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Conclusions and Recommendations



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Technical Advisory Group Members

Peter Figueroa

Donald A. Henderson, Chairman

Akira Homma

*John La Montagne**

Joseph Z. Losos

Fernando Munoz Porras

Walter Orenstein, Rapporteur

*Roberto Tapia Conyer**

Ciro A. de Quadros, Secretary, Ad Hoc

** Unable to attend*

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CONCLUSIONS AND RECOMMENDATIONS

Introduction

Immunization is widely recognized to be one of the most cost-effective prevention measures. In the Americas, the impact is demonstrated by the elimination of polio since 1991, the elimination of measles transmission in most countries of the region, and marked reductions in neonatal tetanus morbidity. Maintaining these great achievements requires continued high level support and resources for vaccines, vaccine delivery, and disease surveillance. Failure to maintain high levels of surveillance, of immunization coverage and of implementation of the disease prevention strategies could lead to return of disease epidemics. It is important that Ministries of Health give high priority to full implementation of immunization programs and assure that adequate resources are devoted to such programs. Likewise, it is critical that international agencies continue to provide assistance to national immunization programs.

It is especially important to sustain polio free status until global eradication occurs and vaccination can be stopped. Polio viruses can quickly be reintroduced into the Region by travelers from the many remaining parts of the world where polio is endemic.

Urgent attention is needed to assure that the year 2000 goal of elimination of measles from the Americas is achieved. To do this, the current level of measles prevention efforts must be sustained and in many countries increased.

Immunization Programs in a Changing Policy Environment

All countries are moving toward delegating greater responsibility for delivery and management of health care services to local levels. This provides an opportunity to promote community participation and commitment of local health authorities. These are necessary for the success of vaccination programs.

However, with decentralization there remains a requirement at the central level to assure that immunization program goals are met in all areas of a country. Because almost all vaccine-preventable diseases can spread widely, successful control or elimination requires coordinated national and international efforts so that no area becomes a reservoir to seed infection into other communities and countries.

Recommendations

- **National governments must maintain authority to monitor the implementation of immunization programs at the state and local level and to take corrective actions should problems be detected.**
- **Vaccination and surveillance programs should be considered essential public goods and funded with public resources.**
- **Within the context of a changing environment to improve access to health services, vaccination coverage should be an indicator of the success of local and state delivery of services and a measure of the success of the health care reform and decentralization process.**
- **National inter-agency committees remain a focal point for guidance in the implementation of plans of action in each country and in coordinating international input. These committees have assumed the additional responsibility of coordinating the collaboration of the private sector and local NGOs. The inter-agency committees deserve the full support of all partners as an initiative which will strengthen the sustainability of vaccine-preventable *disease programs*.**
- **The following indicators should be used to monitor sustainability of national immunization programs in the Americas:**
 - Coverage (national and district levels)
 - Program Access (BCG and DPT1 coverage)
 - Program Efficiency - Drop-out Rates (DPT1/DPT3 and DPT1/Measles)
 - Percentage of total immunization program costs financed by the country
 - Percentage of recurrent¹ program costs financed by the country
 - Approval of legislation establishing a specific budget line to finance vaccines and syringe costs.

¹ Vaccines, syringes, cold chain, local staff costs, including per diem and transportation.

Measles Elimination

Substantial progress has been made towards achieving the goal of measles elimination in the Americas. Transmission has been interrupted in many countries of the Region. The PAHO vaccination strategy (catch-up, keep-up and follow-up), where fully implemented, has proven to be highly effective. However, low levels of incidence can lead to a false sense of security. In the absence of measles transmission, susceptibles accumulate in a community, as a result of failure to vaccinate all children and because primary vaccination does not protect 5 to 10% of those vaccinated. These susceptibles can sustain future measles outbreaks. To maintain a measles-free state will require ongoing efforts to minimize susceptibility using the complete strategy.

