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Ad hoc Meeting of Experts on Surveillance of HPV-Associated Disease in the Americas

In October 2006, the Immunization Unit of the Pan American Health Organization (PAHO) convened a two day *Ad Hoc* Meeting of Experts to discuss and advise on the most appropriate and effective strategies for the conduct of human papillomavirus (HPV) surveillance in Latin America and the Caribbean. The meeting's purpose was to determine how HPV surveillance could be operationalized and what supporting information and laboratory systems would be required.

Four PAHO Member States, Brazil, Chile, Costa Rica, and Mexico were represented at this meeting. Experts from McGill University in Canada, the Ludwig Institute in Brazil, the National Cancer Institute and the Centers for Disease Control and Prevention (CDC) in the United States, and the World Health Organization in Switzerland also participated. This abridged report focuses on the salient points emerging from the meeting.

Dr. Carlos Castillo-Solórzano, Acting Chief, Immunization Unit, opened the meeting and Dr. Jon Andrus, Lead Technical Advisor on Immunization, chaired the proceedings. In his opening address, Dr. Castillo-Solórzano briefly summarized the key facts in relation to the epidemiology of cervical cancer in Latin America and the Caribbean and reviewed the important elements of PAHO's technical cooperation activities with its Member States in relation to new vaccine introduction. He noted that HPV vaccine introduction presents multiple and unique challenges when compared with other vaccines currently used. Some of these included the following: (1) HPV vaccines are being targeted to non-traditional EPI age groups; (2) proposed HPV surveillance systems cannot be based on the observation of early clinical signs and symptoms, such as a fever and rash in the case of measles; (3) the vaccine impact will not be immediately observable; and (4) the need for consensus-building across a very wide spectrum of stakeholders.

A Snapshot of Country Perspectives

During this meeting, the CDC representative gave an outline of the developing US perspectives on HPV surveillance including its purposes, the endpoints being considered for monitoring vaccine impact, some identification of potential information sources and the associated challenges. The representatives from Brazil, Chile, Costa Rica, and Mexico shared some of their perspectives regarding HPV vaccine introduction. The Mexican representative indicated that they had already initiated internal discussions around the issue of HPV vaccine and had noted that vaccine cost would be a key determinant of their introduction plan. She emphasized that because reducing inequities in health was an important goal for Mexico, direct vaccination of most vulnerable groups with lowest human development index was being given priority consideration. It was envisaged that HPV vaccination could be initially introduced in the 50 poorest municipalities for adolescents up to age 17 years, with subsequent expansion to other poor regions. She also noted that the treatment and follow-up of cytologically screened positive women in the Social Security sector had become more focused as these services were now guaranteed free of charge.

The Costa Rican representative indicated that the national cervical cancer screening program in that country was functioning effectively and that it had resulted in a reduction in the incidence and mortality of invasive

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SIGN and TechNet21 Meetings

The annual SIGN and the 9th TechNet21 meetings were held back to back in October 2006 in Mexico. Both events were organized by the World Health Organization, which serves as the global secretariat for both networks, and co-hosted by the Ministry of Health of Mexico and PAHO. With the assistance of Mexico's National Center for Excellence in Health Technology (CENETEC), both meetings were webcasted for the first time. Partner agencies such as UNICEF and PATH also provided key assistance.

Both meetings provided opportunities for the exchange of ideas between the public and private sectors. It also facilitated a closer collaboration toward the common goal of ensuring the quality, safety, and efficiency of new technologies related to immunization.

SIGN Meeting

The SIGN meeting took place from 24-26 October with participation from more than 51 countries. The objectives of the meeting were to promote injection safety, the protection of health workers, the rational use of injections, improved waste disposal, and the introduction of new technologies.

