe), 102 cases were epidemiologically linked to importation or had virologic evidence of importation, and 14 were of unknown source. Among the 127 cases in U.S. residents, 91% were in individuals who were unvaccinated or of unknown vaccination status. A large proportion of school-aged children with measles were unvaccinated because of personal or religious exemptions. The largest outbreak, predominantly affecting homeschooled children in Illinois, involved 30 cases.

Between 2003 and 2007, 7-11 cases of rubella were reported in the United States (yearly incidence: <1 reported case/million population). In 2008, there were provisional reports of 20 cases, of which 10 were importations from a variety of countries. Of the 20 case-patients, 17 were unvaccinated or of unknown vaccination status.

There have been 3 reports of CRS since 2003, the last occurring in 2006. All 3 cases were in children born to foreign-born mothers who had acquired infection abroad.

Vaccination coverage with MMR vaccine remains high among US children. According to the 2007 National Immunization Survey, 92% of U.S. children aged 19-35 months had received at least 1 dose of MMR vaccine and 89% of adolescents aged 13-17 years had received 2 doses.

Conclusions
Data support the continued elimination of measles and rubella in the United States. However, the recent resurgence of measles in Western Europe and the re-establishment of endemic measles in the United Kingdom highlight the critical need to maintain high vaccination coverage rates and respond aggressively to imported cases and outbreaks to sustain elimination.

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Introduction
Measles is an infectious disease found worldwide, except in countries and regions that have maintained successful vaccination interventions. In the Americas, such interventions resulted in the elimination of the disease in 2002. However, there is a risk that the virus will be reintroduced through imported cases. On 1 May 2008, doctors at a private clinic reported a suspected measles case to the epidemiological surveillance system. The objective of this abstract is to describe the action taken by Peru’s Ministry of Health to prevent the emergence of secondary cases.

Methods
A clinical, epidemiological, and serological assessment of the case was conducted. This was accompanied by case-finding activities, vaccination, and monitoring of contacts, together with an active institutional search for suspected measles cases in the district.

Results
Male patient, 19 years of age, from India, who worked on a gas tanker. On 28 April, he experienced malaise and a sore throat. On 30 April, he developed a fever, and on 1 May, a maculopapular rash. He was transferred by boat and taxi to the clinic. The patient had left India on 19 April bound for Guayaquil, with stopovers in London and Miami. On 21 April, he reached Guayaquil. From there, he went to Puerto Bolivar, boarding the ship that same day and never leaving it until 1 May.

On receiving the report, staff in the General Bureau of Epidemiology recommended the first measures for isolating the patient: seclusion in a private room with a closed door; use of an N95-N100 mask by the patient, and care from staff tested for measles immunity. The case was clinically assessed, and blood samples were taken in coordination with the National Institute of Health; the tests proved positive for measles within 12 hours. The likely date of infection was 10-24 April, and secondary cases were anticipated from 4 to 22 May. In coordination with the clinic, the Health Bureaus of Callao and the City of Lima drew up a list of contacts among the crew, patients, family members, and workers that had been exposed to the patient. They were vaccinated and followed until 22 May. Some 264 people were followed, with 199 of them vaccinated in the first 72 hours. Five people could not be located.

From 19 to 23 May, an active institutional search for suspected measles cases in the last month was conducted in all health facilities in Lima and Callao. A total of 1,140,734 diagnoses were reviewed; 47 suspected cases were identified, 22 of which had not been captured by the regular surveillance system. A blood sample was taken from the cases and they were followed. There were no secondary measles cases.

The patient was transferred from the clinic to a public hospital on 2 May. He was discharged on 5 May and returned to his ship, which weighed anchor that same day after the quarantine order was lifted as a result of the crew’s immunity.

Conclusions
In May 2008, an imported measles case was detected in Lima, Peru, with no occurrence of cases secondary to the importation. Epidemiological surveillance systems play a key role in the timely detection of such cases and the coordination of immediate control measures to reduce or prevent secondary cases and, with them, the resumption of endemic transmission.

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1 General Bureau of Epidemiology, Ministry of Health, Peru.
Improving Congenital Rubella Syndrome Surveillance, Colombia, 2005-2008

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Introduction

In response to the recommendations of Resolution CD44.R1 of the Pan American Health Organization, in September 2003, Colombia made a commitment to eliminate rubella and congenital rubella syndrome (CRS) by 2010. During the period 2005-2006, a national measles-rubella vaccination campaign was conducted, targeting men and women aged 14-39 years and achieving 96.3% coverage. That same year marked the start of the implementation of CRS surveillance strategies.

Methods

Sentinel surveillance began in 2005. Based on the ECLAMC(a) network, it used newborns with low birth weight or birth defects as the criterion for inclusion. In 2006, a national CRS surveillance protocol was adopted and applied countrywide. In 2008, sentinel surveillance was implemented in seven health institutions of Bogotá, with the report of 140 cases; other institutions reported an additional 23 cases, for a total of 163 suspected cases. Case inclusion criteria were as follows: mother with no prenatal care. The surveillance data and laboratory results for rubella, cytomegalovirus, herpes simplex 1 and 2, parvovirus B19, and toxoplasma for the period 2005-2008 were reviewed and analyzed.

Results

In the 2005 sentinel surveillance, 840 suspected cases in 6 cities were reported; 669 (79.6%) for low birth weight, 105 (12.5%) for suspected CRS, 52 (6.2%) for birth defects, and 14 (1.7%) for unspecified reasons (no data). In the 840 suspected cases, the most frequent signs and symptoms were heart disease (5.1%), hepatosplenomegaly (3.9%), and microcephaly (1.2%). A 0.24% positivity was found for rubella but without clinical manifestations of CRS and a 6.0% positivity for the other infectious agents (Table 1). In 2008, sentinel surveillance was implemented in seven health institutions of Bogotá, with the report of 140 cases; other institutions reported an additional 23 cases, for a total of 163 suspected cases. Case inclusion criteria were as follows: mother with no prenatal care, 29.4% (48), birth weight <2,500 grams, 20.9% (34) and clinical manifestations suspected to be caused by gestational or congenital syphilis, 20.9% (34), jaundice, hepato- or splenomegaly, 12.3% (20); heart disease alone or in combination with another condition, 7.4% (12); alterations in the central nervous system (hydrocephalus, microcephaly), 6.8% (11); cataracts, 12.2% (2), and other 1.1% (2). Other characteristics of the suspected cases were as follows: 50.9% (83) were male, the average age on admission was 7 days (median=2, range=1-132), average weight 2,828 g (median=2,900 g; range=660-4,040 g). The laboratory results yielded a positivity for syphilis of 20.9% (34), with a reactivity for other infectious agents as follows: cytomegalovirus, 0.6% (1); herpes viruses, 1+2 0.6% (1); toxoplasma, 0.6% (1), and polyclonal reactions, 1.8% (3). There were no confirmed CRS cases in the Bogotá study (Table 2).

Conclusions

No CRS cases have been confirmed in Colombia since 2005. Of the surveillance strategies used, the greatest success has been achieved with sentinel studies, which have permitted greater case capture compared with routine surveillance. With the information from the two sentinel studies, it can be seen that the criterion of low birth weight is not relevant for the capture of CRS cases. CRS surveillance has received major legal backing from the presidential decree of August 2007 (National Public Health Plan), which requires implementation of a surveillance system for birth defects, with emphasis on rubella, syphilis, toxoplasmosis, and perinatal, neonatal, and child mortality.

(a) ECLAMC: Estudio Cooperativo Latinoamericano de Malformaciones Congénitas (Latin American Cooperative Study on Congenital Malformations); (b) TORCH stands for Toxoplasma gondii; other viruses (HSV and others); rubella; cytomegalovirus (CMV); herpes simplex (HSV); and syphilis.

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Challenges in IgM Interpretation and Case Classification During Measles and Rubella Elimination Phase
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Introduction
Vaccination programs have made measles and rubella rare in American countries, but failure to appreciate the importance of measles and rubella-like illness and to alert the surveillance and laboratory systems to their importance might result in avoidable outbreaks and congenital rubella syndrome (CRS). Clinical diagnosis of rash diseases is unreliable and laboratory confirmation essential. The presence of specific IgM is used to determine whether patients are protected or have recently acquired measles or rubella. For a case classification it is essential to obtain laboratory, epidemiological, and demographic data. However, in the elimination phase, it could prove difficult to conclude case classification based only on laboratory IgM test and epidemiological data. The process to rule out or confirm positive-IgM cases requires a standardized methodology to assure proper and consistent case classification throughout the Region.

Methods
The laboratory components of the strategy for classification of measles and rubella cases to support documentation of their elimination should include the adequate collection of a second serum sample, the collection of samples for virus detection, and differential laboratorial diagnosis for dengue virus, parvovirus B19, and herpes virus 6 (in children aged <2 years).

Results
IgM detection in sporadic cases or in a case of rash with a recent vaccination has been more frequently observed and the appropriate collection of a second serum sample and/or virus detection has been crucial in laboratory interpretation and case classification. Serum collection on most of suspect measles or rubella cases in the Americas is performed within 3 days of rash onset, and around 20% of the true positive cases can present negative IgM results due to the date of sample collection. If these cases are strongly suspected to be measles or rubella due to recent travel, exposure, and/or the case has no history of vaccination, the presence of IgG can rule out the case. If IgG is absent, results from a second sample (IgM and IgG) and/or molecular testing can help classify these cases.

Differential laboratorial diagnostic tests have been used in Brazil and have permitted the etiological definition of outbreaks and sporadic cases classification. In a pilot study on rash diseases in Rio de Janeiro State, 73% and 43% of the herpes virus 6 IgM-positive cases fulfilled the clinical criteria of measles and rubella suspect cases, respectively. Also, herpes virus 6 IgM-positive has also been detected in children recently vaccinated with IgM-positive for measles and/or rubella.

Conclusions
Efforts should be done for the collection of the second serum sample and specimens for virus detection for correct case classification in the measles and rubella elimination phase. In the Americas, in recent measles or rubella single cases or outbreaks the genetic information provided valuable information about the transmission pathway of the virus and the classification of imported cases. Laboratory testing for other viruses should be considered and close collaboration between epidemiologists and the laboratory is essential for decision on laboratory differential diagnosis and case classification. The rubella IgM assays on serum samples from pregnant women should always be interpreted with caution. Rubella IgM test is not recommended as routine antenatal care unless there is a history of rash or contact with a rubella-like rash.

In the elimination phase the rapid conclusion of each single case and a proactive role of the laboratory and epidemiologist for case classification are required. Countries that still have pending cases should make efforts for case classification. It is important that each case be reviewed by a committee established at national level that could include an external consultant. Also, countries should utilize available resources such as sending samples to reference laboratories for virus detection, differential diagnosis and IgM/IgG confirmation, when dealing with special cases.

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2 Secretariat of Health Surveillance, Ministry of Health, Brazil.
3 Universidade Federal Fluminense, Rio de Janeiro, Brazil.
4 Comprehensive Family Immunization (FCH), Pan American Health Organization, Brazil.
5 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
Prioritizing Vulnerable Populations

Are Two Better Than One? Did a Second Routine Dose of Measles Vaccine Hasten Measles Elimination in the Americas?

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Introduction

The Region of the Americas reached measles elimination (ME) in 2002 using a strategy of high first-dose routine measles vaccine coverage (MCV1) and a second vaccination opportunity through mass campaigns every 4-6 years. A second routine dose (MCV2) at school entry was added in some countries (two-dose) but not in others (one-dose); the impact of MCV2 on ME is unclear.

Methods

ME was defined as the first year between 1992-2002 with sustained interruption of indigenous measles virus transmission. Country data on socioeconomics, demographics, vaccination coverage, and estimated proportion of children (<15 years) susceptible to measles were compiled. Time to ME between one-dose and two-dose countries was compared using Kaplan-Meier curves with and without propensity score methods.

Results

One-dose (n=14) and two-dose (n=7) countries did not differ in median MCV1 coverage for years 1999–2001 (94% for both) or median coverage for three measles campaigns (94% vs. 91%). Mean percent of susceptible children after MCV1 and campaigns were similar in one-dose (7.4%, 95% CI: 5.5–9.2) and two-dose (5.9%, 95% CI: 3.9–7.9) countries. Compared with one-dose countries, two-dose countries had significantly (p<0.05) higher median gross national income per capita (USD 486 vs. 217), percent urban population (75% vs. 58%), and female literacy (96% vs. 84%), and lower infant mortality (18 vs. 32 per 1000 live births); no difference in time to elimination was found between one-dose and two-dose countries in crude (p=0.79) and propensity score subset (p=0.51) analyses.

Conclusions

Two-dose and one-dose countries had similar times to elimination despite apparent socioeconomic differences. MCV2 may not have hastened ME because high coverage with MCV1 and campaigns achieved a threshold immunity needed to eliminate measles.

Comparison of Time to Measles Elimination in Countries With a One-Dose and Two-Dose Routine Measles Vaccination Schedule,*

Latin America, 1992-2002

*All countries also providing a second opportunity for vaccination through campaigns

Source: Country reports to PAHO.

1 Global Immunization Division, Centers for Disease Control and Prevention (CDC), Atlanta, USA.
2 National Center for Immunization and Respiratory Diseases, CDC, Atlanta, USA.
3 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
Validating the Quality of the 2008 Measles and Rubella Follow-up Campaign in Honduras

Molina I1, Mendoza L1, Palma M1

Introduction

As a step towards the goal of eliminating measles and rubella in the Americas by the year 2010, Honduras conducted its fourth measles and rubella follow-up campaign in its 20 Departmental Regions. Its objective was to administer one dose of measles-rubella (MR) vaccine to 95% of children aged 1-4 years, regardless of their vaccination status, in order to reduce the accumulation of people susceptible to becoming sick or dying of measles or rubella.

Methods

A plan of action was prepared for the follow-up campaign, scheduled for 21 April to 24 May 2008 across the entire country. The target was 853,795 children aged 1-4 years, in two phases: vaccination of the target population for three weeks and rapid coverage monitoring (RCM) and a search for unvaccinated people during the fourth week. The data were consolidated in Excel spreadsheets, which were analyzed weekly, and a final report was prepared. Following the campaign, verification of administrative coverage using “crossed” RCM was programmed. This was done by personnel from a different health service, with support from an external team from the Pan American Health Organization (PAHO). For this, organization, microplanning, and selection of the clusters in the health centers and geographical areas of influence in the country's 298 municipalities were conducted. Forty-five percent (659) of the country’s health centers were selected, covering 55% of the total target population to be vaccinated. Forms used in the field for data collection and consolidation were reviewed, revised, and validated with the national team of the Expanded Program on Immunization.

Results

At the national level, the campaign was extended until 15 June 2008. Of the target population from 1-4 years, 81% (688,170) was vaccinated. Of the Departmental Health Regions, only one (5%) exceeded the expected 95% coverage, while the remaining 19 (95%) did not. According to the results of the first external RCM conducted by PAHO in the country’s 298 municipalities, 1,274 RCMs were conducted in 1,700 localities, confirming by vaccination card that 94% (44,241) of the population aged 1-4 years was vaccinated. It was found that 75% (15) of the Health Regions exceeded 95% coverage and only 25% (5) of the regions (Metro DC, Metropolitan SPA, Gracias a Dios, Lempira, and Olancho) did not, where those vaccinated ranged from 81% to 91%. For this reason, a door-to-door search was conducted to find people still not vaccinated. In this second RCM, 100% of the Regions achieved 95% coverage, with the exception of one municipality in Gracias a Dios, which is why a third RCM was conducted. By municipality, only 14% (57) exceeded 95% administrative coverage, but comparison with the coverage from the first RCM found that 87% (260) of the municipalities exceeded 95%. Among the principal constraints identified were problems at the national level with the official denominator, lack of transportation, and the limited number of vaccinators.

Conclusions

In compliance with the goal of measles and rubella elimination, Honduras conducted its fourth follow-up campaign without achieving the coverage expected, according to administrative data. However, the use of RCM methodology to certify coverage of the campaign by PAHO in the country’s 298 municipalities showed during the first RCM that 87% of the municipalities achieved 95% coverage and that the official population figures did not match the population found at the local level. There were problems with the population denominator in 40% of the Departmental Regions. Furthermore, this methodology made it possible to identify municipalities that did not attain the targeted coverage and facilitated additional vaccination efforts until coverage of over 95% was attained in each municipality.

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1 Expanded Program on Immunization, General Directorate of Health Promotion, Secretariat of Health, Honduras.
Introduction
In 2002, Paraguay added the MMR vaccine to the regular vaccination schedule administered at 1 year of age. Over the past seven years, annual coverage has reached 77% to 91%, with an 86% average. In 2003, the country conducted the last follow-up campaign against measles and rubella using the MR vaccine. In 2008, the cumulative percentage of measles and rubella susceptibles due to low coverage was 74% (148,736) of the estimated live birth cohort that year. Furthermore, the incidence of mumps cases in the country continues, with the age group of 1-4 years at the greatest risk (average incidence rate of 9.5/100,000 inhabitants); June, September, and October are the months with the highest number of reported cases. The decision was therefore made to conduct a national vaccination follow-up campaign in May 2009, targeting children aged 1-8 years and using the MMR vaccine in children aged 1-4 years. Since cases of aseptic meningitis and parotitis have been reported after vaccination with MMR, associated especially with vaccines containing the Leningrad-Zagreb or Urabe mumps strains, Paraguay decided to develop and implement a plan to monitor events supposedly attributable to vaccination or immunization (ESAVIs) during the follow-up campaign.

Methods
Literature review and discussions with experts, laboratory staff, and staff from Paraguay's Expanded Program on Immunization (EPI).

Results
The objective of the plan for ESAVI monitoring is to document the incidence of aseptic meningitis and parotitis attributable to vaccination and immunization with MMR (Leningrad-Zagreb strain) during the national vaccination campaign in Paraguay and to assess the impact of MMR vaccine use in follow-up campaigns. For this purpose, the following case definitions have been adopted:

- **Aseptic meningitis:** a) suspected case: every person aged 1-4 years with a clinical diagnosis of meningitis; b) probable case: every suspected case with a history of MMR vaccination within 30 days of symptom onset; c) confirmed case: every probable case with pleocytosis (>5 leukocytes/mm³), an absence of microorganisms in the Gram stain, and cerebrospinal fluid (CSF) cultures negative for bacterial microorganisms, in the absence of antibiotic treatment prior to obtaining the first CSF sample; and d) case confirmed by viral detection: PCR positive for the mumps virus in CSF or neurological tissue.
- **Parotitis:** a) suspected case: every case with an acute uni- or bilateral increase in the volume of the parotid region; b) probable case: every suspected case with a history of MMR vaccination within 30 days of symptom onset; and c) confirmed case: every probable case with any titer of IgM antibody or an increase in the titers of IgG antibody compared with the first sample, or seroconversion of negative to positive.

Cases of aseptic meningitis and post-vaccination parotitis reported to the EPI will be followed up to 30 days after the end of the campaign. The EPI's Immediate Response Group (GRI, for its Spanish acronym) and the national team of supervisors will coordinate universal surveillance of ESAVIs and train hospital physicians countrywide in the detection, investigation, follow-up, and classification of cases. Data will be analyzed as a whole in order to estimate case incidence and the case-fatality rate, determine the association with the vaccine, learn its characteristics and associated risk factors, and publish the findings. Active case-finding will be conducted, moreover, to complement the ESAVI monitoring system during the campaign.

Conclusions
The goal of the follow-up campaign is to vaccinate 586,306 girls and boys aged 1-4 years with MMR vaccine. Based on the estimate of susceptibles, some 20 to 25 cases of aseptic meningitis and 245 parotitis cases are expected to be attributed to the vaccination. Monitoring of the magnitude and impact of these events will make it possible to evaluate the implications of using the MMR vaccine (Leningrad-Zagreb) in follow-up campaigns.

1  Expanded Program on Immunization, Ministry of Health and Social Welfare, Paraguay.
2  Comprehensive Family Immunization (FCH), Pan American Health Organization, Paraguay.
3  Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
Introduction
After the global eradication of smallpox in 1979 and the certification of polio eradication in the Americas in 1994, the Region adopted the goal of measles elimination in 1994. In 2003, the Directing Council of the Pan American Health Organization/World Health Organization (PAHO/WHO) adopted Resolution CD44.R1 for the elimination of rubella and congenital rubella syndrome (CRS) by the year 2010. The implementation of the elimination strategies resulted in the interruption of endemic measles transmission in 2002. Meanwhile, rubella virus transmission during the first quarter of 2009 is limited to one single country.

In 2007, the 27th Pan American Sanitary Conference reflected with great satisfaction on the remarkable progress to date of the initiative to interrupt the endemic transmission of the rubella virus. Recognizing that considerable efforts were needed to strengthen and expand partnerships between public and private sectors, it approved Resolution SCP27.R2, thereby requesting Member States to begin the documentation and verification process of endemic transmission of measles and rubella viruses in the Americas. To that end, PAHO/WHO developed a Plan of Action.

Methods
The experiences and lessons learned from the certification process for the eradication of other vaccine-preventable diseases in the Region were examined. Country reports, the progress report of rubella and CRS elimination, and the recommendations from the Technical Advisory Group (TAG) on measles and rubella elimination were reviewed. Meetings to discuss specific points of the documentation and verification process with regional experts on measles and rubella were organized. The initial protocol of the Plan of Action was validated in one country and later modified according to recommendations. In August 2008, the proposed plan was presented to an expert panel for final drafting.

