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Meeting of Ad-Hoc Panel of Experts on Rubella and Measles



Some members of the Expert Panel (from left to right): Dr. Carlos Castillo-Solórzano, Dr. Peter Strebel, Dr. Louis Cooper, Dr. Stanley Plotkin, Dr. Michael Katz, Dr. Alan Hinman, and Dr. Jon Andrus. Washington, D.C., 3-4 March 2004.

During its September 2003 session, PAHO's 44th Directing Council endorsed the goal of rubella and congenital rubella syndrome (CRS) elimination by 2010 and urged countries to draft national plans of action within one year. It also requested the Director of the Organization to elaborate a regional plan of action and mobilize resources in support of the rubella and CRS elimination goal.

These recommendations were based on rapid reduction in diseases burden from the implementation of an accelerated rubella control strategy; the extensive experience gained by the

Region in vaccinating large and heterogeneous population groups; the cost-benefit data from the English-speaking Caribbean; the availability of a safe, affordable, and efficacious vaccine; and the existing political commitment of Member countries.

Within this context, PAHO's Immunization Unit (IM) held a Meeting of an Ad-Hoc Panel of Experts on Rubella and Measles in Washington, D.C., from 3-4 March 2004. The goals of the meeting were to review the current strategies for rubella and CRS elimination, review current PAHO measles surveillance indicators and definitions for measles elimination, and make suggestions for revisions where needed.

The meeting brought together experts and health officials from Brazil, Canada, Chile, Honduras, Mexico, the United King-

dom, and the United States. PAHO IM staff and consultants, as well as staff from WHO, also attended. The experts reaffirmed that the strategies to eliminate rubella and CRS being advocated by PAHO are correct. These include routine highlevel coverage of children; mass vaccination campaigns of adults to reduce the pool of susceptibles; inclusion of rubella vaccine in "follow-up" measles campaigns; and high-quality surveillance of rubella and CRS.

A table on the following two pages lists several of the issues addressed by the experts.

