



Immunization Newsletter

Pan American Health Organization

VOLUME XXIX, NUMBER 2 ► APRIL 2007

- 1 AFP Surveillance in Canada
- 1 EPI Evaluation in Uruguay, 2006
- 6 Human Hookworm Vaccine Initiative
- 7 Update on Pro-Vac Initiative
- 8 Pan American Games & Rubella Alert

AFP Surveillance in Canada

Elimination of indigenous wild poliovirus transmission was certified in Canada and the rest of the Region of the Americas in September 1994. However, until global eradication of poliomyelitis is achieved, Canada recognizes there is an ongoing risk for importation of wild polioviruses.[1] Therefore, Canada maintains an acute flaccid paralysis (AFP) surveillance system with the overall goal to ensure prompt investigation of AFP cases to rule out poliovirus infections, in keeping with recommendations from the World Health Organization (WHO).[2] This article describes the results of AFP surveillance for 2006 in Canada and highlights challenges.

Methods

Canada's AFP case definition includes any patient aged <15 years with onset of focal weakness or paralysis characterized as flaccid (reduced tone) without other obvious cause (e.g., trauma). Key surveillance indicators are based on WHO quality assurance criteria. They are as follows:

- 1) Sensitivity of surveillance: The ability to detect at least one case of non-polio AFP (including Guillain-Barré Syndrome/GBS) per year for every 100,000 children aged <15 years;
- 2) Stool specimen collection from AFP cases: The collection of adequate stool specimens for poliovirus examination from at least 80% of AFP cases within 14 days of paralysis onset; and
- 3) Case follow-up: Follow-up exam conducted at least 60 days after paralysis onset to verify the presence of residual paralysis in at least 80% of AFP cases.

Canada's AFP surveillance systems consists of two complimentary pediatric surveillance networks actively monitoring for AFP cases in children aged <15 years. One is hospital-based and the other is pediatrician practice-based. The IMPACT (Immunization Monitoring Program, ACTive) hospital-based sentinel network consists of twelve pediatric tertiary care centers where AFP surveillance began in 1991. The Canadian Paediatric Surveillance Program (CPSP) consists of a over 2,300 pediatricians who began supplementing national case detection and documentation in 1996.

Virological investigation of cases includes collection and testing of stool specimens, cerebrospinal fluid (CSF), throat swabs and/or polio-specific serology. Additionally, bacterial culture for *Campylobacter* in stool was

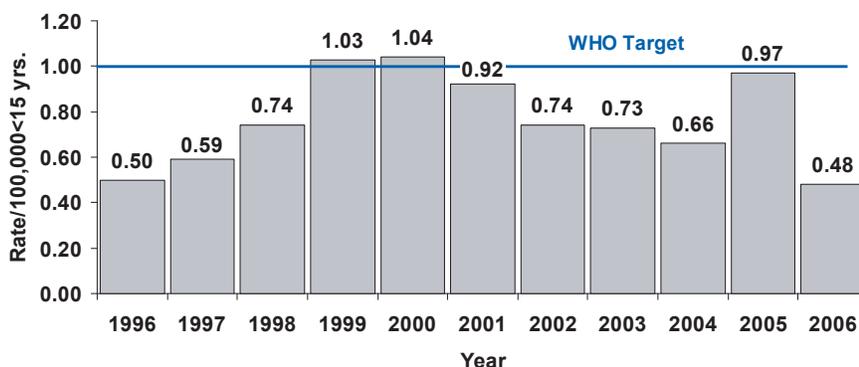
Summary of EPI Evaluation in Uruguay, November 2006

The Pan American Health Organization (PAHO) offers its Member States the opportunity to evaluate their national immunization programs through an international multidisciplinary evaluation of the Expanded Program on Immunization (EPI). The EPI evaluation serves as a tool for monitoring program advances and assessing the degree of development and technical capacity available to face new challenges. The third evaluation of the National Immunization Program (NIP) of the Republic of Uruguay took place from 6-17 November 2006.

Background

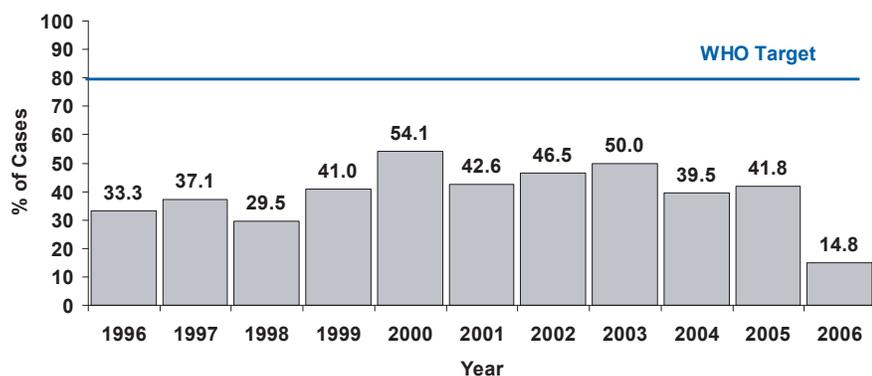
Uruguay has been a pioneer country with regards to vaccine introduction. It was the first country in Latin America to introduce MMR (1982, with a second dose in 1992), Hib (1994), and varicella vaccines (1999). It is also one of the first countries to recommend seasonal influenza vaccine. Currently, Uruguay's routine immunization schedule includes BCG at birth, pentavalent vaccine (DTP-Hib-Hep B) and OPV at 2-4-6-12 months, MMR and varicella vaccines at 12 months, DTP and MMR vaccines at 5 years, and Td vaccines at 12 years, with booster doses of the latter every 10 years. Additionally, influenza vaccine is administered annually in campaigns targeting seniors and children aged 6-23 months. The 23-valent

