EPI Newsletter

Expanded Program on Immunization in the Americas

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WHO Commemorates its 50th Anniversary!

On April 7, the World Health Organization (WHO) celebrated its 50th anniversary. WHO's work has benefited the well-being of children worldwide. Among the Organization's achievements is the global eradication of smallpox, a deadly and disfiguring disease that was preventable through vaccination. Following a 10-year international effort led by WHO, the last case of naturally occurring smallpox was reported in Merka, Somalia, on October 26, 1977. The Americas was the first region of the world to achieve smallpox eradication, with the last case of naturally occurring smallpox reported in Rio de Janeiro, Brazil in 1971.

Source: PAHO/WHO

The fight to protect children against vaccine-preventable diseases has been at the forefront of WHO's collaboration with its Members States, and it is the area of greatest impact. As one of the regional offices of WHO, PAHO has seen tremendous improvements in immunization coverage for children under 1 year of age for these diseases, from 25-30% in 1977, to levels above 80% in 1997. In 1991, the Americas became the first region in the world to eradicate poliomyelitis. Worldwide, countries are united in the goal to eradicate polio by the year 2000.

These extraordinary conquests in the Americas and worldwide have been the product of the collective action of countries, donors and beneficiaries alike, in pursuit of a common objective. This collaboration has enabled many countries to acquire the necessary tools to improve their health situation by themselves in a sustainable way.

Following the successful eradication of polio in the Americas, the Ministers of Health adopted a resolution in 1994, calling for the eradication of measles transmission from the Americas by the year 2000. The challenge to eradicate measles from the Americas has mobilized PAHO to revitalize the close and effective partnerships between countries established during the polio eradication years.

These partnerships formed through WHO/PAHO's work in health will play a critical role in the years to come. There are still countries and sectors of the population within countries that lack access to basic immunization services. Others are ready to incorporate a wider range of vaccines as part of the EPI. Much remains to be done to improve the quality of immunization services delivery and to find financing mechanisms that allow countries to maintain and improve vaccination coverage in a sustainable way. With the process of decentralization underway, attention is also needed to ensure that basic immunization remains a priority in all areas of each country, so that no area becomes a reservoir to seed infection into other communities and countries.

In this issue:

Paraguay and Brazil Discuss Joint Strategies for the Eradication of Measles

On February 12-13, 1998, a technical meeting was held in Curitiba, Brazil, to establish immediate strategies for controlling measles outbreaks in the border municipalities between Paraguay and Brazil. A project was prepared for technical cooperation between countries (TCC) to eradicate measles from the municipalities along the border between the two countries. TCC projects are a key component of PAHO's technical cooperation because they foster collaboration among countries in the Region to solve a particular health problem or set of problems. Representatives from the Ministries of Health of Brazil and Paraguay and at the regional and municipal levels attended the meeting. Also present were members of the Brazilian Cooperation Agency (ABC) within the Ministry of Foreign Affairs of Brazil, the Ministry of Health of Argentina, and PAHO country staff in Paraguay and Brazil.

Background

The measles epidemic that began at the end of 1996 in Brazil and lasted through 1997, with more than 26,000 confirmed cases, affected several countries in Latin America, including Paraguay. The two countries share a large border with a heavy flow of people. Therefore, there is a mutual interest to act jointly in activities for epidemiological surveillance and immunization to reach the Regional goal of measles eradication by the year 2000.

In Brazil, the border population of Paraná State with Paraguay is estimated at 370,000, spread among 11 municipalities, of which nine have achieved vaccination coverage over 95%. Two municipalities reported confirmed measles cases in 1997: Foz do Iguaçu with 77 cases and Santa Terezinha do Itaipú with 9 cases. In the state of Mato Grosso do Sul, the border population is estimated at 183,713, also distributed among 11 municipalities. Despite the lack of laboratory-confirmed measles cases, five clinically confirmed cases were reported. Vaccination coverage was over 95% in two municipalities.

In Paraguay, there was a resurgence of measles cases due to an importation from Brazil, with 198 laboratory-confirmed cases. The highest incidence occurred in the 10th health region (Ciudad del Este) with 105 cases, and the 14th health region (Canindeyú) with 14 cases, both bordering on the states of Paraná and Mato Grosso do Sul, respectively.

The tourist and commercial traffic across the Ponte Internacional da Amizade, which connects Ciudad del Este and Foz do Iguaçu is an important risk-factor in the transmission of measles virus in the region. The total border population is 701,423, and vaccination coverage in this area fluctuates between 40 and 60%.