The year 1996 was a notable year for the program with only 2109 confirmed cases of measles. However, in 1997, epidemic measles developed in Sao Paulo, Brazil with spread to other states in Brazil and at least four other countries of the Region. To date, over 4,000 laboratory confirmed cases of measles have been reported. At least two to three times that number may have occurred. Over one half of the cases occurred in unvaccinated persons 20-29 years of age. Several other countries have reported smaller but similar outbreaks in which substantial transmission appears to have occurred among adults.

The lack of a timely follow-up campaign and a deficient vaccination program appear to have been responsible, in part, for a rapid accumulation of susceptible children in Sao Paulo. Another contributing factor was the presence of many susceptible young adults due to migration from areas with low measles incidence, who would have not been targeted in follow-up campaigns. Epidemiological information about this outbreak is still incomplete. Little is known concerning the dynamics of measles transmission and risk factors for acquiring measles infection. A careful epidemiologic investigation is needed.

The Sao Paulo epidemic vividly illustrates the importance of all countries appreciating that the measles elimination effort is not a local or even a national campaign but a hemisphere-wide program which can only be as strong as its weakest component. This is true on a global scale as well because many cases in this Region have been linked either epidemiologically or virologically to importations from outside this hemisphere. Thus, better worldwide measles control is important to the continued success of measles elimination in the Americas.

Recommendations

General

- **The occurrence of epidemic measles in a major urban area poses, by far, the most serious threat to the overall program because of the possibility of widespread disease dissemination. Accordingly, it is important that program success in all urban areas**

(population of $\geq 1,000,000$) be monitored on an ongoing basis by national authorities and reported to PAHO. The status of all cities should be published regularly and, for cities which are failing to sustain their efforts, special efforts should be made by national and international authorities to persuade responsible city officials of the need for corrective action.

- Over the next year and for the foreseeable future, surveillance throughout the Americas is critical in order to ascertain the extent and characterization of measles spread from the Sao Paulo epidemic. When measles is introduced, it is important to know the characteristics of individuals introducing infection and the characteristics of those acquiring infection. It is important to determine the likelihood of such outbreaks dying out with or without interventions. In particular, it is critical to evaluate whether adults are capable of sustaining transmission of measles over long periods when immunity levels are high among children. Only if such information is available, will it be possible to respond appropriately.

Vaccination Strategies

- Routine vaccination of infants (keep-up vaccination) is a critical component of the PAHO measles elimination strategy. To obtain a higher measles vaccine effectiveness, the age of routine vaccination should be increased from 9 months to 12 months of age. Once the age has been increased, coverage should be monitored among children 12-23 months of age. Efforts need to be made to vaccinate $\geq 90\%$ of infants at their first birthday in every district of every country. In countries with rubella/CRS control programs, MR or MMR vaccine should be used for routine infant vaccination.
- To maintain high population immunity among preschool-aged children, follow-up measles vaccination campaigns should be conducted whenever the estimated number of susceptible children 1-4 years of age approaches the number of children in one birth cohort. In countries with routine vaccination coverage in the 80-90% range, these campaigns should be conducted every 4 years. In these campaigns, all children 1-4 years of age should be vaccinated, regardless of previous vaccination or disease history status. Those countries with rubella/CRS control programs should use MR or MMR vaccine.
- High coverage for the follow-up campaigns is critical since in most countries they represent the last opportunity to provide measles vaccine to children who previously escaped vaccination. Immediately after these campaigns, the coverage in every district of the country should be determined. Those districts which did not achieve at least 90% of the target population should immediately conduct supplemental (mop-up) activities which may include door to door vaccination.

- The ultimate goal of the measles elimination effort is case prevention by reducing susceptibility through vaccination. The occurrence of cases represents a failure to anticipate disease risk and to take corrective action to prevent outbreaks. The most practical means for identifying susceptibility is to monitor coverage of routine immunization and immunization campaigns to estimate age-specific immunity levels. Serosurveys cannot be recommended for routine use because they often fail to detect the significant pockets of susceptibles who resist participating in surveys, they can be expensive, and they are methodologically difficult to perform and interpret.
- To assure high measles immunity among school-aged children, the vaccination status of all children entering school should be ascertained. Those students who are unable to provide documentation of prior measles vaccination should be vaccinated before being allowed to attend school.