Figure 1. Non-Polio AFP Detection Rate, Canada, 1996-2006



Source: Immunization & Respiratory Infections Division, Public Health Agency of Canada.

Figure 2. Percentage of AFP Cases with Adequate Polio-Specific Stool Investigation, Canada, 1996-2006



Source: Immunization & Respiratory Infections Division, Public Health Agency of Canada.

added to Canada's AFP surveillance in 2001 to explore possible links between *Campylobacter* infection and GBS. Finally, to assist with case diagnosis, neurological investigation of AFP cases consists of CSF examination, nerve conduction studies, electromyography, MRI, or CT scan.

Results

Non-Polio AFP Detection Rate: During 2006, a total of 77 reports were received through the two pediatric surveillance networks, including 27 AFP cases, 8 excluded reports, and 38 duplicate reports (single events captured two or more times through either network). Six of the eight reports (10%) were excluded based on age >15 years at paralysis onset, and two (3%) based on another obvious cause. The final 27 confirmed cases for 2006 represent a non-polio AFP detection rate of 0.48/100,000 children aged <15 years of age (Figure 1).

Age, Sex, and Immunization Status: In 2006, AFP cases ranged in age from 11 months to 14 years (median 7.4 years). As in previous years, cases reported in 2006 were evenly distributed across age groups. The male-to-female ratio was 1.2:1.0.

Of the 27 AFP cases reported in 2006, 48% had detailed documentation of routine childhood immunization. Eleven of these had received age-appropriate polio immunization with inactivated poliovirus vaccine (IPV). An additional six cases had polio vaccination information reported as "up-to-date", but with no accompanying details. Three cases, who were born or traveled abroad, had documented vaccination with oral polio vaccine (OPV) or a combination of OPV and IPV doses.

Virological Investigation for Polio or Other Enteroviruses: Polio-specific stool testing ap-

pears to be decreasing, with only seven (15%) of cases investigated in 2006 (Figure 2). Of these seven cases, only four were tested for poliovirus or non-polio enterovirus isolation within two weeks of paralysis onset. Two of the cases with stool collected were missing stool specimen collection dates and one had stool collected after two weeks of paralysis onset, when the sensitivity of virus isolation is decreased. There were two instances where stool collection was requested but was not conducted. While there was no positive identification of polioviruses from any of the virological investigations, another viral etiology was identified in three cases (mononucleosis, mycoplasma infection, and influenza B).

***Campylobacter* Investigation:** Testing for *Campylobacter* steadily increased to 24% of AFP cases in 2005. In 2006, investigations increased to 33% of AFP cases and none were positive for *Campylobacter*. Given the short period for this type of investigation and the relatively low number of cases investigated each year, it is not possible to draw any conclusions regarding *Campylobacter* infection and the development of GBS at this time.

Neurological Investigations: The majority of cases (100% in 2006) continue to undergo one or more neurological investigations. Cases are diagnosed based on the clinical and neurological evaluation. Table 1 shows the distribution of diagnosis for AFP reported since 1996. The majority are diagnosed as GBS. In 2006, there were only two diagnoses of transverse myelitis/post-infectious inflammatory myelitis compared to an average of six in previous years (range 2-10). The remaining two other cases included idiopathic Bells Palsy and peripheral neuropathy secondary to mycoplasma infection.

Hospitalization and Outcome: All but one

(96%) of the 2006 AFP cases were hospitalized. The average length of stay was 14 days with a range of 1 to 39 days. Outcome at the time of the initial report was missing for two cases. Of the remaining 25 cases for whom outcome was reported, 5 (20%) had fully recovered, 17 (68%) had partially recovered with residual weakness or paralysis, and 3 (12%) had not recovered but their condition was progressing.

Only one-third of cases (9/27) had the 60-day follow up exam reported. Five of nine had fully recovered, one had residual paralysis, one still has exam pending, and one died.

