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Immunization Newsletter

Pan American Health Organization

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In this issue:

Update on the Status of HPV Vaccines

Two prophylactic HPV vaccines are currently available on the global market for the prevention of cervical cancer due to specific high-risk types of human papillomaviruses (HPV). They are Gardasil, a quadrivalent vaccine formulated by the Merck Company and containing vaccine-like particles (VLPs) against HPV genotypes 6, 11, 16, and 18, and Cervarix, a bivalent vaccine produced by GlaxoSmithKline and containing VLPs against genotypes 16 and 18. HPV types 16 and 18 account for roughly 70% of cervical cancers globally, while types 6 and 11 are most frequently associated with benign genital warts, a cause of significant morbidity. Both vaccines are highly efficacious.

Efficacy

In women who are not infected with any of the vaccine-related HPV genotypes (i.e., HPV-naïve), the quadrivalent vaccine provides 96% efficacy against persistent infection, 99% efficacy against HPV 6, 11, 16, or 18 cervical or genital lesions, 95-100% efficacy against early cervical cancerous changes, and 100% efficacy against vulvar and vaginal intraepithelial neoplasia. The bivalent vaccine is 96% efficacious against persistent infection, 100% efficacious against HPV 16- or 18-cervical lesions and 89-90% efficacious against early cervical cancerous changes. Some of the key efficacy measures have been summarized in Table 1.

There is also new evidence from follow-up studies to suggest that both vaccines offer cross protection against HPV types 45 and 31, which, although less common, are also associated with a high relative risk of cervical cancer. The bivalent vaccine has been found to reduce the incidence of infection with these two genotypes, and recipients of the quadrivalent vaccine were found to produce neutralizing antibodies against them. The clinical significance of these findings, including whether the incidence of early cervical cancerous changes is reduced, is currently under investigation (1). More evidence has recently emerged regarding the ability of the quadrivalent vaccine to prevent disease rather than to cross-neutralize non-vaccine types. Clinical trial results have estimated vaccine efficacy against cervical intraepithelial neoplasia (CIN) 2-3 and adenocarcinoma in-situ (AIS) due to HPV types 31 and 45 at 62%, and at 43% for similar lesions attributable to HPV types 31, 33, 45, 52, and 58 (Table 2).

Table 1. HPV Vaccine Efficacy Measures

End Points of Efficacy	Quadrivalent Vaccine Efficacy (95% CI)	Bivalent Vaccine Efficacy (95% CI)
Persistent Infection	96% (94.0-100) [a]	96% (75.2-99.9) [c]
CIN Grade 2	100% (81.0-100) [b]	100% (-7.7-100) [c]
CIN Grade 2+		90.4% (53.4-99.3) [d]
CIN Grade 3	100% (76-100%) [b]	

CI: Confidence Interval CIN: Cervical Intraepithelial Neoplasia

(a) Villa et al. Efficacy of a prophylactic quadrivalent human papillomavirus (HPV) types 6/11/16/18 L1 virus-like particle (VLP) vaccine through up to 5 years of follow-up. Abstract presented at the Meeting of the EUropean Research Organization on Genital Infection and Neoplasia (EUROGIN), April 2006, Paris, France.

(b) Garland et al. Quadrivalent Vaccine against Human Papillomavirus to Prevent Anogenital Diseases. N Engl J Med 2007. 356:1928.

(c) Harper et al. Sustained efficacy up to 4.5 years of a bivalent L1 virus-like particle vaccine against human papillomavirus types 16 and 18: follow-up from a randomised control trial. The Lancet 2006;367:1247-55.

(d) Paavonen et al. Efficacy of a prophylactic adjuvant bivalent L1 virus-like-particle vaccine against infections with human papillomavirus types 16 and 18 in young women: an interim analysis of a phase III double-blind, randomised controlled trial. The Lancet. 2007;369:2161-70.

PAHO's Pro-Vac Initiative

The Pan American Health Organization (PAHO) estimates the annual mortality in Latin America and the Caribbean due to rotavirus-induced diarrhea to be 16,000. It also estimates that, annually, another 22,000 children die from invasive pneumococcal disease and 32,000 women die prematurely from cervical cancer caused by human papillomavirus. 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 be grounded in a greater body of evidence that reflects national conditions. This represents a significant departure from a history of policy driven by Regional mechanisms, such as PAHO's Technical Advisory Group on vaccine-preventable diseases.

In response to the need for support for evidence-based vaccine introduction decisions, PAHO and its partners –including the Gates Foundation, various academic centers, the ADIPs[1], the U.S. Centers for Disease Control and Prevention (CDC), and the World

[1] ADIP: Accelerated Development and Introduction Plan.