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\rightarrow	What definition of rubella elimination should be used in the Americas?	 Elimination of rubella and CRS in the Americas is the interruption of endemic rubella virus transmission in all countries. There are no indigenously acquired cases of CRS. Re-establishment of endemic transmission is a situation in which a chain of transmission continues uninterrupted for a period ≥12 months. Other definitions and classifications should be comparable to those established for measles.
\rightarrow	Is there any reason to modify the current approach to vaccination of women of childbearing age?	 Experience in mass vaccination of millions of women of childbearing age has allowed follow-up of several thousand women who were vaccinated without being aware of pregnancy. Follow-up of their pregnancies has yielded very reassuring results. Although ~3.6% of infants born to susceptible women vaccinated in early pregnancy were IgM positive, NONE had anomalies compatible with congenital rubella syndrome. Virus isolation studies are continuing. Other countries undertaking mass vaccination of adult women should conduct similar studies.
\rightarrow	What are the potential benefits of the rubella initiative on strengthening the health system?	 Helps strengthen surveillance and services to newborns (e.g., hearing screening, birth defects surveillance). May potentially improve services and follow-up to children with birth defects such as impaired hearing and learning disabilities. Provides contact between official health services and adults, particularly adult males, who often are not in contact with these services. Increases awareness of health issues for women. Offers an opportunity to link child health and child education services. Strengthens infrastructure and quality of services. Creates cost savings for the health system. Helps establish structure/mechanism for introducing future vaccines for use in adults (e.g., HIV, human papillomavirus).
\rightarrow	Given the program will be moving to integrated measles/rubella surveillance, do the current case definitions need to be modified? If so, to what?	 Full integration of measles and rubella surveillance requires definition of a suspected measles/rubella case. Since younger health care workers are not familiar with measles, the following is proposed for a case definition: a fever and rash illness or when a health care worker suspects measles or rubella infection. All notified suspected cases should be reported to the EPI notification system as well as to standard disease surveillance systems.
\rightarrow	What criteria/indicators should be used/ established to document the adequacy of integrated surveillance?	 For purposes of discussion, integration is defined as not having totally separate reporting / surveillance systems for measles and rubella. Except for outbreak settings, all specimens will be tested for both measles and rubella. Indicators should be developed for adequacy of combined / integrated measles / rubella surveillance. Many of the existing measles indicators can be used as is; some may require modification. An important indicator of sensitivity of surveillance is the reported rate of suspected cases. It would be useful to have a minimum indicator of sensitivity comparable to the AFP rate used in polio. Participants asked that national experiences be reviewed so that proposals for a baseline rate could be discussed at the November 2004 Technical Advisory Group on Vaccine-preventable Diseases (TAG) meeting (i.e. 1-5/100,000 is being used in Mexico and the United Kingdom). The age group to which the baseline rate would be applied also needs to be established. An indicator of surveillance relates to the results of lab testing.
\rightarrow	Are the case definitions for surveillance of CRS useful?	 Case definitions for surveillance of CRS are very useful. It must be remembered that there is a difference between surveillance and diagnosis. A sensitive definition for reporting suspected CRS to trigger investigation is important in the context of elimination. The present definition appears adequate for surveillance: a health care worker at any level of the health care system should suspect CRS in an infant when (1) One or more of the following birth outcomes are detected: congenital cataracts, hepatosplenomegaly, patent ductus arteriosus, purpura, or hearing impairment and (2) An infant's mother was known to have had laboratory confirmed rubella infection during pregnancy AND after a thorough physical examination, for any reason, there is clinical suspicion of CRS in the infant. For diagnosis, a more specific definition might be appropriate. Laboratory confirmation remains the gold standard. For purposes of monitoring trends, CRS surveillance should be strengthened throughout the Americas through collaboration with the regional Perinatal Information System from CLAP (Latin American Center for Perinatology and Human Development) and the ECLAMC (Latin American Collaborative Study of Congenital Malformations).
\rightarrow	What should be the guidelines for CRS case investigation and follow-up?	• The present system of sentinel CRS surveillance is appropriate for countries in early stages of elimination activities. As the program matures, surveillance should probably extend to secondary hospitals as well as tertiary centers. In the end stages, attempts should be made to identify/investigate every case.