Representatives from Bolivia, Brazil, Colombia, Honduras, and Mexico were present at the meeting. Bolivia presented its experience with 2 IMMUNIZATION NEWSLETTER > VOLUME XXVIII, NUMBER 6 > DECEMBER 2006

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SIGN Safe Injection Global Network

Safe Injection Global Network (SIGN)

Unsafe injection practices are increasingly recognized as a major source of infection with bloodborne pathogens. The SIGN alliance is a voluntary coalition of stakeholders aiming to achieve safe and appropriate use of injections. For more information on SIGN, see http://www.who.int/injection_ safety/sign/en/.

The 2006 SIGN meeting produced a number of relevant recommendations in the areas of integrated infection control strategies, health care workers safety, injection safety, quality and access to safe injection devices, and waste management. A full copy of the report will be available shortly at http://www.who.int/injection_safety/sign/meetings/en/ index.html

waste management during the recent rubella elimination campaign (May-June 2006). Brazil presented on hepatitis B immunization among health care workers. Colombia presented the study conducted on the reuse of single-use medical devices. Honduras shared its experience on vaccination safety. The details of these reports can be found on the website (see box above).

PAHO gave an overview of its Regional Plan for Quality Control and Safety of Syringes, a collaborative activity between the Essential Medicines, Vaccines, and Health Technology Unit and the Immunization Unit. The plan's main objective is are to ensure the quality and safety of products used by Regional immunization programs, from procurement to final disposal, including storage, distribution, and use. (1)

TechNet21 Meeting

The TechNet21 meeting was held from 26-27 October with 130 participants in attendance who shared their experiences in the areas of vaccine management, equipment management, and integration of support systems. A session on research provided information on new technologies such as less heat/freeze sensitive vaccines, aerosol administration of measles vaccine, and intra-dermal jet injection.

PAHO made two presentations on behalf of the Region of the Americas. The first was a regional overview of current priorities. One priority is to review the PAHO Revolving Fund's supply chain and its plan of action envisioned for 2007 to "do more with less" by reducing costs and improving services to member countries. Another priority is to examine the critical role of the cold chain in the supply chain in terms of warehousing, distribution, and utilization.

PAHO's second presentation was an overview of the impact of rotavirus vaccine introduction on cold chain equipment needs in Brazil, Panama, and Venezuela during 2006. The presentations highlighted the challenge of working with countries and suppliers to anticipate the impact new vaccines will have on cold chain capacity.

Conclusion

Participants in the SIGN and TechNet21 meetings recommended that the "back-to-back" format be maintained as it encourages the exchange of experience between both communities of experts. Participants also acknowledged that the wide distribution of information via the Internet was useful and asked that it be repeated in the future. In the case of the TechNet21 meeting, the information was sent via its network to more than 1,000 users who, although they could not attend, were able to benefit from the meeting.

UNICEF and other partners expressed interest in the incident reporting system implemented by PAHO. The system reports problems related to quality of syringes and other products purchased through the PAHO Revolving Fund. Staff from the Immunization Unit and the Essential Medicines, Vaccines, and Health Technology Unit provided a short briefing about the system that was created on PAHO's SharePoint site.¹ Objectives of the incident reporting system site are to provide a forum for information on quality and safety issues, conduct follow-up and monitoring of incidents, disseminate alerts, and serve as a repository for product information for

the benefit of EPI personnel.

Reference:

1. Pan American Health Organization. Regional Plan for Quality Control and Safety of Syringes. *Immunization Newsletter* 2005; 28(5).

Technical Network for Strengthening Immunization Services (TechNet21)

The Technical Network for Logistics in Health (TechNet) was first established in 1989 to provide updates in technology to a professional network of logistics experts and immunization professionals who are involved in the management of immunization and other primary health care operations at the country and international levels. In 2001, its name was updated to Technical Network for Strengthening Immunization Services, to reflect its widening audience. Its acronym was changed to TechNet21. TechNet21 serves as a forum for experts to discuss ways to improve immunization services. Members of the forum meet every 18 to 24 months to share their experiences and information. For further information, see http://www.technet21.org/

The 2006 TechNet21 meeting produced a number of relevant recommendations in the areas of vaccine management, equipment management, integration of support systems, and research. A full copy of the report is available at http://www.technet21.org/Mexico/TechNetMexicoMeet-ingReport2006.pdf.



