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FOURTH MEETING OF THE EPI TECHNICAL ADVISORY GROUP (TAG)

ON ERADICATION OF POLIOMYELITIS IN THE AMERICAS

ANTIGUA, GUATEMALA

20-22 APRIL 1987

In the 7 months since the third meeting of the Technical Advisory Group (TAG) in Brasilia, major efforts were devoted to securing the necessary external resources to carry out the eradication program. This has now been achieved, and commitments or pledges have been made that will provide more than USÑ$50Ñmillion to support the eradication program in the period 1986-1990. This total includes $20.6 million from USAID (in addition to substantial funds to be supplied in direct bilateral support), $16 million from UNICEF, $15 million from Rotary International, $7 million from PAHO, and $5.5 million from the Inter-American Development Bank.

Other important accomplishments since the third TAG meeting include the completion of the Laboratory Manual and the Field Guide, which is ready for publication. A course in surveillance and investigation of poliomyelitis has been conducted in Brazil with participants from 14 countries. In addition, a course in serological and virological techniques in polio diagnosis was conducted in Brazil and attended by personnel from 14 different countries. At the end of the course, participants received small quantities of cell lines, antisera, reagents, and supplies necessary to carry out these studies. Six laboratories (Argentina, Brazil, Colombia, Guatemala [INCAP], Mexico, Trinidad [CAREC]) have been identified to serve as sub-Regional reference laboratories and a specialized course will be conducted in Atlanta in September, 1987. Supplies and equipment are being ordered for these laboratories and should be in place before the end of the year. Efforts are underway to recruit 4 sub-Regional epidemiologists (to be located in Brazil, Honduras, Mexico, and Haiti).

The Interagency Coordinating Group met in January and found that, although there was good coordination of activities at the Regional level, there were still problems of coordination at the country level. They recommended the formation of coordinating committees in each country and the full involvement of these committees in the development and implementation of national plans of action. Such activities are now in progress. In the country work plans now being developed, issues of financial commitment and accountability are being addressed directly.

Several National Vaccination Days have been held since the last TAG meeting and, in a good example of multinational coordination, the Central American republics held a Central American Vaccination Day on April 5. An important feature of this activity was a joint television appearance by the Presidents of the various countries.

Against this background, the Fourth Meeting of the TAG was held in Antigua, Guatemala, April 20-22, 1987. The meeting was inaugurated by Dr. Carlos Armando Soto Gomez, Minister of Health and Social Welfare, and Dr. Fernando Antezana, PAHO/WHO Country Representative. The meeting was chaired by Dr.ÑD.ÑA. Henderson; Dr. Alan Hinman served as rapporteur. A complete list of participants and the agenda of the meeting are attached. The following represents a brief summary of the main agenda items and the conclusions and recommendations of the TAG.

CURRENT STATUS OF POLIOMYELITIS IN THE AMERICAS

In 1986, a provisional total of 811 cases of polio was reported from the Americas, compared to 867 cases reported in 1985. Brazil contributed more than 2/3 of the 1986 cases, compared with slightly more than 1/2 of 1985 cases. Mexico reported a significant decline in reported cases, from 148 cases in 1985 to 66 cases in 1986. On the other hand, Colombia experienced more than a doubling in the number of cases reported, from 36 cases in 1985 to 75 cases in 1986.

During the first 14 weeks of 1987, the number of probable and confirmed cases reported from the Americas is slightly lower than was observed in the same period in 1986, despite improved surveillance (210 compared to 221). Of particular concern is the fact that both Brazil and Colombia are reporting approximately the same numbers of cases in 1987 as in 1986, and El Salvador, Ecuador, Peru, and Venezuela are all reporting higher numbers of cases.

REPORTS FROM SPECIFIC COUNTRIES

EL SALVADOR

Routine health facility based immunization services in El Salvador have been augmented beginning in 1985 with National Vaccination Days (NVD) whose objective is to increase rapidly vaccine coverage with each of the EPI antigens. Following the 1986 NVD, polio vaccine coverage for children 1 year, 1 year and 2-4 years of age stood at 46%, 80% and 88%, respectively. This increased coverage has been accompanied by a reduction of cases of paralytic poliomyelitis from the levels observed during the previous 10 years. In 1986, 43 suspected cases were identified by the passive surveillance system implemented by the Ministry of Public Health, of which 15 were confirmed following investigation.