\rightarrow	Are there additional tests or collection methodologies that should be incorporated into the laboratory network system? For elimination purposes, when should a second specimen to measure IgM be collected? Are there any special groups in which test samples should routinely be repeated? What is the appropriate use of IgM and avidity tests in pregnancy?	 Serum IgM testing within 5 days of rash onset may be negative in persons who are infected with rubella. For surveillance purposes of identifying chains of transmission, this is adequate in the earlier stages of elimination activities but will not be as elimination is approached. In later stages, it may be necessary to take a second specimen if the initial IgM test (taken within 5 days of rash onset) is negative. This will allow testing of paired sera for both IgM and IgG. Assessing suspected rubella in pregnant women will require taking a second specimen if the initial IgM taken within five days of rash onset is negative. This will allow testing of paired sera for both IgM and IgG. Avidity testing can be a useful adjunct to IgM testing in assessing how recently infection occurred. However, it may not be helpful in re-infection, which may result in an IgM response. In some areas of some countries, pregnant women are routinely tested for both IgG and IgM antibodies. Unless there is a suspicion of recent exposure to rubella, IgM testing should not be done because of the low, but real, possibility of false positivity or true detection of persistently positive IgM circulating antibodies. Studies to assess the utility of other approaches to diagnosis, including RT-PCR (reverse transcriptase-polymerase chain reaction) testing of oral fluids or other pharyngeal samples, should be pursued actively by PAHO. At the same time, the practical issues involved in widely disseminating PCR testing need to be addressed. 					
→	What should be the guidelines for obtaining specimens for rubella virus culture?	 In countries where the incidence of rubella is still high, specimens should be obtained from a range of settings sufficient to establish the distribution of circulating strains of rubella virus. In every country, one or more persons should be identified with the responsibility to assure collection of specimens for rubella virus isolation. This could well be the person responsible for measles virus isolation. As elimination is approached, efforts should be made to isolate rubella virus from all sporadic cases and from every chain of transmission, both for diagnostic purposes and to characterize the origin of the virus. Isolates obtained from these efforts should be characterized to enable appropriate use of molecular epidemiology. Development of, for example, oral fluid (or other pharyngeal sample) RT-PCR technology could obviate the need for virus isolation for purposes of diagnosis. 					
\rightarrow	What are the most appropriate definitions of measles elimination and re-establishment of endemic/indigenous measles transmission for use in PAHO?	 Measles elimination in the Americas is the interruption of endemic measles virus transmission in all countries. Re-establishment of endemic transmission is a situation in which a chain of transmission continues uninterrupted for a period ≥12 months. Imported cases are cases exposed outside the Western hemisphere during the 7-21 days prior to rash onset as supported by epidemiological and/or virologic evidence. Measles import-related cases are locally-acquired infections occurring as part of a chain of transmission originated by an imported case as supported by epidemiologic and/or virologic evidence. Measles cases with unknown source of infection are cases where source has not been identified after a thorough investigation. 					
\rightarrow	Are the surveillance indicators proposed by PAHO appropriate?	 An indicator for rate of rash illness investigated should be established, based on the experience in the countries. Current indicators appear useful. 					
→	What surveillance criteria in PAHO should be used to assess interruption of indigenous transmission (post-eradication)?	 A range of indicators will be needed, including level of population immunity, adequacy of surveillance and investigation, laboratory capacity and performance. 					
\rightarrow	What criteria in PAHO should be used to certify measles elimination?	 In addition to criteria relating to duration of interruption of transmission and other factors mentioned above, operational criteria relating to program performance will be needed (e.g., review of clinic registries). 					
→	What should be the priority research issues for rubella and measles elimination?	 Impact of rubella program on routine immunization services and on strengthening health services. Epidemiologic/economic implications of immunizing adult males in rubella programs. Document the health/economic burden of rubella and CRS in the Americas and the costs and benefits of rubella elimination. Document the impact of rubella and rubella elimination on sectors other than health – e.g., education. Evaluate tests (e.g., RT-PCR, avidity testing), alternative clinical specimens (e.g., oral fluid, dried blood spots), and testing algorithms in PAHO countries. Review country experience with surveillance indicators/strategies. Evaluate different approaches to CRS surveillance. Evaluate the hemispheric Vaccination Week. Review surveillance of events supposedly attributable to vaccines and immunization (ESAVI) and injection safety practices in PAHO. 					

Towards Elimination of Rubella and Congenital Rubella Syndrome



Among the activities marking the celebration of the Vaccination Week in the Americas, El Salvador and Ecuador are conducting vaccination campaigns among men and women to eliminate rubella and congenital rubella syndrome. In El Salvador, 2.9 million persons aged 15-39 years will be vaccinated, while in Ecuador 5.1 million persons aged 16-39 years are being targeted. This strategy is designed to rapidly reduce the circulation of the rubella virus, as well as to prevent the shift of disease burden to susceptible young adults, particularly women of childbearing age. Both campaigns will be ongoing until 31 May 2004.

This intervention has a high cost-benefit ratio, generates savings for the health system, and is an opportunity to reduce inequities in the care of young adults and in maternal health. In addition, this activity promotes a culture of prevention and plays a critical role in reducing mortality and congenital malformations among children. During vaccination campaigns, advocacy, promotion, and social mobilization generate enormous benefits for strengthening health services directed at the adult population. The use of the combined measles-rubella (MR) vaccine further strengthens measles elimination in the Americas.