¹ Share Point is a tool designed to facilitate distance collaboration and information-sharing through the web.

HPV SURVEILLANCE from page 1

cervical cancer and in the increased detection of pre-cancerous lesions. He noted that Costa Rica was considering HPV vaccine introduction for women aged 10-25 years before initiation of sexual activity.

Both Brazil and Chile indicated that HPV vaccine introduction was being considered in their respective countries and that cost-effectiveness studies were being planned. The Brazilian representative noted that although universal vaccination coverage is the preferred goal of that country, HPV vaccine may have to be considered as a special antigen for risk populations given the current high vaccine prices. She commented that it would be prohibitively expensive to vaccinate the 26 million women, aged 9-26 years, for whom the vaccine has been approved in Brazil.

HPV Surveillance

1. Objectives

The main objectives of HPV surveillance were defined as follows:

- To gather baseline data for assessing the pre-vaccine disease burden and compiling the evidence for informed decision-making regarding HPV vaccine introduction;
- To monitor the impact and effectiveness of HPV vaccine introduction; and
- To determine whether or not policy changes may be indicated.
- 2. Endpoints of interest for surveillance

Given the wide spectrum of disease associated with an HPV infection and the experience using

some of the endpoint indicators of vaccine efficacy in the clinical vaccine trials, it was agreed that the discussion on endpoints for surveillance would be focused on the six variables outlined in Table 1. Given that both vaccines will contain the high-risk oncogenic HPV types 16 and 18, the most important common endpoints of interest for monitoring vaccine impact would relate to cervical cancer and its precursor lesions. In those countries where the quadrivalent vaccine is being used, monitoring of genital warts would be important for an impact assessment. Genital warts, however, were considered to be a soft endpoint because many affected individuals are not sufficiently inconvenienced to seek medical care and the real population magnitude of this problem would be underestimated. Additionally, in many countries genital warts are not included in any obligatory national notification of sexuallytransmitted infections.

In addition to the endpoints presented in Table 1, it was recognized that an HPV surveillance system could also include pharyngeal papillomatosis and anogenital cancer. However, a deluxe or topof-the-line model HPV surveillance system would be too costly and too complex for developing countries to sustain over the long term. Countries were therefore advised to adopt and implement those surveillance strategies which were sustainable and affordable for them. The experts reiterated that where financial resources were constrained, limited funds should best be used for enhancing HPV vaccination coverage.

3. <u>Potential important data sources</u> Important data sources for any HPV surveillance

Table 1. Endpoints for HPV Surveillance and Measurement Indicators								
Endpoints	Measurement Indicators							
Genital HPV infections	Changes in prevalence							
Genital warts (depends on vaccine product being used)	Changes in prevalence							
Cervical cancer precursors, specifically CIN 3* based on histological determination	Changes in the overall prevalence							
Invasive cervical cancer based on histological determination	Changes in the incidence profiles							
Invasive cervical cancer mortality	Changes in mortality profiles							
HPV type-specific changes in histologically-defined CIN 3* lesions	Changes in type-specific incidence in CIN 3* precursor lesions							
* Cervical Intraepithelial Neoplasia Grade III								

system were identified and included the following:

- National, sub-regional, and regional laboratories that will participate in the Global HPV laboratory network;
- Colposcopy and other hospital-based or clinic services to which women are referred for diagnostic evaluation of an abnormal Papanicolaou smear (Pap smear) result and where histologic results are generated;
- National registries which capture all cases of histologically-defined cervical intraepithelial neoplasia Grade III (CIN 3);
- Cancer registries, where they exist, to provide data on the changing cervical cancer incidence;
- National vital registration systems to provide for data on changing cervical cancer mortality data; and
- HPV vaccine registers as a means to link vaccination status to future disease outcomes.