Discussion

The AFP rate in Canada is below the expected rate (Table 2). Since 1996, the WHO target was met only twice (in 1999 and 2000). However, the number of cases captured multiple times by IMPACT and CPSC was high. In 2006, there was an average of two reports (initial notification report or full case investigation report) for each confirmed case, suggesting a sensitive surveillance based on multiple case detections (capture and re-capture). Late reports may still increase the 2006 detection rate. Nine confirmed AFP cases, with onset in 2005, had case investigation report forms submitted in 2006, the largest ever number of late reports. These late reports elevated the 2005 AFP rate to its highest level within five years (0.97/100,000). Canada's lower than expected AFP rates may be a result of under-detection of cases or, alternatively, they may be a true reflection of lower baseline levels for non-polio AFP in Canada and other developed countries.

Over the past 10 years, the proportion of cases with adequate stool investigation has been consistently below the WHO surveillance target of 80% of cases (Table 2). Surveillance quality could be improved through increased stool sampling and virological testing for polioviruses and non-polio enteroviruses. Given that most AFP cases in Canada are diagnosed as either GBS or transverse myelitis, clinical signs and symptoms consistent with these conditions may favor neurological investigation over virological testing. However, the clinicians participating in AFP surveillance and investigation in Canada are reminded that the importance of polio-specific stool investigations and other virological investigations should not be minimized. Negative results of appropriate polio-specific investigations are as essential as a positive result in AFP case evaluations. Polio-specific laboratory investigations remain vital for WHO-recommended evaluation and documentation of all cases, including those in which poliomyelitis is not being consid-

Table 1. Neurological Diagnosis of AFP Cases, Canada 1996-2006

Diagnosis	Number of Cases (% of total)										
	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Polio	0	0	0	0	0	0	0	0	0	0	0
Guillain-Barré Syndrome	21 (70.0)	29 (82.8)	34 (77.3)	50 (82.0)	49 (80.3)	42 (77.7)	33 (76.7)	33 (75.0)	27 (71.1)	36 (66.7)	23 (85.2)
Transverse myelitis/Post infectious inflammatory myelitis	6 (20.0)	2 (5.7)	6 (13.6)	7 (11.5)	4 (6.6)	8 (14.8)	7 (16.3)	4 (9.1)	7 (18.4)	10 (18.5)	2 (7.4)
Encephalitis/ Encephalomyelitis/ Encephalopathy	1 (3.3)	1 (2.9)	1 (2.3)	0	0	0	0	3 (6.8)	0	2 (3.7)	0
Myelopathy	0	1 (2.9)	0	0	0	0	0	0	0	1 (2.2)	0
Radiculopathy/ Radiculoneuritis	1 (3.3)	1 (2.9)	0	0	0	1 (1.9)	1 (2.3)	0	0	1 (2.2)	0
Other	0	0	0	4 (6.6)	8 (13.1)	3 (5.6)	2 (4.7)	4 (9.1)	4 (10.5)	5 (9.1)	2 (7.4)
Not specified/ Undetermined diagnosis or etiology	1 (3.3)	1 (2.9)	3 (6.8)	0	0	0	0	0	0	0	0
Total	30 (100)	35 (100)	44 (100)	61 (100)	61 (100)	54 (100)	43 (100)	44 (100)	38 (100)	55 (100)	27 (100)

ered as a possible diagnosis. Non-polio viruses that may also cause AFP can be investigated through prompt virological investigation of stool or other clinical specimens.

Reporting of 60-day follow-up status to verify or rule out residual paralysis is below the WHO surveillance target of 80%, reaching only approximately 30% in 2006 (Table 2). Lack of 60-day follow-up information may be related to the timing of report completion and submission, or other factors related to the surveillance and reporting process. Better documentation of 60-day follow-up with observation of any residual paralysis and timely completion and submission of case report forms would strengthen Canada's surveillance and documentation.

Conclusion

Surveillance quality could be improved through increased stool sampling and virological testing for polioviruses and non-polio enteroviruses. In addition, better documentation of 60-day follow-up with observation of any residual paralysis and timely completion and submission of case report forms would strengthen Canada's surveillance and documentation.

While stool-testing rates and 60-day follow-up documentation are below WHO-recommended targets in Canada, polio-compatible disease is ruled out based on alternate diagnoses established through extensive neurological and other clinical and laboratory investigations.

Surveillance partners in Canada are reminded that with re-infection of several previously polio-free countries, including some African countries with close ties to the Americas, constant risk of polio importations remains. All countries, including Canada, must maintain high quality AFP surveillance and high vaccine coverage to prevent re-introduction of wild poliovirus to the Americas. [3] ■

Authors: Jeannette Macey (Acting Head, Disease Surveillance) and Tammy Lipskie (Epidemiologist), Immunization and Respiratory Infections Division, Centre for Infectious Disease Prevention and Control, Public Health Agency of Canada.

References:

1. WHO. Resurgence of wild poliovirus type 1 transmission and effect of importation into polio-free countries, 2002–2005, Weekly epidemiological record, 17 February 2006, No. 7, 2006, 81, 63–68 <http://www.who.int/wer/2006/wer8107/en/index.htm>
2. PAHO. Norms and standards in epidemiology: Guidelines for epidemiological surveillance. Epidemiol Bull Jun 1999; 20(2): 11-3.
3. PAHO. XVII Meeting of the Technical Advisory Group on Vaccine-Preventable Diseases. Final Report, Guatemala, 2006.