We salute the political commitment of the national authorities who, through presidential decrees, have declared the vaccination campaigns to be of national interest and have assigned the resources required for such effort. We also recognize health workers for their dedication and enthusiasm. Finally, we congratulate international cooperation agencies who have contributed to the success of the campaigns with their technical and financial support.



Measles Elimination in Mexico

Background

The indigenous transmission of measles appears to have been has been interrupted in Mexico and the rest of the Americas since 2002¹. However, 108 confirmed cases have been reported in Mexico since April 2003 and transmission is ongoing. Isolation of the virus and genetic sequencing have linked these cases with importations of H1 measles viruses from other parts of the world. Ongoing transmission in Mexico highlights the risk of importation of measles virus.

A PAHO mission was invited to visit Mexico from 19 to 23 April 2004. The objectives of the visit were 1) to evaluate the circulation of the measles virus in Mexico during the past 12 months; 2) to review the steps taken to interrupt transmission; and 3) to identify the lessons learned and the challenges for interrupting the transmission of the measles virus in Mexico.

This article presents the findings and the agreed upon plan of action following the above-mentioned joint review of the measles situation in Mexico conducted by Mexican health authorities and the PAHO delegation.

In accordance with the provisions of the Plan of Action for Measles Elimination in the Americas, adopted by PAHO's 38th Directing Council in September 1995 and the recommendations of the Technical Advisory Group (TAG) on Vaccine-Preventable Diseases.

Findings

1) Mexico has implemented the measles elimination strategies recommended by PAHO.²

In 1993, Mexico carried out a catch-up campaign to achieve the rapid interruption of measles transmission. Children under 14 years were targeted for measles vaccination and 96% coverage was achieved. In 1998 and 2002-2003, mop-up campaigns targeting children 1-4 years of age were carried out to protect susceptible preschoolers; these campaigns attained coverage levels of 95%.

Regarding routine vaccination to maintain measles elimination, official data on vaccination coverage indicated national coverage levels of 95% for children 1 year of age, 98% for children 2 years of age, and 99% for children under 5 for December 2003. This coverage has been maintained for the past four years. Rapid coverage monitoring in several states performed over a number of years using the WHO methodology³ generally yielded similar or higher rates.

Similarly, the 2000 national measles seroprevalence survey of children aged 1 to 9 years (6,270 samples) conducted by Mexico's National Institute of Public Health found 99% seropositivity for measles (95% confidence interval: 98.8-99.3). There were no significant differences for gender or urban/rural environment. These data demonstrate good vaccination coverage achieved through the various vaccination strategies employed for measles elimination.

Mexico also has a sensitive surveillance system in place resulting in early case detection. The efficiency of the system has been recently reflected in the case investigations conducted in areas with measles cases in 2003-2004: the Federal District (DF) and the States of Mexico and Hidalgo. These investigations have been coordinated among the federal, state and local levels, with the participation of all health institutions. Specific activities have included:

- Clinical and epidemiological studies of the cases;
- Active case-finding, searching for cases in the area around the residence and places known to have had confirmed cases, as well as workplaces, child-care centers, street markets, and schools;
- Vaccination of the susceptible population and children aged 6-11 months;
- · Retrospective case-finding in health units; and
- · Rapid coverage monitoring.

2) 2003-2004 Measles Outbreak

The first known case in this outbreak appeared in Mexico City with date of onset of 13 April 2003. Between April 2003 and April 2004, 108 confirmed cases of measles, 44 in 2003 and 64 in 2004 (up to epidemiological week 16 of 2004), were reported to the Epidemiological Surveillance System for Exanthematous Febrile Diseases. Of the 108 confirmed cases, 102 were confirmed by laboratory and 6 by epidemiological link. The source of infection could not be determined in 32 (31%) of them. Of the confirmed cases, 77 have occurred in the Federal District, 24 in the State of Mexico, 4 in the State of Hidalgo, 2 in the state of Coahuila and 1 in the state of Campeche. The most affected age groups are young adults and children under 1 year of age (Figure 1).