Because costs and complicated laboratory support for continuous monitoring of a slowly evolving condition presented challenges, case-control study methodology is an important and viable alternative for assessing vaccine effectiveness.

Other important points emerging from the discussions are presented below:

- Given the potential complexity and costs of implementing a full range of HPV surveillance strategies, it will not be possible for every country to develop such an expanded complement of surveillance strategies. Instead, it was recommended that some countries, where the capability and infrastructure existed, could undertake some of the more sophisticated elements of a surveillance system, for example, type-specific HPV testing of CIN3 lesions, while others may be able to contribute to another endpoint.
- Neither abnormal Pap smears nor cervical cancer and any of its precursor lesions are legally notifiable in any country in the Americas.
- Some assessment of HPV type-specific changes would be warranted to confirm declines in HPV genotypes contained in the vaccines, as well as to ascertain whether or not the vaccine genotypes are being replaced. The team recommended that this should be a periodic exercise undertaken in a few selected countries.
- The performance characteristics of the Pap smear test, particularly its positive predictive value, will change over time as vaccination coverage increases and there is a concomitant decline in the incidence of cervical cancer and its precursor lesions. Therefore, the use of cy-

tologically-defined endpoints was not recommended, even though it was recognized that cytology registers existed in many countries.

- It is critically important to achieve high HPV vaccination coverage rates in those areas or populations which are underserved with regard to screening. If this is not attained, further inequities will be created as these populations will benefit neither from screening nor from vaccination.
- Serologic assessment of coverage is not currently recommended owing to its costs and the absence of standardized commercially available VLP (vaccine-like particle) assays.

HPV Vaccination and Cervical Cancer Screening

During the meeting, it was repeatedly recognized that surveillance of HPV-associated disease was intimately linked to the national cervical cancer screening programs in countries and that the introduction of HPV vaccine invariably required a re-assessment of existing screening algorithms given issues of costs, cost-effectiveness, and overall program efficiency.

In order to maximize the effect of vaccination and screening for improved cervical cancer control, the expert team recommended the introduction of HPV vaccination approximately three years prior to the median age of sexual debut together with at least two cervical screenings during a woman's lifetime, preferably at 35 and 40 years of age. HPV DNA assays are recommended as primary screening tools, given that viral persistence in older women is a better marker of the risk for developing cervical cancer. Inexpensive, rapid HPV DNA assays will become available within the next 2-3 years and will greatly revolutionize the cervical cancer screening algorithms currently used. Primary and secondary preventive interventions for cervical cancer over the life

Viral persistence and progression Cervix Clearance Clearance HPV-infected Regression HPV Precancer Strategy Proposed Strategy HPV vaccination HPV vaccination

The Natural History of HPV Infection and Cervical Cancer. The peak prevalence of transient infections with carcinogenic types of HPV (blue line) occurs among women during their teens and 20s, after the initiation of sexual activity. The peak prevalence of cervical precancerous conditions occurs approximately 10 years later (green line) and the peak prevalence of invasive cancers at 40 to 50 years of age (red line). (The peaks of the curves are not drawn to scale.) The conventional model of cervical-cancer prevention is based on repeated rounds of cytologic examination, including Papanicolaou smears, and colposcopy (small blue arrows). Alternative strategies include HPV vaccination of adolescents (large beige arrow), one or two rounds of HPV screening at the peak ages of treatable precancerous conditions and early cancer (large reddish-brown arrows), or both.

Source: Schiffman M, Castle PE. The Promise of Global Cervical-Cancer Prevention. N Engl J Med 2005; 353;20:2101-2104. Copyright © 2005 Massachusetts Medical Society. All rights reserved. Adapted with permission, 2006.

course are depicted in Figure 1.

Based on this consultation, PAHO's Immunization Unit will continue to develop and pilot-test some prototype HPV surveillance systems for use in Latin America and the Caribbean.