Table 2. Canadian Performance in 2006 Compared to Key WHO Performance Targets for AFP Surveillance

WHO Performance Targets	Observed Performance Canada, 2006
One non-polio AFP case per 100,000 children aged <15 years	0.48/100,000
One adequate stool specimen to be collected for poliovirus culture within two weeks of paralysis onset in <u>at least 80%</u> of AFP cases	4/27 (15%)
Follow-up exam conducted at least 60 days after paralysis onset to verify the presence of residual paralysis in <u>at least 80%</u> of AFP cases	8/27 (30%)

URUGUAY from page 1

polysaccharide pneumococcal vaccine is also administered to persons at risk who are covered under the public health system.

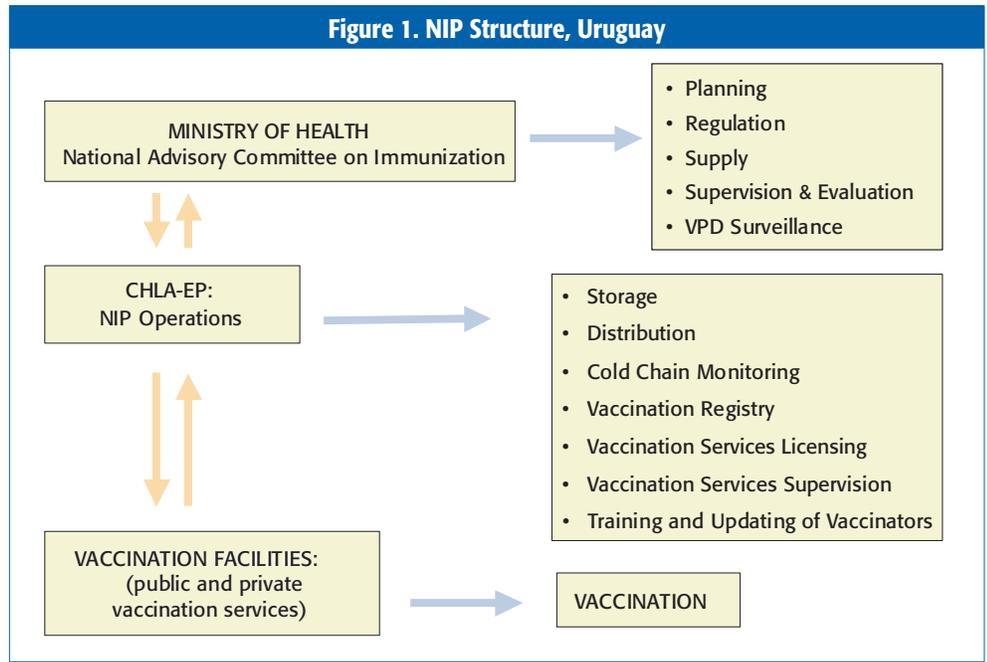
In 1987, a ministerial decree assigned responsibility for NIP implementation to the *Comisión Honoraria para la Lucha Antituberculosa y Enfermedades Prevalentes* (CHLA-EP). CHLA-EP is under the direction of the Ministry of Health and receives technical advice from the National Advisory Committee on Immunization Practices (NACIP).

The NIP is a model of public-private inter-institutional cooperation on three levels (Figure 1): the Ministry of Public Health (MOH), CHLA-EP, and vaccination facilities from the public sector (under the MOH, CHLA-EP, and departmental governments) and the private sector.

Currently, Uruguay is implementing a new health policy focusing on primary health care, preventive interventions, and public/private health care financed by a National Health Insurance Program. This reform aims to introduce universal health access, equity in expenditures and financing, and quality of health services, while restoring the system’s sustainability.

Methodology

The evaluation was conducted following the international multidisciplinary EPI evaluation methodology, consisting of a qualitative and quantitative assessment that incorporates interviews



with key individuals at the political, managerial, and operational levels. This multidisciplinary approach allows for a thorough review of the different components of the immunization program.

Twenty-two persons from the MOH and CHLA-EP and 10 international consultants comprised the evaluation team. Ten of the 19 Departments of Uruguay were selected, accounting for 72% of the total population. A total of 303 individuals were interviewed at political, managerial, operational, and user levels, including staff from 4 agencies.

Main Findings and Recommendations

The main findings and recommendations in the areas of operations and surveillance are presented in Table 1. The evaluators highlighted the following findings as remarkable:

- The NIP receives sustained political commitment backed by a law, which translates into resources that ensure universal and free vaccination.
- The NIP organization provides a model of public/private interinstitutional cooperation.
- Uruguay has been a pioneer country in the introduction of new vaccines (such as MMR, Hib, varicella, and influenza).
- Health workers are highly motivated and committed to the program, especially within the country’s interior.
- The NIP has an excellent cold chain component.
- There is a high degree of satisfaction among service users (97% of interviewees indicated they were satisfied with the services received in vaccination centers and posts).

