EPI Newsletter

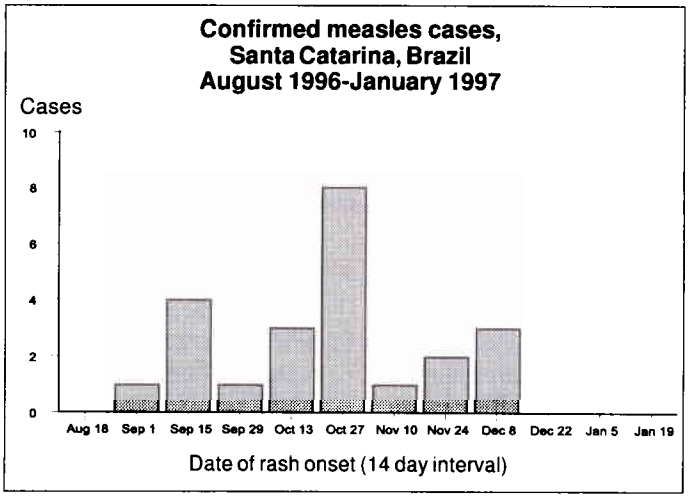
Expanded Program on Immunization in the Americas

Volume XIX, Number 1 **IMMUNIZE AND PROTECT YOUR CHILDREN** February 1997

Measles in Brazil: Indigenous or Imported?

On 24 September 1996, the Santa Catarina State public health department received a report of a suspected measles case. The patient was a 32 year old woman from São José County who had been seen by a physician on 22 September 1996 because of fever, rash and cough. She was initially thought to have an allergic reaction and was treated with antihistamines.

Two days later, the patient returned for re-evaluation accompanied by her 6 month old grandson, who was acutely ill with a fever and rash illness. The infant was referred to a pediatrician and was diagnosed clinically as having measles. The woman's rash had increased in severity and her respiratory symptoms had worsened. She was then hospitalized with the diagnoses of measles and pneumonia.



Both cases were confirmed as measles when serum specimens tested positive for measles IgM antibodies using an indirect assay at the Public Health Laboratory (LACEM) in Florianópolis. The specimens were later reconfirmed using the highly specific measles IgM capture test in the measles laboratory of the Oswaldo Cruz Foundation (FIOCRUZ) in Rio de Janeiro.

A visit to the woman's home revealed that her 19 year old son-in-law, a gas station attendant, had a history of fever and rash illness, with rash onset on 6 September 1996. A blood specimen collected from him in late September was positive for measles IgM antibody. The source of his measles infection is unknown.

Field investigation conducted in the Florianópolis health district, including 18 counties of Santa Catarina between September and December of 1996, ascertained a total of 58 suspected measles cases (see graph). Of these, a total of 24 (41.4%) were confirmed as measles, 23 via laboratory confirmation and 1 case was confirmed by epidemiologic linkage to a laboratory confirmed case. The remaining 34 suspected measles cases had a blood specimen collected and tested negative for measles IgM, and were thus discarded. The last confirmed case had rash onset on 18 December 1996. No additional cases have been detected since then, despite the existence of enhanced measles surveillance.

Urine specimens were collected for measles virus isolation from several suspected measles cases. These specimens were centrifuged, resuspended in viral transfer media, frozen and transferred to the FIOCRUZ measles laboratory. Measles virus was isolated from two of the submitted specimens. Genomic analysis of the measles virus isolates is currently being conducted in collaboration with the Centers for Disease Control and Prevention's measles laboratory in Atlanta, Georgia, USA. Provisional data of the nucleotide sequence of the isolated virus suggests that the virus isolated from Santa Catarina is similar to a virus which has been circulating in Europe in recent years, suggesting the likelihood of an importation.

Thirteen confirmed cases were reported from São José County, 4 from Antônio Carlos County, 2 from the capital city of Florianópolis, and one case each from Biguaçu,

In this issue:

Palhoça, Aguas Mornas, Criciuma and Brusque Counties. Of the laboratory confirmed cases, 4 (17.4%) had histories of measles vaccination; the remaining cases were unvaccinated. Of the confirmed cases with histories of measles vaccination, 2 (50%) had received measles vaccine in the month before rash onset.