Presidential Leadership Award from Women in Government

On 18 November, Women in Government, an organization of women state legislators in the United States, presented its Presidential Leadership Awards to individuals and groups that are advancing efforts to eliminate cervical cancer worldwide. The ceremony was held in Washington, D.C., during the Women in Government's summit on cervical cancer and HPV vaccine.

As one of the award recipients, the Pan American Health Organization (PAHO) was recognized because of its work in the Americas, which has helped improve cervical cancer screening rates and increase access to lifesaving technologies such as HPV vaccines. In addition to eight distinguished individuals, Women in Government also recognized the Bill and Melinda Gates Foundation and the National Breast and Cervical Cancer Early Detection Program, a program affiliated with the U.S. Centers for Disease Control and Prevention. Accepting the award on behalf of PAHO, Dr. Jon Andrus, the lead technical advisor of the Immunization Unit, said "It's not just about having a vaccine that can prevent cervical cancer. The challenge of national immunization programs around the world is to deploy this important lifesaving technology to those women who need it most. The problem is that 80 percent of women who die of cervical cancer are generally poor and live in underserved areas, and will be the ones to benefit most as we work hard to create affordable prices and access to this vaccine for them."

The International Agency for Research on Cancer estimates that more than 37,600 deaths due

Figure 1. Integration of HPV Vaccination with Screening

PAN AMERICAN HEALTH ORGANIZATION

to cervical cancer occur annually in the Region. The organization has therefore developed an HPV vaccine introduction plan that includes the following steps:

- Building political will through advocacy;
- Disseminating relevant information and knowledge in order to support evidencebased decision-making;
- Encouraging or conducting relevant research, such as economic analyses and acceptability studies:
- Designing surveillance systems and tools;
- Mobilizing cross-sectional support through effective social marketing and communication; and
- Mobilizing the essential financial and technical resources to facilitate HPV vaccine introduction.



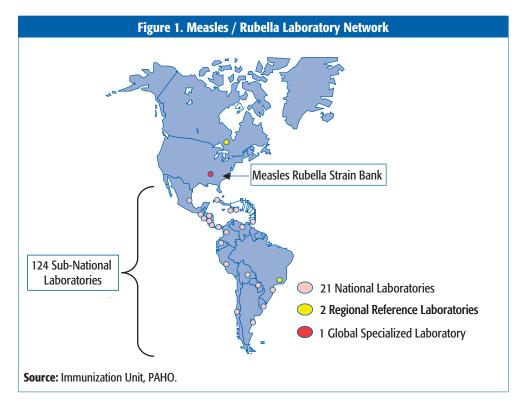
Dr. Andrus and Dr. Merle Lewis, Regional Advisor, Immunization Unit, receiving the Presidential Leadership Award on behalf of PAHO. Standing to the left is Dr. Donnica Moore, a women's health expert who served as the event's emcee. Standing to the right is Susan Crosby, President of Women in Government.

Photo: Marty Lavor

Measles and Rubella Laboratory Network in the Region of the Americas

The Measles/Rubella Laboratory Network continues to be fully functional in support of measles and rubella surveillance in the Region of the Americas. The network was established in 1995 and has been providing crucial information to confirm or discard suspect cases, identify circulating virus strains, and evaluate the impact of mass campaigns activities. Laboratory

analyses include IgM and IgG antibody detection, virus isolation, detection of viral nucleic acid, and molecular characterization. The Measles/Rubella Laboratory Network is composed of 21 national laboratories, 124 sub-national laboratories, 2 regional reference centers, and 1 global specialized laboratory (Figure 1). The main activity of national and sub-national laboratories



is to test specimens from suspect measles/rubella cases by IgM ELISA. Some national laboratories are also responsible for virus isolation and quality control of sub-national laboratories.