Argentina also experienced an outbreak in 1997, which is still ongoing. During that year, the first confirmed cases appeared in the province of Misiones, which borders on Paraguay and Brazil. Measles then spread to metropolitan Buenos Aires and the capital city. A total of 762 cases were reported of which 112 were confirmed. Seven of these were in the province of Misiones. In 1998, at the time of the meeting, 47 cases were confirmed, all in the metropolitan area. Three-quarters of the reported cases have occurred in children under 5 years of age. The Ministry of Health scheduled a measles *follow-up* vaccination campaign for children under 5 in May. At the same time, the Ministry is implementing routine vaccination with measles-mumps-rubella (MMR) vaccine for children ages 12 months to 6 years.

Conclusions

There have been 205 confirmed measles cases in the border area between Brazil and Paraguay, which has a population of approximately 1,500,000 inhabitants. The following problems were identified in the border municipalities of both countries:

- Limited exchange of information on the occurrence of measles cases
- Underreporting of measles cases
- Lack of timely control measures
- Lack of coordination among the responsible authorities in the border areas
- A heavy flow of persons in the border areas
- The presence of indigenous villages in four border municipalities in Mato Grosso do Sul
- Passive and unstructured surveillance in some regions and municipalities
- Difficulties in the interpretation of coverage data
- Lack of coordination to develop adequate vaccination and epidemiological surveillance strategies

On the basis of these findings, there was consensus on setting up three local border committees. These committees will be comprised initially of those in charge of surveillance in the municipal and regional health secretariats and the National Health Foundation of the border municipalities in Brazil, as well as those responsible of the health regions in Paraguay (in equal numbers between the two countries). Among its initial functions will be establishing joint flows of information on epidemiological surveillance operations, (weekly negative notification of cases and notification of suspected and confirmed cases) and planning of joint operations in support of measles eradication.

A project was developed and approved to provide technical support for the joint activities between the two countries at the local level. This project seeks to improve communication between municipal health secretariats in Paraná and health regions in Paraguay on the border of these two countries to strengthen surveillance activities and immunization programs for measles and other vaccine-preventable diseases; and to further stimulate joint solving of health problems.

Source: Meeting Report.

Districts at Risk for Measles in El Salvador

Following the re-introduction of measles virus in Central America through an outbreak in Costa Rica in 1997, El Salvador reviewed the vaccination coverage levels of children under 1 year of age in all its 262 districts, to determine which had not reached coverage levels of at least 90%.

Background

One of the recommendations for measles from the Technical Advisory Group Meeting (TAG) held on September, 1997 in Guatemala, is to target vaccination efforts to areas at relatively higher risk for measles transmission. These include those districts with coverage for measles vaccine <90% in children under 1 year of age, especially in urban areas with high population density.

In October 1997, the Ministry of Health analyzed all 262 districts in El Salvador, to determine their relative risk for measles outbreaks. The average number of "at risk" districts during the period 1995-1997 has been approximately 70 districts per year. The number of children susceptible to measles accumulated every year in these districts has been approximately 15,000. In 54 of these districts, low coverage has been recurrent, that is <90% for at least 2 years since 1995, and in 20 of the 54 districts, low coverage has been occurring for the past 3 years. The population of children under 1 year living in those districts is between 30,000 to 35,000, or 26% of the country's official population data in this age group.

The following criteria were used to define high-risk districts:

- Average vaccination coverage obtained from all districts from January to June 1997.
- Population density in these districts.
- Number of children under 5 years of age susceptible to measles that had accumulated in the last 3 years.

Based on the country's trend of average vaccination coverage, the expected number of high-risk districts at the end of 1997 would have been 84, mostly located in rural areas. Sixty-five have low population density (fewer than 500 children under 1 year of age), representing 26% of the target population; 10 have between 500 and 1,000 children under 1 year of age; 4 have between 1,500 and 3,000 children under the age of 1 year old; and 5 districts situated in urban areas have over 3,000 children in that age range (42% of the target population).

Based on this analysis, the Ministry of Health of El Salvador organized in November and December 1997, a *mop-up* measles vaccination campaign in these 84 districts, aimed at children under 5 year of age, to increase population immunity and reduce the risk of measles outbreaks. House-to-house vaccination was carried out in these districts, using the current routine vaccination schedule, that is one dose of measles vaccine at 9 months, and one dose of MMR at 15 months. Including first doses and boosters, a total of 36,560 doses of measles vaccine and 8,637 doses of MMR were administered to children under the age of 5 years.