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PRO-VAC from page 1

Health Organization– collaborated to conduct technical workshops with national immunization program managers in 2004 and 2006 (1). 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, the London School of Hygiene and Tropical Medicine, the 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 indirectly benefited from Pro-Vac[2] with successful applications for New Vaccine Support: all countries that applied were approved.

PAHO's Pro-Vac Initiative:

Enhancing Evidence-based Capacity to Make Informed Policy Decisions on the Introduction of New Vaccines in the Americas

Over the next five years, PAHO seeks to mobilize $5.3 million to continue this work. The Bill and Melinda Gates Foundation looks to sustain support. The objectives are as follows:

- 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 (2).

Pro-Vac coordinated partnerships will align available national and international expertise to provide technical cooperation to Ministries of Health. The expertise mobilized, along 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, Pro-Vac is pursuing a subregional approach to generate and share evidence amongst neighboring countries (Table 1). Support provided to Pro-Vac will be strategically used to benefit all low- and middle-income countries, leading to a Region-wide impact starting in countries most likely to be the first introducers. PAHO increases the value of investing in the Pro-Vac Initiative by sharing the experience, evidence, tools, and the valuable expertise of partners and the Key Center networks with middle-income countries. In this fashion, PAHO, with the support of the Gates Foundation and other partners, can meet the mandate to support evidence-based vaccine introduction decisions expressed by the Ministers of Health of the Americas in Resolution CD47.R10 adopted at PAHO's 2006 Directing Council (3). ■

[2] Also known as the Initiative to Promote the Implementation of Economic Analysis for Vaccine Introduction in Countries of Latin America and the Caribbean.

Table 2. Pro-Vac Twelve-month Vision

	Country	Subregion	Vaccine(s)
Country Activies Committed	Bolivia	Andean	Pneumococcus
	Cuba	Caribbean	Pneumococcus
	Guyana	Caribbean	Pneumococcus / Rotavirus / HPV
	Honduras	Central America	Pneumococcus / Rotavirus
	Jamaica	Caribbean	HPV
	Nicaragua	Central America	Pneumococcus
Country Activities Planned	Brazil	Southern Cone	Pneumococcus
	Paraguay	Southern Cone	Rotavirus
Regional Activity Committed	GAVI Country Economic Workshop		
Regional Activities Planned	E-learning Module Development Economics of HPV Workshop Key Center Network Development		

References:

(1) Immunization Newsletter, Vol. XXVIII, Number 5. Multiyear Project Proposal for the Promotion of Evidence-based Policy Decisions for New Vaccine Introduction in Latin America and the Caribbean (Pro-Vac). (October 2006).

(2) Andrus JK, Toscano C, Lewis M *et al*. A model for enhancing evidenced-based capacity to make informed policy decisions on the introduction of new vaccines in the Americas: PAHO's Pro-Vac Initiative. *Public Health Reports* 2007;122(6):811-16.

(3) Available on PAHO's website at: www.paho.org/english/gov/cd/CD47.r10-e.pdf.

HPV from page 1

It is to be noted that women infected with one, but not all, of the quadrivalent vaccine-related genotypes acquired protection against those types to which they had not yet been exposed. No therapeutic benefit has been demonstrated among women infected with vaccine-containing types with either vaccine. Therefore, vaccination should be initiated before the onset of sexual debut in order to derive maximum benefit.

Safety

HPV vaccines are not whole virus preparations but are VLPs, which are produced using recombinant technology. These vaccines do not contain any live biologic product or DNA. Therefore, they are not capable of producing infection or cancer. The incidence of serious adverse events post-HPV vaccination is not significantly higher among vaccine recipients compared to placebo recipients. However, study vaccinees did have more frequent occurrences of injection site pain, edema, and erythema. It is reassuring to note that no unique adverse events have been reported among vaccinated women who had already been naturally infected with HPV types contained in the vaccine.

Table 2. Cross Protection Elicited by the Quadrivalent Vaccine Against CIN 2-3 and AIS

Causal HPV Type	Quadrivalent HPV Vaccine	Placebo	Efficacy (%)	95% CI
HPV 31-35	8	21	62.0%	10,85
HPV 31-33-45-52-58	27	48	43.0%	7,66

CI: Confidence Interval

Source: HPV Type 6/11/16/18 Vaccine: First Analysis of Cross-protection Against Persistent Infection, Cervical Intraepithelial Neoplasia (CIN) and Adenocarcinoma In-Situ (AIS) Caused by Oncogenic HPV Types in Addition to 16/18. Brown D, for the FUTURE Study Group, Indiana University School of Medicine. Abstract presented at the 47th Interscience Conference on Antimicrobial Agents and Chemotherapy, American Society for Microbiology, Chicago, 2007.