Surveillance and Laboratory

- Measles surveillance is critical for ensuring progress towards the goal of measles elimination in the Americas. The purpose of measles surveillance is to detect virus circulation in a timely manner, to ascertain risk factors for measles, to obtain appropriate specimens for laboratory confirmation from suspected cases, and to provide information that will guide further prevention efforts.
- A standardized measles surveillance system is essential for monitoring progress toward the successful achievement of Region-wide measles elimination. All countries should provide the necessary data to the Region-wide measles elimination surveillance system (MESS).
- Communication and training efforts must be part of developing better surveillance systems. PAHO should support the development of training manuals, courses, and messages for use in the different countries of the Region.
- Each country should periodically evaluate the quality of its surveillance system. PAHO has developed a protocol for rapid evaluation of surveillance systems which should be disseminated to all countries of the region. A plan should be made for these evaluations in all countries as soon as possible.
- Laboratory confirmation is an essential part of the regional measles surveillance system. All isolated cases of measles and at least three cases from each chain of transmission should be confirmed by the laboratory. A single serum specimen collected at first contact with the health care system is sufficient for confirming measles.

- Suspected measles cases, with epidemiologic links to laboratory confirmed cases are themselves considered to be laboratory confirmed. Cases meeting the clinical case definition but which have neither laboratory confirmation nor epidemiologic links to a laboratory confirmed case represent failures of the surveillance system.
- Available data suggest that two commercially available measles IgM assays (Behring and Chemicon) are the most satisfactory tests for routine use. They are sensitive, specific and rapid (2-3 hours to perform). A positive result can be considered confirmatory of measles. Specimens that present special problems can still be sent to regional reference laboratories for confirmation by the CDC capture IgM assay.
- Virologic surveillance is important. Clinical specimens for viral isolation should be obtained from every chain of transmission. Urine, the most practical specimen to collect, should be obtained within 7 days of rash onset and forwarded to a laboratory to be properly processed. At present, virus isolation is performed at FIOCRUZ and CDC.

Outbreak Response

- If more than one birth cohort of susceptible preschool children has accumulated in an outbreak area, a mass campaign should be promptly conducted. All schoolchildren should be screened and all those who have not received at least one dose of vaccine should be vaccinated. All children presenting to a hospital emergency room or other health care facility during a measles outbreak should be vaccinated, regardless of prior vaccination status, provided there are no contraindications. During outbreaks, the routine age for measles vaccination should be lowered to 6 months.
- Countries should not implement indiscriminate campaigns to vaccinate all adults against measles. Most adults are likely to be immune and achieving significantly higher levels of coverage among adults is extremely difficult. However, where surveillance has identified specific risk groups for measles among adults, such as university students, health care workers, or others, targeted vaccination efforts may be useful.
- When importations are detected, countries should notify the country or countries where infection is likely to have been acquired. PAHO should facilitate cross country notifications.

Management Indicators

The following indicators are essential for monitoring the performance of the program:

Notification:

≥ 80% of reporting sites report on a weekly basis the presence or absence of suspected measles cases.

≥ 80% of reporting sites report at least one suspected measles case per year.

Investigation:

≥ 80% of suspected measles cases are investigated within 48 hours of report.

≥ 80% of suspected measles cases have a blood specimen collected if there is not an epidemiological link to a laboratory confirmed measles case.

≥ 80% of measles chains of transmission have an identified source of infection.

Laboratory:

≥ 80% of specimens with results within 7 days of receipt in laboratory.

Poliomyelitis

The hemisphere continues to be free of wild virus polio and surveillance indicators for the Region, as a whole, show that most countries are continuing to conduct adequate surveillance for AFP cases. However, the TAG noted a substantial deterioration in surveillance in some of the countries of the Region raising concerns that future importations of wild virus could be missed. Surveillance for polio must be maintained in all countries, at the same level as in 1994 when the Region was certified as polio free, until polio is certified as eradicated from the globe and vaccination is stopped.