Figure 1. Measles cases in Mexico, by age groups, from week 16 2003 to week 16 2004



Source: Health Secretariat, Mexico

Measles serology testing has been performed at the Institute for Diagnosis and Epidemiological Reference (INDRE), Mexico's national epidemiological reference laboratory, and the Centers for Disease Control and Prevention (CDC) in the United States, using the ELISA test for the detection of measles IgM.

Furthermore, pharyngeal and urine samples have been tested for culture and polymerase chain reaction (PCR) assay in INDRE and in CDC. The past 12 months have yielded 13 positives with 100% homologous sequences corresponding to genotype H1, which were very similar to the H1 strain currently circulating in Japan. However, the source of importation has not been identified. Preliminary data indicate that three nucleotides of the virus differ from those of the H1 virus isolated from a case in Chile imported from Japan in 2003. The H1 genotype has recently surfaced in Korea and China, suggesting that this part of Asia was the source of the importation of the virus.

Mexico's National Health Security Committee declared a national emergency, which calls for assertive action to interrupt transmission. This Committee has agreed to:

- Strengthen the Plan of Action for interrupting transmission.
- Eliminate circulation of the measles virus while moving forward with the program for eliminating rubella and congenital rubella syndrome through simultaneous and vigorous nationwide action.
- Procure and distribute 16.5 million doses of measles-rubella (MR) vaccine for administration to the susceptible population (aged 13 to 39 years).
- · Distribute the general guidelines for immediate implemen-

² Pan American Health Organization. Technical Paper No. 41: Measles Eradication Field Guide. 1999. Washington, D.C.

³ Pan American Health Organization. The Use of Rapid Coverage Monitoring: The Vaccination Campaign against Measles and Rubella in Ecuador. EPI Newsletter 2003; 25(2):1-3.

Strategies to interrupt transmission of the measles virus in Mexico

Given the existence of a national technical plan and the policy to interrupt measles transmission, the Mexican health authorities and the PAHO team agreed that the following general steps should be taken to bolster current efforts and ensure optimal implementation of the plan of action:

- 1. Mexico has made intensive efforts to control the outbreak in the affected municipalities. However, as recommended by the National Health Security Committee and the National Vaccination Board (CONAVA), it is important that intensive vaccination campaigns be waged to interrupt circulation of the measles virus.
 - The priority in these intensive campaigns is to vaccinate all adolescents and young adults aged 13 to 39 in Mexico with the MR vaccine. This is the group at highest risk, according to the epidemiological information on the measles cases and the national seroprevalence survey.
 - Vaccination activities should be carried out swiftly, preferably in a 4-6 week time span.
 - Given the time required for optimal planning of the campaign and the availability of all the necessary resources, September 2004 is suggested as the best time for ensuring successful implementation of this vaccination campaign. However, the group recognizes that transmission will continue and that there is significant risk of a rise in the number of cases and the spread of outbreaks to other parts of the country. In light of this, the group stresses the importance of establishing contingency plans and ensuring the immediate availability of the necessary resources, particularly the MR vaccine.
- 2. The success of the vaccination campaign hinges on a timely supply of the necessary resources. The target population consists of roughly 51 million individuals between the ages

tation of the respective Plan of Action in the states.

- Activate, without exception, the state Committees for Health Security, Epidemiological Surveillance (CEVE), and Vaccination (COEVA). They should meet on a continuous basis and will be in charge of timely monitoring the steps taken under the Plan of Action.
- At the federal level, hold monthly meetings so that CEVE and COEVA committees can report to their counterparts at the central level. The first meeting will be held from 13-14 May in Mexico City and will be attended by health services directors, program heads, and state epidemiologists.