Results

A total of 116 districts (32 additional districts participated in the *mop-up* campaign to increase population immunity) carried out house-to-house vaccination activities during this campaign. The population of children less than l year of age in these districts is 91,115 children, representing 57% of this population group in the country (160,023). A total of 69,552 houses were visited, of which 52,494 were found occupied. A total of 41,597 children under 5 years of age were found in these houses.

The *mop-up* vaccination campaign against measles carried by El Salvador in targeted districts was very effective. The campaign succeeded in achieving higher measles vaccination coverage in districts that otherwise would not have reached the recommended 90% coverage by the end of 1997. <u>The most important achievement of this effort was the reduction from 84 to 61 in the number of districts at risk for measles</u>.

As a result of the campaign, there was an increase in districts reaching higher than 90% coverage (201 of 262 districts). However, there still remain 61 districts at risk, four of them due to high population density (more than 3,000 children under 1 year of age.)

Recommendations

- Continue strengthening routine infant vaccination programs by assuring daily immunization services and avoiding missed opportunities to vaccinate.
- During the next National Immunization Day, target resources toward districts at higher risk.
- Continue monitoring vaccination coverage by district at least every three months, as well as their performance in meeting the epidemiological indicators for surveillance, which are critical for the eradication of measles.
- Avoid the accumulation of susceptibles, especially in the districts with high population density and high influx of foreign visitors. These factors favor the reintroduction of measles virus to the country, and constitute an impediment to the eradication of measles in the Region of the Americas.
- Strengthen epidemiological surveillance throughout the country, primarily in the "silent" districts, that is those that have never reported suspected measles cases or have low rates of weekly negative notification.

Source: Ministry of Health of El Salvador.

Editorial Note: The Pan American Health Organization urges countries to follow the example of El Salvador by characterizing in more detail vaccination coverage obtained at the district level, and the population living in those districts that have not been vaccinated.

Central America Meeting Initiates Surveillance System for Hib and *Streptococcus pneumoniae*

Nicaragua hosted the first regional meeting on March 2-7, to develop a proposal for an epidemiological surveillance system for bacterial meningitis and pneumonia among children under 5 years of age, particularly those attributed to *S. pneumoniae* and *H. influenzae* type b. These microorganisms represent the most important etiological agents of acute respiratory diseases affecting children in Central America. The establishment of a regional surveillance system will allow the quantification of disease burden and assist countries in phasing in new vaccines, such as Hib, in their routine immunization programs.

Simultaneous workshops were held with representatives from Public Health Laboratories and epidemiological surveillance. Laboratory staff from participating countries were trained in microbiological techniques for both diseases. Also presented were a prototype agenda and a model workshop that can be replicated in their respective countries. The microbiology group of the National Institute of Health in Colombia was responsible for the design and implementation of the laboratory training. It followed a model workshop held in 1992, as part of the *S. pneumoniae* surveillance study sponsored by PAHO and the Canadian International Development Agency.

During the session with epidemiologists, a proposal was prepared for the establishment of inclusion and exclusion criteria, case definitions, as well as requirements for standardizing surveillance. The participation during the discussions of clinicians from hospitals in Managua was important, since they will play a major role in implementing these criteria and in ensuring the adequate completion of case investigation forms. Participants prepared forms to be used, in an effort to standardize the information entered into a sub-regional database. The generic protocol of the Global Program for Vaccines of the World Health Organization was used as a sample in preparing the proposal, as well as surveillance protocols of Nicaragua, and El Salvador and the pilot study that is being carried out in Guatemala City.

The meeting culminated with a joint session of laboratory staff, clinicians and epidemiologists, and highlighted the need for close collaboration during the development of the surveillance system. This meeting also stressed critical aspects in collecting and processing samples which should be taken into account during the planning stages of the surveillance system, and for the selection of participating hospitals and centers.

Recommendations

- Adapt the protocols already in place for surveillance in Nicaragua and El Salvador to include the standardized definitions endorsed during the meeting.
- Recommend that the study being conducted in Guatemala adopt the same definitions, to be able to use the information in a regional context.
- In the remaining countries, organize a surveillance system according to the proposal discussed.
- Prepare workshops at the national level for standardizing laboratory procedures, according to the workshop carried out in Managua.