Recommendations

- **All countries must assure that adequate resources are devoted to polio surveillance. AFP surveillance must continue with ascertainment of at least one case annually of AFP per 100,000 < 15 years of age.**
- **For laboratory diagnosis, only one stool, collected within 15 days of onset of paralysis, is needed. Such specimens should be collected from at least 80% of AFP cases.**
- **An inventory of all laboratories in the hemisphere which have wild polio virus stocks should be completed as a first step toward the eventual destruction of all wild polio viruses as part of the global certification process.**
- **OPV remains the vaccine of choice in the Americas because it induces gut immunity, thus preventing spread of wild viruses if introduced; it is easy to administer; and it is relatively inexpensive.**
- **Recommendations specific to the laboratory are included in the laboratory report.**

Neonatal Tetanus

Acceleration of NNT elimination activities in the Region of the Americas began in 1988 and great progress has been made. The annual number of cases in the Region decreased from 1,470 in 1988 to 312 in 1996, and the number of districts with multiple cases of NNT has also decreased.

Recommendations

- **Td should replace TT any time TT is indicated for vaccination of women of childbearing age, other adults, and older children to also improve protection against diphtheria.**
- **Surveillance and NNT case investigations should be improved in risk areas of endemic countries, particularly in areas from which information on coverage and cases is lacking.**
- **Vaccination of all women of child-bearing age in all risk areas is essential to continue control of the disease.**

Rubella and Congenital Rubella

Available data indicate that rubella is prevalent throughout the Americas. Cases of CRS and fetal infection have been documented in Barbados, Belize, Brazil, Cuba, Jamaica, Mexico, Panama, and Trinidad. It has been estimated that there are more than 20,000 infants born with CRS each year in the Americas in the absence of major epidemics.

There is more information regarding rubella susceptibility in the Americas. Serological surveys in at least 13 countries have documented a wide range of susceptibility in women of child bearing age or young adults of both sexes. Persons living on islands or in rural areas are more likely to be susceptible than those living in urban areas, with as many as half of adults of childbearing age in these settings being susceptible. Consequently, it is clear that the potential exists in many countries for major epidemics of rubella (with consequent CRS), in addition to the ongoing endemic incidence. All countries have at least some risk of rubella and CRS in the absence of effective immunization. Countries without direct evidence of the magnitude of risk

may wish to consider serological studies such as surveys of pregnant women or women at delivery. There are several sources of safe and effective vaccines at relatively low price.²

Recommendations

- **At this time, it is premature to establish a hemispheric goal of rubella elimination, but this could well be a logical development as progress continues with measles elimination.**
- **All countries should incorporate rubella vaccine (as MR or MMR) into childhood vaccination programs, both as part of routine childhood immunization at 12-15 months and as part of the follow-up campaigns reaching children 1-4 years of age every 4 years. This will provide immediate protection to the vaccinees and, over the course of several years, will prevent epidemic rubella among children. However, it will have only a limited immediate impact on the transmission of rubella among adults or the occurrence of CRS.**
- **Countries implementing childhood rubella programs should make efforts to reduce the accumulation of susceptible adult female groups, such as post-partum vaccination, immunization in family planning clinics, and other settings where females can be vaccinated. Women should be vaccinated with MR or MMR vaccine to take advantage of the opportunity to increase immunity to measles.**
- **While women known to be pregnant should not be vaccinated, others should be. Reasonable precautions are to ask a woman if she is pregnant, and if not, to vaccinate.**
- **Surveillance of CRS (and rubella) should be initiated throughout the Americas and should begin before, or at the same time as, implementation of a rubella vaccination program.**
- **Countries wishing to prevent and control CRS promptly should carry out a one time mass campaign to vaccinate all females 5-39 years of age with rubella or MR vaccine. Operationally, adult women could be vaccinated post-partum, premaritally, at workplaces or in colleges.**
- **Countries wishing to prevent and control both rubella and CRS promptly should carry out a one time mass campaign to vaccinate both males and females 5-39 years of age with rubella or MR vaccine.**

²Note: current prices indicate that MR can be purchased for only a few cents more than rubella vaccine alone.

Hepatitis B

It has been estimated that between 140,000 to 400,000 new cases of acute hepatitis B occur annually in the Americas. Two thirds of them are believed to occur in South America, primarily in areas within the Amazon Basin.