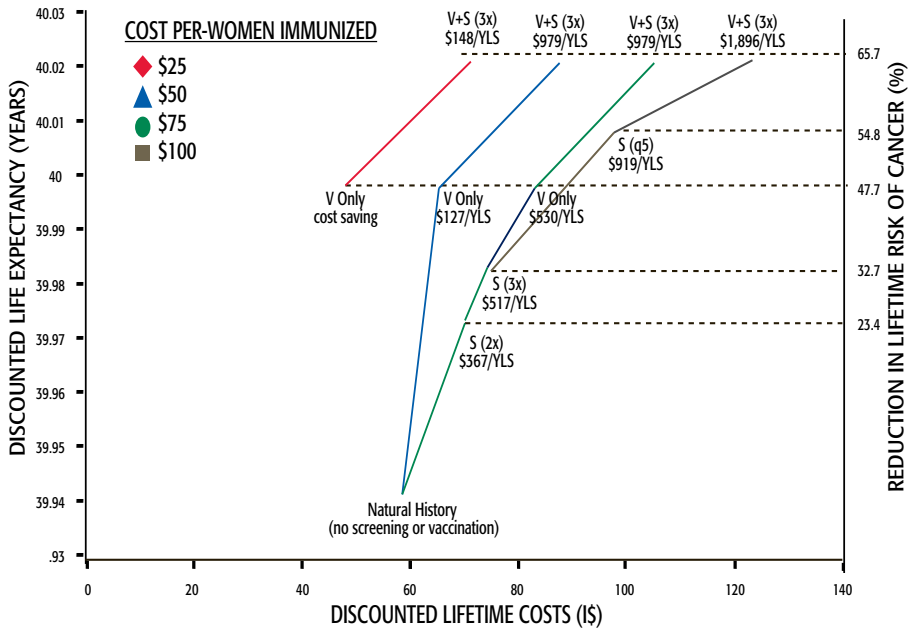
Co-Administration

Studies already undertaken have determined that hepatitis B vaccines can be safely co-administered with HPV vaccines. However, additional co-administration studies are being conducted to assess HPV vaccine immunogenicity when it is concurrently administered with combined DTP and meningococcal vaccines.

Cost Effectiveness of HPV Vaccines

Currently, the cost per vaccine dose, not including administration fees, is over US $100. Manufacturers have expressed their willingness to adjust vaccine price according to country-specific economic conditions. Using decision models, Garnett *et al*. examined Brazilian data to compare different cervical cancer control approaches with varying vaccine prices, inclusive of three doses, wastage, delivery, and programmatic costs (3). If the costs per woman immunized could be maintained at I$25, then vaccination alone would be cost-saving as compared to doing nothing, and would result in a 48% reduction in cervical cancer incidence. For the same price, vaccination and screening three times in a lifetime would be cost-effective for an incremental cost-effectiveness ratio (ICER) of I$148 per year of life saved and would result in a 66% reduction in cervical cancer incidence. When the cost per vaccinated woman rises to I$100, the ICER increased and the advantage of including vaccine versus screening alone was lost. In this model, the most significant factor influencing cost-effectiveness of HPV vaccination was the price of HPV vaccine (Figure 1).

Figure 1. The Impact of HPV Vaccination and Screening on Cervical Cancer, Brazil



Source: G.P. Garnett et al. Chapter 21: Modelling the impact of HPV vaccines on cervical cancer and screening programmes. *Vaccine* 24S3 (2006) S3/178-S3/186.

HPV Vaccines and Cervical Cancer Screening

Cytologic screening with the Papanicolaou smear (Pap smear) has been the mainstay of secondary cervical cancer prevention over the past 40-50 years, having been applied in the industrialized countries with resounding results. However, its application in developing countries has not uniformly resulted in the significant reductions in disease burden observed in the developed world. More recently, as understanding of the molecular biology of HPV improved, sophisticated screening tests have been developed to detect the presence of high-risk oncogenic HPV types in cervical cells and tissues. Additionally, much recent research has focused on the evaluation of alternatives to the Pap smear screening modalities for use in low-resourced settings, in order to address the challenges associated with Pap smear use in developing countries. Such alternative strategies include visual inspection with acetic acid (VIA) and visual inspection with Lugol's iodine (VILI).

Primary prevention for cervical cancer has always included health promotional messages on risk-reduction strategies, which have emphasized safe sexual practices, including abstinence, sexual partner reduction, delaying first intercourse, and condom use. Avoidance or reduction of tobacco use is also advised as smoking has shown a moderate and statistically significant association with cervical cancer. Though the exact mechanism for this relationship is unknown, tobacco-related compounds have been detected in the cervical mucous of smokers and may contribute to oncogenic changes through direct damage to DNA and/or by reducing the host's immunologic capacity to clear HPV infection (2).