GUATEMALA

In 1986 the Ministry of Public Health in Guatemala initiated NVD. Currently it is expected that NVD will be carried out toward the end of 1987. After the 1986 NVD, poliovaccine coverage was raised among children 1 and 1-4 years of age to 33% and 46%, respectively. It is unlikely that such low coverage will have a major effect on poliovirus transmission. Of the 65 suspected cases reported in 1986, 33 were confirmed. Few of the reported cases were investigated fully but outbreak control measures were instituted in many under the direction of area and district authorities.

HONDURAS

Honduras also utilizes the NVD strategy in addition to routine immunization services, and enjoys the highest coverage rates of the three Central American countries reported in detail. Poliovaccine coverage among children 1 and 1-4 years of age in 1986 was 63% and 88% respectively, as calculated by a cohort system. Of the 77 suspected cases investigated during the period 1985-86, 11 were confirmed; the ratio of confirmed to suspected cases of 1:7 is the lowest among the three countries, and may reflect the use of excessively rigid guidelines for case confirmation. Case investigation and

the implementation of outbreak control measures appear to be more aggressive in Honduras than in the other 2 countries reported in detail. In the first 14 weeks of 1987, 14 probable cases have been reported from Honduras.

GENERAL COMMENTS BASED ON EXPERIENCES IN THE THREE COUNTRIES

Vaccine coverage is calculated using different methods in each country, and depends upon target population estimates extrapolated from census data collected 10-15 years previously. These methods should be standardized, in view of the comparative monitoring and evaluation functions for which these data are used nationally and internationally.

Active case-finding through the review of hospital emergency room and outpatient records in all three countries revealed unreported cases which met the suspected case definition. Another common observation is that each of the countries appears to be having difficulties with the current guidelines for case investigation and classification. Undue emphasis has been placed in some cases on laboratory findings, particularly where inappropriate intervals had elapsed between the onset of symptoms and taking a specimen for viral isolation or between first and second serum specimens.

In view of these findings, a number of interventions are indicated. A regional or departmental epidemiologic structure should be created in Guatemala as a matter of urgency. In-service training for health care providers concerning notification, referral, and case investigation and classification procedures should be conducted in each country. In particular, it should be emphasized that the final classification of cases should be based primarily on clinical and epidemiological data and carried out by an epidemiologist rather than a clinician. Weekly reporting and active case finding should be instituted at hospitals and rehabilitation facilities (at all levels) in each country. A proposal from Rotary International which calls for increased private sector assistance in the promotion of community awareness about polio eradication and the means by which this may be achieved is welcome.

Outbreak control measures ("bloqueos vacunales") should be carried out automatically in each of the three countries following the classification of a suspected case of polio as a probable case, as described in the PAHO Field Guide. Data concerning the date and extent of control activities should be routinely collected and analyzed in all cases. Cases reported from frontier areas should have coordinated bi-national investigation and containment.

The cold chain monitoring system in Honduras is practical and effective. Such a system should be adapted and put into practice in other countries where it may provide practical operational data with which to maintain cold chain hardware and fuel supplies more effectively. The establishment of cold chain facilities in those Guatemalan Departments that still lack them should be completed as a matter of urgency.

Funding is now available for the formal establishment of the Poliovirus Reference Laboratory at INCAP in Guatemala. Arrangements for the shipping and handling of specimens from the three countries to INCAP for viral studies possible through negotiations between the country programs and the Laboratory Director. A practical time-table for the transmission of results to the

country programs should be established. An early activity of this laboratory should be to explore the role of non-polio enteroviruses in causing paralysis (as has been reported from El Salvador and Honduras).

BRAZIL

Major improvements in the quantity and quality of surveillance information from Brazil were apparent in the presentation on that country. In 1986, 54% of probable and confirmed cases had complete laboratory evaluation (stool specimen and 2 blood specimens) and only 8% had no laboratory specimens. Unfortunately the time elapsed between the onset of symptoms (or the taking of specimens) and the availability of laboratory results (111 days, on average, between the acute blood specimen and results) severely limited the utility of the laboratory information. Of cases with known serotype in 1986 (44% of total), 57.9% were due to type 3 poliovirus.

A major effort has been made to use the classification system recommended by TAG with final classification of all probable cases within 10 weeks. One manifestation of this effort is that, in the 12th week of 1987, Brazil classified all remaining suspected or probable 1986 cases as confirmed or not polio. Approximately 60% of the 1029 total reported suspected cases were confirmed, the remainder were discarded. In the majority of the discarded cases no definitive diagnosis was available but of those with a definite diagnosis, facial paralysis (Bell's palsy) was the most common diagnosis. Guillain-Barre Syndrome was the second most common diagnosis, accounting for 7.7% of those with known other diagnosis; all cases were in persons 15 years of age or older.