Results
Measles and rubella elimination is defined as the interruption of endemic transmission of measles and rubella viruses and the absence of CRS cases associated with endemic transmission for a period ≥12 months. The Plan of Action for documenting and verifying the elimination has six main components: (1) sustainability of national immunization programs; (2) analysis of measles, rubella, and CRS epidemiological data; (3) review of the surveillance system’s quality; (4) surveillance of measles and rubella viruses; (5) analysis of protected cohorts, including vaccination coverage, routine vaccination, and post-partum vaccination; (6) integration and assessment of all the pieces of evidence. The documentation and verification process will be developed over a three-year period and with high quality surveillance.

Conclusions
The Plan of Action for the documentation and verification of measles, rubella, and CRS elimination is presented to the XVIII TAG Meeting on vaccine-preventable diseases for consideration. The plan will guide countries and their national commissions in the preparation and building of evidence to establish that the endemic transmission of measles and rubella has been interrupted based on data that are valid, comprehensive, representative, and consistent.

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1 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
Experience and Progress of Costa Rica in Documenting and Verifying Measles and Rubella Elimination
Morice A1, Avila-Agüero ML1, and the Working Group for documenting rubella and CRS elimination2

Introduction
In 1986, Costa Rica introduced the measles, rubella, and mumps vaccine (MMR). In 2000, it launched a National Plan of Action for the elimination of rubella and congenital rubella syndrome (CRS) and the consolidation of measles elimination. In 1999, the last case of indigenous measles was confirmed, and no endemic transmission of rubella and CRS has been detected since late 2001. This abstract presents the methodology and results of the process that, in compliance with Resolution CSP27.R2 of the 27th Pan American Sanitary Conference (2007), will provide evidence confirming that Costa Rica has reached the goal of eliminating these diseases.

Methods
Trends in rubella, measles, and CRS incidence were analyzed, identifying changes in their seasonality, cyclic, and demographic pattern; laboratory alternatives were implemented to improve knowledge about the rubella and measles genotypes; population immunity was determined by calculating vaccinated population cohorts, complementing this with the seroprevalence surveys available in the country; surveillance quality indicators were evaluated; retrospective rubella, measles, and CRS case-finding was conducted, using diverse methodologies and information sources to ultimately determine the robustness, validity, and representativeness of the surveillance and population immunity data.

Results
From 1977 to 2001, circulation of the rubella virus was endemic in the country, with epidemics occurring every five to seven years. The last rubella outbreak in Costa Rica (1998-99) revealed a shift in susceptibility toward the population aged 25-34 years (rate=80 per 100,000) and 15-24 years (rate=26 per 100,000). The vaccination campaign targeting men and women aged 15-39 years conducted in May 2001 (coverage 98%) reduced the incidence from n=32 rubella cases that year to n=0 confirmed cases in 2002. Routine MMR coverage was maintained at over 90%, and the follow-up campaigns (1997 and 2002) recorded coverage of 87% and 86%, respectively. Information sources such as nominal registries and coverage monitoring are being used to identify the unvaccinated and analyze population immunity. From 2002 to 2008, the National Reference Laboratory tested an average of n=249 (range=169 to 327) and n=252 (range=169 to 326) samples per year for IgM measles and rubella, respectively (rate=6 per 100,000). In 2007-2008, a total of 54 IgM samples positive for measles and/or rubella or undetermined were reported. All the cases were discarded, since they were associated with postvaccination reactions or false positives associated with dengue or parvovirus B19. In 2003, one imported measles case from India was detected, and in 2006, one rubella case; neither generated secondary cases. Retrospective measles and rubella case-finding (2006-07) yielded 59 suspected cases out of a total of 27,999 diagnoses, all of them being discarded by laboratory or epidemiological criteria. Preliminary results of retrospective CRS case-finding (2002-2008 birth cohort) in the National Children’s Hospital and three special education centers identified n=101 and n=102 suspected cases, respectively. At present, the cases evaluated have been attributed to congenital genetic malformations, prematurity, or infections such as cytomegalovirus.

Conclusions
The available epidemiological information in Costa Rica indicates that its vaccination strategies have interrupted endemic circulation of the rubella and measles viruses. This evidence will be studied by a national expert committee created by Executive Decree. The documentation process included the National Center for Congenital Disease Registry for active CRS surveillance, strengthened the national clinic for congenital infections, and will expand neonatal deafness screening coverage through national legislation. This effort is leading to an improvement in the quality of life and reducing the social and economic cost of a vaccine-preventable disability.

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1 Ministry of Health and Social Development, Costa Rica.
2 Composed of professionals from different disciplines in the Ministry of Health, the Costa Rican Institute for Research and Education in Nutrition and Health, the Costa Rican Social Security Fund, and the National Children’s Hospital.
Introduction

Surveillance evidence over three years that there is no circulation of wild viruses in the world and full laboratory containment of wild polioviruses are the conditions set by the Global Commission for the Certification of the Eradication of Poliomyelitis to certify that all regions of the World Health Organization (WHO) have eradicated poliomyelitis. The 126th Session of the Executive Committee of the Pan American Health Organization, held on 27 June 2000, adopted Resolution CE126.R4, which recommended that the Directing Council urge Member States to “initiate activities related to the containment of any laboratory material that may harbor specimens of wild poliovirus, to ensure that global certification of eradication is eventually accomplished.” Of the three polio-free WHO Regions, Europe and the Western Pacific have already submitted their final reports. The report from the Americas, the first Region of the world to have eradicated poliomyelitis, is still pending.

Methods

The reports submitted by the countries of the Hemisphere during the first meeting of the American Regional Commission for Poliovirus Laboratory Containment and Certification of Polio-free Status (AMR RCC), held in Washington, D.C. from 22-23 March 2004, as well as the reports submitted to the second, third, and fourth meetings of the AMR RCC, held in 2008, were reviewed.

Results

The AMR RCC has accepted the final reports of the national committees for laboratory containment of wild polioviruses from the following countries: Bolivia, Chile, Costa Rica, Dominican Republic, El Salvador, Haiti, Honduras, Mexico, Nicaragua, Panama, USA, and all the English-speaking Caribbean countries. At its next meeting, scheduled for July 2009, the AMR RCC will review the final reports of Argentina, Brazil, Canada, Colombia, Ecuador, Guatemala, Paraguay, Uruguay, and Venezuela.

Conclusions

The AMR RCC has programmed its activities so that at its upcoming meeting in July 2009, the documentation that it must present to the Global Commission for Certification of Poliomyelitis Eradication will be complete. The RCC must receive therefore all final reports of the national containment committees that have not yet been submitted.

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1 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
Progress Towards Containment of Polioviruses in Brazilian Laboratories

Hage E1, Colatto A2, Malaspina F3, Flannery B4

Introduction
In 1994, three years after the last confirmed poliomyelitis cases in the Americas, Brazil was certified by the International Commission for the Certification of Poliomyelitis Eradication (ICCPE) as a “polio-free country”. Following revised criteria established by the Global Commission for the Certification of the Eradication of Poliomyelitis and the World Health Organization, documenting containment of polioviruses in laboratories became a mandatory condition for countries to be certified as having eradicated polio by the Global Commission.

The goal of the Global Plan of Action for Laboratory Containment of Wild Polioviruses is to prevent transmission of polioviruses from laboratory sources prior to and following global polio eradication. Prior to global eradication, when polioviruses are still circulating in some parts of the world, countries must complete four defined activities: conduct an inventory of all laboratories to identify stored materials containing wild polioviruses or potentially containing infectious polioviruses and encourage laboratories to destroy unnecessary materials; organize a network of laboratories that maintain these materials; orient laboratories to ensure adequate levels of biosafety for manipulation of these materials; and plan for the implementation of the post-eradication phase.

Methods
In 2004, the Brazilian Ministry of Health conducted an initial laboratory inventory by mailing a questionnaire to the 27 states. Due to poor response to the mailed questionnaire, a second questionnaire in digital format was designed and launched in 2008 on the Ministry of Health website. The database for the inventory is all laboratories included in the National Registry of Health Establishments, a mandatory registration system for health laboratories in Brazil. A system of risk classification was created to prioritize institutions/laboratories from lowest to highest probability of having infectious materials, based on a literature search and information about the type of laboratory (diagnostic, research, industry). The on-line questionnaire was piloted in the state of Paraná in August 2008. New strategies were added in January 2009 to reach 100% of laboratories, including creating state sub-committees for polio containment with representation of public health laboratories, and epidemiologic and sanitary surveillance services. These groups will oversee the completion of the electronic questionnaire and the inventory of stored materials in the states. Following the conclusion of the national inventory, the sub-committees will be responsible for supervising the destruction of materials containing polioviruses and potentially infectious materials that are no longer needed, and for evaluating biosafety conditions for storage of materials deemed necessary.

Results
The initial questionnaire (in print) mailed in 2004 had a low completion rate: 289 Brazilian laboratories responded to the questionnaire, of which 6 stored or manipulated potentially infectious materials and 4 stored wild polioviruses. The on-line questionnaire launched in 2008 targets over 20,000 laboratories registered in the national database. The pilot of the on-line questionnaire demonstrated its efficiency: in a period of 60 days, 216 laboratories and 76 institutions participated in the questionnaire; 5% were functioning prior to 1994, 41% had -20ºC or -70ºC freezers, 26% had the capacity to store materials for more than 6 months, and none had polioviruses or materials potentially containing infectious polioviruses. The electronic questionnaire was launched nationally in January 2009. Brazil plans to complete its laboratory inventory with a goal of 100% participation of laboratories by June 2009.

Conclusions
Brazil has not yet concluded all the activities included in the plan of action for containment of polioviruses in laboratories. The Ministry of Health expects greater response to the electronic questionnaire and, with support from the state sub-committees, to conclude the first phase of the containment process as quickly as possible.

1 Department of Epidemiological Surveillance (DEVEP), Secretariat of Health Surveillance (SVS), Ministry of Health, Brazil.
2 Division of Public Health Laboratories (CGLAB), DEVEP, SVS, Ministry of Health, Brazil.
3 Comprehensive Family Immunization (FCH), Pan American Health Organization, Brazil.
Introduction

The debate surrounding polio vaccination policies has arisen as a result and should be viewed in the context of global polio eradication, a World Health Organization initiative adopted by the countries of the world after the World Health Assembly set the goal of global poliomyelitis eradication in 1988, in Resolution WHA41.28. The last polio case in the Americas was reported in 1991, and in 1994 the American Hemisphere was certified as free of the indigenous circulation of the wild poliovirus. This goal was achieved with routine and supplementary vaccination using oral poliovirus vaccine (OPV), whose use continues to this day. As of March 2009, our Region has maintained its status as a polio-free Hemisphere, using the same vaccine with which eradication was achieved. Some countries, concerned about the risk of paralytic polio associated with the OPV vaccine, have begun to consider the appropriateness of using inactivated polio vaccine (IPV).

Methods

The policies of the Pan American Health Organization’s (PAHO) immunization program are based on the recommendations of the PAHO Technical Advisory Group (TAG) on Vaccine-preventable Diseases. The recommendations of each of the previous TAG meetings have been reviewed.

Results

• During polio eradication in our Hemisphere and in each one of its subsequent recommendations, TAG has maintained that the OPV vaccine should remain the vaccine of choice as long as global polio eradication has not been achieved.
• During the 2000-2001 outbreak in the Dominican Republic and Haiti, caused by the virus derived from the Sabin vaccine, the epidemic was interrupted and the circulation of the virus ended with the use of the OPV vaccine.
• The global polio eradication initiative is evaluating vaccination alternatives for use once polio has been eradicated worldwide (See map of polio cases by district and country.)

Conclusions

Polio vaccination policies should continue to be established in our Hemisphere based on the immunization program’s TAG recommendations.

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1 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
Prioritizing Vulnerable Populations

New Test Algorithm for Poliovirus Results
Bispo de Filippis AM', Ruiz Matus C', Landaverde M'

The eradication of polio from the Western Hemisphere was achieved in 1991 and the Region was certified as free of the circulation of the indigenous wild poliovirus (WPV) in 1994. Although remarkable progress has been made towards achievement of global polio eradication, endemic transmission of WPV 1 and 3 has never been interrupted in four countries: Afghanistan, India, Nigeria, and Pakistan.

In 2008, WPV were isolated from 1,652 patients with poliomyelitis in 23 countries: four of those countries are endemic. Vaccine-derived polioviruses (VDPVs) were isolated from 79 patients in three countries. Over 60% of all polio cases reported globally in the last years have been due to poliovirus imported into polio-free areas.

To accelerate and secure the interruption of the WPV and VDPVs transmission worldwide, in 2005, the Second Meeting of the Advisory Committee on Poliomyelitis Eradication (ACPE) recommended as one of the strategic priorities, the reduction of the time for laboratory confirmation of cases and introduced a shortened algorithm for specimen processing and virus identification. Result timeliness can be affected by field collection, transportation, and laboratory performance. Transportation is a major factor affecting timeliness of results: many efforts are made to reduce the transportation time, but with limited success. In the laboratory, timely detection of poliovirus in AFP stool specimens is crucial because it allows public health interventions to stop transmission chains of WPV and VDPVs. In the Americas, the average time for completing laboratory procedures is 42 days. The new algorithm allows for a 50% reduction of the laboratory target test time, from the current 42 days to a maximum of 21 days.

Considering that the new algorithm was designed to reduce the time for laboratory results to be available and to increase the sensitivity of poliovirus detection, a concern was raised about the possibility of loss of sensitivity for non-polio enteroviruses (NPEV) isolation. Therefore, the new algorithm was first implemented by 5 laboratories in the Americas, as a “pilot phase” to evaluate whether the new algorithm is adequate for the current status of Region, where the poliovirus isolation rate is lower than for NPEV. Results of the first evaluation were presented during the Regional Polio Laboratory Meeting in May 2007.

The PAHO Laboratory Network concluded that the new algorithm improved the sensitivity for poliovirus detection in a shorter time without loss of sensitivity for NPEV. However, an increase in reagents was noted. The mean time for polio results was 12 days and for NPEV ranged from 18 to 25 days.

The Polio Eradication Surveillance System (PESS) is being reviewed to include the new time indicator for polio laboratory results. The new algorithm should be fully implemented in the PAHO LabNet by the second semester of 2009. The new target for timely reporting of results will change to >80% of virus isolation results within 14 days after the arrival of the specimen in the laboratory and >80% of intratype differentiation (ITD) results reported within 7 days after poliovirus isolation. For completeness of polio laboratory results, including ITD, the new target is expected to be within 21 days.

1 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
Session 2: The Unfinished Agenda

Mumps
Pertussis
Neonatal Tetanus
Influenza
Yellow Fever
Introduction

The measles-mumps-rubella (MMR) vaccine has gradually been implemented in the routine program of all countries and territories of the Region of the Americas (with the exception of Haiti). Although data are limited, reductions in the number of reported mumps cases followed the introduction of routine first MMR dose (MMR1) in several countries. Despite regional high coverage with routine MMR1 and the introduction of a second routine MMR dose in many countries, large mumps outbreaks have occurred in recent years. On the other hand, follow-up campaigns, which are an essential component of the measles and rubella elimination initiatives to provide a second vaccination opportunity, generally target children aged <5 years with MR vaccine, on average every 4 to 5 years.

Methods

Available regional data on mumps cases reported over the last decade were examined through the revision of country reports to the Comprehensive Family Immunization Project, with particular emphasis placed on those countries that have experienced outbreaks since 2005.

Results

As of February 2008, mandatory notification of mumps occurs in 27 (77%) countries of the Region, with 36 out of 38 countries and territories (94.7%) reporting cases at Regional level. However, data are incomplete and provide only a glimpse of the true epidemiological situation of the disease. The experience of several countries reporting mumps cases has been a gradual but significant reduction in disease incidence, ranging from 80% to 99% reduction of cases, followed by outbreaks on average 10 years or more post vaccine introduction. At the Regional level, mumps incidence has increased from 3.39 per 100,000 in 2004 to 5.27 per 100,000 in 2007 (preliminary data) due to recent outbreaks in Uruguay (2005-2006), El Salvador (2006), the United States (2006), Canada (2007), and Venezuela (2007-2008). The analysis of incidence rates (per 100,000) by age group and year (2004-2006) for 6 countries (Argentina, Chile, El Salvador, Guatemala, Mexico, and Paraguay) demonstrated the following: for 2004, incidence rates in age groups aged <1 year, 1-4 years, 5-9 years, 10-14 years, and >15 years was 9.1, 39.7, 39.4, 19.6, and 3.6, respectively; for 2005, incidence rates for these age groups were 10.8, 41.3, 39.2, 19.5, and 4.1; and for 2006, 11.1, 38.4, 38.0, 23.1, and 4.14.

Conclusions

The mumps component of the vaccine does not provide the same high levels of protection as the measles and rubella components and is considered inadequate to provide population protection. For this reason, it is necessary to better understand the epidemiology of mumps in the Americas. Waning immunity is another potential contributor to Regional outbreaks, as well as low coverage with the first MMR dose in poor performing municipalities. The purpose of this analysis is to inform recommended changes in vaccine policy or strategies to better control the disease and prevent future outbreaks. All countries must include mumps in their list of notifiable diseases, routinely monitor disease incidence to increase availability of regional mumps information, and support decision-making on vaccination strategies. Countries that plan to incorporate mumps vaccine strains associated with increased risk of aseptic meningitis into mass immunization strategies should ensure that adequate monitoring of events supposedly attributable to vaccination or immunization (ESAVIs) is in place, implement appropriate strategies for communicating risk, and train health workers in proper case management to handle ESAVI reports.
Montiel L1, Sarmiento H2, Merino N2, Pinto B3, Hernández R3, Porras N4, Roger Zapata T4, Ghisays G4

Introduction
Mumps is a benign, self-limiting viral disease, whose principal manifestation is compromise of the salivary glands. Some 15 to 20% of infections are asymptomatic, but serious complications can occur, among them encephalitis in 15% of cases, permanent neurological sequelae, pancreatitis in 4% of cases, neurosensory deafness in 1 in 20,000 cases, and orchitis in 40% of post-pubertal boys, with infertility as a rare sequela. Infection in the first trimester of pregnancy is associated with a 25% miscarriage rate. In Venezuela, mumps outbreaks occurred in 1997 and 1998, with 34,496 and 19,968 reported cases, respectively. There were no reports of deaths or severe complications associated with the outbreaks. In 2007 and 2008, a large-scale outbreak occurred, with a total of 219,778 cases. The incidence data for this disease are based on cases confirmed by clinical and laboratory diagnosis. Prior to this outbreak, mumps was not notifiable in the country.

Methods
The cohorts protected since the introduction of the MMR (measles-mumps-rubella) vaccine in 1999 were reviewed. The case incidence was analyzed by age group and epidemiological week of the 2007–2008 outbreak. Case reporting began improving in February 2008, when the operational case definition was implemented. Serological diagnosis was obtained through the detection of IgM antibodies with the ELISA technique and total antibodies with hemagglutination inhibition (HI). The isolation was done in VERO_E6 cell culture and confirmed by indirect immunofluorescence (IIF). Genotyping was based on sequencing of the SH gene, which was done at the U.S. Centers for Disease Control and Prevention (CDC) in Atlanta.

Results
Use of the MMR vaccine with mumps virus antigen began in 1999. Average vaccination coverage of children aged 1 year are <85% per year on average. The MR vaccine was used to control the 2001 and 2006 measles outbreaks, and in the rubella elimination campaign, where 97% coverage was achieved. The MMR vaccine was not used so as to prevent potential adverse events, such as aseptic meningitis and postvaccinal parotitis referred to in the literature. In Venezuela, the Urabe and Leningrad-Zagreb (L-Zagreb) vaccine strains are used. The national schedule does not include the administration of a second dose.

The cumulative number of susceptibles in the cohort born between 1983 and 1997 was 6,797,994, and for the period 1998 to 2007, 2,303,202, for a total of 9,101,196 people, who at the time of the outbreak were between the ages of 1-24 years. The outbreak began in epidemiological week 15 of 2007, with 19,071 cases reported that year. In 2008, 200,707 cases were reported. The higher case rate affected the 5–9, 10–14, and 15–24 age groups; the 10–14 age group was the most affected, with a rate of 1.81 per 100,000. Many of these people were not eligible to receive the MMR vaccine at the time of its introduction in 1999. The outbreak affected all 24 states in the country, with the highest incidence rates recorded in Zulia, Apure, Amazonas, Anzoátegui, and Cojedes. Between November 2007 and December 2008, the laboratory studied 1,007 cases, 350 of which were serologically confirmed. In order to isolate the circulating strain, 14 saliva samples from patients with a clinical diagnosis of mumps were processed; 12 of them tested positive and 6 of them were genotyped at the CDC, which reported genotype G in all cases.

Conclusions
The main cause of the outbreak was the significant clustering of susceptibles, representing people not vaccinated because they were ineligible at the time the vaccine was introduced. This explains the high incidence rates in the 10-24 age group. It seems these people did not develop natural immunity either, owing to the reduction in the circulation of the mumps virus stemming from sustained use of the MMR vaccine over the last 10 years. The high rates in the 5-9 age group are due to the low coverage achieved in that cohort during the same period. Much has been said about the inherent risks of using the MMR vaccine, especially the Urabe or L-Zagreb strain, and potential adverse events such as aseptic meningitis and parotitis. It is necessary to compile information that will contribute to the formulation of potential changes in recommendations on the MMR vaccine use, both for campaigns to maintain measles/rubella elimination in the Americas and to deal with potential mumps outbreaks. Other aspects, such as vaccine efficacy, the vaccination schedule, and potential variations in the circulating wild strain that could differ from current vaccine strains, should not be ignored.