The availability of HPV vaccines now offers an additional, effective tool for primary prevention of cervical cancer. It must be emphasized that this primary preventive tool is not a replacement for secondary prevention through screening.

Cervical Cancer Screening in an HPV Vaccine Era

Screening will still be required in an HPV vaccine era as the current vaccines do not contain all of the known high-risk oncogenic HPV types. While HPV types 16 and 18 are responsible for approximately 70% of the global cervical cancer burden, vaccinated women will still be at risk for infection with the other oncogenic types not contained in the vaccine. They will still need to be screened. Additionally, all of the women who are age-ineligible to receive the current vaccines must continue to be screened for cervical cancer.

Comprehensive Cervical Cancer Prevention

The availability of HPV vaccines together with cervical cancer screening offers the opportunity for comprehensive cervical cancer control through the application of these two complementary tools. This also allows us to conceptualize cervical cancer prevention over the life cycle of a woman as we can immunize adolescents prior to initiation of sexual activity to prevent infection with HPV types 16 and 18 when they become sexually active, and we can screen older women at later ages to detect and treat any abnormal or pre-cancerous lesions. Together, these two strategies will result in a significant reduction in the cervical cancer burden, even though this impact will not be observed for 10-20 years.

Evidenced-Based Decision-Making Regarding HPV Vaccine Introduction

The decision to introduce HPV vaccine into national immunization schedules should be based on data reflecting the local situation to the extent possible. Therefore, any decision for vaccine introduction and the selection of a specific HPV vaccine for use must be informed by evidence,

the most salient of which should include:

- The magnitude of the HPV-associated disease burden (e.g., invasive cervical cancer, high-grade cervical pre-cancerous lesions; and genital warts);
- The economic costs of the individual disease burden;
- The costs and cost-effectiveness of the vaccine;
- The type of health infrastructure already available or required to ensure efficient vaccine delivery, particularly for adolescent girls;
- The incremental additional costs required for an expanded cold-chain capacity, surveillance systems, social mobilization and communication;
- Cultural and political acceptance of the vaccine;
- The costs and cost-effectiveness of other preventive strategies directed at the disease of interest; and
- The sustainability of vaccine introduction into national immunization programs.

Unanswered Questions

1. Duration of Protection: Even though adequate levels of vaccine-induced antibodies have been maintained during the 5.5 years of observation among vaccinees in HPV vaccine trials, researchers are unable to project th duration of protection that will be conferred. Hence, the question regarding the need for booster doses remains. It would, however, be inappropriate for countries to withhold vaccination for this reason, while many more young women develop persistent infections with high-risk oncogenic HPV types, increasing their risk for cervical cancer.

2. Efficacy in Males: The quadrivalent HPV 16, 18, 6, 11-containing vaccine has been tested in males, aged 9-15 years, with excellent results regarding its immunogenicity and safety. On the basis of these studies, this vaccine was licensed for use in young males in some countries such as Australia, Denmark, and Mexico. However, it is important to note that no efficacy results regarding its capacity to prevent ano-genital cancers or pre-cancers in males are currently available, though results of such trials should be available by the end of 2008.

3. Efficacy in HIV-infected Populations: Even though HPV vaccine trials are currently underway to address the important issue of vaccine efficacy in HIV-infected populations, the results are not yet available.

Summary

Two highly effective and safe vaccines exist that will greatly assist with efforts to control cervical cancer in the future. Many countries in Latin America and the Caribbean are very interested in the application of these vaccines owing to the high cervical cancer burden and the substantial associated costs borne by this Region. The Immunization Unit will work collaboratively with PAHO Member States to build the evidence base required for informed decision-making through its Pro-Vac Initiative. Additionally, PAHO will work in a cross-functional manner with Member States to strengthen national programs with a re-orientation towards comprehensive and integrated cervical cancer prevention and control. Additional research addressing as yet unanswered questions will help elucidate and guide decision-making, and results are eagerly anticipated. ■

References:

(1) World Health Organization. Human papillomavirus and HPV vaccines: technical information for policy-makers and health professionals. (WHO/IVB/07.05). Available on line at http://www.who.int/vaccines-documents/ DocsPDF07/866.pdf (15 Dec. 2006).

(2) Castellsague X, Munoz N. Cofactors in human papillomavirus carcinogenesis-role of parity, oral contraceptives, and tobacco smoking. *J Natl Cancer Inst Monograph* 2003;31:20–28.

(3) Garnett GP, Kim JJ, French K, Goldie SJ. Modelling the impact of HPV vaccines on cervical cancer and screening programmes. *Vaccine* 2006; 24S3:178-186.