Mexico's plan to interrupt measles transmission revolves around two elements:

a) Epidemiological surveillance:

The CEVE committees should guarantee application of the epidemiological surveillance guidelines and their monitoring at the local level. They should also guarantee thorough interinstitutional coordination, the clinical and epidemiological investigations of each reported, case and the monitoring and supervision of surveillance and control activities in all units of the sector in the federative entities. 13 and 39. Apreliminary estimate based on previous years' vaccination activities in this age group and the purchase of 16 million doses of MR vaccine indicates that at least 26 million additional doses of MR vaccine are needed to conduct a vigorous, intensive countrywide vaccination campaign to interrupt transmission of the measles virus.

- 3. The global supply of vaccine is limited. In order to guarantee that producers have this number of doses on hand and can guarantee their availability, health authorities must inform the market of their needs as soon as possible.
- It is important for the states and districts to draw up detailed plans of action that include the application of optimal modalities for vaccinating all young adults in the target age group.
- 5. To guarantee that the states make the commitment and carry out this plan in an optimal manner, the Health Secretariat will once more convey the decisions of the National Health Security Board to each state and draw up guidelines emphasizing the aspects described earlier.
- To improve the detection, investigation, and classification of cases and contacts, the Health Secretariat will coordinate the review of all probable cases with acute febrile exanthema to the states and confirm all cases where there is evidence of an epidemiological link with clinically- or laboratory-confirmed cases.
- 7. To strengthen the national laboratory network, the Health Secretariat has made a commitment to take the following steps:
 - Train and strengthen state laboratories in the diagnosis of exanthematous febrile illnesses
 - Strengthen the role of the national reference laboratory (INDRE) in quality control, and performance evaluation in all laboratories of the national network.
- b) Vaccination activities for outbreak control:
- Immediate implementation of mop-up campaigns in high schools and professional schools throughout the country and vaccination of the population aged 13 to 39 years in all health units.
- Implementation of prevention and control measures when a case is reported through "blocking strategies" in high-risk areas (areas with cases and low coverage), by vaccinating the population aged 6 to 11 months and those aged 13 to 39 with no history of vaccination since 2000.
- Vaccination of health workers and tourism sector employees with no history of vaccination since 2000.

Challenge

The current measles situation in Mexico poses a critical challenge for national authorities to maintain measles elimination in the Americas. As long as the measles virus continues to circulate in other parts of the world, the countries of the Hemisphere will be at risk for imported cases. The lessons learned in Mexico in stopping transmission will be important for other countries of the Region.

Coverage Rates: DPT-3, OPV-3, Measles, and BCG Region of the Americas, 2003

Occurations	DPT3		OPV3		Measles		BCG	
Country	2002	2003	2002	2003	2002	2003	2002	2003
Anguilla	99	99	91	99	99	99	99	99
Antigua & Barbuda	98	99	93	99	99	99	N/A	N/A
Argentina	93		94		95		99	
Bahamas	94		93		94		N/A	N/A
Barbados	87	86	86	86	91	88	N/A	N/A
Belize	89	96	93	95	89	94	97	99
Bermuda	71	92	71	92	75	77	N/A	N/A
Bolivia	93	95	93	94	99	99	99	94
Brazil	96	96	97	99	95	99	99	99
British Virgin Islands	98	99	99	99	99	99	80	99
Canada*	93		93		95		N/A	N/A
Cayman Islands	93	92	93	92	91	83	92	75
Chile	99		99		99		94	
Colombia	80	93	82	92	93	93	87	97
Costa Rica	94	88	94	88	94	89	92	87
Cuba	99	73	99	99	93	99	99	98
Dominica	98	99	98	99	99	96	99	99
Dominican Republic	73	75	76	73	89	80	96	90
Ecuador	87	89	88	99	82	99	99	99
El Salvador	81	88	81	87	93	99	92	90
Grenada	98	98	98	98	96	99	N/A	N/A
Guatemala	95	94	95	94	92	94	96	97
Guyana	91	90	93	91	93	94	91	95
Haiti	39	50	41	48	34	52	45	54
Honduras	95	92	95	92	97	95	94	91
Jamaica	86	81	86	81	86	78	90	88
Mexico	91		92		96		92	
Montserrat	92	91	94	91	99	99	99	99
Nicaragua	85		85		98		93	
Panama	89	86	85	83	89	83	92	87
Paraguay	87	85	87	86	87	91	84	88
Peru	95	94	95	95	95	95	92	94
St. Kitts & Nevis	97	99	97	99	99	93	99	99
St. Lucia	88	84	90	85	98	86	95	92
St. Vincent & Grenadines	99		99		99		91	
Suriname	73	74	73	74	73	69	N/A	N/A
Trinidad & Tobago	96		96		87		N/A	N/A
Turks & Caicos	93		93	96	86	91	92	75
Uruguay	95	91	95	91	95	95	99	99
USA			90		92		N/A	N/A
Venezuela	63	67	77	83	78	81	90	88