As a result of the evaluation, the following general recommendations were made:

- Incorporate national immunization experts into the administrative health reform team to share lessons learned, limitations, and operational strategies for integrated health care.
- Ensure that the current reform process guarantees the sustainability and strengthening of the NIP’s achievements.
- Incorporate coverage with complete vaccination schedule as one of the progress indicators of the health reform process.

Immunization Program Information System

The coverage component of the immunization program information system was assessed through an evaluation process complementary to the traditional PAHO EPI evaluation methodology. The functionality of the information system was evaluated (at the national, department, and operational levels), the accuracy of both the denominator and numerator was determined, and rapid coverage monitoring (RCM) was conducted to validate coverage at the local level. The generalization of RCM results is limited because RCMs are not conducted through random sampling. The table below presents the main findings and recommendations regarding the immunization program information system.

Findings	Recommendations
<ul style="list-style-type: none"> • The computerized registry of all children allows generating information on coverage by birth cohort and conducting individualized monitoring activities to locate defaulter children. • Uruguay’s registry system for coverage monitoring is very reliable, both in the registration of doses and the integrity of the denominator. • Coverage levels for vaccination of adolescents and adults are not monitored. 	<ul style="list-style-type: none"> • Use the registry system for monitoring vaccinated children as a model for other countries in the Region of the Americas. • Expand the registry of vaccinated individuals and measure coverage of vaccines not included in the current system (for example dT and influenza).

Table 1. Uruguay Evaluation, 2006: Main Findings and Recommendations

	Findings	Recommendations
O P E R A T I O N S	<ul style="list-style-type: none"> There is no single manual for immunization practices and regulations. 	<ul style="list-style-type: none"> Prepare a manual of regulations that integrates the different components of the program.
	<ul style="list-style-type: none"> High vaccination coverage has been sustained over time; however, pockets of low coverage exist. Delays in vaccine uptake are observed. 	<ul style="list-style-type: none"> Improve data analysis by local geographic area in order to guide, evaluate, and implement supplementary vaccination activities, when necessary. Link the vaccination registry system to the geographic information system of the MOH, thus contributing to integration with other health programs. Strengthen the management of the NIP through decentralization, including the planning and programming of goals by local geographic area. Revise strategies for capturing and vaccinating populations to improve timely uptake and expansion of coverage in low-coverage areas (marginalized areas and areas of extreme poverty).
	<ul style="list-style-type: none"> Feedback is limited and detailed analysis of coverage by locality is sporadic, complicating the identification of pockets of susceptible individuals. 	<ul style="list-style-type: none"> Coordinate, analyze, and provide monthly feedback on vaccination coverage information.
	<ul style="list-style-type: none"> There is no National Regulatory Authority for vaccines. 	<ul style="list-style-type: none"> Implement a National Regulatory Authority for vaccines.
	<ul style="list-style-type: none"> The team that manages the process of BCG production and quality control in the Calmette laboratory is dedicated and very professional. However this laboratory has not been accredited by the World Health Organization. 	<ul style="list-style-type: none"> Analyze the continuation of local BCG production, taking into account that the vaccine is produced in a laboratory that has not been prequalified by WHO, and determine if production costs are competitive.
	<ul style="list-style-type: none"> Even though monitoring activities for events supposedly attributed to vaccination or immunization (ESAVIs) for BCG are conducted, other ESAVIs are not reported or investigated. 	<ul style="list-style-type: none"> Establish regular ESAVI monitoring.
S U R V E I L L A N C E	<ul style="list-style-type: none"> VPD notification is mandatory. A plan exists for the strengthening and development of epidemiological surveillance. Government Bureaus have named a person responsible for this topic in each Department. Uruguay remains free of polio, measles, and rubella virus circulation. 	<ul style="list-style-type: none"> Continue efforts to strengthen advances gained within the framework of the reform process.
	<ul style="list-style-type: none"> Health facilities do not receive periodic feedback on epidemiological VPD surveillance or coverage. Information (monthly bulletin) is limited to the dissemination of cases reported by mandatory disease notification through the Web. Weekly negative reporting of VPDs targeted for eradication (acute flaccid paralysis) and elimination (measles and rubella) is less than 80%, and silent areas exist. 	<ul style="list-style-type: none"> Promote information dissemination related to the VPD situation and trends at all levels.
	<ul style="list-style-type: none"> The epidemiological VPD surveillance is not linked to the NIP, neither at the managerial nor operational level of the Departments. 	<ul style="list-style-type: none"> Strengthen coordination with NIP. Strengthen training in VPD surveillance. PAHO proposes the implementation of a workshop on this topic in 2007.
	<ul style="list-style-type: none"> Joint surveillance activities are not conducted in border areas, representing a permanent risk for VPD control. 	<ul style="list-style-type: none"> Incorporate the NIP in the border health agenda.
	<ul style="list-style-type: none"> Varicella vaccination has resulted in a 47% reduction of cases (from 3,458 to 1,616) with the greatest impact in children aged <5 years. Incidence rates before vaccination (1999) were higher in children aged <5 years (56.9 x 10.000), while in 2005 the highest rate was in children aged 5-9 years (28,7 x 10.000). This suggests the disease now affects older age groups. 	<ul style="list-style-type: none"> Strengthen surveillance and monitor changes in varicella incidence patterns by age and, if necessary, assess the possibility of covering other age groups at greater risk for contracting the infection. Incorporate the identification of varicella antibody levels into the serological survey that is being discussed to measure antibodies against rubella.
	<ul style="list-style-type: none"> The number of mumps cases has been declining significantly since 1992. However, during 2005 the country faced an outbreak with a total of 2,144 cases. Attack rates by age were greater in persons born between 1981 and 1984 and the majority of cases occurred in the group aged 19-23 years. These cohorts were vaccinated with one dose of MMR. Administration of a second dose at 5 years of age was implemented starting in 1992. 	<ul style="list-style-type: none"> Characterize the details of the 2005-2006 mumps outbreak and publish the findings to guide the development of vaccination recommendations for the control of this disease in Uruguay and the Americas.
<ul style="list-style-type: none"> The accumulation of measles susceptibles was calculated in cohorts of children born between October 2001 and September 2005. The result suggests that approximately 23,000 children aged 1-4 years, or almost 50% of a birth cohort, are susceptible to measles. The level of rubella immunity in the population aged >22 years cannot be verified. There is no active CRS surveillance and retrospective case searches have not been conducted; therefore, the absence of CRS cases cannot be confirmed. The accreditation of the reference measles/rubella laboratory is pending. 	<ul style="list-style-type: none"> Conduct a <i>follow-up</i> campaign with the MR vaccine targeting children aged 1-4 years, to immunize susceptible children in these cohorts, and at-risk groups (young adults) to decrease the risk of the reintroduction of endemic circulation of measles and rubella viruses, as well as to reach the rubella and CRS elimination goal. Initiate the documentation process to verify rubella and CRS elimination. This includes retrospective case search for rubella and CRS, utilizing different information sources, and the implementation of a seroprevalence study. Achieve measles/rubella laboratory accreditation and maintain the systematic completion of proficiency tests. 	