Pertussis in the Americas

A meeting on pertussis in the Americas was held on 16 October 2007 at the Headquarters of the Pan American Health Organization (PAHO) in Washington, D.C. Representatives from Ministries of Health of Argentina, Costa Rica, Mexico, the U.S. Centers for Disease Control and Prevention (CDC), the World Health Organization (WHO), and PAHO participated in the meeting.

The objectives of the meeting were to analyze the status of pertussis in Latin America (Figure 1) and discuss whether the current recommendations issued by the Technical Advisory Group (TAG) on vaccine-preventable diseases should be modified. Presentations made included an overview of pertussis in the world, Latin America, and the U.S., as well as outbreaks in Argentina and Mexico. The reasons that brought Costa Rica and the U.S. to introduce the Tdap vaccine were also examined, along with the available epidemiological evidence justifying the current and proposed new immunization schedules.

Major Conclusions and Recommendations

General:

- Pertussis is a neglected disease that deserves more attention because of its potential to cause outbreaks when DTP3 coverage falls. Therefore, at the next TAG meeting, the agenda should include a session on pertussis that would cover the epidemiologic situation in the Region, current methods of control, country experiences and presentations of outbreak investigations, and a review of the current TAG recommendations to determine if revisions are required.

Surveillance:

- Surveillance is a challenge because of the difficulties with diagnosis, in particular laboratory confirmation.
- Opportunities exist to strengthen surveillance, especially when linked to the SIREVA surveillance network of bacterial invasive disease and transfer of technology with capacity development from such partners as the CDC.
- PAHO should be recommending that, whenever specimens are obtained for PCR,[1] specimens also should be collected for culture at the same time. PCR seems to be replacing culture. However, culture remains the gold standard and has important public health implications because PCR still has problems with false positives.
- To prevent countries from making wrong policy decisions based on erroneous surveillance data, additional effort to enhance surveillance is essential in the Region. The presentation by the CDC highlighted how an outbreak of pertussis in a U.S. city was incorrectly determined to be pertussis because of limitations of PCR technology used.
- CDC is developing standardized PCR technology that should improve predictive values of these tests, as well as methods for serology. These results could also be presented to TAG.

1 Polymerase Chain Reaction.

Outbreak Investigations:

- Outbreaks should be investigated, particularly to determine the age distribution, vaccination status of pertussis cases, and other risk factors.
- While surveillance remains a challenge, investigation of all outbreaks provides invaluable data for strengthening disease control strategies.

Country Presentations:

- The epidemiology of pertussis varies widely by country.
- Argentina had a large pertussis outbreak in Neuquén Province from Epidemiological Week 20, 2004 to Epidemiological Week 23, 2007 (Figure 2). A total of 1,248 confirmed cases were reported, 957 of them among children aged 1-10 years. DTP3 coverage in Neuquén Province in 1998-2003 was 87%. To determine whether the outbreak was failure to vaccinate or vaccine failure, Argentina should conduct a well-designed case-control study. The cold chain also needs a systematic evaluation.
- Costa Rica decided to target new mothers for vaccination in response to the perceived increased risk of pertussis in neonates. This strategy will need careful monitoring and evaluation in order to determine its effectiveness.
- In Mexico, there is significant under-reporting. This needs urgent attention if policy decisions on pertussis are going to be fully supported.

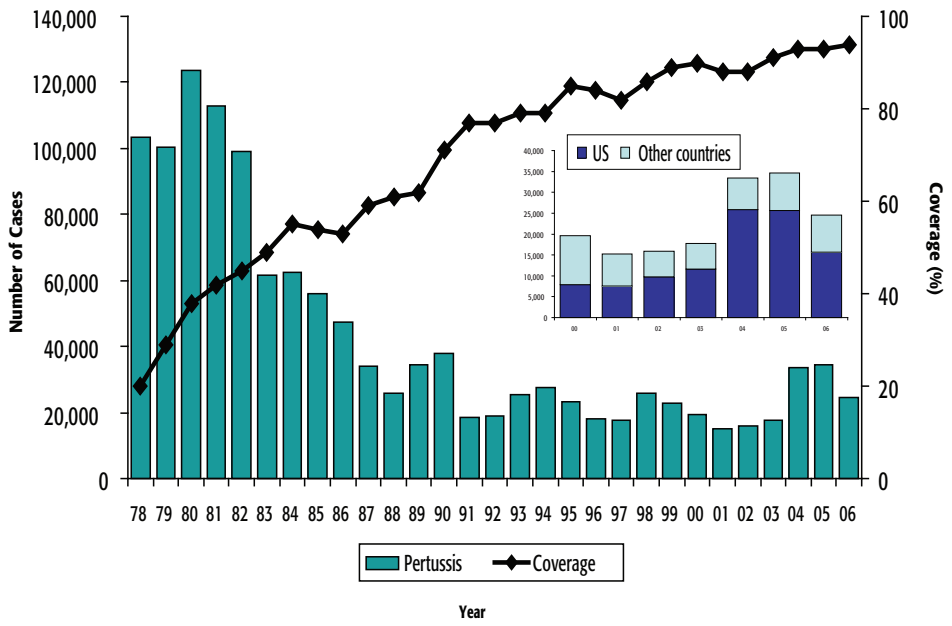
Vaccination:

- There is no reason for countries to change from whole cell pertussis- (wP) to acellular pertussis- (aP) containing vaccines. The wP antigen is much more cost-effective.
- Adding booster doses to the country immunization schedule depends upon the local national situation.
- For newborns aged <2 months, culture specimens need to be improved. wP vaccine can be given as early as 6 weeks of age. This recommendation should be reinforced during outbreaks, particularly when younger newborns are being reported as cases, while making every effort to obtain the best specimens possible.

Research:

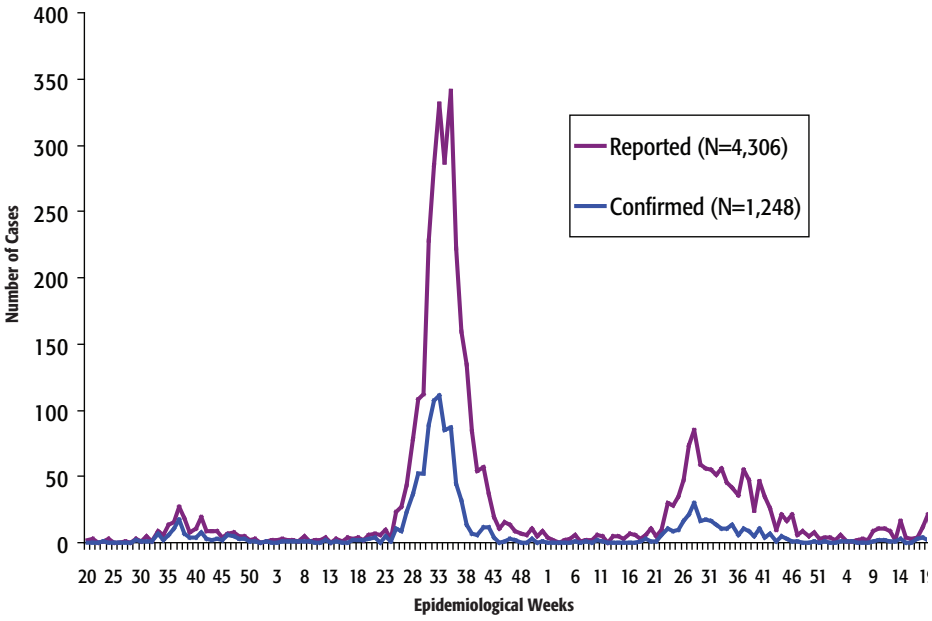
- It was noted by the group that the role of asymptomatic carriers seems more hypothetical than real, but this needs continued evaluation.
- Vaccination in pregnant mothers was discussed and the group felt more research is required before a general recommendation is made.

Figure 1. Pertussis Cases and DTP3 Coverage, The Americas, 1978-2006



Source: Country reports to Immunization Unit, PAHO.

Figure 2. Epidemiological Curve of Reported and Confirmed Pertussis Cases, Epidemiological Week 20, 2004 to 23, 2007, Neuquén Province, Argentina



Source: Immunization Program, Direction of Epidemiology, Ministry of Health, Neuquén Province, Argentina.

Summary

The group felt that more emphasis should be placed on outbreak investigation and research. The topic will be re-visited at PAHO's next TAG. ■

Rotavirus Vaccines

The rotavirus vaccine is one of the new vaccines being introduced by immunization programs. Since 2006, two vaccines are approved by the National Regulatory Agencies of their manufacturers' country of origin: Rotarix (GlaxoSmith-Kline) and Rotateq (Merck). Both vaccines are now available for sale.

As part of its policy for support to new vaccine introduction, the Immunization Unit of the Family and Community Health Area of the Pan American Health Organization, recommends that countries take all the required steps prior to vaccine introduction so that national immunization programs are successful in incorporating other biologicals.