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**Mumps in the United States: Lessons Learned from the 2006 Outbreak and Challenges for Elimination**

*Seward J*

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**Introduction**

After implementing a routine one-dose mumps vaccine policy in the United States in 1977, and a 2-dose MMR vaccine policy in 1989, dramatic declines in the mumps incidence occurred. A mumps elimination goal by 2010 was established in 1998. During 2001–2005, less than 300 mumps cases were reported annually and epidemiological patterns were suggestive of elimination. However, a large mumps outbreak in 2006 led public health officials to re-evaluate this elimination goal and mumps epidemiology in the highly vaccinated US population.

**Methods**

Mumps cases are reported to the Centers for Disease Control and Surveillance from state health departments via the Nationally Notifiable Disease Surveillance System (NNDSS) using a standardized case definition. Data from eight states most severely affected by the 2006 outbreak were also analyzed.

**Results**

From 2000-2005, an average of 280 cases of mumps was reported annually (incidence <1/million population). The highest incidence was in children 5-9 years of age (median age 10 years) and key surveillance indicators (lab confirmation, vaccination status) were <50% complete. During 2006, 6,584 confirmed and probable mumps cases were reported from 45 states. The national incidence of mumps was 2.2 cases per 100,000 persons with the highest incidence in 8 Midwestern states and the highest attack rate (6 per 100,000) in persons 18-24 years of age (median age 22 years). Between January 1 and July 31, 2006, 5,127 cases occurred in these eight states. Eighty five persons were hospitalized; no deaths occurred. Among cases for which vaccination status was known, 63% had received two doses of mumps-containing vaccine. Sixty-four percent of cases were females, and 88% were non-Hispanic whites. Genotype G was the predominant genotype isolated during the outbreak, from cases in 12 states. Studies conducted on college campuses showed that, despite extremely high 2-dose vaccine coverage (95%-99%), the force of infection was sufficiently high to sustain transmission, 2 doses of mumps vaccine were 79-88% effective in protecting against mumps parotitis in exposed room contacts, and mumps neutralizing antibody IgG antibody levels to Jeryl Lynn strain were significantly lower among students who received their 2nd mumps vaccine dose >15 compared with <5 years previously. Diagnostics tests (capture IgM and PCR) showed low sensitivity in 2-dose vaccinated case-patients. Following the 2006 outbreak, there were 800 reported mumps cases during 2007 and 386 (provisional) during 2008. In this post-outbreak period, although the highest incidence rates for mumps are in children 5-9 years old, the median age of cases is 19 years and reported incidence remains higher in persons 18 and older than before the 2006 outbreak.

**Conclusions**

Despite high vaccine coverage in pre-school, school and college students, the largest outbreak of mumps in over two decades occurred during 2006. The outbreak was characterized by two-dose vaccine failure. This outbreak highlights the need to 1) better understand mumps epidemiology in the US; 2) improve diagnostic testing for mumps, especially in vaccinated persons; 3) evaluate the waning immunity and vaccine effectiveness; and 4) consider vaccine and vaccine policies for mumps outbreaks and for achievement of mumps elimination in the US.

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**Introduction**

Pertussis, or whooping cough, is one of the diseases that generally receives little attention in the global public health context and yet warrants study, given its potential for outbreaks when coverage with the diphtheria-tetanus-pertussis vaccine (DTP) is low. In the past 10 years, the total annual number of reported cases in the Americas has ranged from 20,000 to 30,000, and vaccination coverage with the third dose of DTP by one year of age has been over 85% (Figure). In October 2007, the Pan American Health Organization (PAHO) convened a meeting of experts to discuss suggesting that the PAHO Technical Advisory Group (TAG) on Vaccine-preventable Diseases modify its current recommendations on pertussis surveillance and prevention.

**Methods**

The agenda included an initial presentation on the pertussis situation worldwide, in Latin America, and in the United States, a study on outbreaks in Argentina and Mexico, the factors that led Costa Rica and the United States to introduce the Tdap vaccine, and the epidemiological justifications for the current immunization schedule and the new ones proposed.

**Results**

- Epidemiological surveillance poses a major challenge, particularly due to the complexity of diagnosis in the different age groups and the complexities of case confirmation through laboratory studies. Under-reporting may be common.
- In order to prevent errors in analysis resulting from poor-quality surveillance data (epidemiological or laboratory-based), it is essential to improve pertussis surveillance in the Region. The presentation by the United States at this meeting offered the example of an outbreak of what appeared to be pertussis and was initially falsely classified as such (with all the implications for control in the field), due to the limitations of the PCR technology employed.
- The presentations showed the importance of adequately studying outbreaks and properly documenting risk factors, specifically the age groups of all cases and their vaccination status and using sensitive and specific laboratory diagnostics.
- Argentina gave a presentation on a moderately localized outbreak. Determining whether it was due to low coverage or vaccine failure will require more information and future investigations could preferably utilize a case-control study. The status of the cold chain also needs examination.
- Costa Rica decided to vaccinate both the father and mother of newborns in response to what it perceived as a greater risk of illness in neonates. This strategy should be carefully monitored and evaluated to assess its impact.

**Conclusions**

- The current emphasis on PCR for pertussis diagnostics in the field makes obtaining a culture appear to be less important. However, since PCR can result in false positives, it should be stressed that obtaining specimens for culture is still essential for confirming the diagnosis, especially in neonates.
- Changes in vaccination policies and control measures should only be justified with adequate documentation and analysis of the basic causes of outbreaks.
- The TAG took the view that there is no reason to shift from the whole-cell vaccine (wp) to the acellular vaccine (aP), since the former is more cost-effective.
- Adding boosters to the primary three-dose schedule will depend on the national situation and TAG recommendations;
- Acquiring more data will aid policy-making.
- For newborns, especially during outbreaks, vaccination can begin at 6 weeks of age. especially if that age group is being affected. The importance of obtaining specimens for culture, especially in neonates, should be underscored.

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Introduction
During recent decades, there were significant changes in the epidemiologic pattern of pertussis (whooping cough) in Costa Rica. Responding to the 2006-2007 outbreak, efforts to improve knowledge about the epidemiology of pertussis led to the adoption of vaccination strategies designed to protect groups at higher mortality risk. The objective of this abstract is to analyze changes in the epidemiology and transmission pattern of Bordetella pertussis and its connection with pertussis immunization strategies adopted in Costa Rica.

Methods
Whooping cough vaccination strategies, case incidence reported to the surveillance system, and changes in mortality by age using the national death registry have been described since 1950. Using mobile averages, the cyclical and seasonal hospital discharge pattern for the period 1990-2008 is identified. The Bordetella pertussis risk groups and transmission mechanisms are described using data from the prospective study of hospitalized children (2001-2004). Laboratory confirmation was obtained through culture and PCR of Bordetella pertussis. The scientific evidence to support the “cocoon strategy” of post partum vaccination and its association with the epidemiologic behavior of the 2006-2007 pertussis outbreak are described.

Results
The introduction of the diphtheria-tetanus-pertussis vaccine in 1950 and inclusion of a 5-dose series in 1974 rapidly reduced the number of pertussis cases. However, a cyclical pattern of 3 to 5 years was maintained (Figure), with seasonal behavior. Late 2000 witnessed an increase in the number of hospitalizations due to pertussis and severity of cases in newborns and infants. The prospective study in hospitalized children revealed 27% positivity in family contacts, with mothers being the most frequent source of infection (50% of contacts). Geographic analysis of the 2006-2007 outbreak showed the spread of the disease in the different provinces, with bimodal behavior. The rate of reported pertussis cases in children aged <1 year was 232.1 per 100,000, with mortality of 11.2 per 100,000 live births in 2007, accounting for more than 1% of total deaths in children aged <1 year. Four percent of laboratory-confirmed cases during the outbreak were adolescents, and 16% were adults aged ≥18. On analyzing the available evidence on the effectiveness of the vaccination strategies, the severity and case-fatality in infants, and the high institutional delivery coverage in Costa Rica (98%), in April 2007 the decision was made to begin vaccinating women during the postpartum period—the cocoon strategy—to quickly raise maternal immunity levels, reduce the role of mothers as carriers, and confer greater protection to infants through breast milk. Following the introduction of this strategy, a decline in the number of cases and deaths was observed. A study of the 13 laboratory-confirmed deaths in 2006-2007 indicated that two occurred after starting post-partum maternal vaccination. No pertussis-related infant deaths were reported in 2008.

Conclusions
Given the current pertussis profile, improvements in surveillance, prevention, and control are needed to reduce neonatal and young infant mortality. Adoption of the “cocoon strategy” should be accompanied by campaigns to support breastfeeding to provide greater protection for infants. Education strategies must also be improved to prevent the disease, identify potential contacts, and institute appropriate protective measures to prevent transmission of the disease to neonates and young infants.

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Pertussis in Argentina
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Introduction
As a result of pertussis outbreaks in 1972, 1976, 1980, and 1984, Argentina added a second DTP booster at age 6 in 1985 (5th dose). As a consequence, case incidence was reduced from 52.4 reported cases per 100,000 population in 1984 to less than 1 case per 100,000 in 2002. However, the downward trend was halted starting in 2003, when 639 cases were reported, followed by 976 cases in 2004, 2,060 in 2005, 1,982 in 2006, and 3,839 in 2007, with reporting rates of 1.8, 2.7, 5.7, 5.5, and 10.4 cases per 100,000 population, respectively (Figure 1).

Methods
Vaccination coverage over the past 25 years with the vaccine containing the pertussis component and pertussis outbreaks across the country during the period 2003-2007 were studied in an attempt to identify the causes of the outbreaks, as well as potential control measures.

Results
In the past 6 years, vaccination coverage with the third dose of the DTP-Hib in children aged <1 year in Argentina ranged from 90% to 95%. Coverage with the fourth dose at 18 months ranged from 80% to 85%, and with the fifth dose administered at 6 years, 85% to 92%. Data show that in 2006 and 2007, the coverage in approximately 60% of the country’s 548 departments was <95% and that approximately 60% of children aged <1 year live in those departments.

During the period studied, 13 of the country’s 24 provinces reported pertussis outbreaks, using case definitions that vary from place to place. The number of cases at the national level had risen steadily since 2004, and although 2006 witnessed a decline in all age groups, except children aged <1 year, the trend persisted in 2007. Although the higher reporting rate continued in children aged <1 year, it should be noted that the greatest increase since reemergence was observed in preschool children (2-4 years) and adolescents and adults (15-49 years).

Of the 1,982 cases reported in 2006, roughly 1/3 were reported by Neuquén Province. Of the 3,839 cases reported in 2007, 31% were from Buenos Aires Province, and only 1,174 (30%) of them were confirmed using the criteria recommended by the Pan American Health Organization: PCR, culture, epidemiological link, or paired serology. It is estimated that at the national level, only 20-25% of reported cases have been confirmed using these criteria.

Conclusions
The accumulation of susceptibles due to the non-optimal DTP-Hib vaccination coverage achieved by the country in recent years, the low vaccine efficacy (estimated at around 85%), and the short duration of the immunity conferred are some of the reasons cited to explain the current epidemiological situation.

The main recommendations included an improvement in epidemiological surveillance and laboratory diagnostic capacity, early detection of outbreaks, and timely implementation of control measures, including mop-up vaccination campaigns in municipalities with DTP-Hib coverage of <95%, as well as the administration of a booster containing acellular pertussis vaccine in adolescents and health workers.

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Strengthening Pertussis Surveillance: Importance of Diagnostics

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Introduction
Although in 2003 pertussis was still responsible for an estimated 279,000 deaths at the global level, and although DTP3 coverage is an indicator of health development and used as a measure of the World Health Organization’s (WHO) Global Immunization Vision and Strategy goal of reaching 90% national vaccine coverage, there is a lack of disease reduction target. Pertussis prevention and control has not received sufficient emphasis in recent years. Surveillance is difficult so that disease burden goes largely unrecognized, which in turn results in less attention being devoted to this disease. Attention tends to exclusively focus on DTP3 coverage which has some imprecision in estimation. WHO recommends the use of a booster dose after primary immunization; nonetheless, coverage with such booster doses is poorly reported.

Methods
The presentation reviews data pertaining to immunization schedules, vaccine coverage, and surveillance data collected from the WHO-UNICEF Joint Reporting Forms. It also reviews current global recommendations as well as existing surveillance and laboratory standards for pertussis.

Results
• Although the reported overall DTP3 coverage exceeds 90%, there is still a difference of 9% between the reported coverage and the WHO/UNICEF best estimates, and the estimated drop-out rate from DTP1 through DTP3 is 10%. Estimated coverage varies from a low 69% in WHO’s South-east Asia Region to a high 96% in the European Region.
• Pertussis surveillance is a real challenge with difficult clinical and laboratory diagnoses. Infants under 6 months, vaccinated children, adolescents, and adults often do not have the typical whoop or cough paroxysm, making clinical diagnosis more challenging in these groups.
• Diagnosis is based on the recovery of the causal organism from nasopharyngeal specimens obtained during the catarrhal and early paroxysmal stages on appropriate culture media. WHO considers culture as the “gold standard” of laboratory confirmation. It is the most specific diagnosis, but is not very sensitive (60%). Polymerase chain reaction is more sensitive and can be performed on the same biological samples as cultures. It is delicate to perform, requires more expensive equipment and carries a risk of false positive results.
• Pertussis immunization schedules vary tremendously by region and countries.
• Altogether it is estimated that notification is extremely poor with <1% of cases reported globally for a total of 152,535 reported cases in 2007.
• At present, global pertussis surveillance data is of insufficient quality to guide global, regional, or most country vaccination strategies. Recent trends suggest a deterioration of global surveillance.
• It is essential that pertussis outbreaks be properly investigated and risk factors clearly identified.

Conclusions
• If one is to improve pertussis control, it is essential that the impact of immunization programs and vaccination strategies be properly assessed. As a result, strengthening of pertussis surveillance and monitoring of pertussis vaccination is of critical importance.
• Laboratory capacity has to be expanded, hopefully building on the bacterial laboratory network.
• There is currently no evidence from surveillance data to change the emphasis of WHO recommendations.

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Introduction

In 1989, the World Health Assembly adopted a resolution calling for the global elimination of neonatal tetanus (NNT) by 1995. This resolution was endorsed by the Directing Council of the Pan American Health Organization (PAHO) and, with a view to meeting that goal, the ministers of health of PAHO Member States initiated specific program activities with support from the Organization and several international agencies.

Methods

Elimination of neonatal tetanus as a public health problem has been defined as the reporting of less than one case of NNT per every 1,000 live births in a municipality or district in a year. The information provided by the countries in their morbidity reports and NNT case investigation forms, collected through their epidemiological surveillance systems, is analyzed.

Results

• In the Americas 1,495 NNT cases were reported in 1988 and 63 in 2007. Case numbers have fallen by 96% (Figure).
• NNT has been eliminated as a public health problem in every country in the Americas except Haiti, which in the past five years has reported some 40-60% of all cases in the Hemisphere.
• Countries have used the recommended strategies to target actions in at-risk districts or municipalities, intensifying surveillance and vaccinating all women of childbearing age.

Conclusions

• Latin America, with the exception of Haiti, has eliminated NNT as a public health problem.
• The strategies implemented in at-risk municipalities or districts have met the proposed objective of eliminating NNT as a public health problem.
• The cases that still occur in the countries of the Region are generally found in remote municipalities with scattered populations and in rural areas.
• Action should be taken in Haiti that will make it possible to complete the elimination of NNT in the Americas.

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Seasonal Influenza Vaccination in the Americas
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Introduction
Seasonal influenza is a viral disease whose annual epidemics are estimated to cause three to five million cases of severe illness and 250,000 to 500,000 deaths worldwide. Vaccination is the main strategy for primary prevention. In the Americas, Bermuda, Canada, Chile, and the United States have used seasonal influenza vaccination for the past several decades, while many other countries and territories have not introduced the vaccine until fairly recently. During the 56th World Health Assembly in 2003, the World Health Organization (WHO) encouraged nations to increase influenza vaccination coverage among high-risk groups, with the goal of achieving 50% coverage in populations 65 years and older by 2006 and 75% coverage in this group by 2010. In 2004, the Technical Advisory Group (TAG) expanded upon these recommendations, advising yearly influenza vaccination of populations older than 60 years, the chronically ill, populations with immunodeficiency, health professionals, and pregnant women in their second trimester. These recommendations were later expanded upon by TAG in 2006 to include children aged 6-23 months. The objectives of this review were to describe the current state of influenza vaccination in the Americas and to discuss challenges remaining for optimizing vaccine use.

Methods
To assess the status of influenza vaccination in the Region through 2008, data were consolidated by country from four sources: a 2004 Pan American Health Organization (PAHO) survey administered by the Immunization Project to Member States, the 2006 WHO’s Global Influenza Survey, annual country reports through the PAHO-WHO/UNICEF Joint Reporting Forms (JRF), and information from PAHO’s Revolving Fund for Vaccine Procurement. The data was then reviewed and information was sent to national authorities for verification and updating. Additional questions regarding criteria used for vaccine introduction and the status of impact evaluations were also posed. For countries that did not return verified information, data from WHO’s 2006 Global Influenza survey and/or informal email communications with national PAHO employees were used. Information from Canada and the United States was retrieved from the Public Health Agency of Canada and the Centers for Disease Control and Prevention, respectively. Information from the Netherlands Antilles was based on data received from Bonaire. The French Caribbean Departments were not included in this review.

Results
Currently, 35 out of 47 countries/territories administer influenza vaccine in their public health sector, compared to 13 countries in 2004. Targeted risk groups vary and include older adults, children, individuals with chronic disease, poultry workers, pregnant women, public safety workers, indigenous populations, childcare providers, and incarcerated populations, among others. Sixteen countries report coverage among older adults, ranging from 21% to 100%; coverage data is not available for most countries and targeted populations. Use of Northern Hemisphere or Southern Hemisphere vaccine formulation is uniform in temperate sub-regions. However, there is mixed use of vaccine formulations by country in tropical zones. Good surveillance systems are not in place in most tropical countries. Political decisions and influenza morbidity and mortality were the most common reasons given for vaccine introduction. In 2008, approximately 166.3 million doses of seasonal influenza vaccine were purchased in the Americas and 30 of 35 countries procured their vaccine through PAHO’s Revolving Fund.

Conclusions
Since 2004, there has been rapid uptake of seasonal influenza vaccine in the Americas. Challenges to fully implement influenza vaccination remain, including difficulties measuring coverage rates and variable vaccine uptake. In addition limited surveillance and vaccine effectiveness data to guide decisions regarding vaccine formulation and timing, especially in tropical countries. Future efforts to improve coverage monitoring will be essential to determine what population groups are not being reached and to create strategies to ensure better compliance. Additionally, to better understand viral circulation, particularly in tropical areas of the Americas, influenza viral surveillance needs to be enhanced. Countries that have not introduced the influenza vaccine would benefit from evaluating local epidemiology and conducting cost-effectiveness studies to develop informed, evidence-based policies.

Note: This abstract is based on the article, Seasonal Influenza Vaccination in the Americas: 1970s-2008, submitted for publication on 27 February 2009.
Influenza A(H1N1) Vaccination in the Americas
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Epidemiological Situation
Beginning in mid-March 2009, surveillance systems in Mexico began to report a sharp increase in cases of a severe influenza-like illness. This increase began when cases of seasonal influenza typically start to wane. The number of reported cases continued to grow in the first weeks of April and geographical expansion was seen with clusters of severe pneumonia cases in young, normally healthy, adults. On 17 April, Mexico intensified surveillance for cases of acute respiratory disease. The country sent specimens from suspect cases to the reference laboratory of the Public Health Agency of Canada and a new influenza A strain (H1N1) of porcine origin was identified.

In the United States, on 24 April, the Centers for Disease Control and Prevention (CDC) reported eight cases of influenza A(H1N1) in the states of California and Texas. This strain was confirmed as being genetically similar to the strain isolated from the cases in Mexico. The number of cases continues to grow.

Given the emergence of the new influenza strain and its subsequent spread throughout the Americas and other regions of the world, the World Health Organization (WHO) declared pandemic phase 4 on 25 April 2009, pandemic phase 5 on 29 April 2009, and pandemic phase 6 on 11 June 2009. As of 15 June 2009, a total of 35,503 cases of influenza A(H1N1) had been recorded, including 163 deaths, in 75 countries, the West Bank and Gaza Strip.

PAHO's Regional Vaccination Plan for Pandemic Vaccination
As part of the Pan American Health Organization’s (PAHO) technical cooperation activities with Member States of the Region, a Regional Vaccination Plan for Pandemic Vaccination was developed and distributed to Member States in May 2009. The plan consists of multiple components and includes the following:

—— Strengthening of Seasonal Influenza Vaccination
As of December 2008, thirty-five Member States and territories administered the seasonal influenza vaccine in the public sector, vaccinating a wide variety of population risk groups. Twenty-six Member States used the Northern Hemisphere vaccine formulation, and nine used the Southern Hemisphere formulation. Most Member States purchased vaccine through PAHO’s Revolving Fund (RF). While there is little evidence that seasonal influenza vaccines confer cross-protection against influenza A(H1N1), strengthening vaccination with the seasonal vaccine is essential to reduce disease burden and to prevent the co-circulation of both seasonal and A(H1N1) influenza strains. The objectives of the Regional effort to strengthen seasonal influenza vaccination are two-fold:

1. To support the introduction of the seasonal influenza vaccine into the public sector of nine Member States and territories that have not done so to date; and
2. To scale-up existing seasonal influenza vaccination in the remaining Member States, where the vaccine has already been introduced.