Source: Meeting Report.

Evaluation of Mexico's Universal Vaccination Program

Background

As a result of Mexico's participation in the World Summit for Children, held in New York City on 30 September 1990, the Universal Vaccination Program (UVP) was established to strengthen the prevention and control of vaccine-preventable diseases. The Program's primary goal is to achieve equity in the vaccination of all children less than five years of age. The National Council on Vaccination was established by Presidential Decree on 22 January 1991, to coordinate and support immunization activities carried out by the institutions of Mexico's National Health System. Since its inception, the Council has monitored the development of the Universal Vaccination Program and has incorporated new operational strategies.

Following a request by the Ministry of Health of Mexico to the Pan American Health Organization, an international team carried out an evaluation of the country's Universal Vaccination Program. This exercise sought to review the development of the Universal Vaccination Program between 1990 and 1997; review quantitatively the progress achieved and activities performed; identify the Program's problems and present possible solutions; and define activities to reach set objectives within the context of the process of decentralization. The evaluation had two other major components: evaluation of the cold chain and logistics program, and a feasibility study of vaccine production through the incorporation of new technologies to Mexico's Gerencia General de Biologicos y Reactivos. The following is a summary of the evaluation in Mexico.

Findings

According to available data encouraging results have been achieved, both in terms of vaccination coverage and impact. These data indicate that in 1996, 97% of children 1 to 4 years age had completed the basic vaccination schedule.

The morbidity and mortality due to vaccine-preventable diseases are at the lowest levels: significant are the absence of poliomyelitis cases during the last 7 years, diphtheria during the last 6 years, and the gradual decline in morbidity due to measles in the last 5-year period.

Principal findings of the evaluation indicate that Mexico's Health Ministry, the Mexican Institute of Social Security and the Institute of Social Security for State Workers are placing a high priority on vaccination activities. This is evident by the allocation of sufficient resources and by the country's strategic vision in terms of adding new vaccines into the regular vaccination schedule, including those that will benefit the adult population and/or prevent congenital defects. Awareness on the importance of vaccination was raised among staff of the National Health System and in the community. The impact of the strategies used by the UVP, which include routine vaccination and intensive vaccination campaigns, confirm that they are adequate and that they should continue to be implemented and strengthened.

Adequate coordination among the institutions that belong to the National Health System has been achieved at all levels, and there has been close collaboration with other public health organizations, particularly PAHO and UNICEF.

Recommendations

The principal observations and recommendations of the evaluation include:

- At the central level, good quality epidemiological surveillance and the capacity for rapid analysis has been achieved. However, at the jurisdictional and local levels there are important areas that require immediate action.
- The quality of information at the local level is questionable, reaches the central level inopportunely and lacks feedback mechanisms to operations.
- Up-to-date training in epidemiological surveillance is lacking for personnel at the operational level—rationale for surveillance is not fully understood.
- The above deficiencies point to the possibility of underreporting in the notification of suspected measles cases, considering that a large number of rubella and dengue cases were reported in 1997 without laboratory confirmation, and the measles outbreak in São Paulo, Brazil, which spread to other areas of Latin America.
- Reporting of laboratory results should be simplified, so that they arrive at the local levels in a timely manner. PROVAC should be adapted for use at the local levels. This would facilitate their involvement in the programming and evaluation of activities.
- The current regionalization should be reviewed, especially in the Federal District, to ensure that it fulfills its objectives of maximizing resources and avoiding duplication.
- Mechanisms are needed to ensure the introduction and availability of Hib vaccine at all health services. This would harmonize vaccination activities at all levels of the country's health institutions.
- As new vaccines are incorporated to the UVP, it will be necessary to immediately begin surveillance activities for the targeted diseases.
- The current vaccination schedule should be reviewed, particularly the need for a booster of DTP vaccine at 18 months.
- Vaccination against rubella should be included for all women of childbearing age.
- Private sector participation is important in all program activities, especially vaccination and surveillance.

Source: Ministry of Health, Mexico.

For a copy of the complete evaluation, please contact the Ministry of Health at Lieja 7, Col. Juarez, Mexico, D.F. Mexico.

3rd Canadian National Immunization Conference

Partnerships for Health through Immunization
The Calgary Convention Centre, Calgary, Alberta, Canada
December 6-9, 1998

Organized by the Laboratory Centre for Disease Control, Health Canada, and the Canadian Paediatric Society.