Recommendations

- **Routine vaccination of all children living in the Amazon Basin is recommended as well as in other areas, if any, with high endemicity (HbsAg prevalence equal or greater than 7%).**
- **Routine vaccination is also recommended for those at high risk of infection, such as health care workers and hospital staff.**
- **Because HBV infection is largely asymptomatic among young children, disease surveillance has a limited role in monitoring the hepatitis B vaccination program. Instead, the vaccination program must be monitored through mechanisms of process indicators (e.g., proportion of children or workers vaccinated) and through studies of asymptomatic hepatitis B virus infection (i.e. serologic studies).**

Yellow Fever

Between 1990 and 1996, 1,287 cases of yellow fever were reported in the Americas. As during the decade of the 1980s, 80% of these cases came from Amazon Basin areas of Bolivia and Peru. However, important risk areas for yellow fever are also present in Brazil, Colombia, and Venezuela.

Recommendations

- **Epidemiological surveillance for yellow fever cases is especially important because of the risk of its introduction into urban areas, now experiencing resurgent infestation with the vector *Aedes aegypti*. Thus, it is recommended that epidemiological surveillance be intensified and that adequate resources for diagnosis be provided.**
- **High risk areas should be identified based on special risk factors as is done now for the neonatal tetanus program.**

- **Incorporate vaccination against yellow fever into national immunization programs in high-risk areas and ensure that adequate quantities of vaccines and other supplies necessary to immunize against this disease are available at local health services.**
- **A stockpile of yellow fever vaccine should be available for use during an emergency.**

***Haemophilus Influenzae* type b (Hib)**

Safe and effective vaccines against *Haemophilus influenzae* type b (Hib) have had an enormous impact in industrialized countries on Hib disease incidence, particularly meningitis and epiglottitis. Similar effects have also been observed in some countries in the region (e.g. Uruguay and Chile) that have introduced Hib vaccine in their national immunization programs. It is possible that a larger impact on pneumonia will be observed in developing countries, as *Haemophilus influenzae* type b is an important pathogen in childhood pneumonias.

At present the price of Hib vaccine is a deterrent to vaccine introduction. It is hoped that increased demand from countries will lead to price reductions.

Recommendations

- **The TAG recommends the introduction of Hib vaccine in national immunization programs provided that adequate additional funds can be identified. However, implementation of Hib should not divert resources needed to sustain and enhance existing immunization efforts.**
- **Good quantitative data on the incidence of Hib disease in the Region are not available, particularly on respiratory disease. It is recommended that well structured surveillance systems be established to monitor illnesses due to Hib and to demonstrate vaccine impact.**
- **Use of the PAHO revolving fund for joint purchase of vaccines should facilitate negotiations to obtain a better price.**
- **It is important to evaluate carefully other vaccination strategies such as a reduced dosage or a reduced number of doses. PAHO should facilitate and help coordinate such studies.**

Diphtheria

Diphtheria incidence has been moving steadily downward throughout the Region. But in Ecuador, special problems have occurred. Ecuador's three major cities (Quito, Guayaquil and Machala) have been affected. During 1994-1995, 724 cases were reported at the national level, of which 84% were older than 15 years of age. Nearly 80% of cases were confirmed by culture. The case-fatality rate was 1.4%.

Outbreaks similar to that of Ecuador have recently been observed in the former states of the Soviet Union. These outbreaks have primarily affected adults with unusually low case-fatality rates. The cause for these outbreaks is not fully understood. Use of Td instead of TT for vaccination of older children and adults whenever tetanus toxoid is indicated should reduce the risk of any future diphtheria outbreaks.

Recommendations

- **It is TAG's belief that at this time special vaccination programs are not warranted. For the present, the routine vaccination program in children should be strengthened and further outbreaks, if they occur, should be carefully studied.**
- **Surveillance should be strengthened to include an investigation form for each suspected case and the determination of vaccination status.**
- **The diagnostic laboratory network should be strengthened to include testing for toxigenic strains.**
- **Norms should be established regarding diagnostic definitions and standard therapy to be applied.**

Pertussis

Pertussis incidence has steadily declined and is now at all-time historical low levels. Vaccination levels are generally satisfactory and there has been a marked reduction in the drop-out rates between the first and third dose of DPT.