To achieve these objectives, resources (monetary and vaccine supplies) have been mobilized. Support has also been given in the determination of population risk groups and operational strategies for vaccine introduction and scale up.

—— Status of Influenza A(H1N1) Vaccine Production
WHO estimates the optimal global production capacity of a novel monovalent H1N1 vaccine at 94 million doses per week, assuming vaccine yield is equal to seasonal influenza and that dose sparing is employed. Using this baseline, speculative estimates are that 2.4 billion doses of influenza A(H1N1) vaccine could be available in 6 months and 4.9 billion doses available after 1 year of production. Due to multiple, pre-existing advanced purchase agreements, large quantities of perspective doses have already been committed. WHO has asked manufacturers to consider donating a percentage of vaccine to United Nation agencies for distribution to developing nations to ensure equity and access. Discussions concerning a pandemic procurement facility are also ongoing.

As of 15 June 2009, 5 vaccine viruses were available (2 classical reassortants and 3 generated by reverse genetics). Three vaccine viruses have completed ferret safety testing and can be used under Bio-Safety Level L2+ conditions for large-scale vaccine production. Other vaccine viruses are expected to be available shortly. Factors such as the use of adjuvant and dose scheduling have yet to be determined.

—— Preparation of Countries for Influenza A(H1N1) Vaccine Introduction
Biologicals and supplies: Vaccine procurement, supply, storage, and distribution will be critical in the introduction of an influenza A(H1N1) vaccine. The supply needs of Member States and territories will be consolidated on a Regional level. Countries and territories should consider the implications of the new vaccine on their cold chain. The RF will play a key role as a procurement mechanism, promoting equity and access to vaccines.

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Training: Training personnel is a priority. At the Regional level, a training of FCH/IM consultants and sub-Regional workshops are being organized. A technical-operational vaccination manual will also be distributed to Member States.

Social mobilization: Communication materials will be produced at the Regional level. These materials will be distributed to the Member States and will also be available via electronic media. It is important that social mobilization messages be clear, objective, and consistent. Most importantly, messages should be transparent about what is known and what is not yet known.

Vaccination strategies: Considering that influenza A(H1N1) vaccine supply will be limited in the beginning stages of production, Member States will need to prioritize risk groups, a process that involves scientific, logistical, ethical, moral, cultural and legal considerations. Member States should rely on the ethical guidelines of National Committees on Immunization Practices, Ethics Committees, and the WHO, as well as the involvement of all sectors.

Vaccination strategies should be set at the national level for each priority group. Suggested strategies include sending vaccination teams into the community to reach individuals at places of work and recreation, as well as to vaccinate captive populations. Vaccination of pediatric populations should be in accordance with local-level routine vaccination programs.

Surveillance of ESAVIs\(^{(a)}\): Anticipated high public demand for the vaccine could also increase the possibility of programmatic errors. PAHO will provide Member States with a tool for ESAVI surveillance; a survey on pre-implementation of the surveillance information system has already been distributed. Countries and territories are advised to create an investigation and response team at national level. Before the onset of campaigns, the flow of ESAVI reporting, investigation, and crisis response should be established.

Evaluation of the impact and effectiveness of the Influenza A(H1N1) vaccine: PAHO is attempting to develop a study protocol that will evaluate the impact of the vaccine through the ProVac initiative.

\(^{(a)}\) Events Supposedly Attributable to Vaccine or Immunization.
Introduction

Over the last three decades, jungle yellow fever virus activity in the Americas was limited to the enzootic area shared by Bolivia, Brazil, Colombia, Ecuador, French Guiana, Guyana, Panama, Peru, Suriname, Trinidad and Tobago, and Venezuela. The last reported outbreak of urban yellow fever occurred in Brazil in 1942, and the last confirmed case of urban yellow fever was reported by Trinidad and Tobago in 1954. Since late 2007, the Region has witnessed intense circulation of the yellow fever virus, with extensive epizootics and outbreaks of human cases.

Yellow fever can be prevented with live attenuated 17D vaccine that has been considered safe and effective. The global supply of vaccine is currently limited. Two large suppliers prequalified by the World Health Organization currently provide vaccines to the Americas: Bio-Manguinhos, which provides 95% of the vaccines purchased by the Pan American Health Organization’s Revolving Fund (RF) for Vaccine Procurement, and Sanofi Pasteur, which meets 95% of the demand for Africa through UNICEF and 5% of the demand from the RF.

Methods

Reports of confirmed yellow fever cases, along with outbreaks and epizootics notified since 2000, were reviewed. Regarding vaccination, yellow fever vaccination plans of enzootic countries, their vaccination coverage, and the campaigns implemented were also reviewed.

Results

From 2000 to 2008 (provisional data), 1,015 confirmed yellow fever cases were reported, with a case-fatality of 51.1%. The highest case numbers were reported by Peru (352), followed by Brazil (273), Colombia (202), Bolivia (85), Venezuela (63), Paraguay (28), Argentina (10), and Ecuador (2). A full 82.8% of the cases were male. Of the cases where the occupation is known, 47.2% were agricultural workers. Ecotourists represent 3.2%. Some 8.9% of the cases reported having been vaccinated against yellow fever, although the vaccination date was not noted.

In 2008, 109 yellow fever cases were reported. Outbreaks occurred in Argentina (8 cases), Brazil (48 cases), and Paraguay (28 cases). Nine of the Paraguay cases were confirmed in metropolitan Asunción as urban transmission. Argentina and Paraguay had gone more than three decades without reporting cases. From October 2008 to February 2009, epizootics were reported in Argentina, Brazil, Trinidad and Tobago, and Venezuela. In 2009, as of epidemiological week 7, seven yellow fever cases had been reported, with 3 deaths.

Currently, 7 of the 13 countries with enzootic areas (Bolivia, Colombia, Guyana, Paraguay, Peru, Trinidad and Tobago, and Venezuela) have added the vaccine to their routine childhood immunization programs, achieving roughly 73% coverage. Four countries (Brazil, Ecuador, Panama, and Suriname) vaccinate children living in enzootic areas. Mass vaccination activities vary from country to country: reactive campaigns to respond to outbreaks or preventive campaigns in stages, targeting the resident population and areas where migrants originate. Peru vaccinated over 10 million people between 2004 and 2007, Brazil, 90 million in the past 10 years, and Bolivia, roughly 5 million through a national campaign in 2007. In response to the 2008 outbreaks, Brazil administered over 14 million doses of vaccine; Argentina, 1.5 million; and Paraguay, over 3 million. As for events supposedly attributable to vaccination or immunization (ESAVIs), in 2007 Peru reported a cluster of 5 cases of viscerotropic disease, and in 2008, Brazil reported 6 cases and Argentina 1.

Conclusions

Yellow fever in the Americas is an important public health problem. The pattern observed in the Region is sylvatic yellow fever transmission. However, the limited urban transmission that occurred in Paraguay in 2008 shows that urban yellow fever remains a threat. The widespread proliferation and high density of *Aedes aegypti* increase the risk of reurbanization. Comprehensive steps should be taken to control *Aedes aegypti* in urban areas bordering on risk areas to prevent reurbanization.

All countries with enzootic areas have implemented yellow fever plans targeting population living in or traveling to risk areas. Most countries have introduced the vaccine in their routine programs, although coverage is unusually lower that coverage for other vaccines. Given the global vaccine shortage, rational vaccine use is essential, as well as maintaining national and regional vaccine reserves to respond to outbreaks.

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1 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
2 Communicable Diseases (HSD), Pan American Health Organization, Washington, D.C., USA.
Risk of Urbanization of Yellow Fever in the Americas: The Experience of Paraguay

Allende I, Cabello A, Carrillo M, Vázquez C, Cousiño B, Martínez N, Benítez L, Viveros C, Manzur J, Torres C

Introduction
The cases of jungle and urban yellow fever reported by Paraguay in 2008, coming after 34 years without a recorded case in that country, have important implications for international public health. The last reported human cases of jungle yellow fever in Paraguay were in 1974, and the last cases of urban yellow fever reported in South America were in 1942. In 2001, in light of persistent outbreaks of jungle yellow fever in Bolivia and Brazil, Paraguay launched an effort to vaccinate the population residing in areas bordering those two countries, with coverage of 28%. In 2006 Paraguay introduced the vaccine into the routine immunization schedule at the national level, with coverage of 26%. Since 2007, however, an extensive epizootic has developed, spanning a large ecological area shared by Brazil, Paraguay, and northern Argentina. In January 2008 the first indigenous cases of jungle yellow fever were detected in hunters in San Pedro Department, located in the north of Paraguay’s Eastern Region; these were followed by cases in the Central and Caaguazu Departments, which are nonborder areas. In the Central Department, where some municipalities are part of the metropolitan area of Asunción, a case cluster was found in the Laurelty neighborhood, in San Lorenzo Municipality. This neighborhood presented indices of infestation by Aedes aegypti of 26%, and this case cluster is the first sign of probable urbanization of the disease.

Methods
To control the yellow fever outbreak, Paraguay formulated a plan that included the strengthening of epidemiological surveillance, care of patients, vector control, targeted and expanded vaccination, and risk communication. Epidemiological research was conducted to characterize the cases and identify the etiologic agent, vectors, and reservoirs, providing a basis for control measures to interrupt the chain of transmission. These measures included an active search for febrile patients, chemical control of the vector, and elimination of breeding sites. The vaccination campaign was accompanied by monitoring of events supposedly attributable to vaccination or immunization (ESAVIs) and rapid coverage monitoring.

Results
A total of 162 suspected cases were detected by the surveillance system from epidemiological week 3 through week 22 in 2008. Of these cases, 28 were subsequently confirmed: 15 in San Pedro Department, 4 in Caaguazu Department, and 9 in San Lorenzo Municipality in Central Department. Among the 28 confirmed cases, there were 11 deaths, for a case fatality of 39%. The surveillance system captured 69% of the cases through active search, while 31% were captured through the health services. Of the confirmed cases, 64% were male and 36% female.

Vector control: During the outbreak in Laurelty and continuing until 30 May 2008, a total of 326 specimens of adult mosquitoes were collected for taxonomic identification and later virological research. The vector control efforts adopted the blockade strategy used for suspected cases of dengue. These actions were launched within 24 hours of the report of the suspected case and covered an initial geographic area of 400 meters; this was subsequently expanded to two concentric rings of 1 and 2 kilometers. The fumigation was conducted in short cycles of 3 and 5 days using backpack sprayers and heavy machines, respectively, with environmental brigades and house-to-house mop-ups, until larval densities were reduced to thresholds of relative epidemiological safety. Targeted vaccination actions were conducted jointly with vector control measures.

Vaccination: Paraguay conducted targeted vaccination in the area surrounding each case in concentric rings of 1 and 2 kilometers, corresponding to the area defined for vector control. The vaccination was expanded to include the metropolitan area of Asunción because of its high indices of Aedes infestation and the large influx of population for employment. A geographic corridor was also included, based on the cases found in the San Pedro, Caaguazu, and Central Departments. Vaccination was accompanied by rapid coverage monitoring and ESAVI surveillance, with 7 severe events reported. Because the outbreak in Paraguay came at a time of global yellow fever vaccine shortage, 2 million doses were obtained from the International Coordinating Group on Provision of Vaccines of the World Health Organization.
Risk communication was regarded as a weak area of the yellow fever control plan in Paraguay. The failure to designate a single spokesperson was one of several factors contributing to a lack of accurate information and resulting panic among the population.

**Conclusions**

In Paraguay, 34 years after the last recorded case, authorities have confirmed a classic outbreak of jungle yellow fever, a transitional “rural” outbreak, and an urban outbreak in the metropolitan area of Asunción. This situation has led the country to redefine its risk areas and adjust its vaccination plan to maintain high coverage in the enzootic areas, among travelers to these areas, and in the routine vaccination schedule.

The strengthening of epidemiological surveillance is fundamental in order to predict future outbreaks; this should include surveillance of epizootics and ictero-hemorrhagic syndromes. The case fatality observed in the recent outbreaks was less than what is typically reported, which could have to do with the implementation of a sensitive surveillance system. The fast and effective actions undertaken in the areas of vector control and vaccination were critical for successful control of the outbreak in the urban setting. Paraguay’s experience demonstrates that there is a continuing risk of urban yellow fever and points to a need for integrated surveillance and control of diseases transmitted by *Aedes aegypti* in areas bordering the zones of yellow fever risk.
Introduction

Peru is one of the countries in the Americas where yellow fever remains endemic. In 2007, 27 yellow fever cases, including 24 fatalities, were reported. On 15 August 2007, a large earthquake hit Peru, with an epicenter near the Southern coast in the Region of Ica. As part of the Peruvian Ministry of Health’s response to the earthquake, vaccination campaigns using a variety of vaccines were conducted in the Ica Region starting on 23 September. On 6 October, an event supposedly attributable to vaccination or immunization (ESAVI) in the Ica Region was notified to the surveillance system; the patient died the same day. Yellow fever vaccine-associated viscerotropic disease (YEL-AVD) was the suspected cause. Five other cases were reported in the following days.

Methods

Case investigation followed the following steps: (1) Clinical and laboratory investigation of ESAVI; (2) YEL-AVD case definition review for the case classification process; (3) Active institutional case-finding of other YEL-AVD cases in hospitals of the Ica Region; and (4) Control of vaccine quality and potency and supervision of laboratory facilities. Specimens obtained from the patients were processed by the National Institute of Health and the Legal Medicine Institute in Peru, the United States Naval Medical Research Center Detachment (NMRCD) in Lima, and the Centers for Disease Control and Prevention (CDC) in the United States. PAHO and CDC provided technical assistance.

Results

The regular AEFI surveillance system identified six probable YEL-AVD cases from the Ica Region, and five other probable cases from other regions. The active institutional case-finding field investigation reviewed 28,788 medical files and 233 death registries from 23 September to 6 November. It found five probable cases in Ica, all of them already identified by the routine surveillance system. After careful investigation, four cases notified from Ica Region were classified as confirmed YEL-AVD cases. One case remained as a probable case, and all other cases were discarded. All confirmed and probable cases were vaccinated with the same vaccine lot. A total of 42,742 doses of the compromised lot were applied in Ica. The YEL-AVD cumulative incidence for that lot was 9.4/100,000 doses. Some clinical characteristics of the confirmed cases are shown in the Table below. The results of the analysis of vaccine quality and potency were within international standards. Inspection of the manufacturing facility showed no deviations from the norm. Molecular analysis of the vaccine viruses isolated from patients and from vaccine vials of the implicated lot showed no abnormalities.

### Table: Viscerotropic Disease Associated with Yellow Fever Vaccination, Ica Region, Peru, 2007

<table>
<thead>
<tr>
<th>Case 1 RCQ</th>
<th>27-Sep</th>
<th>28-Sep</th>
<th>4-Oct</th>
<th>5-Oct</th>
<th>6-Oct</th>
<th>Lab Tests</th>
<th>YF-specific Lab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 23 years</td>
<td>Vaccination</td>
<td>Fever, headache, malaise, joint pain, muscle pain.</td>
<td>Nausea, vomiting and watery diarrhea.</td>
<td>Admitted to Ica Regional Hospital</td>
<td>Multisystemic failure. Death.</td>
<td>TGO: 78 U/L TGP: 65 U/L TBil 0.8 mg/dL DBil 0.2 mg/dL Ibil 0.7 mg/dL</td>
<td>Elisa IgM (+) in serum, RT-PCR (+) in serum, IHC staining (+) in liver, lung, kidney, brain.</td>
</tr>
<tr>
<td>Age 24 years</td>
<td>Vaccination</td>
<td>Fever, headache, malaise, muscle pain.</td>
<td>Nausea, vomiting and watery diarrhea.</td>
<td>Admitted to Chinchaca Hospital. Transferred to Lima.</td>
<td>Multisystemic failure. Death.</td>
<td>TGO: 735 U/L TGP: 167 U/L TBil 6.3 mg/dL DBil 0.2 mg/dL Ibil 0.1 mg/dL</td>
<td>Elisa IgM (+) in serum, RT-PCR (+) in serum, IHC staining (+) in liver, lung, kidney</td>
</tr>
<tr>
<td>Age 79 years</td>
<td>Vaccination</td>
<td>Fever, malaise, abdominal pain and dysphnea (2 months previous).</td>
<td>Vomiting and watery diarrhea.</td>
<td>Admitted to Nazca Hospital</td>
<td>Multisystemic failure. Death in Ica Regional Hospital.</td>
<td>TGO: 416 U/L TGP: 231 U/L TBil 2.9 mg/dL DBil 2.3 mg/dL Ibil 0.7 mg/dL</td>
<td>Elisa IgM (+) in serum, RT-PCR (+) in serum, IHC staining (+) in liver, spleen.</td>
</tr>
<tr>
<td>Age 49 years</td>
<td>Vaccination</td>
<td>Headache, gastrointestinal and vaginal hemorrhage.</td>
<td>Intense headache, malaise, joint pain.</td>
<td></td>
<td></td>
<td>TGO: 91 U/L TGP: 128 U/L TBil 5.2 mg/dL DBil 4.2 mg/dL Ibil 1.0 mg/dL</td>
<td>Elisa IgM (+) in serum, RT-PCR (+) in serum, IHC staining (+) in kidney.</td>
</tr>
</tbody>
</table>
Conclusions

Four confirmed YEL-AVD cases and one probable YEL-AVD case were detected in Ica Region, a non-endemic yellow fever area. After clinical, virological, epidemiological, and pathological evaluations, the cause of the cluster remains largely unexplained. The cluster occurred following a mass vaccination campaign in a natural disaster area where ESAVI monitoring was heightened. Yellow fever vaccination remains the most cost-effective tool for yellow fever prevention. However, given recent ESAVIs, efforts must be made to strengthen epidemiological surveillance, focus vaccination efforts in areas at risk for yellow fever, and comply with vaccine recommendations and contraindications.
Serious Adverse Events Associated with Receipt of Yellow Fever Vaccine
During a Mass Immunization Campaign, Peru, 2007
Barrett A1

Yellow fever remains a substantial public health problem in tropical regions of South America and Africa, and there is a risk of introduction and spread in non-endemic regions infested with the urban vector *Aedes aegypti*. There is no specific treatment for yellow fever. Vaccination using the live, attenuated 17D vaccine remains the most effective measure for prevention and control of yellow fever. With the strong support of the Pan American Health Organization (PAHO) and the World Health Organization (WHO), most countries in the endemic region now incorporate 17D vaccines into their Expanded Program on Immunization (EPI). The 17D vaccine has been administered to hundreds of millions of people over 70 years, with a long history of confidence in its safety and effectiveness. Nevertheless, new precautions concerning yellow fever 17D vaccines have recently been recognized because of the occurrence of rare but serious adverse events.

Yellow fever vaccine-associated viscerotropic disease (YEL-AVD) represents a rare but life-threatening complication first described in the medical literature in 2001. Up to September 2007, a total of 36 YEL-AVD cases had been reported worldwide following administration of yellow fever vaccines (17D and 17DD substrains) from 5 manufacturers. The mean age was 49 years (range 4-79 years), the male:female ratio was 2:1, and the case-fatality rate was 60%. Reported risk factors include age >60 years and thymic disease/thymectomy. In September-October 2007, a mass yellow fever immunization campaign was conducted in Ica Department, Peru, following a major earthquake, with approximately 63,000 doses delivered. Five persons, aged 23 to 79 years, who received yellow fever vaccine (17DD substrate) developed suspected YEL-AVD. This was the first time that multiple YEL-AVD cases had clustered within a short timeframe (patients were immunized between 23 September and 1 October 2007) and delimited space (Ica Department, Peru). Four persons died (case-fatality rate 80%). All four fatal cases occurred within a population of ~43,000 who had received a single lot of 17DD vaccine (designated 050VFA-121Z, referred to below as 121Z) manufactured by a WHO-prequalified producer, Bio-Manguinhos from Brazil. A second lot of Bio-Manguinhos vaccine (123Z) had been used in ~20,000 persons in the mass campaign in Ica Department, without any associated cases of YEL-AVD. The vaccine lot used in a fifth (non-fatal, but hospitalized) case is unknown.

A number of hypotheses were considered to explain the higher rate of YEL-AVD in Ica, including altered pathogenicity of the vaccine virus, altered susceptibility of the individuals experiencing the adverse events, and altered susceptibility of the population as a whole. The possibility that the 121Z lot contained a genetic change responsible for enhanced virulence was the focus of an extensive investigation. Overall, within the limits of the testing performed, no evidence could be found to suggest that the vaccine lot 121Z had anything inherently wrong with it to explain the higher frequency of viscerotropic disease in persons receiving that lot. Possible host factors (advanced age, autoimmune disease) may have contributed to susceptibility in two of the four cases.

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Session 3: Future Challenges

Rotavirus and Pneumococcus
Human Papillomavirus
Evidence-based Decisions
Introduction

It is estimated that rotavirus is responsible for 611,000 (454,000-705,000) deaths from diarrhea worldwide\(^{(4)}\) and around 15,000 deaths and 75,000 hospitalizations of children under 5 years in Latin America annually.\(^{(5)}\) In 2005, the World Health Organization (WHO) estimated that 1.6 million people die each year from pneumococcal disease and of these, 0.7 million are children under 5 years, mainly children under 2.\(^{(6)}\) In Latin America and the Caribbean (LAC), pneumococcal disease is estimated to cause 327,000 cases of pneumonia and around 4,000 cases of meningitis.\(^{(6)}\) The high morbidity and mortality from these diseases and the availability of new vaccines pose a great challenge to the governments of the Region of the Americas. This abstract reviews activities in the Region to support decision-making and assess the impact of the introduction of new rotavirus and pneumococcus vaccines and their contribution to the achievement of the Millennium Development Goals.