Conclusion

Uruguay's NIP has achieved remarkable successes, including high vaccination coverage levels, early introduction of new vaccines, a personal-

ized coverage information system, VPD surveillance, and high prestige in the community. New challenges are the control, elimination, and eradication of VPDs, the sustainable introduction of new vaccines, reaching those in pockets

of low coverage, and strengthening VPD surveillance. As the NIP seeks to adapt to the health sector reform, the use of coverage and other immunization indicators will be critical to evaluate progress. ■

The Human Hookworm Vaccine Initiative: Development and Testing of an Orphan Product for a Neglected Tropical Disease



Dr. Peter Hotez,
Principal Investigator,
Human Hookworm
Vaccine Initiative, Sabin
Vaccine Institute.

Introduction

Human hookworm infection is a neglected tropical disease affecting 576 million people worldwide. In the Americas, approximately 50 million people are infected with hookworm, with the highest prevalence and intensities in Brazil and Central America. The high rates of re-infection that occur following anthelmintic deworming are a major barrier to the public health control of hookworm and other soil-transmitted helminth

infections. Therefore, there is an urgent need for the development of new control tools for hookworm, including vaccines.

Methods and Results

The *Na*-ASP-2 hookworm vaccine, has been developed, manufactured, and is being tested in early clinical trials. The vaccine is comprised of a 21.3 kDa recombinant protein expressed in yeast and adsorbed to Alhydrogel[®]. The *Na*-asp-2 gene encodes a protein secreted from *Necator americanus* infective larvae, which facilitates parasite invasion. Preclinical *in vitro* studies showed that anti-ASP-2 antibodies recognized the native antigen and inhibit larval invasion. Immunization of dogs and hamsters with animal hookworm ASP-2 orthologues resulted in reduced hookworm burden and blood loss relative to controls, following challenge infections with *Ancylostoma caninum* and *A. ceylanicum*, respectively. Additional epidemiological data from Minas Gerais, Brazil indi-