Because of the continued occurrence of polio throughout 1986 and the continuing number of cases reported thus far in 1987, it is anticipated that an additional (third) National Vaccination Day will be held in Brazil in November of this year in all parts of the country except the South, which has been relatively free of disease and also has high coverage from routine services as well as the NVD.

OPV VACCINE TRIAL, BRAZIL

In the period February-June 1986, an outbreak of paralytic poliomyelitis caused by type 3 viruses (P3) occurred in the northeast region of Brazil. The outbreak was linked to a low seroprevalence of neutralizing antibody against P3, in spite of relatively high rates of coverage (75-80%) with 3 or more doses of trivalent oral polio vaccine (TOPV). To determine whether alternative vaccines might improve rates of seroconversion, 734 children in Recife were randomly assigned to receive a single dose of either:

T-C - the current TOPV with 1,000,000, 100,000, and 300,000 TCID50 of P1, P2, and P3, respectively

T-N - a TOPV with 600,000 TCID50 of P3, or

M-3 - a monovalent OPV with 300,000 TCID50 of P3.

Of the 734 children, 441 (60%) returned for collection of the second serum specimen and were included in the analysis. The results of neutralization antibody assays before and after vaccination showed generally high rates of seroconversion and/or increases in antibody titer against both P1 and P2 among children who received either T-C or T-N. Post-vaccination seroprevalences in these two groups ranged from 78-94% for P1 and 84-98% for P2 overall. However, when responses to P3 were evaluated, seronegative children who received T-N were 4 times as likely to seroconvert than those who received T-C (p 0.001; 95% C.I. 1.8-9.6). Similar differences were observed when the M-3 group was compared with T-C (p 0.0005), even though both groups had received the same dose of P3 antigen.

These findings, combined with a generally favorable evaluation of the cold chain, provided additional evidence that the outbreak of polio in Northeast Brazil was potentiated by type-specific failure of the current TOPV. On the basis of these findings, Brazilian health officials have decided to substitute the new formulation for use nationwide. This approach seems quite appropriate in light of the experience in the Northeastern part of the country. However, it does not seem indicated to extend this approach beyond Brazil at present, given that existing formulations of OPV are in widespread use throughout the world and have been very effective in the control and elimination of poliomyelitis in many countries under widely different climatic and social conditions.

MEXICO

In 1986, Mexico began holding NVDs in January and March, distributing OPV to all children less than 5 years old through more than 80,000 vaccination posts throughout the country. In 1987, DTP also was administered in 10 states during the second NVD. Coverage in each of the 4 NVD has been estimated at more than 90% nationwide and there has been a major decline in reported cases of polio, beginning immediately after the second NVD in 1986 and continuing to present. Of the 66 confirmed cases reported in 1986, 41 were reported before the second NVD (in mid-March) and 25 after. Of the 66 confirmed cases, 41 were confirmed on clinical grounds, 11 had virus isolations (including 4 who were also serologically confirmed) and 18 were serologically confirmed (including 4 who also had virus isolation). 90% of the cases were in children less than 5 years old. Of 44 discarded cases, 38% had no definitive diagnosis but 11 (25%) were diagnosed as having GBS - all of these were in children less than 10 years old. 22/66 cases were in children who had received 3+ doses of OPV. Thus far in 1987, only 13 cases have been reported in Mexico.

OTHER COUNTRIES

Brief presentations were made about the status of programs in Bolivia, Colombia, and Peru with even briefer discussions about Haiti, Dominican Republic, Ecuador, Paraguay, and Venezuela. In Colombia, NVD using OPV, DTP and measles vaccine were begun in 1984. Notwithstanding high coverage, there was an increase in incidence in 1986 which has continued into 1987. Although most cases occurred in inadequately vaccinated children, 19% occurred in children who had received 3+ doses of OPV. Because of the occurrence of 4 cases in infants less than 6 months of age, the Ministry of Health has

recommended administration of a dose of OPV at birth. Surveillance at the national level has not yet been standardized and there are delays in arriving at final classification of cases. In Bolivia, no cases were reported in 1984 and 1985 but 7 suspected cases were reported in 1986. Three of these were discarded, possibly due to inconclusive laboratory results. Major problems at present include the lack of a national program coordinator and inadequate reporting. In Peru, 3 NVD resulted in the raising of immunization coverage from 20% to 52%. Improved surveillance is being introduced but presently is only operative in Lima. This is reflected by the fact that 67% of reported cases are from Lima. Laboratory support is not adequate because of supply problems. Newborn administration of OPV has been introduced but further NVD are not presently planned. Of concern is the fact that 47% of cases are in children who have a history of 3+ doses of OPV.