Objectives are to present a forum for discussion and information exchange related to the practical aspects of immunization programs in Canada and means of improving them. This will cover issues such as vaccine supply and delivery, education, assessment of vaccine programs, regulations and legislations, and global immunization efforts. The conference will look at both programmatic and disease-related issues, with primary focus being on programmatic issues. The main focus will be on childhood immunization. There will also be an examination of progress towards the achievement of established Canadian national goals for the reduction of vaccine-preventable diseases of infants and children.

To access information as it becomes available, or to be put on the conference mailing list, visit the Conference Website at:

http://www.hc-sc.gc.ca/hpb/lcdc/events/cnic/index.html

Or fax your request to:

Chuck E. Schouwerwou, BA,CMP
Conference and Committee Coordinator
Division of Immunization

613-952-7948

Poliomyelitis Surveillance

Attention to the four poliomyelitis surveillance indicators approved by the International Commission for the Certification of Poliomyelitis Eradication (ICCPE) in 1994, has gradually been deteriorating during the last years since the Region of Americas was declared free from wild poliovirus. These indicators are designed to measure the performance of health services and the sensitivity of the surveillance system to detect wild poliovirus circulating in the community. Sensitivity is the most important characteristic of the poliomyelitis surveillance system and it is measured by the rate of acute flaccid paralysis (AFP) per 100,000 under 15 per years of age.

As of the week 11 (March 21) of 1998, the AFP rate reached its lowest level yet in the Americas. Only three countries (Bolivia, Chile and Honduras) presented the rate at acceptable levels (see Table). The other countries in the Caribbean region and Latin America showed rates lower than 1 AFP case per 100,000 children under 15 years of age. This analysis does not include data for the United States and Canada, because both countries follow a different surveillance system.

Considering the size of the population of children under 15 years of age in those three countries (11 million) compared to the size of the corresponding population (190 million) in the Region (Caribbean and Latin America), it can be concluded that only 6% are currently protected by a sensitive AFP surveillance system. This leaves 94% living in countries where the low sensitivity of the surveillance system does not allow for the timely identification of the circulating virus. If an importation occured from another region where the virus is still circulating, the possibility of stopping the spread of the wild poliovirus would be minimal.

The Americas' experience also shows that even in 1991, when the sensitivity of AFP surveillance system was extremely high, it still took 8 months to identify circulating wild poliovirus in Peru. This raises the possibility that the poliovirus might today be circulating silently in the Region.

Immediate attention is needed to overturn the declining attention to the AFP surveillance indicators. As the members of the ICCPE have pointed out, "it would be tragic, if after the extraordinary efforts that have been made to free the Americas from polio, we were to let down our guard and allow the poliovirus to become established once again."

AFP Surveillance Indicators

Country	80% weekly reporting units	80% of cases investigated within 48 hours	80% of cases with 1 adequate stool sample taken	AFP Rate ≥ 1:100,000 in children < 15 years
Honduras	■	■	■	■
Bolivia		■	■	■
Chile	■	■		■
Colombia	■	■	■	
Cuba	■	■	■	
Ecuador	■	■	■	
El Salvador	■	■	■	
Nicaragua	■	■	■	
Venezuela	■	■	■	
Dominican Republic		■	■	
Peru	■	■		
Brazil		■		
Mexico		■		
Panama	■			
Paraguay	■			
Argentina				
Costa Rica				
Guatemala				
Haiti				
Uruguay				

■ - Meet criteria * Data as of 21 March 1998

Source: SVI/PAHO (PESS

Regional Update

- In April and May of 1998, SVI/PAHO will conduct three sub-regional meetings for the Southern Cone and Brazil, the Andean region and Central America (including the Latin Caribbean countries and Mexico). These meetings will provide a forum for discussion and for the exchange of information and experiences of the national immunization programs. Key in these discussions will be the Region's progress toward measles eradication. Participants will include country EPI Managers and representatives from USAID, UNICEF, Rotary International and non-governmental organizations.
- From 22 March through 3 April 1998, an evaluation of the national immunization program in Brazil was carried out by the Ministry of Health and PAHO. The purpose was to evaluate the development of the program, determine its capacity and available resources, and gauge its potential for growth to allow the sustainable incorporation of new vaccines into the basic immunization schedule.
- In May 14-15, an international meeting will be held in Cuzco, Peru on yellow fever, to review the epidemiological situation and latest outbreaks, and to discuss strategies for routine immunization for this disease in high-risk areas.
- The Ministry of Health of Haiti has announced that it will conduct a *follow-up* measles vaccination campaign in 1998, with cooperation from PAHO and other agencies.
- During May and June, *follow-up* measles vaccination campaigns are scheduled in Argentina, Uruguay and Venezuela.