Recommendations:

- **Routine immunization should be reinforced to achieve and maintain $\geq 90\%$ DPT3 coverage.**
- **Whole-cell vaccines have proved to be both safe and effective and are preferred to the acellular vaccines by most countries, both because of their successful performance and their lower cost.**

Vaccines of Quality

Quality of vaccine is assured through both quality control of the final product, as well as Good Manufacturing Practices (GMP) during the entire manufacturing process. Both manufacturers and governments using vaccines are responsible for quality. Manufacturers must adhere to GMP that assure high quality of every lot (consistency of production). Governments must have adequate capacity to monitor manufacturers and their products.

The Special Program for Vaccines and Immunization (SVI) has organized a Regional Network of National Control Laboratories and more recently, a Regional Network of National Control Authorities with the objective of strengthening and harmonizing the vaccine quality control system in the Americas. The SVI implemented a Certification Program for Vaccine Producers and is encouraging them to conduct feasibility and viability studies of their production activities.

Recommendations

- **Local vaccine manufacturers should participate in the PAHO Certification Program for Vaccine Producers.**
- **Local manufacturers should perform feasibility and viability studies of vaccine production to demonstrate their capability to supply vaccines of quality to immunization programs in a timely and continuous manner.**
- **Governments in the Region must institute National Control Authorities (NCA) appropriate to their vaccine production and purchasing policies.**
- **The NCA must be responsible for licensing vaccines, lot release, post-marketing surveillance, laboratory testing of vaccines, GMP inspections and evaluating vaccines if they are to be used for clinical trials in the country.**

- **National Control Authorities in countries where vaccine is produced must have a National Control Laboratory (NCL) responsible for performing laboratory testing of vaccines prior to release. The NCA and the NCL must be independent of the producer.**
- **National immunization program managers and National Control Authorities in all countries should cooperate to implement a national system of surveillance of and response to adverse events following vaccination. PAHO has reviewed and updated the *Guidelines for Implementing a Surveillance System for Adverse Events following immunizations*.**
- **Immunization program managers should use only vaccines of known quality in their immunization programs.**

Research and Development: the Regional Vaccine Initiative.

Although governments recognize that vaccine and immunization are key to the control, elimination and eradication of vaccine-preventable diseases, this recognition has not been translated into concrete actions to promote and support research and development for vaccine production. Research and development teams in the region are few and not coordinated among themselves or with vaccine producers. The introduction of new vaccines into national immunization programs in the region may be facilitated if some existing public laboratories participate in the process.

Results obtained by the Pneumococcal Surveillance Network demonstrate the importance of inter-country collaboration and coordination to standardize laboratory and epidemiological methodologies for monitoring a specific pathogen, to determine regional burden of disease, and to define particular characteristics of the burden such as serotype distribution or antimicrobial resistance. This system can be established and developed as the basis for a more comprehensive surveillance network for vaccine-preventable diseases.

Recommendations

- **Formal programs for vaccine research and development must be established with appropriate financial resources, together with strong coordination at the country and regional level in order to potentiate existing research, development and production capabilities.**
- **This initiative should give priority to the development of polysaccharide based vaccines as this methodology will provide vaccines against several important childhood pathogens such as *Haemophilus influenzae*, *Neisseria meningitidis*, *Streptococcus***

pneumoniae, *Salmonella typhi*, and *Shigella* sp., responsible for significant mortality and morbidity in the Region.

- The Network should include other countries in the Region as well as other important vaccine preventable diseases such as *Haemophilus influenzae* and *Neisseria meningitidis*. This improved network will also be an important epidemiological support to the Regional Vaccine Initiative
- The Network should collect information on cases and correlate those data with laboratory information to answer questions such as whether the increasing trend of antibiotic resistance has been associated with increased disease severity, complications, and cost. These data will be important in guiding clinical management and future policies for pneumococcal vaccination.