OTHER

Cold chain equipment is now available throughout the Region. The primary remaining problems are in management and supervision of the cold chain. Most programs do not have an organized program for handling biologicals but deal with distribution on an ad hoc basis. Although equipment exists, poor condition and poor maintenance are still encountered. Additionally, although personnel have been trained in cold chain techniques, many have not incorporated this knowledge into daily practice (e.g., not monitoring and recording temperatures). Most of these problems can be readily solved by proper supervision of cold chain activities. A simple step to take to ensure adequate potency of OPV is to ensure that once OPV has been removed from a refrigerator for transportation it is not to be returned - if it is not completely used by the end of the day it should be discarded.

In addition to the role of Rotary International in providing financial support and OPV to immunization programs, the possibility of involving local Rotary clubs in other programmatic activities (e.g., public education, surveillance, organization and implementation of containment efforts) was discussed. No fixed protocol has been developed for this involvement but a detailed manual for Rotarians about EPI will shortly be distributed widely. Involvement of Rotarians can be significantly enhanced by providing regular feedback to Rotary Clubs from the health authorities about the polio situation within the country (as is now being done in Brazil).

There was detailed discussion of a research agenda and priorities for the Region; this is summarized in the Conclusions and Recommendations.

CONCLUSIONS AND RECOMMENDATIONS

The assurance of adequate external financial support added to national resources and the national political will now permits the program to be developed as was originally envisaged. The task now is to use these resources wisely and to apply them expeditiously in order to achieve the goal of eradication by 1990. Substantial progress has been made, but because of delays in obtaining funds, the eradication program has fallen behind schedule and will have to be intensified in order to meet the target. In this regard, several points are important; many of these have been made in earlier TAG reports but bear repeating.

1. Surveillance and investigation. Surveillance is clearly the critical element in disease control and eradication and must be given the highest priority. Although surveillance is improving in many countries, it is still not adequate in any country and remains to be established in many.

   a. A reporting network should be established consisting of at least one reporting unit in each municipio (or comparable small geopolitical unit) which should report each week whether or not suspected cases have been seen and their number. All health units (including hospitals and rehabilitation units) where cases are likely to be seen must be included as reporting units. A roster should be kept indicating whether or not each reporting unit has reported each week and steps should be taken to ensure that all units report promptly and regularly. Such a reporting network should include health facilities from all providers of health care (e.g., private sector, Social Security, Ministry of Health) and should be in place and operational in all countries before the end of 1988.

   b. "Suspected" cases which should be reported include all cases of paralytic illness occurring in persons less than 15 years of age as well as adults in whom the diagnosis of poliomyelitis is suspected. All cases of Guillain Barre Syndrome in persons less than 15 years of age should be considered "probable" polio unless proven otherwise. Recent experience suggests that the diagnosis of GBS is inappropriately made in some children. Development of specific diagnostic criteria for GBS could be quite helpful in this regard.

   c. The case definitions/classifications developed by TAG should be used in all countries, with particular attention paid to the time limitations for the various categorizations. All "suspected" cases should be visited by an epidemiologist trained in the clinical diagnosis of polio within 48 hours and classified either as "probable" or "not polio". It must be stressed that this classification is to be made by the epidemiologist based on the clinical and epidemiological information available, not by the attending clinician. Within 10 weeks, "probable" cases should be classified as either "confirmed" or "not polio".. If insufficient evidence is available at 10 weeks to readily categorize a "probable" case, it should be categorized as "confirmed." All "probable" and "confirmed" cases should be reported to PAHO even before final categorization.

   d. A detailed list should be maintained of all "suspected" cases and explanations provided for their categorization as "probable", "confirmed", or "not polio". It is particularly important to document why cases are discarded as "not polio". It may be useful to request review of individual cases by an expert or a panel of experts to assist in final categorization.

e. In countries where polio has not been reported recently it is particularly important that special visits be made to hospitals and rehabilitation centers to review charts and discharge summaries to determine if cases have been seen that might represent polio.

f. The Field Guide provides detailed recommendations for development and implementation of surveillance systems. It should be widely distributed and used.

g. Efforts should be made to ensure virus isolation and serotyping on as many cases of polio as possible to detect other P3 outbreaks should they occur. If outbreaks of P3 are detected, consideration should be given to alternative approaches to control (e.g., use of monovalent vaccine or enhanced potency TOPV).