Reported Cases of Selected Diseases

Number of reported cases of measles, poliomyelitis, tetanus, diphtheria, and whooping cough, from 1 January 1998 to date of last report, and the same epidemiological period in 1997, by country.

Country/Territory	Date of last report	Measles				Polio		Tetanus				Diphtheria		Whooping Cough	
		Confirmed 1998			Confir-med*			Non Neonatal		Neonatal					
		Labo-ratory	Clini-cally	Total	1997	1998	1997	1998	1997	1998	1997	1998	1997	1998	1997
Anguilla	21 Mar	0	0	0	0	0	0	...	...	0	0	0	0	0	0
Antigua & Barbuda	21 Mar	0	0	0	0	0	0	...	0	0	0	0	0	0	0
Argentina	21Mar	46	0	46	10	0	0	...	...	...	...	...	...	...	...
Bahamas	21 Mar	0	0	0	1	0	0	0	0	0	0	0	0	0	0
Barbados	21 Mar	0	0	0	0	0	0	...	0	0	0	0	0	0	0
Belize	21 Mar	0	0	0	0	0	0	...	0	0	0	0	0	0	0
Bermuda	21 Mar	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Bolivia	21 Mar	0	0	0	0	0	0	1	0	1	3	5	0	18	22
Brazil	21 Mar	314	7	321	83	0	0	...	...	...	...	...	...	...	...
British Virgin Islands	21 Mar	0	0	0	0	0	0	...	0	0	0	0	0	0	0
Canada	21 Mar	2	__	2	251	0	0	...	...	...	...	...	...	...	...
Cayman Islands	21 Mar	0	0	0	0	0	0	...	0	0	0	0	0	0	0
Chile	21 Mar	0	0	0	0	0	0	...	...	...	0	...	0	...	...
Colombia	21 Mar	1	6	7	18	0	0	0	1	3	9	2	2	81	88
Costa Rica	21 Mar	0	0	0	0	0	0	...	...	...	...	...	...	...	...
Cuba	21 Mar	0	0	0	0	0	0	...	...	...	...	...	...	...	...
Dominica	21 Mar	0	0	0	0	0	0	...	0	0	0	0	0	0	0
Dominican Republic	21 Mar	0	0	0	0	0	0	4	2	0	0	3	3	5	1
Ecuador	21 Mar	0	0	0	0	0	0	0	2	6	9	5	4	62	61
El Salvador	21 Mar	0	0	0	0	0	0	...	...	...	...	...	0	...	0
French Guiana	...	...	...	...	...	0	0	...	...	...	...	...	...	...	...
Grenada	21 Mar	0	0	0	0	0	0	...	0	0	0	0	0	0	0
Guadeloupe	21 Mar	0	0	0	28	0	0	...	...	...	...	...	...	...	...
Guatemala	21 Mar	0	0	0	4	0	0	0	...	1	...	0	...	364	...
Guyana	21 Mar	0	0	0	0	0	0	...	...	0	0	0	0	0	0
Haiti	21 Mar	...	...	...	0	0	0	0	...	12	17	0	...	...	...
Honduras	21 Mar	0	0	0	3	0	0	...	0	...	0	...	0	...	...
Jamaica	21 Mar	0	0	0	0	0	0	...	0	0	0	0	0	0	0
Martinique	...	0	0	0	...	0	0	...	...	...	...	...	...	...	...
Mexico	21 Mar	0	0	0	0	0	0	...	23	...	7	...	...	...	0
Montserrat	21 Mar	0	0	0	0	0	0	...	0	0	0	0	0	0	0
Netherlands Antilles	...	...	...	...	...	0	0	...	...	...	...	...	...	...	...
Nicaragua	21 Mar	0	0	0	0	0	0	1	2	0	0	0	0	0	15
Panama	21 Mar	0	0	0	0	0	0	0	0	0	0	0	0	66	4
Paraguay	21 Mar	0	0	0	1	0	0	...	...	...	...	...	...	...	0
Peru	21 Mar	0	0	0	20	0	0	18	11	4	4	1	0	229	167
Puerto Rico	21 Mar	0	__	0	0	0	0	...	...	...	...	...	...	...	...
St Vincent/Grenadines	21 Mar	0	0	0	0	0	0	...	0	0	0	0	0	0	0
St. Kitts/Nevis	21 Mar	0	0	0	0	0	0	...	0	0	0	0	0	0	0
St. Lucia	21 Mar	0	0	0	0	0	0	...	0	0	0	0	0	0	0
Suriname	21 Mar	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Trinidad & Tobago	21 Mar	0	0	0	0	0	0	...	0	0	0	0	0	0	0
Turks & Caicos	21 Mar	0	0	0	0	0	0	...	1	0	0	0	0	0	0
United States	21 Mar	7	__	7	11	0	0	...	...	...	...	...	...	...	...
Uruguay	...	...	...	...	0	0	0	...	...	...	...	...	...	...	...
Venezuela	21 Mar	0	0	0	3	0	0	5	4	1	2	0	0	165	55
TOTAL		**370**	**13**	**383**	**433**	**0**	**0**	**29**	**46**	**28**	**51**	**16**	**9**	**990**	**413**