Methods

The general guidelines for epidemiological surveillance of rotavirus diarrhea and bacterial pneumonia and meningitis in children under 5 years were reviewed, and descriptive data from countries that systematically reported to the Pan American Health Organization (PAHO) in 2008 are presented. Also presented are the special studies currently under way, together with an update on the countries that have added the rotavirus vaccines and pneumococcal conjugate vaccine to their immunization programs.

Epidemiological surveillance of rotavirus diarrheal diseases and bacterial pneumonia and meningitis is conducted in selected sentinel hospitals using the definitions for suspected and confirmed cases and the standard laboratory methodologies established in the PAHO surveillance guides.\(^{(e,f)}\)

Results

LAC countries have been among the first in the world to introduce the rotavirus vaccine into their immunization programs: Brazil, El Salvador, Mexico, Nicaragua, Panama, and Venezuela in 2006; Ecuador in 2007; Bolivia in 2008; and Colombia, Guyana, Honduras, and Peru in 2009. Mexico and Uruguay added the pneumococcal conjugate vaccine to their immunization programs in 2008, and Barbados, Costa Rica, Guyana, Honduras, Nicaragua, Peru, and Venezuela will be introducing it in 2009 (Figure).

Surveillance data for rotavirus diarrheal diseases are reported by 11 countries of the Region. As of February 2009, Bolivia, Chile, Ecuador, El Salvador, Guatemala, Honduras, and Nicaragua had reported their data for 2008. A total of 149,853 hospitalizations of children under 5 years were studied; 14% (20,863) of these cases had been admitted for diarrhea and of these, 57% (11,904) were classified as suspect rotavirus cases. Of the cases with stool samples, 28% tested positive for rotavirus.

Seven countries report epidemiological surveillance of bacterial pneumonia and meningitis: Bolivia, Ecuador, El Salvador, Guatemala, Honduras, and Nicaragua had reported their data for 2008. A total of 8,829 hospitalized cases of bacterial meningitis in 2008, of the 8,829 hospitalized susceptible pneumonia cases, 79% of cases with a chest x-ray were classified as probable bacterial pneumonia, with a case-fatality of 5%.

Special studies are also being pursued, in addition to conducting epidemiological surveillance. El Salvador and Nicaragua are studying the efficacy of the rotavirus vaccine. Brazil and Mexico are participating in a safety assessment of the rotavirus vaccine centered on intussusception. In 2009, a study on the efficacy of the pneumococcal conjugate vaccine and an international evaluation of the rotavirus vaccine introduction will be conducted in Nicaragua and Ecuador, respectively. These studies represent a collaborative effort on the part of the Ministries of Health, PAHO/WHO, the U.S. Centers for Disease Control and Prevention, the U.S. Food and Drug Administration, and the Program for Appropriate Technology in Health (PATH).

Conclusions

Many lessons have been learned in the Region of the Americas from the introduction of new vaccines, chiefly rotavirus. Epidemiological surveillance helps with estimating the burden of disease and assessing vaccine impact. Therefore, surveillance should be strengthened and, in countries where it does not exist, implemented. Special studies show how the new vaccines behave in a

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\(^{(3)}\) Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
routine immunization program. The experience of LAC countries with new vaccine introduction confirms the benefits of coordination among the technical, operational, financial, and political spheres.\(^{(g)}\)

**References:**

(b) Pan American Health Organization. Experts meet in Mexico to discuss rotavirus. *Immunization Newsletter.* 2004;26(5).
(f) Organización Panamericana de la Salud. Vigilancia de las neumonías y meningitis bacterianas en menores de 5 años. OPS 2009; PST No. 633.
**Introduction**

In 2004 and 2005, a growing number of cases and deaths from diarrhea in children was recorded in El Salvador, primarily in the first quarter of each year. This led the authorities in early 2006 to begin sentinel hospital-based rotavirus monitoring, following the technical guidelines issued by the Pan American Health Organization (PAHO). The object was to obtain data to justify the introduction of a vaccine, which took place in October of that year, using a 2-dose schedule. The purpose of this study is to show case trends subsequent to vaccine introduction.

**Methods**

Descriptive study. Data from international indicators in seven national sentinel hospitals were used for the period 2006-2008. The case definition was as follows: a child under 5 years hospitalized for acute diarrhea lasting up to 14 days. Confirmatory tests used was ELISA. Review of national epidemiological surveillance, sentinel hospital, laboratory, and national mortality data.

**Results**

In 2006, 164,230 cases of diarrheal disease in children under 5 years were recorded. In 2007, the figure was 124,224, or a 24% reduction. In 2008, it fell to 103,491, or a 17% reduction over the previous year. Seventy-two percent of investigation forms and samples were studied during the first year of surveillance, rising to 92% in the second year, and 96% in the third year. Despite the growing number of cases investigated, the percentages of laboratory-positive rotavirus cases were 52%, 36%, and 11%, respectively, denoting a statistically significant reduction. As to mortality, in 2006, 44 cases associated with diarrhea were recorded, with rotavirus confirmed in 10. In 2007, the figure was 29, with rotavirus confirmed in 3. In 2008, no case of this pathology was confirmed. Predominant circulation of G1P8 was identified in 2007-2008, following vaccine introduction.

**Conclusions**

Sentinel surveillance is conducted, with 96% of cases investigated. There is evidence of a reduction in cases and case-fatality following the vaccine introduction.

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**Introduction**

When Paraguay joined the SIREVA network in 1998, the comparison between bacterial agents isolated in Paraguay with isolates from other countries in the Region became possible. Combining laboratory data with epidemiological surveillance is a public health priority, as it allows for a full assessment of the true burden of disease. Pneumonia and meningitis continue to cause high morbidity and mortality in children aged under 5 years. After the introduction of the vaccine against *Haemophilus influenzae* type b (Hib) in Paraguay in 2002, *S. pneumoniae* (*Spn*) became the principal causal agent isolated. The increase of antibiotic-resistant *Spn* serotypes not covered by the vaccines currently available is a real concern in this age group. A hospital-based sentinel surveillance system was implemented in Paraguay with the following objectives: a) to obtain standardized epidemiological data on bacterial pneumonia and meningitis for children under 5 years, b) to identify and characterize the circulating bacterial agents, and c) to identify patterns of *Spn* antimicrobial susceptibility.

**Methods**

Prospective, cross-sectional multicenter, sentinel surveillance. Starting in epidemiological week (EW) 11/2007 and including data until EW 53/2008. Children under 5 years, with suspected pneumonia or meningitis hospitalized in six hospitals that are part of the surveillance network were included. The isolates obtained from cerebrospinal fluid (CSF), blood, and pleural fluid were characterized at the National Public Health Laboratory (*Laboratorio Central de Salud Pública*).

**Results**

A total of 2,267 suspected cases were hospitalized for pneumonia. Of them, 79% (1,792/2,267) were identified as probable cases by X-ray and 7.5% (135/1,792) were confirmed by bacterial isolation. In the 135 confirmed cases, *Spn* was isolated in 62% (84/135); 81% were sensitive to penicillin, and 19% had intermediate sensitivity to penicillin by minimum inhibitory concentration (MIC). Non-b *Haemophilus influenzae* (non-b Hi) was isolated in 2.9% (4/135), and Hib was isolated in 1.4% (2/135). Of the remaining 45 bacterial pneumonia isolates, 20 were *Staphylococcus aureus* and the other 25 were possible contaminants. Of the total *Spn* isolates, 54.7% (46/84) were characterized. Serotype 14 was the serotype most frequently isolated (56.5%, 26/46), followed by serotypes 1 and 5 (these two serotypes were more common in children aged under 2 years). The other serotypes were sensitive to penicillin. The case fatality rate for confirmed bacterial pneumonia was 21% (28/135).

Regarding meningitis, 290 children were admitted as suspected cases. A total of 54% (156/290) were classified as probable cases on the basis of the characteristics of their CSF, and 30% (47/156) were confirmed through isolation of the causative agent. Of the total isolates, 68% (32/47) were isolates in CSF, 19% (9/47) in blood culture, and 13% (6/47) in both CSF and blood. Most of the cases from which bacteria were isolated from blood culture only did not have a CSF sample. Only two children with symptoms had CSFs that were not characteristic of bacterial meningitis. Of the confirmed cases, 49% (23/47) had *Spn*, 19% (9/47) had *Neisseria meningitidis*, and 15% (7/47) had Hib. Of the other 8 cases, one neonate had *Streptococcus* group B, one had Bacillus ssp, one *Streptococcus viridans*, two Gram negative bacillus, and three were considered contamination. Of the *Spn* isolates, 69.5% (16/23) were characterized. The serotype most commonly isolated was 14 with 38% (6/16) followed by serotypes 7F, 19F, 12F, and 1. Of all *Spn* isolates characterized, 69% (11/16) were sensitive to penicillin, and 31.25% were resistant to penicillin (all non-sensitive strains were serotype 14). *Neisseria meningitidis* serogroup B was isolated most frequently followed by W135. The case fatality rate for confirmed bacterial meningitis was 43% (20/47).

**Conclusions**

Hospitalization for pneumonia and meningitis in children under 5 years is common. *Spn* was isolated frequently, and it was usually sensitive to penicillin. However, serotype 14 was associated with decreased sensitivity. Serotypes commonly isolated were 14, 5, and 1; the latter two were more common in children under 2 years. For pneumonia, Hib isolation was low, and less than non-b Hi. The case fatality rate was higher in meningitis cases.
Adverse Events Associated with New Rotavirus Vaccines: Passive Surveillance Network in Latin America
Peña Ruz J¹, de Oliveira LH², SANEVA Network

Introduction
Until several years ago, the only registered rotavirus vaccine was the tetravalent human-resus reassortant (G1-4) rotavirus vaccine (RRV-TV), marketed as RotaShield® by Wyeth-Lederle. Less than a year after it was licensed, the vaccine was withdrawn from the market. Retrospective studies confirmed a causal relationship between intussusception and vaccination with RotaShield®. In view of the causal relationship established, intussusception has become an important safety parameter in the evaluation of the rotavirus vaccines recently developed.

Aware that the introduction and use of new vaccines in our Region pose a major and historically unprecedented challenge, a network of sentinel countries (SANEVA) was created in March 2006 to monitor adverse events associated with new vaccines. Coordinated by the Pan American Health Organization (PAHO), its participants consist of representatives from national regulatory authorities and the Expanded Programs on Immunization of Argentina, Brazil, Mexico, Panama, and Venezuela. The findings from surveillance of the use of the rotavirus vaccine Rotarix® are presented here.

Methods
A database was created for events supposedly attributable to vaccination or immunization (ESAVIs) reported to the participating institutions as required by the systems in each country in the network. The information was sent bimonthly to the coordinator (PAHO), who performed a general consolidation of the data that was validated by the members of the network. The Brighton Collaboration case definition for intussusception was used.

Results
As of October 2008, 13,000,000 doses had been administered and 891 reports of ESAVIs associated with the Rotarix® vaccine had been received, among them 169 cases of intussusception, 52 cases of programmatic error (intramuscular and subcutaneous administration), and 363 systemic events (diarrhea, vomiting, and fever) (Table). Data from the SANEVA Network show a much lower incidence of intussusception than expected: 0.13 vs. 4–5 x 10,000 children under 1 year, revealing a correlation with age. A total of 58 programmatic errors regarding intramuscular administration have been reported, 90% of them in the private sector. To date, this error in the mode of administration has not resulted in complications.

Conclusions
The surveillance system in Latin America is passive that is, the data fed into the system come from spontaneous reporting by health professionals. This implies that the systems in the majority of the countries are not very sensitive, since there is under-reporting of ESAVIs. In the particular case of rotavirus vaccines, the experience shows that another type of early detection system for ESAVIs, such as an active surveillance system, is needed. When introducing new vaccines, epidemiological studies, such as case or case-control studies, are important. This would provide us with timely, evidence-based information on the safety of the new vaccines.

It is important to point out that the data from the SANEVA Network indicate a far lower incidence of intussusception in children under 1 year than expected. Retrospective and prospective studies of prevalence rates of intussusception conducted in Latin American countries in children under 1 year showed rates of 47 x 100,000 children in Venezuela and 51 x 100,000 children in Chile. There is a higher percentage of intussusception in males, a finding that coincides with the baseline data from epidemiological intussusception studies. Regardless of the dose, the highest number of intussusception reported through the SANEVA Network corresponds to children aged 4 to 6 months, which is correlated by data from O’Ryan et al mentioned earlier.

The clearest and most troubling aspect has been intramuscular administration, which is not an adverse event related to the quality and safety of the vaccine, but a programmatic error linked to incorrect vaccine use. To date, this has not led to complications in the subjects involved. Almost 90% of these reports originated in private distribution channels. This situation needs to be studied in depth and corrected immediately.

From the ESAVIs reported and analyzed by the SANEVA Network, we can conclude that no signs suggesting a safety problem with the Rotarix® vaccine have been detected. The events reported most often were within expectations, based on the data from the clinical trials conducted pre-licensure.

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² Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
## Intussusception with Rotarix® Vaccine

<table>
<thead>
<tr>
<th>Country</th>
<th>Start of Vaccination</th>
<th>Doses Administered</th>
<th>Coverage</th>
<th>Number of Intussusception related to vaccination</th>
<th>Incidence/10,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argentina</td>
<td>…</td>
<td>Doses administered 266,150</td>
<td>Private Sector</td>
<td>18</td>
<td>0.68</td>
</tr>
<tr>
<td>Brazil</td>
<td>March 2006</td>
<td>1st dose: 6,294,680</td>
<td>2008</td>
<td>46</td>
<td>0.051</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2nd dose: 4,888,185</td>
<td>1st dose: 89.9%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total: 11,182,865</td>
<td>2nd dose: 76.4%</td>
<td></td>
<td></td>
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<tr>
<td>Mexico</td>
<td>March 2006</td>
<td>1st dose: 904,478</td>
<td>2008</td>
<td>46</td>
<td>0.28</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2nd dose: 744,523</td>
<td>1st dose: 79.3%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total: 1,649,001</td>
<td>2nd dose: 61.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Panama</td>
<td>March 2006</td>
<td>1st dose: 104,143</td>
<td>2007</td>
<td>42</td>
<td>2.37</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2nd dose: 72,455</td>
<td>1st dose: 85.4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total: 176,598</td>
<td>2nd dose: 58.9%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

…: not available

Source: PAHO/SANEVA/JPR.

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**References:**


Introduction

Rotavirus is responsible for nearly 600,000 deaths in children under 5 years, 2 million hospital admissions, and 130 million diarrhea cases worldwide, with 80% of the deaths occurring in developing countries. The live-birth cohort in Ecuador is approximately 290,000 per year. Acute diarrheal disease is the second leading cause of morbidity and mortality in the population under 5 years; 1 out of every 3 children under 5 years has one episode of rotaviral diarrhea every year. Vaccination would result in a 70% reduction in the total direct medical costs attributable to rotavirus.

Methods

The vaccine of choice was Rotarix®: protection is obtained with two doses (at 2 and 4 months of age); it produces immunity at an earlier age, has a high percentage of cross-immunity with other serotypes, and is prequalified by the World Health Organization. It should not be administered after the age of 6 months.

A plan was developed and a multidisciplinary committee formed. Cold chain capabilities were assessed to plan the investment. Brazil and Panama shared their lessons learned and the National Commission of the Expanded Program on Immunization studied the decision. A vaccination protocol, training video, and brochure of frequently asked questions were put together, and an individual practice workshop was held on how to prepare the vaccine. The daily record form was modified and the Children's Vaccination Card File system was set up in each health unit. The sentinel surveillance system for severe diarrheal diseases was designed. In the three initial months of vaccine introduction, all infants under 6 months of age were to receive at least one dose.

Results

During the three-month introductory period (October 2007), 103,751 first doses were administered (71.56% of those who could receive at least one dose), and 24,608 second doses were administered (51%), with at least a one-month interval. In 2008, coverage with two doses was 82% nationally, with a range of 52 to 99% in the 24 provinces. The percentage of health areas is less than 80% (Table).

<table>
<thead>
<tr>
<th>Percentage of Health Areas by Range of Coverage, Ecuador, 2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of health areas</td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>12</td>
</tr>
</tbody>
</table>

The ROTA1-ROTA2 dropout rate is 19%, with a range of 7 to 36% between provinces. The indicator of consistency between PENTA2 and ROTA2 is 80% at the national level, with a range of 55 to 92% between provinces. Passive surveillance has not reported serious events supposedly attributable to vaccination or immunization (ESAVIs) or errors in administration. Epidemiological surveillance has just been starting since late 2008.

Conclusions

Vaccinating at the recommended age so as not to miss the opportunity has meant a change for health workers and the population. Little use is made of the card file to follow up with the second dose before children are 6 months old. Coverage in the health areas and provinces is not uniform. Ongoing supervision and evaluation need to be strengthened. It is essential to improve ESAVI surveillance and hospitalized cases of severe diarrheal disease to assess vaccine impact and identify circulating serotypes. The population should receive greater education about vaccinating at the recommended age.

Bibliography:


1 Expanded Program on Immunization (EPI), Ministry of Health, Ecuador.
2 Comprehensive Family Immunization (FCH), Pan American Health Organization, Ecuador.
Efficacy Study of the Pentavalent Rotavirus Vaccine, Nicaragua, 2007-2008
Patel M1, Pedreira C2, de Oliveira LH2, Tate J1, Orozco M3, Mercado J4, Gonzalez A4, Malespin O5, Amador JJ5, Umana J4, Balmaseda A4, Perez MC4, Gentsch J1, Kerin T1, Andrus JK3, Parashar U1

Introduction
In October 2006, the Ministry of Health of Nicaragua added the pentavalent rotavirus vaccine (VR5) to its regular program following negotiations between the manufacturer (Merck) and the Government of Nicaragua that yielded an agreement by Merck to provide the vaccine free-of-charge for a three-year period. Although clinical trials of the vaccine have demonstrated excellent efficacy and safety levels, there is a lack of detailed data on the results of studies in developing countries and no published data on vaccine efficacy when administered at the same time as the oral polio vaccine (OPV). In this context, Nicaragua’s Ministry of Health decided to conduct a study to determine the efficacy of the rotavirus vaccine in the country’s routine immunization program. The study has two secondary objectives: 1) to determine the efficacy of incomplete vaccination schedules and vaccine efficacy against specific rotavirus strains, and 2) to identify potential risk factors for unsatisfactory vaccine efficacy, for example the concomitant administration of OPV, low socioeconomic level, or a breast milk diet.

Methods
Case-control study at four hospitals in the country. The cases are children at an eligible age for the vaccination, treated for laboratory-confirmed rotavirus diarrhea. These were paired by age with two control groups: 1) children living in the same neighborhood as the case and 2) hospitalized children or children brought in for a consultation at the same hospital as the case for a pathology other than diarrhea or a vaccine-preventable disease.

Results
From 14 May 2007 to 30 June 2008, 285 cases of rotavirus diarrhea were identified, or 18% of the total diarrhea cases captured. Of these, 93% were admitted to the hospitals in the study and 88% required intravenous rehydration. In 85% of the cases, virus of the G2P[4] strain was isolated. Analysis with the two control groups combined yielded an efficacy of 45% (IC95%=14-65) with three complete doses of VR5 for cases of any severity, which is similar to the efficacy found when cases and control groups were compared separately; efficacy of 60% (IC95%=32-76) for serious cases, and 78% (IC95%=39-92%) for very serious cases. Compared to the neighborhood and hospital controls, the cases had a higher probability of being cared for at a day-care center and their mothers a lower probability of having a higher level of formal education. These variables did not alter the efficacy estimates when they were included in the final model. Since all the children received VR5 concomitantly with OPV, the efficacy with and without the administration OPV could not be assessed.

Conclusions
VR5 in Nicaragua was less efficacious than in industrialized countries. However, the protection against very serious diarrhea was high, attaining reasonable levels. Continuing the study in Nicaragua, combined with the results of studies in Asia and Africa, will facilitate a more thorough evaluation of the level and duration of the protection offered by VR5 in different scenarios and with different vaccine strains.

1 Centers for Disease Control and Prevention, Atlanta, USA.
2 Comprehensive Family Immunization (FCH), Pan American Health Organization, Nicaragua.
3 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
4 Ministry of Health, Managua, Nicaragua.
5 Program for Appropriate Technology in Health, Managua, Nicaragua.
Introduction
Diarrhea is among the most common causes of death among children <5 years in developing countries worldwide and rotavirus is the most frequent causative agent in this age group, accounting for approximately one-third to one-half of all hospital admissions and more than 500,000 childhood deaths each year. In this abstract we review data from the global rotavirus surveillance networks to describe the prevalence of severe rotavirus disease in various World Health Organization’s (WHO) Regions of the world.

Methods
In each of the WHO Regions, active, hospital-based surveillance for rotavirus disease among children <5 years who are admitted to the hospital overnight for intravenous hydration was initiated in various countries using a generic WHO protocol.

Results
A total of 62,584 (range: 3,374–26,065 per WHO Region) hospitalized patients aged <5 years with acute diarrhea were tested for rotavirus during the study period at all sites combined. The overall median detection rate of rotavirus among all countries was 40%. The median rotavirus detection rate was lowest in the Region of the Americas (34%) and highest in the South-East Asian and the Western Pacific Regions (45%). The most common strains in all Regions, except the Eastern Mediterranean and African Regions, were G1P[8], G9P[8], and G2P[4], accounting for approximately two thirds of strains in these Regions. In the Eastern Mediterranean and African Regions, specimens characterized in the category “other” accounted for 50% and 46% of strains, respectively; this category included specimens in which either the G or P type (or both) of the infecting strain could not be characterized.