Faced with the decision to include the rotavirus vaccine in their immunization schedules, countries will have the choice between two available vaccines. The decision must be taken by countries since current data don't allow an express recommendation of one vaccine over the other. To help countries in the decision-taking process, Table 1 summarizes some of the characteristics of both vaccines. ■

Table 1. Characteristics of the Available Rotavirus Vaccines

Vaccine	Rotarix	Rotateq
Manufacturer	GlaxoSmithKline	Merck
Composition	G1 P[8]	G1, G2, G3, G4 P[8]
Number of Doses	2	3
Recommended Vaccination Age	• Preferable to complete schedule before age 16 weeks • First dose: Age 6 weeks minimum • Maximum Administration Age: 24 weeks	• Complete the schedule between age 6-32 weeks • First dose: Age 6-12 weeks • Maximum Administration Age: 32 weeks
Interval Between Doses	Minimum 4-week Interval	Recommended Interval: 4-10 weeks
Mode of Administration	Oral	Oral
Presentation	Lyophilized	Liquid
Cold Chain Space	• Box of 10 doses: 1,560.0 cm^3 (1 child with complete schedule: 312.03 cm^3) • Box of 1 dose: 259.8 cm^3 (1 child with complete schedule: 519.60 cm^3)	• Box of 10 doses: 798.0 cm^3 (1 child with complete schedule: 239.40 cm^3)
Conservation in Cold Chain	2°C – 8°C	2°C – 8°C
Efficacy*	Demonstrated in clinical studies	Demonstrated in clinical studies
Effectiveness	Study in process	Study in process
Serious Adverse Events	Not demonstrated in clinical studies	Not demonstrated in clinical studies
WHO Prequalification	Yes	Probably December 2007
Price	Revolving Fund: US $7.50 per dose	Revolving Fund: not established yet

* Currently it is not possible to compare efficacy levels of both vaccines due to methodology differences in available studies.

PAHO's Revolving Fund: Doing More With Less

In November 2007, managers of the Expanded Program on Immunization (EPI) from Caribbean countries met in Tobago for their 24th annual meeting. The main objectives of the meeting were to share experiences and lessons learned and provide updated information on relevant technical and programmatic topics. One topic of particular importance was the Pan American Health Organization (PAHO) Revolving Fund for vaccine procurement. A presentation highlighted the results of recent assessments of the Revolving Fund and the supply chain of vaccines to PAHO member countries. Later, EPI managers issued a declaration in favor of sustaining immunization programs in the Region of the Americas.

The Revolving Fund

PAHO's Revolving Fund has nearly 30 years experience serving countries to ensure a supply chain of safe, affordable vaccines that is linked simultaneously with high-quality technical assistance. This stable vaccine supply chain has been critical for countries of the Caribbean to achieve their disease reduction targets of polio eradication and measles and rubella elimination, and add new vaccines into immunization schedules.

Results of recent assessments of the Revolving Fund and the supply chain of vaccines highlighted operational errors, in particular those involving on-time shipment, purchase orders, and payment of orders. The studies identified strengths in cold chain adequacy, including adequate overall capacity, but weaknesses in terms of better forecasting of capacity for new vaccine introduction. Strengths of the vaccine distribution system included a national plan for distribution, but weaknesses were that the plan is not necessarily implemented. Also, inventory procedures such as limits for minimum and maximum inventory need to be set, and inventory forms must be systematically used and analyzed. Weaknesses in control of vaccine wastage were that lost quantities are often not recorded, data are insufficient to analyze vaccine consumption, and quantities of vaccine received and used are not often reconciled.

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Reported Cases of Selected Diseases, 2005-2006

Number of reported cases of pertussis, diphtheria, tetanus, neonatal tetanus (NNT), and mumps