* Canada uses Pentacel vaccine (DTaP-IPV-Hib)

N/A: Data not applicable

... : Data not available

Data updated: 18 May 2004

Vaccines: Preventing Disease and Protecting Health

The countries of the Americas have made tremendous strides in improving the health of the Region's peoples since the Pan American Health Organization was established just over 100 years ago. These improvements were due in great part to the implementation of national immunization programs (NIPs). These programs, particularly those that operated over the last 25 years since the Expanded Program on Immunization (EPI) was established in the Americas, have brought several

vaccine-preventable infectious diseases under control. Until recently, NIPs used just a few vaccines developed several years ago. Over the last decade, however, major advances in biotechnology made it possible to develop several new vaccines, and many candidate vaccines are now under way. Consequently, one of the challenges for health policy makers has now been to introduce these newly developed vaccines into NIPs.

Given the accelerated progress in research and development

in the field of vaccines and to commemorate its first bicentennial, the Pan American Health Organization convened a conference so that experts at the vanguard in the field of vaccines and immunization could review the state of the art and look ahead to years to come. The Conference, "Vaccines, Prevention, and Public Health: A Vision for the Future," was held in Washington, D.C. from 25 to 27 November 2002 and gathered more than 300 experts from the world over.

Papers presented at the conference marked the beginning of the book "Vaccines: Preventing Disease and Protecting Health." In early sections, the book relates successful efforts to fight diseases with vaccines, including the eradication of polio from the Americas and the potential contribution of new

The EPI Newsletter is published every two months, in Spanish, English and French by the Immunization Unit of the Pan American Health Organization (PAHO), Regional Office for the Americas of the World Health Organization (WHO). Its purpose 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 their possible solutions.

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.

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measles vaccine formulations to reducing measles mortality worldwide. It also looks at the challenges posed in using vaccines to cope with emerging and re-emerging diseases, such as HIV/AIDS and bioterrorism.

In subsequent sections, the authors examine innovative efforts under way to test the efficacy of vaccines against diseases such as meningococcal infection, *Haemophilus influenza* type b infection, varicella, and hepatitis A. They



also look at efforts to develop a new generation of vaccines against cholera and typhoid, shigellosis, and *Helicobacter pylori* infection. The advances in vaccine development against influenza and hepatitis C are also presented.

The book includes sections on the quest for vaccines against tuberculosis, HIV/ AIDS, dengue, malaria, and hookworm. New concepts in vaccine development, and use of adjuvants and delivery systems, such as DNA vac-

cines and oral vaccines derived from transgenic plants, are also discussed. Later sections deal with the use of vaccines against pathogens used in potential bioterrorist attacks, with a particular emphasis on agents causing smallpox and anthrax. Regulatory and safety issues related to vaccines are also presented from the perspectives of the public sector, the pharmaceutical industry, and the vaccine consumer. The final chapter highlights the ongoing challenges of vaccine development, disease prevention, internal and external financing and sustainability of immunization programs, and the impact of health sector reform on these issues.

¹de Quadros CA, ed. *Vaccines: Preventing Disease & Protecting Health.* Washington, DC: Pan American Health Organization; 2004.



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