Conclusion
Data generated from global rotavirus surveillance networks highlight the burden of rotavirus hospitalizations, including those in low-income countries that are eligible for financial support for vaccine purchase through the GAVI Alliance. These surveillance networks will be useful platforms for assessing vaccine performance and detecting possible changes in epidemiology of rotavirus disease and strain patterns post vaccine introduction.

Bibliography:

Centers for Disease Control and Prevention, Atlanta, USA.
Long-term Effect of 7-valent Pneumococcal Conjugate Vaccine Use on Invasive Pneumococcal Disease in the United States

Verani JR1, Whitney CG1, Pilishvili T2, Farley MM2, Schaffner W2, Thomas A2, Reingold A3, Harrison LH4, Lynfield R5, Bennett NM6, Hadler JL7, Beall B1, Moore MR1

Introduction
In the United States, and globally, pneumococcal disease—including otitis media, pneumonia, sepsis, and meningitis—is a major cause of illness and death in children. Until recently few tools were available to prevent these infections. In 2000, a new conjugate vaccine covering 7 of 90 pneumococcal serotypes was licensed for use in young children in the United States. The vaccine was recommended for all children aged <2 years (2-4-6 months and 12 to 15 months) and for high-risk children aged 2-4 years. The 7 vaccine serotypes caused 80% of severe infections in children in the United States at the time the vaccine was licensed. Although vaccine shortages slowed uptake between 2001 and 2004, by early 2007 88.9% of children aged 19-35 months had received at least 3 of the 4 recommended doses, according to the National Immunization Survey of the Centers for Disease Control and Prevention. We assessed the impact of 6 years of continuous 7-valent pneumococcal conjugate vaccine (PCV7) use in children on invasive pneumococcal disease incidence among children and adults.

Methods
We identified cases of laboratory-confirmed invasive pneumococcal disease through eight sites in the United States continuously participating in Active Bacterial Core surveillance from 1998 through 2006. We calculated changes in age- and serotype-group specific invasive pneumococcal disease incidence rates in 2006 compared to 1998-1999 (before introduction) and estimated the number of cases prevented in the United States.

Results
From 1998-1999 to 2006, invasive pneumococcal disease incidence declined from 24.4 per 100,000 in 1998-1999 to 13.5 per 100,000 in 2006 (-45%, 95%CI -47 to -42%). Invasive pneumococcal disease rates caused by vaccine serotypes declined from 15.5 to 1.3 per 100,000 and were significantly lower (88%-100%) in 2006 for all age groups. Invasive pneumococcal disease rates caused by serotype 19A and other non-PCV7 serotypes increased from 0.8 to 2.7 per 100,000 and from 6.1 to 7.7 per 100,000, respectively, with significant increases observed among all age groups. During 2001-2006, an estimated 11,000 to 15,000 fewer cases of invasive pneumococcal disease occurred annually among children <5 years and 9,000 to 18,000 fewer cases occurred annually among persons ≥5 years in the United States. Overall, >170,000 invasive pneumococcal disease cases and 10,000 deaths were prevented since PCV7 introduction.

Conclusions
The data from the United States, one of the first countries to introduce pneumococcal conjugate vaccine, indicate that the vaccine is providing major benefits for reducing morbidity and mortality due to pneumococcal disease. The burden of pneumococcal disease has decreased among all age groups, and the marked public health benefits of PCV7 use in the United States remain evident six years after introduction. Increases in non-vaccine serotype invasive pneumococcal disease have been noted, yet remain modest small relative to overall vaccine benefits.

1 Centers for Disease Control and Prevention, Atlanta, USA.
2 Emory University School of Medicine, Atlanta, USA.
3 Vanderbilt University, Nashville, USA.
4 Oregon Department of Health, Portland, USA.
5 University of California Berkeley, USA.
6 University of Pittsburgh School of Medicine, Pittsburgh, USA.
7 Minnesota Department of Health, St. Paul, USA.
8 University of Rochester, Rochester (NY), USA.
9 Connecticut Department of Health, Hartford, USA.
Introduction

Human papillomavirus (HPV) infection is a major cause of morbidity and mortality in Latin America and the Caribbean. However, there is no consolidated data on the incidence and prevalence of HPV infection or the frequency of the infection in neoplastic and preneoplastic lesions in different geographic locations. Also, there are no recent consolidated data on the disease burden potentially generated by the virus. The purpose of the study was to estimate the disease burden generated by HPV and of the diseases associated with the infection by the virus, provide estimates of the health and economic benefits of HPV vaccination and screening in selected countries of Latin America, and evaluate the quality of the studies conducted in these countries.

Methods

We conducted an exhaustive and systematic review of the scientific literature published since 1990, focusing on the studies that measure the prevalence of HPV infection and HPV-related disease in women and in men. The databases used for the literature review were PubMed, LILACS, SciELO, CAB, EMBASE, ICNAHL, and Cochrane. We defined inclusion and exclusion criteria. We calculated the general prevalence in different populations, by age groups, and by specific genotypes of the virus. In order to calculate the incidence of cervical HPV infection, we used data provided by two of the three prospective cohort studies conducted in Latin America. The incidence was calculated as incidence density whose denominator was person-time of follow-up. We calculated the incidence rates by age, by specific genotypes, using a modern taxonomic classification based on the recent epidemiological and phylogenetic data of the scientific literature (Sabin Team). The disease burden was calculated using the International Agency for Research on Cancer’s (IARC) statistics of cancer cases related to HPV in the region. The proportion of cervical cancer attributable to HPV was assumed to be 100%, while for oropharyngeal cancer we calculated the attributable risk based on the case control studies. We performed a descriptive analysis that summarizes the findings of all the studies identified by subgroups (e.g., women with normal cytology, by age groups). We calculated the general prevalence through fixed effect and estimated the prevalence by age groups through mixed models.

Results

In 43 studies among women with normal cytology, the determined global prevalence of HPV by PCR was 18.7% (95% CI 15.4-22.0%). For women with ASCUS this prevalence was 56.1% (95% CI 39.7%-72.4%), for LSIL, 79.0% (95% CI 71.9%-86.1%), for HSIL, 96.8% (95% CI 93.5%-100%), and for invasive cervical cancer, 94% (95% CI 89.4%-98.5%). Seven studies were conducted among healthy men. For them, the prevalence of HPV was 21.7% (95% CI 1.7%-41.6). The frequency of HPV-16 was 2.6% (95% CI 1.8-3.2) for women with normal cytology and 49.3% (95% CI 45.5%-53.1%) for cases with invasive cervical cancer. The prevalence of HPV-18 was 1.0 (95% CI 0.6-1.3) and 10% (95% CI 7.6%-12.5%) in the same groups. The incidence of HPV in the prospective cohorts was 8% per year. The highest incidence was for women under 25.

In Latin America and the Caribbean 83,000 cancer cases attributable to HPV occur annually. The most frequent are cervical, 78,000 cases (94%) and oropharyngeal cancer, 12,740 cases (1.5%). The vast majority of cervical cancer cases occur in Argentina, Brazil, Colombia, Mexico, and Peru, where 49,000 new cases are estimated per year (62.8%).

Conclusions

Through this meta-analysis, we calculated the prevalence, the incidence, and the disease burden attributable to the infection by HPV. Cervical cancer represents more than 90% of the disease burden attributable to HPV, generating around 40,000 annual deaths and 100,000 years of life lost in the region. The introduction of a vaccine that prevents the infection by virus 16 and 18 could diminish the disease burden by 40 to 50% depending on the coverage of vaccination and the effectiveness of complementary measures such as strengthened screening.
Update on Human Papillomavirus Vaccines

Markowitz L1, Andrus JK2

Introduction
Two prophylactic human papillomavirus (HPV) vaccines have been developed, a quadrivalent vaccine directed against HPV 6, 11, 16 and 18, and a bivalent vaccine against HPV 16 and 18. There are challenges to implementation of HPV vaccination programs in both developed and developing countries.

Methods
Data from HPV vaccine trials were reviewed as well as information on programs and post-licensure monitoring in countries that have implemented HPV vaccination.

Results
Both the bivalent and quadrivalent HPV vaccines have high efficacy in females for prevention of HPV 16/18-related cervical precancers; the quadrivalent vaccine also has high efficacy against HPV 6/11-related genital warts. Available data through 5-6 years post-vaccination show excellent duration of protection. New data available for the quadrivalent HPV vaccine demonstrate high efficacy against genital warts in males. The quadrivalent and bivalent HPV vaccines have now been licensed in over 90 countries worldwide; however, far fewer have initiated public sector vaccination programs. Most countries recommend routine vaccination of girls in early adolescence and many also recommend catch-up vaccination. The quadrivalent vaccine is the only vaccine currently licensed in the United States; over 22 millions doses were distributed through the end of 2008. The bivalent vaccine is being used for vaccination programs in the United Kingdom and other countries in Europe. Some countries with school-based vaccination programs, such as Australia and the United Kingdom, have achieved high vaccine coverage in the first year of their program. Post-licensure monitoring of vaccine safety is ongoing. The high cost of HPV vaccine has been an impediment to introduction in developing countries. Demonstration projects conducted by PATH are ongoing in 4 countries of the world, including Peru.

Conclusions
New data continue to become available from HPV vaccine trials; these need to be considered for policy decisions. Developed countries are in early stages of their HPV vaccine programs; efforts are ongoing to obtain resources for vaccine introduction into low resource countries where the burden of cervical cancer is the greatest.

1 Centers for Disease Control and Prevention, Atlanta, USA.
2 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
HPV Vaccine and Cervical Cancer Prevention: Integrating Strategies
Andrus JK1, Luciani S2, Jauregui B3

Introduction
Cervical cancer caused by human papillomavirus (HPV) is a major preventable public health problem among women. The World Health Organization (WHO) and the International Agency for Research in Cancer (IARC) estimate that cervical cancer kills more than 273,000 women per year. Greater than 80% of those deaths occur in women living in developing countries. Significant disparities in the age-adjusted mortality rates for cervical cancer exist between the sub-regions of the Americas with estimates of 16.0, 15.0, and 12.9 cervical cancer deaths per 100,000 population for the Caribbean, Central America, and South America, respectively. These rates are also substantially higher than 2.3 cervical cancer deaths per 100,000 population in North America.

Methods
Documents from meeting reports, recent scientific publications, technical and policy statements were reviewed from global, regional, and national sources, including the PAHO Regional Strategy for Cervical Cancer Prevention and Control in Latin America and the Caribbean (LAC).

Results
Despite the availability of cervical cancer screening, countries in LAC have not experienced the same declines in mortality rates as have been observed in North America. Opportunities exist for improving the effectiveness of current programs through rapid scale up of new cervical cancer prevention strategies, including 2 recently developed safe and efficacious vaccines, and new technologies and alternative approaches for screening and pre-cancer treatment. To that end, the PAHO Regional Strategy for an integrated, accelerated collaborative work will be presented. The Regional Strategy, endorsed by Ministers of Health of the Americas calls for increased action to strengthen programs, through an integrated package of services including the provision of health information, screening, diagnosis, treatment, and the use of evidence-based policy decisions on whether and how to introduce HPV vaccines.

Conclusions
The public health importance of this disease cries for urgent acceleration of comprehensive, integrated disease prevention strategies. Cervical cancer is a disease that is highly preventable through the application of available cost-effective tools. If efforts are coordinated well, such work has the potential to make a tremendous impact on the health of women, particularly women living in impoverished communities.

1 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
2 Chronic Disease Prevention and Control (HSD), Pan American Health Organization, Washington, D.C., USA.
PAHO’s ProVac Initiative: Enhancing Evidence-based Capacity to Make Informed Policy Decisions on the Introduction of New Vaccines in the Americas

Andrus JK1, Jauregui B1, Ruiz Matus C1

The Pan American Health Organization (PAHO) estimates annual mortality in Latin America and the Caribbean due to rotavirus-induced diarrhea to be 16,000; another 22,000 children die each year from invasive pneumococcal disease; and 32,000 women die prematurely each year from cervical cancer caused by human papillomavirus (HPV). Vaccines against these priority diseases present opportunities to make substantial gains in health, contributing to the achievement of the Millennium Development Goals. The relative value of these vaccines depends on the burden of disease, vaccine cost, and the available resources for introducing the vaccines into national immunization programs. As burden of disease and resources available vary between countries and subregions, the decision to introduce these relatively more expensive, new vaccines requires that policy decisions are grounded in a greater body of evidence that reflects national conditions.

In response to the need for support for evidence-based vaccine introduction decisions, PAHO and partners—including the Gates Foundation, various academic centers, the Accelerated Development and Introduction Plans (ADIPs), the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO)—collaborated to conduct technical workshops with national immunization program managers in 2004 and 2006. These workshops provided an introduction and training on conducting economic evaluations of new vaccines. As a part of this work, PAHO and leading researchers from Emory University, London School of Hygiene and Tropical Medicine, University of Medicine and Dentistry of New Jersey, the ADIPs, and CDC developed models for evaluating the priority new vaccines. A model for HPV vaccine is under development with Harvard University.

GAVI-eligible countries benefited from ProVac with successful applications for New Vaccine Support; all countries that applied were approved.

Over the next 5 years, PAHO has been awarded $5.3 million by the Bill and Melinda Gates Foundation to continue this work. The objectives of the initiative are now clearly defined and include:

- Strengthening policy infrastructure and process,
- Developing and improving upon tools for economic analysis,
- Strategizing sub-Regional impact,
- Collecting data and conducting analyses,
- Making evidence-based decisions,
- Effectively planning for vaccine introduction when appropriate, and
- Promoting partnerships.(a)

ProVac coordinated partnerships will align available national and international expertise to provide technical cooperation to Ministries of Health. Expertise mobilized, in harmony with other existing partnerships, will support countries in conducting the comprehensive economic evaluations of new vaccines, developing advocacy cases for policy, and strengthening expert technical advisory bodies.

Recognizing that it is impractical to pursue economic evaluations of priority vaccines in every country, ProVac is pursuing a subregional approach to generate and share evidence amongst neighboring countries. Support provided to ProVac will be strategically used to benefit all low and middle income countries, leading to a Region-wide impact in countries most likely to be the first introducers. PAHO increases the value of investing in the ProVac Initiative by sharing the experience, evidence, tools, and the valuable expertise of partners and the Key Center networks with low-income countries. Work is focused on meeting the mandate to support evidence-based decisions on new vaccines expressed by the Ministers of Health of the Region in the 2006 PAHO Directing Council Resolution (CD47.R10) This presentation will also describe the project implementation plan and the activities to be rolled out in the next few years.

Reference:

1 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
Cost-effectiveness Analysis of the Rotavirus Vaccine in Bolivia

Iñiguez V1, Ethiene K2, Rowlinson E3, Rivera R4, Kelly F5, Mamani N6, Leon J7, Halkyer P8, Flores J9

Introduction

The impact of acute diarrheal disease associated with rotavirus on children under 5 years and the projected introduction of available vaccines against this virus have led to the need to conduct a study in Bolivia at the beginning of 2008 to assess the potential cost-effectiveness of the rotavirus vaccine in children under 5 years.

Methods

The benefits and cost-effectiveness ratio of the Rotarix® vaccine in Bolivia were analyzed from the perspective of the health system, using data on the incidence of the disease, direct medical costs, and vaccine coverage and efficacy rates. The data were obtained over a one-year period from six sentinel hospitals in four Bolivian cities—Hospital Boliviano Holandés, El Alto; Hospital Materno Infantil, La Paz; Hospital del Niño, La Paz; Hospital Albino Patiño, Cochabamba; Hospital Manuel Ascencio Villarroel, Cochabamba; and Hospital Mario Ortiz Suarez, Santa Cruz—and extrapolated to the national level based on the 2006 birth cohort. A discount rate of 3% was used. Program costs and benefits were updated for 2008.

Results

A rotavirus immunization program would prevent 419 deaths, 7,439 hospitalizations, and 30,445 outpatient consultations in the first year of life. Direct medical costs without a vaccination program total US $1,775,231.60 per year. Vaccination would cut health expenditure to US $425,848.47, representing an avoided cost of US $1,349,383.10. Universal vaccination at a cost of US $19 would result in a cost-effectiveness ratio of US $213 per DALY (disability-adjusted life year), making the intervention highly cost-effective since it is 14 times smaller than the national gross domestic product (GDP) per capita. The effect of changes on 20% of the following variables was considered: rotavirus incidence and mortality, vaccine efficacy in rotavirus-associated mortality and morbidity, costs of treatment of acute diarrheic disease by rotavirus, and estimated price of the vaccine. Cost-effectiveness results were sensitive to the following variables: rotavirus mortality, vaccine efficacy to prevent rotavirus mortality, and vaccine price. The increase in mortality and vaccine efficacy to prevent deaths showed a lower incremental cost-effectiveness ratio.

Conclusions

Rotavirus vaccination is a highly cost-effective intervention that will reduce the burden of disease, and result in cost savings in health expenditure from rotavirus diarrhea in Bolivia.

1 Molecular Biology and Biotechnology Institute, Universidad Mayor de San Andrés, La Paz, Bolivia.
2 Hubert Department of Global Health, Emory University, Atlanta, USA.
3 Comprehensive Family Immunization (FCH), Pan American Health Organization, Bolivia.
4 Expanded Program on Immunization, Ministry of Health and Sports, Bolivia.
Economic Impact of Pneumococcal Disease and Cost-Effectiveness of Pneumococcal Conjugate Vaccination in Ecuador in 2008
Vasconez N1, Constenla D2, Jauregui B2, Andrus JK2

Introduction

*Streptococcus pneumoniae* (*S. pneumoniae*) is an important cause of morbidity, mortality, and healthcare system costs in Ecuador. The purpose of this analysis is to estimate the economic burden of *S. pneumoniae* and the cost-effectiveness of pneumococcal heptavalent vaccine (PCV7) introduction in Ecuador. Local experts were trained in data collection in Quito and Guayaquil. This training, coordinated by the Ministry of Health and PAHO’s ProVac Initiative has helped to strengthen national capacity and help local experts perform and coordinate economic evaluations of new vaccine introduction in their own countries.

Methods

We gathered available data to estimate the cost-effectiveness of pneumococcal vaccine introduction in Ecuador. Estimates from the World Health Organization (WHO) Global Disease Burden project were used for pneumococcal disease incidence and mortality estimates. To derive assumptions about the resource utilization and costs required for treating children aged under five years with pneumococcal disease, we administered surveys to physicians and administrators of various public and private hospitals. The health service utilization information derived from these surveys was combined with data from Demographic and Health Surveys to estimate the distribution of visits and hospitalizations across the different types of providers. Similarly, health service cost data obtained from finance departments of various hospitals were combined with WHO-CHOICE (CHOosing Interventions that are Cost-Effective) data to estimate the daily cost of hospitals and outpatient visits.

To conduct the cost-effectiveness analysis we used a ProVac integrated model developed in Microsoft Excel, in which we captured the costs and effects of vaccination on pneumococcal pneumonia, pneumococcal meningitis, and other forms of pneumococcal invasive non-pneumonia, non-meningitis (NPNM) disease in 20 cohorts of children aged under five years. The perspective for the current analysis is societal. All future costs and DALY (Disability-adjusted Life Years) estimates were discounted at a rate of 3%. Sensitivity analyses evaluated the impact of uncertainty on estimates.

Results

In Ecuador, pneumococcal disease resulted in 21,606 annual pneumococcal cases in children aged under five years (Table 1). In terms of the economic burden, the health care cost of pneumococcal disease born by society during a typical year was US $764,854. Vaccination would prevent 56% (US $428,318 per year) of those health care costs. If vaccine price was the current PAHO Revolving Fund price of US $26.35 per dose and vaccine coverage is the same as the diphtheria-tetanus-pertussis (DTP) vaccine in Ecuador, then vaccine-related costs would amount to US $420.3 million annually. The cost-effectiveness ratio combining results from 20 birth cohorts was US $2,640 per DALY averted (Table 2). At lower cost of US $13 and US $7 per dose, these annual costs would be much lower with the cost per DALY dropping to US $1,280 and US $668, respectively. Incremental cost-effectiveness ratios were sensitive to changes in vaccine price, discount rates, disease incidence, case fatality ratios, and vaccine efficacy.

<table>
<thead>
<tr>
<th>Pneumococcal disease in children aged &lt;5 years in Ecuador</th>
<th>During a typical year</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cases</td>
<td>21,606</td>
<td>9,529</td>
</tr>
<tr>
<td>Pneumococcal pneumonia (severe)</td>
<td>20,141</td>
<td>8,883</td>
</tr>
<tr>
<td>Pneumococcal meningitis</td>
<td>168</td>
<td>74</td>
</tr>
<tr>
<td>Pneumococcal invasive NPNM</td>
<td>1,297</td>
<td>572</td>
</tr>
<tr>
<td>Total deaths</td>
<td>513</td>
<td>226</td>
</tr>
<tr>
<td>Pneumococcal pneumonia (severe)</td>
<td>216</td>
<td>95</td>
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<tr>
<td>Pneumococcal meningitis</td>
<td>56</td>
<td>25</td>
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<tr>
<td>Pneumococcal invasive NPNM</td>
<td>241</td>
<td>106</td>
</tr>
<tr>
<td>Total children with sequelae</td>
<td>45</td>
<td>20</td>
</tr>
<tr>
<td>Minor sequelae</td>
<td>34</td>
<td>15</td>
</tr>
<tr>
<td>Major sequelae</td>
<td>11</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 1. Benefits of Pneumococcal Conjugate Vaccination

* Benefit of vaccination is based on the vaccine effectiveness, which incorporates information on the vaccine efficacy and coverage.