Country	Pertussis		Diphtheria		Tetanus (Non-NNT)		Neonatal Tetanus		Mumps	
	2005	2006	2005	2006	2005	2006	2005	2006	2005	2006
Anguilla	…	0	…	0	…	0	…	0	…	0
Antigua and Barbuda	0	0	0	0	0	0	0	0	0	0
Argentina	2,060	1,607	0	0	14	5	0	0	10,727	11,461
Aruba	…	…	…	…	…	…	…	…	…	…
Bahamas	0	0	0	0	0	0	0	0	0	0
Barbados	…	0	…	0	…	0	…	0	…	0
Belize	0	0	0	0	0	1	0	0	30	24
Bermuda	…	0	…	0	…	0	…	0	…	0
Bolivia	1	6	0	0	15	8	5	2	0	…
Brazil	1,328	797	27	9	420	444	10	8	…	…
Canada	2,231	1,945	0	0	4	2	0	0	83	37
Cayman Islands	…	0	…	0	…	0	…	0	…	1
Chile	1,213	1,285	0	0	8	7	0	0	1,579	1,494
Colombia	139	233	1	0	72	59	9	4	2,366	2,243
Costa Rica	7	1,037	0	0	0	1	0	0	46	…
Cuba	0	0	0	0	0	3	0	0	346	882
Dominica	…	0	…	0	…	0	…	0	…	0
Dominican Republic	63	17	39	16	54	65	4	4	…	…
Ecuador	…	23	0	0	16	43	6	4	1,037	0
El Salvador	5	5	0	0	7	5	1	0	488	980
French Guiana	…	…	…	…	…	…	…	…	…	…
Grenada	0	0	0	0	0	0	0	0	0	0
Guadeloupe	…	…	…	…	…	…	…	…	…	…
Guatemala	0	48	0	0	6	6	0	2	1,807	…
Guyana	0	0	0	0	0	0	0	0	0	0
Haiti	496	…	204	260	119	47	71	53	594	…
Honduras	134	138	0	0	19	18	0	0	408	456
Jamaica	8	1	0	0	12	9	0	0	3	2
Martinique	…	…	…	…	…	…	…	…	…	…
Mexico	349	171	0	0	71	50	1	4	8,651	8,322
Montserrat	…	0	…	0	…	0	…	0	…	0
Netherland Antilles	…	…	…	…	…	…	…	…	…	…
Nicaragua	0	148	0	0	8	6	1	0	219	151
Panama	28	132	0	0	1	3	0	0	203	205
Paraguay	13	6	0	0	17	9	2	2	148	234
Peru	127	84	0	0	44	28	2	4	…	0
Puerto Rico	…	…	…	…	…	…	…	…	…	…
Saint-Kitts & Nevis	0	0	0	0	0	0	0	0	0	0
Saint-Lucia	…	0	…	0	…	0	…	0	…	1
Saint-Vincent and the Grenadines	0	0	0	0	0	0	0	0	0	0
Suriname	0	0	0	0	1	0	0	2	0	…
Trinidad and Tobago	0	0	0	0	0	0	0	0	0	13
Turks and Caicos Islands	0	0	0	0	0	0	0	0	0	0
United States of America*	25,616	13,144	0	0	30	22	0	0	314	6,339
Uruguay	0	15	0	0	1	2	0	0	2,193	1,646
Venezuela	836	1,183	1	0	33	34	2	4	3,095	2,935
Virgin Islands (UK)	…	0	…	0	…	0	…	0	…	0
Virgin Islands (US)	…	…	…	…	…	…	…	…	…	…
Total	**34,654**	**22,025**	**272**	**285**	**972**	**877**	**114**	**93**	**34,337**	**37,426**

* USA 2006 data are provisional … - Not available NA - not applicable Updated: 16 January 2008

Source: Country reports to Immunization Unit, PAHO.

DECLARATION from page 6

The plan of action to address deficiencies was discussed. For inventory management issues, countries should access software being promoted by WHO and UNICEF, as well as revitalize their overall inventory management systems. For vaccine distribution countries were asked to evaluate their freezing problems, share these experiences with other countries, and consider the use of Freeze-Tags. All this issues should be addressed in the country assessments routinely conducted by Ministries of Health with support from PAHO.

The Tobago Declaration

Signed by all EPI managers of the Caribbean, the Tobago Declaration (see box at right) notes the remarkable achievements obtained by countries of the Americas in the fight against vaccine-preventable diseases, and the need to introduce new vaccines. The declaration further highlights the crucial role played by PAHO's Revolving Fund in promoting Pan Americanism. ■

Tobago Declaration for Sustaining Immunization Programmes in the Region of the Americas

The 24th Caribbean EPI Managers' Meeting in Tobago, 2007:

Noting:

- The historic achievements of the Expanded Program on Immunization in the Caribbean and Latin America in eradication of polio, elimination of measles, rubella and its major sequela, congenital rubella syndrome;
- Additionally, the virtual elimination of diphtheria, pertussis, neonatal tetanus; thereby preventing significant morbidity and mortality among children;
- Further, the maintenance of a disease-free status of yellow fever in most of the countries in the endemic zone;
- The simultaneous introduction of vaccines such as hepatitis B and *Haemophilus influenza* type b; further substantially reducing the morbidity and mortality of these diseases;
- The critical need to introduce new vaccines against pneumococcus and human papillomavirus, which cause diseases of substantial public health significance; and

Further noting the tremendous achievements throughout the Americas in improving health by controlling vaccine-preventable diseases.

Recognizing the critical role of the leadership of the countries of the Region in collaboration with the Pan American Health Organization, particularly its stewardship of the Revolving Fund for affordable vaccines, assuring cost-effective and equitable access to all vaccines in concert with the principle of Pan American solidarity.

Urges the governments of the Region to continue their support for this cost-effective mechanism of assuring safe access to safe and timely supplies of affordable vaccines.

Calls upon PAHO to continue to maintain its current model of technical cooperation in the Region in association with the management of the Revolving Fund, which has endured uninterrupted supplies of safe and affordable vaccines.

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

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