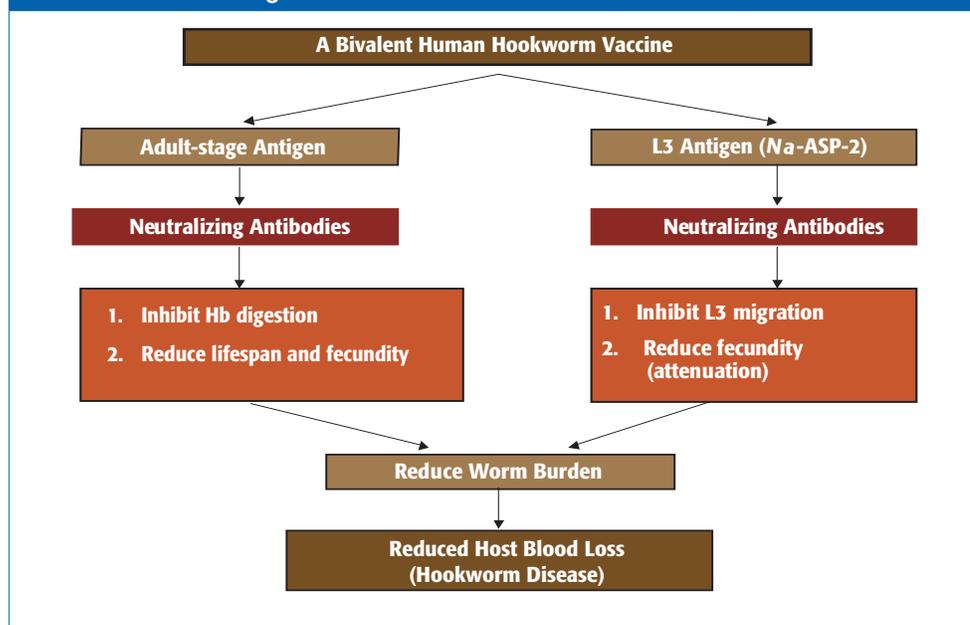
cate that anti-ASP-2 antibody responses among a subset of the population are associated with a reduced risk of acquiring heavy hookworm infection. Data from a Phase 1 clinical trial indicate that the vaccine is well tolerated and immunogenic. A series of clinical studies leading to a proof-of-concept study assessing the ability of the vaccine to reduce host hookworm burden and blood loss in school-aged children will be initiated in Minas Gerais State, Brazil, later in the year. In addition, technology transfer of product manufacturing processes for the *Na*-ASP-2 hookworm vaccine is currently underway in collaboration with Brazilian manufacturer, Instituto Butantan. A second antigen from adult hookworms is also under development. Several adult-stage antigen candidates have been shown to inhibit hemoglobin digestion resulting in diminished host blood loss, worm burdens, and fecal counts in preclinical studies. Downstream studies will evaluate a bivalent human hookworm vaccine comprised of *Na*-ASP-2 and the selected adult-stage antigen (Figure 1).

Conclusions

If the human hookworm vaccine is shown to be efficacious, global access will rely primarily on successful technology transfer of product manufacturing processes in hookworm-endemic countries, and the development of consensus guidelines for integrating vaccinations with school-based deworming programs. ■

Authors: Hotez PJ¹, Alexander N², Bethony J^{1,3}, Bottazzi ME¹, Brooker S², Brown AS¹, Correa-Oliveira R², de Quadros CA¹, Deumic V¹, Diemert D¹, Fujiwara R^{1,3}, Geiger S^{1,3}, Goud G¹, Keegan B¹, Loukas A⁴, Martins E⁵, McGlone B², Miles AP¹, Plietskatt J¹, Raw F¹, Rodrigues LC^{2,5}, Scott CP¹, Stoever K¹, Whitmore M¹, Zhan B¹, Russell PK¹

Figure 1. A Bivalent Human Hookworm Vaccine



1 Sabin Vaccine Institute and Department of Microbiology, Immunology, and Tropical Medicine, The George Washington University, Washington D.C., USA.

2 Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK.

3 FIOCRUZ, Rene Rachou Research Centre, Belo Horizonte, Brazil.

4 Division of Infectious Diseases and Immunology, Queensland Institute of Medical Research, Queensland, Australia.

5 Instituto Butantan, São Paulo, Brazil.

Update on PAHO's Pro-Vac Initiative

At its most recent meeting from 17-18 April 2007, the Strategic Advisory Group of Experts (SAGE) of the World Health Organization reiterated the importance of having an expanded body of evidence to support investment commitments for new vaccine introduction. The relationship between cost, investment, and evidence was emphasized as increasing vaccine prices demand greater financial investment justified by more comprehensive evidence.

Furthermore, country-specific data will help to strategically guide technical cooperation and resource mobilization, and achieve the greatest sustainable improvements in health. To that end, the Pan American Health Organization is leading the Pro-Vac Initiative to strengthen the national capacity to make evidenced-based, informed decisions to introduce new and under-

utilized vaccines, and to promote the transition from Regional to national priority setting for immunization.¹

Within the Region, many countries considering new vaccine introductions are conducting studies to generate the evidence vital to their decisions (Table 1). Burden of disease studies provide accurate, country-specific evidence regarding the potential health impact of new vaccine introductions, while economic evaluations help build the case for investing in new vaccines. These studies are being supported by field staff from the PAHO Immunization Unit, and the Pro-Vac Initiative and its partners.

¹ Pan American Health Organization. Multiyear Project Proposal for the Promotion of Evidence-based Policy Decisions for New Vaccine Introduction in Latin America and the Caribbean (Pro-Vac). *Immunization Newsletter*; 2006;28(5).