1 Expanded Program on Immunization, Ministry of Health, Ecuador.
2 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
Prioritizing Vulnerable Populations

Table 2. Projected Cost-effectiveness of Pneumococcal Conjugate Vaccination in Ecuador (US$, 2007)*

<table>
<thead>
<tr>
<th></th>
<th>US $</th>
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<tbody>
<tr>
<td>Cost per DALY averted</td>
<td>2,640</td>
</tr>
<tr>
<td>Cost per life year gained</td>
<td>2,716</td>
</tr>
<tr>
<td>Cost per case averted</td>
<td>1,971</td>
</tr>
<tr>
<td>Cost per hospitalization averted</td>
<td>23,197</td>
</tr>
<tr>
<td>Cost per death averted</td>
<td>93,289</td>
</tr>
<tr>
<td>Incremental vaccination cost per year</td>
<td>420,333,636</td>
</tr>
<tr>
<td>Health service cost savings per year</td>
<td>428,318</td>
</tr>
</tbody>
</table>

* This projected cost-effectiveness estimate is based on a vaccine price of US$26.35 per dose.

Conclusions

The pneumococcal conjugate vaccine appears to be very cost-effective in Ecuador. The cost-effectiveness ratio of US $2,640 per DALY averted estimated by this study was less than one time Ecuador’s GDP per capita in 2006. Vaccination appears to be very cost-effective according to this WHO criterion. However, it may not be affordable. The economic evaluation should be considered in the context of affordability and financial sustainability.
Introduction

The purpose of this analysis is to estimate the economic burden of Streptococcus pneumoniae (S. pneumoniae) and the cost-effectiveness of pneumococcal heptavalent vaccine (PCV7) introduction in Honduras. As part of PAHO’s ProVac Initiative and in collaboration with the Ministry of Health, local experts were trained in data collection to perform a cost-effectiveness analysis. This training has helped strengthened national capacity to assist local experts in conducting and coordinating economic evaluations of new vaccine introduction in their own countries.

Methods

We gathered available data to estimate the cost-effectiveness of pneumococcal vaccine introduction in Honduras. Data from the World Health Organization (WHO) Global Disease Burden project were used to estimate pneumococcal disease incidence and mortality. To determine pneumococcal disease management, we conducted physician surveys and surveys in the finance departments of various public and private hospitals. The health service utilization information derived from these surveys was combined with data from the Honduras Demographic and Health Surveys to estimate the percentage of cases taken to each type of health facility. Similarly, health service cost data obtained from finance departments of various hospitals were combined with WHO-CHOICE (CHOosing Interventions that are Cost-Effective) data to estimate the daily cost of hospitals and outpatient visits.

To conduct the cost-effectiveness projections we used a ProVac integrated model developed in Microsoft Excel, in which the effects of vaccination on pneumococcal pneumonia, pneumococcal meningitis, and other forms of pneumococcal invasive non-pneumonia, non-meningitis (NPNM) disease in children aged under five years were captured with a societal perspective. All future costs and DALY (Disability-adjusted Life Years) estimates were discounted at a rate of 3%. We performed sensitivity analyses to evaluate the impact of uncertainty on estimates.

Results

Pneumococcal disease resulted in 16,598 annual pneumococcal cases in children aged under five years in Honduras (Table 1). In terms of the economic burden, the health care cost of pneumococcal disease born by society during a typical year was US $865,919. By applying the mean percentage disease averted (57%) to the disease costs, we estimated that the healthcare cost savings due to vaccination would amount to US $493,573 per year.

If vaccine cost was the current PAHO Revolving Fund price of US $26.35 per dose and vaccine coverage for all children in Honduras is the same as the diphtheria-tetanus-pertussis (DTP) vaccine, then vaccine-related costs would amount to US $321.8 million annually. The cost-effectiveness ratio was US $1,560 per DALY averted and US $54,067 per death averted from a societal perspective (Table 2). At lower costs of US $13 and US $7 per dose, these annual costs would be lower with the cost per DALY dropping to US $772 and US $418, respectively. Incremental cost-effectiveness ratios were sensitive to changes in vaccine price, discount rates, disease incidence, case fatality ratios, and vaccine efficacy.

<table>
<thead>
<tr>
<th>Pneumococcal disease in children aged &lt;5 years in Honduras</th>
<th>During a typical year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No vaccine</td>
</tr>
<tr>
<td>Total cases</td>
<td>16,598</td>
</tr>
<tr>
<td>Pneumococcal pneumonia (severe)</td>
<td>15,266</td>
</tr>
<tr>
<td>Pneumococcal meningitis</td>
<td>156</td>
</tr>
<tr>
<td>Pneumococcal invasive NPNM</td>
<td>1,176</td>
</tr>
<tr>
<td>Total deaths</td>
<td>641</td>
</tr>
<tr>
<td>Pneumococcal pneumonia (severe)</td>
<td>304</td>
</tr>
<tr>
<td>Pneumococcal meningitis</td>
<td>65</td>
</tr>
<tr>
<td>Pneumococcal invasive NPNM</td>
<td>272</td>
</tr>
<tr>
<td>Total children with sequeliae</td>
<td>36</td>
</tr>
<tr>
<td>Minor sequeliae</td>
<td>27</td>
</tr>
<tr>
<td>Major sequeliae</td>
<td>9</td>
</tr>
</tbody>
</table>

* Benefit of vaccination is based on the vaccine effectiveness, which incorporates information on the vaccine efficacy and coverage.
Table 2. Projected Cost-effectiveness of Pneumococcal Conjugate Vaccination in Honduras (US$, 2007)*

<table>
<thead>
<tr>
<th>Cost per DALY averted</th>
<th>US $1,560</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost per life year gained</td>
<td>US $1,588</td>
</tr>
<tr>
<td>Cost per case averted</td>
<td>US $1,911</td>
</tr>
<tr>
<td>Cost per hospitalization averted</td>
<td>US $22,478</td>
</tr>
<tr>
<td>Cost per death averted</td>
<td>US $54,067</td>
</tr>
<tr>
<td>Incremental vaccination cost</td>
<td>US $321,760,425</td>
</tr>
<tr>
<td>Health service cost savings per year</td>
<td>US $493,573</td>
</tr>
</tbody>
</table>

* This projected cost-effectiveness estimate is based on a vaccine price of US $26.35 per dose.

Conclusions

Vaccination can effectively reduce the disease burden and healthcare costs of pneumococcal disease in Honduras. Based on the WHO criterion of the incremental cost-effectiveness ratio being less than the per capita GDP of a specific country, the pneumococcal conjugate vaccine appears to be cost-effective in Honduras as its cost-effectiveness ratio of US $1,560 per DALY averted was less than three times Honduras' GDP per capita in 2006. It is important to emphasize that even if a vaccination appears to be cost-effective according to this criterion, it may not be affordable. Even an intervention that provides good value for resources invested may have prohibitive financial requirements that could not be accommodated by the health care systems of the countries studied.
Session 4: Program Management

Immunization and Family Health
Vaccination Week in the Americas
Data Quality
Integrated Surveillance
Vaccine Safety
Immunization Programs in the Conceptual Framework of Family and Community Health

Tambini G¹, Zacarias F²

Introduction

Immunization programs are tailored to specific age groups: neonates, infants, children, adolescents, young people, young adults, and the elderly. They are part of a comprehensive approach that includes preventive actions throughout the life cycle of each individual in the context of the family and the community. This approach is a good example of the application of the conceptual framework on family and community health, which is described below.

Methods

The conceptual framework on family and community health has been developed through a series of steps and activities that include a) bibliographic research; b) analysis of national experiences; c) review of the Regional experience; d) interviews and dialogue with experts in national bodies and academic institutions; e) group work and discussions with focal points of family and community health in the countries; and f) preparation of a comprehensive document currently undergoing technical and editorial review prior to publication.

Description

The conceptual framework and approach based on family and community health are grounded in the premise that health is a fundamental human right supported by the values of equity and solidarity. The four principles that guide this approach include the involvement and collaboration of families and communities, the integration of health services, and the timeliness of health interventions and actions. These actions include health promotion; risk reduction and disease prevention (the principal objective of immunization programs); intersectoral action in health; and promotion of equitable access to quality health services.

From a strategic standpoint, the actions necessary for implementing the approach based on family and community health are consistent with the actions that have contributed to the success of immunization programs in the Americas:

a. Advocacy and mass communication to persuade and involve other partners and institutions;
b. Development of policies and programs, with a clear idea of the needs and strategies for their implementation, as well as the evaluation mechanisms;
c. Establishment of partnerships, associations, and networks;
d. Mobilization of resources—human and financial, national and international;
e. Training of human resources at all levels;
f. Technical cooperation aimed at solving specific problems;
g. Promotion of applied research and generation of new knowledge;
h. Surveillance, monitoring, and evaluation to measure progress, achievements, and impact;
i. Dissemination of information to publicize the findings and give feedback to decision-makers, health services, communities, and families.

Conclusions

Like the implementation of immunization programs, implementation of the family and community health approach at the local level is highly relevant for the successful renewal of primary health care; for response to the needs, demands, and expectations of the population; and for achievement of the health-related objectives of the Millennium Development Goals.

¹ Family and Community Health, Pan American Health Organization, Washington, D.C., USA.
Project Belén: An Alternative Intervention for Addressing Health, Nutrition, and Development Problems in an Extremely Poor District in Peru

Día, A1; Guerra-Garcí, A2; Peña M1; Silva Santisteban A2

Introduction
Despite efforts by countries and international cooperation agencies with regard to attaining the Millennium Development Goals and the partial achievements of many of them, the challenge of bridging gaps between and within countries persists. To this end, the Pan American Health Organization/World Health Organization (PAHO/WHO) has been implementing different initiatives aimed at comprehensively addressing the social determinants of health in conjunction with different national and international social actors, such as the “Faces, Voices, and Places,” initiative and the Pan American Alliance for Nutrition and Development. In this context, in 2007 the PAHO/WHO Representative Office in Peru responded to an appeal by two organizations of clowns (Bolaroja-Peru and Dr. Patch Adams’ Gesundheit! Institute-USA) to contribute to the design and implementation of a local development project in one of the poorer areas of the country where a solid relationship with the community had already been established through use of the arts (clowning in this case). The objective of this project is to improve the health and living conditions of the most vulnerable people in the District of Belén (Iquitos, Peru), through a highly participatory process that uses the arts as a focus for bringing people together and mobilizing them.

Methods
In August 2007, the first local participatory planning workshop was held. It was attended by District and Regional authorities, and representatives of grassroots organizations, neighborhood councils, local nongovernmental organizations (NGOs), schools, health services, cooperation agencies, and other stakeholders. On that occasion, the main social and health problems that affected the district were identified, a series of actions was proposed for addressing these problems, and the Network for Belén was created for the purpose of moving forward with the joint implementation of the solutions and strengthening the coordination of activities by social sectors and actors.

Results
To date, numerous activities have been conducted and have consolidated the work of the Network, in particular the following: 1) periodic follow-up meetings; 2) the first Belén Festival in August 2008, which combined use of the arts and social public health actions; 3) training for local government officials and local NGO technical teams; 4) a population and housing census done by the residents themselves, with support from PAHO/WHO and the Cayetano Heredia University; and 5) mobilization of technical and financial resources from different national and international entities.

Conclusions
The experience gained with the implementation of the Belén project shows that the arts are a valuable resource for developing a link to the community. They facilitate working with groups of people who are living in extremely vulnerable conditions and people’s genuine involvement in the activities that are planned for this purpose. Furthermore, use of the arts in participatory and community empowerment processes makes them a powerful public health tool.

1 PAHO/WHO Representative Office in Peru.
2 Cayetano Heredia University and the Bolaroja Association, Peru.
Introduction

In 2009, Vaccination Week in the Americas (VWA) celebrates its 7th anniversary as a Regional initiative that works to promote equity and access to vaccination, transition from child to family immunization, and Pan Americanism, while maintaining immunization high on the political agenda. VWA activities strengthen national immunization programs by targeting populations with otherwise limited access to regular health services, such as those in border and rural areas, urban margins, indigenous communities and low performing municipalities. Ministers of Health of the Americas endorsed Resolution CD44.R1 supporting the implementation of the VWA at the Directing Council of the Pan American Health Organization (PAHO), in 2003. Country involvement in VWA is flexible and in accordance with national health goals. Over its tenure, VWA has flourished, growing to include participation of all countries and territories in the Region.

Methods

The planning process for VWA is multi-faceted and begins five to six months prior to launching with the distribution of planning workbooks. Countries establish their own goals, target populations, and objectives. International collaboration occurs for the organization of bi- and tri-national launching events and border activities. Regional meetings and workshops also facilitate the VWA planning process. Each year a Regional social communication campaign is established and materials are distributed to country offices from PAHO headquarters.

Results

Over the history of VWA, more than 250 million individuals have been vaccinated with a wide variety of antigens. In 2008, approximately 60 million people were immunized and 45 countries and territories participated in the initiative. Some countries choose to use VWA to focus exclusively on social communication, and others use the opportunities generated through the week to integrate other preventative interventions with vaccination. In 2008, multiple launching events occurred along bi- and tri-national borders in the Region and counted on the participation of high-ranking authorities as well as local community leaders. The events illustrate the increasing political priority given to VWA and the ability of the initiative to transcend political borders in the name of public health.

Conclusions

VWA is a country-led initiative that has evolved over the past seven years into an international call for action, not only with regards to immunization, but also as a yearly opportunity to revitalize primary health care. The success of VWA has come to serve as a model for other Regions of the World Health Organization (WHO), such as the European Region, which celebrates its 4th annual European Immunization Week in 2009. Representatives from other WHO Regions have also expressed interest in piloting their own vaccination weeks, leading to the possibility of a global vaccination week in the future.

1 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
Health Caravan: Vaccination, a Right and Responsibility of All, Costa Rica, 21-25 April 2008
Bustamante X, Picado F, Salazar H, Machado V, Fernández P

Introduction
Vaccination Week in the Americas (VWA) 2008 focused on rural border areas, migrant communities, and residents of remote, transborder, and urban or urban fringe areas with low coverage. Its primary objective was to encourage people to value and support vaccination as a right and responsibility in Costa Rica.

Methods
The communication strategy included a conceptual framework and four strategic lines of action:
1. Formal transborder events with Panama and Nicaragua: targeting the representatives of related entities (local government, education, NGOs, others), health officials, local residents, and the press.
2. Health Caravan: targeting people living in the towns along the Inter-American Highway in the northern and southern parts of the country, conducted in two stages. The first, starting out in La Cruz and passing through the Liberia, Canes, Chomes, Esparza, and San Ramón cantons, and ending at the Plaza de las Garantías Sociales. The second, starting out in Moravia and passing through El Guaro de Cartago, Pérez Zeledón, and Buenos Aires, and ending in San Vito. The closing Caravan started out in San Vito and proceeded to the border area with Panama in the community of Río Sereno, where an event was held, followed by the completion of the tour on the Panamanian side.
3. Design of the VWA logo: targeting all age groups.
4. Interpersonal and mass communication: messages for the entire population, with all age groups targeted.

The strategy was developed with the Technical Committee on Immunization and staff from the health areas of the Costa Rican Social Security Fund (CCSS) and the policy-making areas of the Ministry of Health (MOH).

Results
The Health Caravan was conducted with extensive participation by staff from the central, regional, and local levels of the MOH and CCSS and a variety of local actors. The local level demonstrated considerable capacity for social mobilization, enlisting the participation of community leaders, mayors, students, the elderly, fathers and mothers, religious leaders, transit workers, the civil guard, the Red Cross, and the private sector. The closing ceremony involved Costa Rican-Panamanian cultural events in the border region of Río Sereno de Sabalito de Coto Brus, in which 100 people participated. At key points along the tour, moving events were held whose joy, innovation, and creativity lent social visibility to the VWA.

Branding materials, such as a logo, pennants, and decals, were designed to complement the materials from PAHO Headquarters. The design used the distinctive colors of the VWA, along with the slogan: “Vaccination, safe protection. A right and a duty for all.” To manage public information, the e-mail campaign “Pass it along. It’s important.” was launched, sending out nine different messages during the week. A media plan was also drafted whose implementation took advantage of opportunities for free radio and television time, with local media and national press coverage every day and 20 press releases issued. In the rest of the country, the health areas engaged in outreach activities, using VWA materials and holding fairs, setting up information posts, giving interviews at local broadcasting stations. All age groups were vaccinated, with vaccination activities covering schools, health facilities, and the communities where vulnerable populations live (i.e., migrants and indigenous people).

Conclusions
The Health Caravan met its objective of motivating the population and raising awareness about the value of vaccination and the individual and social responsibility of supporting the country’s efforts to maintain good coverage and prevent diseases. The strategy was innovative and facilitated the involvement of a variety of local actors, including the community, who were the protagonists. The Health Caravan held local events that gave social visibility to vaccination and its significance as the right and responsibility of all age groups. The media maintained its commitment and sensitivity, reinforcing the notion in the population that vaccination is important. Some materials could only be printed in limited amounts, reducing the VWA’s potential for a greater graphic impact.

1 Pan American Health Organization, Costa Rica.
3 Immunization Program, Ministry of Health, Costa Rica.
Prioritizing Vulnerable Populations

Vaccination Week in the Americas in the Republic of Paraguay
Torres C1, Barbosa M1, Montesano R2

Paraguay, an active member of the Pan American Health Organization (PAHO), has participated in the adoption and achievement of targets related to the elimination and eradication of vaccine-preventable diseases. In this regard, it supported the PAHO Directing Council’s Resolution CD44.R1 to conduct Vaccination Week in the Americas (VWA), whose main objectives are to advancing equity and access to vaccination and promote Pan-Americanism. From its beginnings, VWA has served as a platform for the country to conduct vaccination activities aimed at protecting vulnerable groups and improving communication and cooperation with the countries of the Region.

The first VWA was held in April 2003. Its goal was to advance measles elimination and increase vaccination coverage. In Paraguay, this was done in the framework of a follow-up campaign for measles elimination, administering measles-rubella (MR) vaccine to all children aged 1-4 years in the country, attaining 93% coverage.

The 2004 VWA was devoted to controlling tetanus and neonatal tetanus. Full immunization in children aged <5 years was completed, and intensive vaccination with Td was conducted in risk groups, especially farmers, women of childbearing age, indigenous people, border communities, and residents of urban fringe areas.

In 2005, the rubella elimination campaign was conducted, during which 3,713,561 doses of MR vaccine were administered to males and females aged 5-39 years, attaining 99.7% coverage.

In 2006, VWA was used for an influenza vaccination campaign, focusing on risk groups: children aged 6-23 months, the chronically ill, and people aged >60 years.

The 2007 VWA focused on increasing coverage in municipalities with low coverage, in addition to a new influenza campaign. The vaccination strategies used were similar to those of elimination campaigns, resulting in the partial coverage catch-up for all biologicals.

A second measles and rubella follow-up campaign had been planned for 2008. However, a yellow fever outbreak in urban and rural areas required intensive yellow fever vaccination, with the use of concentric blocks around cases and vaccination in the general population, which was an important factor in preventing the spread of the disease. Using this strategy, 2,231,107 people aged 1-59 years were vaccinated. The cumulative yellow fever coverage increased to 61% and the outbreak was controlled. That same year, vaccination against seasonal influenza was also administered in children aged 6-36 months, adults aged >60 years, and other risk groups, and activities were conducted to complete full immunization of children aged <5 years (Figure).

In 2009, the cumulative number of susceptible people by over 100% in a birth cohort in the group aged 1-8 years has made the follow-up campaign pressing. Plans have been made to administer 586,306 MMR doses to children aged 1-4 years and 574,250 MR doses to children aged 5-8 years, in addition to 1,309,292 doses of oral polio vaccine to children from 2 months to 8 years. Full immunization of children aged <5 years will also be initiated or completed.

The Expanded Program on Immunization in Paraguay has taken advantage of VWA to conduct disease elimination activities; bring vaccination services to indigenous communities, remote rural areas, and urban fringe areas; conduct cross-border vaccination and surveillance activities; and effectively control the 2008 yellow fever outbreak. From 2003 to 2009, some 11.5 million vaccination actions have been conducted in the country, fully meeting the VWA objectives.

1 Expanded Program on Immunization, Ministry of Health and Social Welfare, Paraguay.
2 Comprehensive Family Immunization (FCH), Pan American Health Organization, Paraguay.
The Quality of Immunization Coverage Data: A Regional Overview

Danovaro C1, Pacis Tirso CL1, Kurtis H1

Introduction

Immunization coverage levels are a key indicator to measure of immunization program performance. Administrative coverage calculation is the most common method used in the Americas. It is done by dividing the aggregated number of doses reported by vaccination services providers, such as health units and private clinics, over a period of time (numerator) by the target population (denominator). This procedure may lead to over or underestimation of coverage due to numerator inaccuracies or inexact estimations of the denominator. We analyzed the national coverage figures reported to the Pan American Health Organization (PAHO) to better understand the quality of these data and to propose recommendations for their improvement.