To improve virologic surveillance, nine national laboratories were trained on virus isolation and detection in 2005. This was done by conducting supervisory visits and holding a regional workshop. For 2007, the goal is to increase the number of laboratories performing virus isolation/detection in the Region from 11 laboratories to 18. The regional reference laboratories are responsible for the validation of IgM tests results of the national laboratories. Regional reference laboratories also assist in ruling out measles/ rubella cases with possible false-positive or indeterminate results by using additional tests for other febrile rash illness, virus isolation and genotyping. In addition to tasks performed by regional laboratories, the global specialized laboratory distributes the proficiency panels to the national laboratories and validates new methods for network capacity-building through training and courses. The global reference laboratory is also responsible for the bank of measles/rubella virus strains isolated in the Region.

False Positive Results

Currently, the main challenge for the Measles/ Rubella Laboratory Network is dealing with sporadic cases of "false positive results", particularly for suspect cases with no travel or vaccine history. As the disease becomes less common due to high vaccine coverage and active surveillance for rash illness and fever, the positive predictive value of laboratory test will diminish, resulting in an increased number of false positive results. Parvovirus B19, human herpes virus 6 and 7, and cytomegalovirus may be clinically misdiagnosed as measles and rubella and their antibodies can cross-react with measles/rubella IgM tests, giving false-positive results.

An in-depth discussion can be found in the second edition of Recent Advances in Immunization, in the chapter entitled Interpretation of Measles and Rubella Serology. A key message in this chapter is that the clinical, epidemiologic, and laboratory data are equally important to decide the final case classification.

Quality Assurance

In the Region of the Americas, an accreditation process was implemented at the end of 2005. The process requires annual evaluation of a laboratory, using timeliness and quality indicators. The accreditation is essential for documenting the quality of the laboratory network. An annual proficiency test is administered to ensure the reliability and quality of serological work performed in the national and regional laboratories. In 2005, the overall proficiency test score of the network was 100%. For 2006, 20 out 23 laboratories reached the score of 100%. In 2006, 70% of national laboratories received an on-site visit and fulfilled the criteria needed to for accreditation.

A standardized, well validated assay for IgM detection is used in all national and regional laboratories since 2005, ensuring data quality and comparison of results within the network. PAHO is providing support to ensure that the laboratory network has adequate supplies and equipment. PAHO also promotes training activities, research, quality assurance, accreditation, data management, and the use of laboratory indicators.

Recommendations

Although considerable progress has been made in ensuring access to quality services throughout the laboratory network, further efforts are needed to improve virologic surveillance. Logistical problems due to shipping of infectious samples must also be resolved since they represent a major obstacle for transporting the specimen to regional laboratories or the specialized laboratory.

Genetic data for rubella virus circulation in the Region needs continued support. Samples for virus isolation must be obtained from every chain of transmission and from all congenital rubella syndrome cases in the first six months of life. If genetic information regarding circulating genotypes is enhanced, molecular epidemiologic data will help to document viral transmission pathway, classify cases, and confirm the elimination of endemic transmission.

The Paramaribo Declaration

At their 23rd Annual Meeting in Suriname from 13-17 November 2006, the Caribbean EPI Managers:

Acknowledging that the 2007 Cricket World Cup is a highly important event for the Caribbean countries:

Recognizing the tremendous progress made in the subregion in immunization and the importance of protecting the achievements, including the eradication of poliomyelitis and the elimination of indigenous measles, and rubella, and congenital rubella syndrome;

Acknowledging that poliomyelitis, measles and/or other vaccine-preventable diseases are endemic in other Regions of the world and are still endemic in many of the countries participating in the 2007 Cricket World Cup;

Realizing the health implications of this event and the high risk of poliomyelitis, measles, and rubella virus importations into the Caribbean subregion;

Recognizing that vulnerable high-risk groups still remain in the subregion and that national immunization programmes face many challenges due to this event;

Acknowledging that highly effective tools, such as surveillance and vaccination, exist and should be enhanced prior, during, and after this event: and

Caribbean have developed preparedness plans for disease surveillance and outbreak containment, focusing on vaccine-preventable diseases.