Next Steps

A key component of the Pro-Vac Initiative is developing simplified, Excel-based models for economic evaluations of new vaccines. Models for rotavirus, pneumococcus, and influenza were first made available to countries at the September 2006 Pro-Vac Workshop. The Pro-Vac team is continuing to improve these models and will release new versions this year. Additionally, a model for human papillomavirus is currently under development.

The Pro-Vac team will also be providing technical cooperation to GAVI-eligible countries as these countries develop economic and financial documents for their 2007 New Vaccine Support (NVS) applications. The Pro-Vac team can be reached by E-mail at ProVac@paho.org. ■

Table 1. Status of Pro-Vac-Related Studies in the Region of the Americas*

Country	Vaccine	Type of Study	Organization	Status
Bolivia	Rotavirus	Economic	Emory University/ Ministry of Health	Ongoing
	Rotavirus	Economic	University Nur (La Paz)/ PAHO	Under analysis
Brazil	Rotavirus and Pneumococcus	Economic	University of São Paulo/ PAHO/Ministry of Health	Ongoing
Ecuador	Rotavirus	Burden of Disease	PAHO/Ministry of Health	Ongoing
El Salvador	Rotavirus	Burden of Disease	PAHO/Ministry of Health/ Centers for Disease Control and Prevention	Planning Stage
Nicaragua	Influenza	Economic	PAHO/Ministry of Health	Planning Stage
Panama	Rotavirus	Burden of Disease	PAHO/Ministry of Health	Ongoing
Paraguay	Rotavirus	Economic	PAHO/Ministry of Health	Ongoing
Venezuela	Influenza	Burden of Disease	Ministry of Health	Ongoing
	Pneumococcus	Burden of Disease	Ministry of Health	Ongoing
Regional	HPV	Economic	Sabin Vaccine Institute/ Harvard University	Ongoing

* As of 13 April 2007.

XV Pan American Games in Rio de Janeiro and Risk of Rubella



From 13-29 July 2007, Rio de Janeiro, Brazil, will be hosting the XV Pan American Games, a continental version of the Olympic Games including Olympic and non-Olympic sports. The Pan American Games are held every four years (one year before the Olympic Games) and the first event took place in 1951, in Buenos Aires, Argentina (http://www.cob.org.br/pan2007/ingles/sobre_comite.asp).

Rubella incidence in Brazil decreased dramatically following large vaccination campaigns targeting women of childbearing age in 2001-2002. However, rubella transmission and outbreaks continue to occur. Since July 2006, the State of Rio de Janeiro is experiencing a rubella outbreak. Seventy percent of all cases are men. Although this outbreak has affected all age groups, persons aged 20-29 years are at the highest risk.

Since it is likely that residents of the Americas and other Regions traveling to Rio de Janeiro will

be exposed to the rubella virus, the Pan American Health Organization recommends that:

1. Any resident of the Americas, including teams participating in the Pan American Games and other tourists, traveling to Rio de Janeiro be immune to rubella **before** departure; and
2. Health care workers in the **public and private sectors** be alerted to the possibility of rubella occurrence.

Travelers can be considered immune to rubella if:

- They have **written proof of receipt of a rubella-containing vaccine**. However, countries can establish an upper age limit beyond which the vaccination requirement does not apply. This age limit should be based on the year of rubella vaccine introduction, rubella vaccine coverage thereafter, and occurrence of rubella epidemics; or
- They have **laboratory evidence of rubella immunity** (rubella-specific IgG antibodies).

Travelers aged >6 months who cannot provide

the above documents should be advised to receive rubella-containing vaccines, preferably as measles-mumps-rubella (MMR) or measles-rubella (MR), ideally at least two weeks **before** departure. Exceptions include travelers with medical contraindications to rubella-containing vaccines. Infants aged <6 months should not be vaccinated. Infants who receive MMR before their first birthday must be re-vaccinated following the country's schedule.

It is essential to **include the private health care sector and facilities providing health care to tourists in the surveillance system**, since people who can afford international travel are more likely to seek care in private health facilities.

In addition to the measures mentioned above, PAHO encourages the practice of requiring **proof of rubella (and measles) immunity for employment in the health care sector** (medical, administrative, and security personnel). PAHO also advises that personnel from the tourism and transportation industries be also immune to rubella (and measles). ■

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.

References to commercial products and the publication of signed articles in this Newsletter do not constitute endorsement by PAHO/WHO, nor do they necessarily represent the policy of the Organization.

ISSN 1814-6244

Volume XXIX, Number 2 • April 2007

Editor: Jon Andrus

Associate Editors: Béatrice Carpano and Carolina Danovaro



**Pan American
Health
Organization**



Regional Office of the
World Health Organization

Immunization Unit

525 Twenty-third Street, N.W.

Washington, D.C. 20037 U.S.A.

<http://www.paho.org/immunization>