Methods

We focused our assessment on routine coverage for DTP3 in children aged <1 year in countries with a population size over 500,000 for the years 2002 through 2007. For countries using nominal registries and administrative data, we evaluated numerator consistency and denominator accuracy using the parameters listed in Table 1. We also reviewed the reported denominator problems and source for 2007. Data was obtained from country reports to PAHO via EPI tables or PAHO-WHO/UNICEF Joint Reporting Form and from the United Nations Population Division. Finally, we compared reported coverage figures with coverage obtained through surveys. We obtained survey data from the WHO-UNICEF coverage estimates and from a survey dataset compiled by Lim et al. Sub-national surveys were excluded.

Results

Of the 25 countries of the Americas with population >500,000 inhabitants, Canada and the United States use coverage surveys, Mexico and Uruguay use electronic nominal immunization registries (Panama started in 2008), and the rest use the administrative method. DTP3 coverage data was available for all countries for all the years evaluated. However, the number of DTP1, DTP2, and DTP3 doses were incomplete. For denominator analyses, data were available for all countries for all years, except for two countries in 2004 and one in 2005. The main results are summarized in the Table.

Of the 19 countries that reported denominator source, 11 used census projections (4 indicated making adjustments, 1 by the departmental/state level, 1 by an entity other than the National Statistics Office, and 2 by the Ministry of Health); 5 use the number of live births from the year before (1 indicated that they adjust by infant mortality, 1 indicated that data are obtained by health care workers checking local level birth registries); 2 used the total number of children in the nominal immunization registry; and 1 uses population data given by each region. The years of the last censuses were 2000 to 2007 (1 country had a census in 2007 after a census in 1992). The most common denominator problems identified by the countries were frequent migration (mentioned by 9 countries), inaccurate census projections (4), and under-registration of births (3).

Between 2002-2008, 23 surveys in 15 countries were identified: 12 Demography and Household Surveys (DHS), 3 Centers for Disease Control and Prevention (CDC) Reproductive Health Surveys, 3 UNICEF Multiple Indicator Cluster Survey (MICS), 3 National Health Surveys (2 FESAL, 1 National multi-purpose survey), and 2 national immunization coverage surveys. At the time of this abstract, data from 13 surveys were available. Nine surveys (in 8 countries) found DTP3 coverage lower than the administrative coverage reported (for 6 of them the difference was ≥10%); 3 surveys (in 2 countries) found similar coverage rates; and 1 survey found higher coverage rates than reported.

Conclusions

In our evaluation, most countries had at least one extreme observation that would warrant further examination. Changes >5% in year-to-year numerators and negative drop-out rates, especially between DTP2 and DTP3, were particularly frequent. The denominator source varies between countries, and our appraisal of denominator accuracy suggested that some countries may be underestimating their denominator. Overestimation of national denominators may also be a problem, but it was more difficult to ascertain using our methodology. The differences between survey estimates and administrative data may be the result of overestimation of administrative coverage or problems with the survey ascertainment of vaccination, survey precision, or a combination of theses factors.

Our analyses were not exhaustive, did not examine vaccination timeliness, and have several limitations. While they identify certain unusual patterns in the reported data, they do not necessarily indicate inaccuracies. Alternatively the non-appearance of an anomaly does not necessarily mean that the data are unproblematic.

We recommend that countries assess coverage data systematically and periodically using the indicators presented here, or others, and document national and local efforts to improve the quality of coverage data. Each country will have to evaluate its denominator problems comparing different data sources and understanding factors such as birth registration completeness and timeliness, migration, and quality of census and its projections. Furthermore, it will be important for immunization programs to

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1 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
participate in the design of health surveys that measure immunization coverage and to review their results as part of their activities to monitor coverage rates.


Summary of Data Consistency and Denominator Accuracy Indicators, Countries with Population >500,000, Latin America and the Caribbean, 2002-2007

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Observations</th>
<th>Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year-to-year difference in DTP3 doses¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5%</td>
<td>31/110</td>
<td>15/22</td>
</tr>
<tr>
<td>&gt;10%</td>
<td>14/110</td>
<td>7/22</td>
</tr>
<tr>
<td>Negative DTP1-DTP3 drop-out rates²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For 2 or more years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>45/131</td>
<td>15/23</td>
</tr>
<tr>
<td>For 3 or more years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative DTP2-DTP3 drop-out rates²,³</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For 2 or more years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>58/102</td>
<td>19/22</td>
</tr>
<tr>
<td>For 3 or more years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year-to-year difference in denominators⁴</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5%</td>
<td>33/131</td>
<td>17/23</td>
</tr>
<tr>
<td>&gt;10%</td>
<td>15/131</td>
<td>7/22</td>
</tr>
<tr>
<td>Differences &gt;10% between country denominator and UN average live birth estimate⁴</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For 2 or more years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>37/135</td>
<td>17/23</td>
</tr>
<tr>
<td>For 3 or more years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>More BCG doses administered than denominator⁵</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>27/129</td>
<td>9/22</td>
</tr>
</tbody>
</table>

¹ One country excluded due to obvious errors in the number of DTP3 doses reported for most years. Only one country had reported a vaccine stock-out that explained change in year-to-year >10%.
² Not all DTP1 and DTP2 doses available for all years.
³ One country did not report DTP2 doses for the study period.
⁴ 2004 denominator data not available for two countries, 2005 denominator missing for one country.
⁵ One country does not administer BCG. 2002 number of BCG doses missing for one country.
**Evaluation of the Quality of Immunization Data in Guatemala**

Barrera L¹, Rodríguez R², Corado M³, Cajas C⁴, Quemé T⁵, Bringuez A⁶, Danovaro C⁶

**Introduction**

The figures for administrative vaccination coverage in Guatemala differ by more than 5% from the findings of the 2002 Maternal and Child Health Survey (ENSMI). There also are significant disparities between three sources of population data: projection of the population aged <1 year based on the 2002 population census of the National Statistics Institute (INE); live births according to the INE, adjusted by late registry; and live births compiled from the municipalities by the Health Management Information System (SIGSA) of the Ministry of Health and Social Welfare (MSPAS). This creates uncertainty in the denominator when estimating administrative coverage. The MSPAS, with technical cooperation from the Pan American Health Organization/World Health Organization (PAHO/WHO) used WHO’s data quality self-assessment (DQS) methodology, adapting it to the conditions in the country, to determine data quality, accuracy, consistency, integrity, and timeliness (doses administered and population). The objectives were 1) to evaluate the quality of the National Immunization Program’s (NIP) information system in terms of planning, monitoring and evaluation, training and supervision, system design, records management, and reporting of suspect measles and rubella cases; 2) to evaluate data accuracy; and 3) to evaluate data timeliness and completeness throughout the information flow.

**Methods**

Knowledge of the NIP information system (standards, structure, design, data entry, flow, analysis, monitoring, and evaluation). Selection of the areas, municipalities, and health services to be evaluated. Preparation, validation, and standardization of the instruments. Formation of teams with health service supervisors, NIP, statisticians, and epidemiologists from the central level and health areas and four PAHO/WHO consultants. Measurement of the consistency between pentavalent and MMR doses recorded at local level and in the aggregated report for three months report, and estimation of the quality indices from the score obtained in the quality questionnaire, by component represented in radar graphs. Analysis and presentation of the results to the national authorities and health areas.

**Results**

Visits were made to 30 local health services in three (10.3%) of the 29 health areas where 11% of the country’s population resides; these health areas are located in the central, eastern, and western part of the country. At national level, weaknesses were found in the design of the system and calculation of the denominator. Regarding accuracy at local levels, the number of doses administered coincided with the number reported to the next level in only one out of five measurements. Most of the disparities involved over-reporting, especially for Penta3 and MMR. Regarding the quality indices by component, one health area performed adequately in the six components, one in four of the six, and the other, in two of the six indicators. Three of the seven health centers met at least four of the six indicators.

The personnel interviewed considered the NIP a priority, were receptive to providing the information, and appeared to identify with the population and be motivated to improve management. Supervision was inadequate and coverage monitoring graphs outdated; there were errors in recording doses for the right age group and lack of standardization in the reporting of doses administered by the Guatemalan Social Security Institute; rapid coverage monitoring was not systematized for the regular program; different spreadsheets were used for consolidation; conceptual problems existed in estimating vaccine waste; and more health services personnel were needed.

The majority of the surveillance indicators have been met, and the response to a suspect measles or rubella case is adequate, but there are weaknesses in the use of the case definition and no active, systematic institutional case-finding.

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² Comprehensive Family Immunization (FCH), Pan American Health Organization, Guatemala.
³ National Epidemiology Center, MSPAS, Guatemala.
⁴ Health Management Information System, MSPAS, Guatemala.
⁵ Integrated Health Care System, MSPAS, Guatemala.
⁶ Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
Conclusions

The immunization data collection system does not permit obtaining reliable coverage estimates due to deficiencies in the numerator and denominator, which makes reliable analysis and interpretation not possible and detracts from credibility at national and international levels. Health services comply with information flow requirements, but the cut-off date (the 25th of each month) is not uniformly honored, generating inconsistency in the data among the different levels. This evaluation produced a series of recommendations, including the development and implementation of a plan to improve the quality, consistency, and timeliness of the vaccination information system at all levels, the adoption and distribution of technical guidelines for vaccination information to all levels, and the establishment of mechanisms for systematic verification of data quality. The country is implementing these recommendations.

Consistency Between Penta3 Doses in the Daily Record and the Consolidated Monthly Record, by Area and Health Services, Guatemala, 2008

<table>
<thead>
<tr>
<th>Health Area</th>
<th>Nb. of Services Evaluated (%)</th>
<th>Range of Consistency for Penta3 Doses</th>
<th>Over-reporting</th>
<th>Same</th>
<th>Under-reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sololá</td>
<td>11</td>
<td></td>
<td>7</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Chiquimula</td>
<td>9</td>
<td></td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Guatemala Sur</td>
<td>10</td>
<td></td>
<td>6</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>30 (100%)</td>
<td></td>
<td>17 (56.7%)</td>
<td>8 (26.7%)</td>
<td>5 (16.6%)</td>
</tr>
</tbody>
</table>
Integrated Surveillance of Vaccine-preventable Diseases in Costa Rica
Trejos ME1

Introduction
In 2007, the World Health Organization (WHO) published a report entitled Global Framework for Immunization Monitoring and Surveillance. The document issues recommendations for improving national surveillance of vaccine-preventable diseases (VPD) within a single unified vision or framework that builds on the strong points of existing surveillance systems rather than imposing specific, vertical systems for the surveillance of new diseases. Costa Rica, with support from the Pan American Health Organization and the U.S. Centers for Disease Control and Prevention (CDC), is developing a strategy to demonstrate this vision of integration within the framework of a national VPD surveillance system.

Integration of VPD surveillance has several key objectives: 1) reducing duplication of efforts, time, and cost; 2) making more efficient use of limited resources; 3) providing surveillance data to local decision-makers, and 4) building on the strengths of surveillance systems already in existence.

Methods
Demonstration in Costa Rica of the integration of population-based and sentinel surveillance that improves the detection of diseases, provides exhaustive standardized surveillance, achieves synergies, saves resources, and facilitates supervision. The core elements of surveillance to be integrated include 1) identification of cases, 2) collection of data and samples, 3) laboratory tests, and 4) data reporting and feedback.

Results
Costa Rica has developed the plans and completed the protocol for integrated VPD surveillance. In the process, it has evaluated the surveillance system, identifying the system components that are suitable for integration and the actions needed to overcome obstacles to integration. It has also selected the hospitals where sentinel surveillance will be conducted as part of the integrated strategy. Costa Rica hopes to demonstrate the advantages of an integrated approach in strengthening VPD surveillance, increasing user acceptance, and improving compliance with the following objectives of the national surveillance system:

1. Defining the epidemiological characteristics, trends, and burden of disease for selected VPDs, before and after vaccine introduction.
2. Monitoring disease epidemiological and microbiological characteristics.
3. Detecting all disease cases to support ongoing efforts to achieve their eradication or elimination (such as polio, measles, and rubella).
4. Detecting unusual or unexpected outbreaks of the diseases selected.

Steps have been taken to develop an electronic data collection system through a Web interface in order to harmonize and manage information on integrated surveillance. The Web-based system will make efficient and timely use of existing databases for the recording of vaccine coverage, population, and surveillance.

Conclusions
A wide range of stakeholders in different roles are contributing to the development of the integrated VPD surveillance strategy. Documentation of the demonstration of integrated surveillance—the project’s evolution through its various phases, its process and progress, drawbacks and advantages, and lessons learned—will allow this experience to be shared with all countries interested in adapting the methodology. The ensemble of contributions will serve as the basis for the eventual preparation of global recommendations.

Reference:

1 Ministry of Health, Costa Rica.
Introduction
To ensure the success of immunization programs, it is of utmost importance to guarantee vaccination safety and to respond promptly to any concerns raised by the public so as to maintain confidence in immunization. The vaccines procured through the Revolving Fund of the Pan American Health Organization/World Health Organization (PAHO/WHO) are prequalified by WHO and are subject to rigorous quality control procedures, in both the country of origin and country of destination. The introduction of new vaccines currently poses multiple challenges for vaccination safety in the Region, particularly with respect to safe injection practices and the monitoring of events supposedly attributable to vaccination or immunization (ESAVIs), as such events can give rise to rumors and a crisis of confidence. To this end, PAHO/WHO will prepare a strategic plan to strengthen vaccination safety in the Region and ensure that all its components are working properly.

Methods
The existing plan for vaccination safety was reviewed through a collaborative interprogrammatic process that included exhaustive analysis of the current situation in the Region, the regional ESAVI surveillance network for new vaccines (SANEVA), roles and responsibilities, and the available educational materials and information systems.

Results
Extensive work has been done to improve vaccination safety in the Americas. Training modules have been developed, and there is an active ESAVI surveillance network in the countries. However, a comprehensive plan is needed to link the different vaccination safety components throughout the Region. Efforts are therefore under way to prepare a strategic vaccination safety plan based on experiences and lessons learned. This plan will cover four main areas: 1) vaccine quality, 2) safe injection practices, 3) ESAVI surveillance, and 4) crisis prevention. The vision and strategic lines of the plan will seek to harmonize and strengthen current surveillance and investigation processes and the countries’ response capacity. The plan will include objectives, milestones, and deliverables, with the goal to strengthen local capacity. Comprehensive training workshops will be held to update the training modules on vaccination safety, seeking to harmonize them with existing tools developed by the Brighton Collaboration and the CIOMS/WHO working group. The plan will also seek to strengthen the capacity for rapid detection and review of ESAVIs at the Regional and country levels. Preparation of guidelines and implementation of an information system will support this objective.

Conclusions
For development and implementation of the strategic plan to strengthen vaccination safety, PAHO/WHO will develop a regional platform that will permit the coordination, articulation, and optimization of the vaccination safety efforts conducted by national health authorities, multilateral agencies, strategic partners, and other stakeholders.

(a) CIOMS: Council for International Organizations of Medical Sciences.

1 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
2 Essential Medicines and Biologicals (THR), Pan American Health Organization, Washington, D.C., USA.
Introduction

The regulation of products for use in public health is an increasingly urgent need that poses continuing and new challenges to regulatory bodies. The National Regulatory Authorities (NRAs) in the countries play a key role in this effort, facilitating the timely availability of products and thus contributing to the ability of immunization programs to meet their vaccination coverage targets. However, new sophisticated technologies used in the development of drugs, especially vaccines, are making it difficult for the NRAs to exercise their supervisory role and guarantee the quality, efficacy, and safety of the biologicals used in the countries.

Methods

With the emergence of new technologies, it is becoming increasingly difficult for NRAs to perform the six basic functions that the World Health Organization has deemed critical to their effectiveness. Laboratory evaluation of vaccines is becoming a less useful tool in light of the great diversity of new products, the increasingly complex analysis that their biological makeup requires, and the lack of trained human resources and financial resources that would allow NRA laboratories to generate knowledge about the products, while manufacturers are working to advance their development. The laboratory tests that can be performed are general ones that do not relate to the specificity and content of the biological ingredients of the product. Inspection of good manufacturing practices is another function that NRAs in the countries of the Region have limited capacity to perform. The efficient implementation of these inspections helps authorities in a realistic assessment of whether manufacturers are maintaining appropriate conditions for vaccine production. In this context, the functions through which the NRAs can conduct efficient and timely evaluation of products entering the market include product registration, a lot release system, evaluation of clinical studies of a product prior to marketing, and post-marketing surveillance of field performance. When implemented effectively, these tools can provide an NRA with more criteria for passing judgment on a product than conducting inspections and laboratory tests under less-than-adequate conditions.

Results

The Essential Medicines and Biologicals Project of the Technology, Health Care, and Research Area is assessing the performance of NRA regulatory functions in the countries of the Region. It is focusing its efforts on rationally limiting the performance of certain functions, especially laboratory tests and inspections for good manufacturing practices, to agencies that have the resources to perform them efficiently. The preparation of a document on harmonizing the registration of vaccines in the Region of the Americas, and guidelines for its implementation, approved by the 5th Pan American Conference on Drug Regulatory Harmonization, is one of the first steps in this harmonization effort that can benefit all those responsible for vaccine regulation.

Conclusions

The Essential Medicines and Biologicals Project proposes harmonization and mutual recognition among NRAs as a unifying mechanism that can help them find solutions to the challenges they face as the entities responsible for guaranteeing the quality, efficacy, and safety of vaccines amid the emergence of a highly diverse market of new and increasingly sophisticated products.
Introduction
The quality and safety of syringes is a very important public health issue for countries and the Pan American Health Organization/World Health Organization (PAHO/WHO) because of its impact on immunization programs. The Regional Plan for Quality Control and Safety of Syringes was established in 2005 by the Immunization Unit and the Essential Medicines, Vaccines, and Health Technology Unit to support the Revolving Fund in the procurement of vaccines, syringes, and other supplies for countries and their Expanded Program on Immunization (EPI). The purpose of the plan is to ensure the quality, efficacy, and safety of syringes. The plan was initially intended for the verification of compliance with international ISO standards, but it has been expanded to cover the entire life cycle of syringes, from procurement to final disposal, including their safe use. In 2009 the Revolving Fund is procuring approximately 70 million syringes: 14 million auto-disable (AD) syringes, and 56 million disposable (standard) syringes.

Methods
Quality: Several steps have been taken to implement and strengthen the procurement and quality control mechanisms for syringes: a) review of technical documentation and verification of compliance with the requirements established for suppliers; b) laboratory tests to confirm that products to be procured through bidding are in conformity and compliance with ISO standards, as well as monitoring of products received by the countries; c) development of institutional capacity in the National Regulatory Authorities (NRAs) to perform quality control tests.

Regional Incident Report System (RIRS): A notification system and database have been set up to register and monitor incidents reported by countries in relation to the quality and safety of syringes. Documentation of such problems allows for follow-up, research, and broadcasting of alerts.

Laboratory network: In order to improve the capacity for verification, efforts are under way with the NRAs to establish quality control laboratories. This work has begun in six countries thus far: Argentina, Chile, Colombia, Jamaica, Mexico, and Nicaragua.

Training: a) Workshops on best practices in injection safety have been held to facilitate proper incorporation of the new AD technologies and promote the safe use of syringes, including good storage practices and proper final disposal of sharp medical waste; b) NRA professionals were trained in how to perform tests, verify conformity with standards, and organize laboratories as part of human resources development; and c) Distance education was provided through the RIRS portal using Elluminate software.

Results
Quality: a) Over the past three years, laboratory tests (physical and visual) have been performed on the products offered through bidding. These tests have revealed deviations and nonconformities in relation to ISO standards. From 2006 to 2008, 38 samples of AD syringes were evaluated, 15 of which were reported to be in non-conformity (40%). With respect to standard syringes, 82 samples were evaluated, with 49 non-conformities (60%). When these data are disaggregated by year, it appears that deviations in AD syringes fell from 72% in 2006 to 18% in 2008. In standard syringes, deviations rose from 45% in 2006 to 69% in 2008; b) The results of AD syringe evaluations were reported to WHO. This led to a review of these products and changes in the PQS bulletin (Performance, Quality and Safety).

RIRS: Countries reported 10 incidents that were investigated. Investigation has been concluded for 9 of them.

Laboratory network: Validation is currently under way for the testing of protocols prepared jointly by PAHO and the ECRI Institute, which is the PAHO/WHO Collaborating Center for the syringe evaluation.

Training: a) Verification of quality: 6 NRA professionals were trained at the ECRI Institute; b) Best practices in injection safety: in 2008, 2 workshops were held in Nicaragua (40 participants, including delegates from Cuba, the Dominican Republic, El Salvador, Guatemala, Honduras, and Panama) and Honduras (43 participants, including delegates from Bolivia and El Salvador); and c) Training on use of the RIRS portal has been provided to personnel from PAHO Headquarters, to focal points in the countries, and to 8 EPI managers.

1 Comprehensive Family Immunization (FCH), Pan American Health Organization, Washington, D.C., USA.
Conclusions

The Region of the Americas has given priority to quality control of syringes, strengthening the capacity of the NRAs to ensure that syringes comply with ISO standards and that the users of health services can depend upon a quality product.


### Summary of Quality Control Test Results on Syringes, 2006–2008

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of providers</th>
<th>Number of tests</th>
<th>Number of syringes evaluated</th>
<th>Number of deviations and nonconformities in relation to ISO standards</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>AD</td>
<td>Standard</td>
</tr>
<tr>
<td>2006</td>
<td>8</td>
<td>12</td>
<td>11</td>
<td>29</td>
</tr>
<tr>
<td>2007</td>
<td>7</td>
<td>12</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>2008</td>
<td>7</td>
<td>15</td>
<td>17</td>
<td>23</td>
</tr>
</tbody>
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