1. Accordingly declare that:

- a) It is critical to intensify epidemiological surveillance and appropriate vaccination activities for all susceptible local populations:
- b) Political commitment is necessary and should be translated into tangible resources to guarantee the implementation of surveillance plans and maintenance of high vaccination coverage;
- c) Health care workers in the public and private sectors at all levels of the system should be alerted to the possibility of importation of measles, rubella, poliomvelitis, and other infectious diseases not commonly seen in the subregion;
- d) Personnel and volunteers from the health, tourism, sports, and transportation sectors should be immune to poliomyelitis, measles, and rubella before the arrival of cricket world cup participants because, in the event of an importation, such personnel, if susceptible, may serve as transmission agents because of their frequent contact with the general public.

- Recognizing that the host countries of the 2. In this context, the Caribbean EPI Managers acknowledge the excellent support provided by PAHO to Member States and gratefully request that:
 - a) PAHO accelerate communications with WHO and other partners to help advise that every visitor coming from outside the Region to participate in the 2007 Cricket World Cup:
 - i. Be immune against poliomyelitis, measles, and rubella prior to arrival at the Cricket World Cup in the Caribbean; and, when appropriate.
 - ii. Be advised to receive poliomyelitis- and/or measles/rubella-containing vaccines, ideally at least two weeks before departure from their country if there is no vaccination card available or written proof of vaccination. This time is required for a newly vaccinated person to develop protection.
 - b) Effective coordination and commitment be provided by all levels of society, including the local, national, subregional, regional, and global levels to maintain the achievements of the Americas, which is a high priority for all countries of the Region; and
 - c) This declaration be further referred to as "The Paramaribo Declaration."

Paramaribo, Suriname, 17 November 2006.

Reported Cases of Selected Diseases, 2004-2005 Number of reported cases of measles, rubella, congenital rubella syndrome (CRS), poliomyelitis, tetanus,

diphtheria, and whooping cough

Country	Measles Confirmed			Rubella Confirmed		CRS		Poliomyelitis		Tetanus Non-Neonatal Neonatal				Diphtheria		Whooping Cough	
	2004	2005	2004	2005	2004	2005	2004	2005	2004	2005	2004	2005	2004	2005	2004	2005	
Anguilla	0	0	0	0			0	0									
Antigua & Barbuda	0	0	0	0	0	0	0	0	0	0	0	0	0	0		0	
Argentina	0	0	6	0	0	0	0	0	25	14	0	0	0	0	976	2060	
Aruba																	
Bahamas	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Barbados	0	0	0	0			0	0	0		0						
Belize	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Bermuda	0	0	0	0			0	0	0		0		0	0	0		
Bolivia	0	0	12	8	0	0	0	0	29	15	4	5	2	0	6	1	
Brazil	0	6**	319	233	16	4	0	0	463	420	14	10	15	27	1146	1328	
Canada	7*	6**		320	1	1	0	0	2	4	0	0	1	0	2697	2231	
Cayman Islands	0	0					0	0	0		0						
Chile	0	0	3	47	0	0	0	0	10	8	0	0	0	0	1059	1213	
Colombia	0	0	45	85	0	5	0	0		72	8	9		1	25	139	
Costa Rica	0	1	0	0	0	0	0	0	0	0	0	0	0	0	13	7	
Cuba	0	0	18	0	0	0	0	0	0	0	0	0	0	0	0	0	
Dominica	0	0	0	0	0		0	0	0		0						
Dominican Republic	0	0	7	6			0	0	49	54	5	4	122	39	53	63	
Ecuador	0	0	79	0	0	0	0	0	4	16	12	6	0	0	0		
El Salvador	0	0	1	0	0	0	0	0	7	7	1	1	0	0	1	5	
French Guiana																	
Grenada	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Guadeloupe	0	0															
Guatemala	0	0	36	4	2	1	0	0	3	6	1	0	0	0	391	0	
Guyana	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Haiti	0	0	3	0		0	0	0	0	119	33	71	37	204	44	496	
Honduras	0	0	1	0	0	0	0	0	13	19	1	0	0	0	104	134	
Jamaica	0	0	0	0	0	0	0	0	11	12	0	0	0	0	5	8	
Martinique																	
Mexico	64	6**	699	38	5	1	0	0	68	71	4	1	0	0	137	349	
Montserrat	0	0					0	0	0								
Netherland Antilles																	
Nicaragua	0	0	6	47	0		0	0	5	8	0	1	0	0	0	0	
Panama	0	0	0	0	0	0	0	0	2	1	1	0	0	0	12	28	
Paraguay	0	0	1	2	1	0	0	0	12	17	5	2	4	0	40	13	
Peru	0	0	1759	3672	1	7***	0	0	52	44	4	2	0	0	201	127	
Puerto Rico																	
Saint Kitts & Nevis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Saint Lucia	0	0	0	0	0		0	0	0		0						
St. Vincent/Grenadines	0	0					0	0	0	0	0	0	0	0	0	0	
Suriname	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	
Trinidad & Tobago	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	
Turks and Caicos	0	0	0	0	0		0	0	0	0	0	0		0		0	
United States of America	37†	66**	10	11	1	1	0	0	34	30		0	0	0	25827	25616	
Uruguay	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	
Venezuela	0	0	96	823			0	0	35	33	0	2	0	1	715	836	
Virgin Islands (US)																	
Virgin Islands(UK)	0	0	0	0			0	0	0								
Regional Total	108	85	3102	5296	27	20	0	0	825	972	93	114	181	272	33452	34654	