2. Vaccination strategy and coverage. Achievement and maintenance of high immunization levels are key to eradication of polio. Several points are worth mentioning.

a. National Vaccination Days should be undertaken at least twice each year in all Group 1 (polio-infected) countries. Multi-national efforts such as the recent Central American Vaccination Day should be encouraged. These days should be separated by at least one month and should include the administration of DTP, measles, and tetanus toxoid (for adult women) wherever possible. As countries gain experience in such programs, it is expected that all will include the administration of several antigens.

b. Every effort should be made to ensure that NVDs help to strengthen the development of permanent, ongoing immunization services.

c. Coverage should be monitored for each municipio (or comparable small geopolitical unit) and a list made of all municipios with coverages of less than 80%.

d. Although PAHO/EPI techniques for assessing coverage are appropriate for ongoing services, it is not clear that they are the most effective means of assessing coverage where National Vaccination Days are an important component of the strategy. PAHO is asked to convene a small working group to develop recommendations for the most appropriate way to assess vaccination coverage in the EPI (including identification of the most appropriate age groups to be monitored). This should be accomplished before the next TAG meeting.

e. Wherever possible, a dose of OPV should be administered immediately after birth. This should not be counted as part of the routine schedule.

3. Laboratory support. Some progress has been made in developing a network of laboratories but substantial work remains to be done to assure that specimens are processed and reported promptly and results are reliable.

   a. At the present stage of the eradication program, laboratory examinations frequently show long delays between the taking of specimens and the availability of results and results are of uncertain reliability in many areas. Thus, in many areas at present, laboratory findings are of little help in reaching a timely diagnosis. However, as programs progress, the laboratory will play an increasingly important role in confirming the diagnosis, indicating the virus type, and whether it is wild or vaccine-like.

   b. As stated in the report of the Second TAG Meeting "establishing and maintaining competent and reliable laboratory support is both difficult and costly. Moreover, for a laboratory to maintain expertise, a monthly average of approximately 50 specimens for enterovirus isolation is needed." This should be kept in mind in determining whether national laboratories should continue to be used for poliovirus isolation or whether the sub-Regional reference laboratories should be used.

   c. Special efforts should be made to assure that all 6 sub-regional reference laboratories are fully equipped and functional before the end of 1987.

   d. If national laboratories are going to continue poliovirus work once the reference laboratories are operational, they should send duplicates of all polio specimens to the reference laboratories.

   e. Arrangements for appropriate shipping and handling of laboratory specimens (and payment of shipping fees) should be in place before the end of 1987.

4. Containment activities. Containment activities should be carried out promptly in response to all "probable" cases of poliomyelitis. This will normally involve at least several hundred to several thousand vaccinations. The purpose of the containment activities is not only to attempt the interruption of wild poliovirus transmission. The occurrence of a case of polio provides an indication that coverage in the immediate area is not good and the containment activities provide an opportunity to improve coverage. Additionally, the publicity surrounding the occurrence of a case usually enhances public interest and acceptance of immunizations.

5. Research priorities. In addition to discussions of research needs growing out of the P3 outbreak in Brazil, there was detailed consideration by TAG of a proposed research agenda for EPI in the Americas. The TAG feels that the primary thrust of research (as in programs) should be in the area of surveillance. The following were identified as priority areas for research during the next 18 months. Resources should be sought to carry out these studies, which are not listed in order of priority.

a. Determination, as quickly as possible, of the best formulation and schedule of administration of OPV under conditions pertaining in the Americas. The occurrence of the type 3 epidemic in Brazil in 1986 and the demonstration of lower-than-desired seroconversion rates to P3 (and to a lesser extent to P1) warrant this action.

b. Review of official country guidelines for contraindications. This should be combined with efforts to ensure official adoption of the guidelines issued by EPI and endorsed by the Latin American Pediatric Association.

c. Identification of the percentage of children visiting health facilities who are eligible to receive immunizations but who are not vaccinated and the reasons for withholding vaccines.

d. Development of techniques to evaluate the effectiveness and efficiency of National Vaccination Days.

e. Comparison of the efficacy of Edmonston-Zagreb (E-Z) and Chicken Allantoic Membrane (CAM) measles vaccines in infants 6 to 9 months of age.

f. Evaluation of efficacy of alternative measles immunization strategies (e.g. 2-dose strategies or mass campaign strategies).

g. Development and utilization of rapid detection techniques for the identification and characterization of polioviruses.

h. Evaluation of the impact of neonatal tetanus in the Americas.

i. Development of effective surveillance methods for pertussis.

6. Next meeting. The Fifth TAG meeting was tentatively scheduled for the week of 25 January 1988, provisionally in Lima. The reason for the prolonged interval between the Fourth and Fifth meetings is to permit fuller implementation of national programs now that adequate external financial resources have been made available.