... Data not available.
—Clinically confirmed cases are not reported.
* Laboratory and clinically confirmed cases.

Vaccines of Quality

*This article is second in a series on vaccine quality (see the February 1998 issue of the **EPI Newsletter**). In this issue the focus is on tests for safety, specific toxicity and those which are utilized to detect possible contamination by microorganisms.*

Tests for safety, innocuity or nonspecific toxicity

These tests are carried out to detect any possible contamination (chemical) that could have occurred during the production process, particularly during the filling process, which could have a harmful effect on the health of those vaccinated. The methodology used consists of the intraperitoneal or subcutaneous inoculation of the final product in two guinea pigs and five mice (every species within an established weight range), followed by a seven-day period of observation. The animals are weighed before the inoculation and on the seventh day. The product is considered innocuous if all the animals survive the observation period and fail to show signs of toxicity, usually demonstrated by weight loss. It is important to point out that this test is designed to detect associated toxicity directly related to components of the vaccine (for example, pertussis). The dose for inoculation depends on the animal species and on the vaccine. This is a test for detecting potentially serious problems. However, its importance has declined considerably with the introduction and application of Good Manufacturing Practices (GMP) and chemical control tests.

Tests for specific toxicity

Included within this group of tests are those directly associated with the inherent toxicity of some vaccine ingredients. Toxoids (for example, tetanus and diphtheria) are produced by a process of chemical detoxification of the toxins. This test confirms that the process has succeeded in eliminating toxicity and that detoxification is irreversible. In the case of vaccines from killed microorganisms, the test is principally used to detect the toxic effect of some vaccine components. For the attenuated viral and bacterial vaccines, these tests ensure that the microorganisms utilized are not virulent and cannot cause adverse reactions or even the disease. In general, these tests are carried out in animals by injecting a preestablished dose of vaccine, followed by an observation period during which signs of toxicity and/or neurological effects characteristic of the toxins or microorganism should not be observed.

Tests to detect contamination by microorganisms

The absence of contamination by microorganisms is an important component in the quality control of vaccine batches. Viral vaccines are usually prepared using animal tissues, embryonated eggs, cell cultures and sera, all potential sources of extraneous viruses. Contamination can also occur through contact with the working personnel, and by using equipment that has not been properly cleaned and/or sterilized. Extraneous viruses are usually detected by in vitro methods using specific cell cultures. Bacterial contamination is demonstrated by inoculating the vaccine into appropriate culture media and monitoring growth, this is otherwise known as the sterility test.

Many bacteria secrete pyrogens or endotoxins, which are sensitive indicators of the presence of bacteria. The pyrogen test is carried out by injecting the product into the ear veins of rabbits and monitoring their rectal temperature. The animals require special housing, because environmental problems can markedly influence results. Increased body temperatures above certain limits is an indication of a pyrogenic product. Endotoxins can be also detected by their clotting effect on extracts from Limulus amebocytes (LAL test).

It is important to understand that quality control tests are done on a limited, randomly selected number of vials and the results are then extrapolated to the whole batch. Thus, extrapolation of satisfactory results to the whole batch requires the assurance that every unit in the batch has been prepared in compliance with Good Manufacturing Practices.

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