* Due to importation

*** plus 10 congenital rubella infection ... no data

** 2005 imported/related to importation: Brazil, 6 cases; Canada, 4 cases; Mexico, 6 cases; USA, 25 cases. † 23 imported cases

Source: Country Reports to Immunization Unit, PAHO.

Recent Advances in Immunization

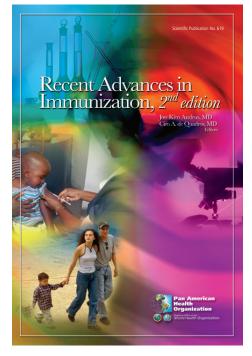
The second edition of *Recent Advances in Immunization* was launched this month during a press conference held at the National Press Club in Washington, D.C. The new publication "provides the strategies and tactics to help us reach the goals of sustaining our immunization achievements and reaching the people who have not benefited from existing and new vaccines," according to Dr. Jon K. Andrus, Lead Technical Advisor with the Immunization Unit and one of the book's two editors.

Dr. Ciro de Quadros, Director of International Programs at the Sabin Vaccine Institute and the other editor, adds that the publication "is a very timely book with details on some new vaccines that haven't been introduced yet. We are witnessing great advances in science and technology but not all mankind is benefiting from them. We hope this book will help make these new technologies available."

The progress of immunization in the Region of the Americas has been extraordinary. However it has also been uneven. While diseases have been eradicated or eliminated, some countries still have a significant proportion of their populations living in districts where coverage remains below 95%, putting them at risk for outbreaks. In addition, countries must consider the introduction of new or underutilized vaccines (against pneumococcus, human papillomavirus, rotavirus, and influenza). Indeed, challenges remain that are driving immunization programs to move from child to family immunization.

Recent Advances in Immunization is intended to be a reference for national immunization managers and other health professionals such as public health, medicine, and nursing students, epidemiologists, and surveillance experts. The topics covered range from adolescent and adult immunization to combination vaccines for childhood immunization, optimal use of BCG vaccine, vaccination safety, interpretation of measles and rubella serology, preparing for the influenza epidemic, introduction of new and underutilized vaccines, and prophylactic human papillomavirus vaccines.

The publication was published in English but will also be translated into French, Portuguese, and



Spanish. For more information on how to obtain a copy, please visit the PAHO Publication webpage at www.paho.org/english/DD/PUB/pub-Home.asp. ■

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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