Cases ranged in age from 6 months to 32 years. Seven cases were younger than one year of age, three cases occurred in children 1-9 years of age, seven cases were in children 10-19 years of age and seven cases occurred in persons $\geq$ 20 years of age. In the Florianópolis health district, the highest age-specific attack rates occurred in infants < 1 year of age (42.8 cases/100,000 population), in adolescents 15-19 years of age (7.4 cases/100k) and in young adults 20-29 years of age (4.5 cases/100k).

Outbreak response activities included an emergency review of vaccination coverage in the affected counties, provision of measles vaccine to infants and children without histories of measles vaccination and enhanced measles surveillance. In addition, a technical team was sent to Antônio Carlos and São José Counties, where visits were made to the households of all confirmed measles cases to gather further information on the possible source of infection and to find additional cases. Visits were also made to health centers, hospitals and schools in these counties to provide measles vaccine to unvaccinated children and to stimulate measles surveillance.

A technical meeting was convened for personnel from the Florianópolis District and Santa Catarina health departments to obtain further information. A lecture was given for pediatricians and pediatric residents at the Children's Hospital in Florianópolis to inform them about the plan to eradicate measles from Brazil and the need to report any suspected measles cases.

Analysis of the coverage attained in the 1992 *catch-up* vaccination campaign aimed at children 1 to 14 years of age, and in the 1995 *follow-up* campaign among children from 1 to 3 years old, indicates that at the state level overall coverage was 94.2% in 1992, and 85.2% in 1995. In 1992, coverage of the group aged 10 to 14 years was 85.3%. Measles vaccination through routine health services between 1992 and 1995 reached 90% of the children under 1 year of age.

It can be estimated that the number of susceptible individuals born after 1992, between those not vaccinated (5% to 10%) and those vaccinated but not immunized (also 5% to 10%), comes to approximately 10 to 15% of all children born (105,000 a year), or 40,000 to 60,000 children aged 1 to 4 years in 1996, many of whom may actually have been revaccinated during the *follow-up* campaign of 1995. Given the coverage levels attained in the 1992 campaign among the group aged 10 to 14 years, it is also estimated that as many as 75,000 adolescents between 14 and 20 years old in the state, may also be susceptible to measles.

The confirmed cases in São José County were clustered in a poor peri-urban area. This led to a selective vaccination effort, in which 14 children from 9 months to 14 years of age living in the area were found to be unvaccinated. In the municipality of Antônio Carlos selective vaccination efforts were undertaken after each report of a confirmed measles case. This included a review of immunization of the 500 students attending the local school. Few previously unvaccinated students were found. Selective vaccination was also conducted among the contacts of the subsequently reported and confirmed cases.

Source: Carla Santos Domingues-MOH Brasilia, Ilse Lisiane-MOH Santa Catarina, Marilda Siqueira-FIOCRUZ, Elisabeth David dos Santos- MOH Brasilia, Bernardus Ganter-SVI/PAHO, Brasilia.

Editorial Note: The outbreak in Santa Catarina is the largest that Brazil has experienced in over 2 years. In 1995, only 13 laboratory-confirmed cases of measles were reported in Brazil. In 1996, prior to this outbreak, only 3 laboratory confirmed cases had been reported, two of which are believed to have been imported from Japan and Italy, respectively. In contrast, in 1991 the year prior to the *catch-up* campaign, over 30,000 measles cases were reported in Brazil.

The initial information from the outbreak investigation suggests that important changes have occurred in the epidemiology of measles in Brazil. Until very recently, measles was circulating freely in Brazil and thousands of cases were reported each year. Moreover, the country experienced major measles outbreaks every few years, with tens of thousands of cases, when the number of susceptible children accumulated to high levels. Most cases occurred among unvaccinated infants and preschool-aged children.

As a result of the implementation of PAHO's measles eradication strategy, measles virus circulation appears to have been interrupted throughout Brazil. Indeed, prior to this outbreak, the last confirmed case of measles in Santa Catarina State was reported in 1993.

While measles surveillance can not be expected to detect every case of measles virus infection in Santa Catarina, in historical comparison, measles transmission does not appear to be extensive. Most cases in this outbreak are occurring among unvaccinated infants, adolescents and young adults. Preschool-age and school-aged children have largely been unaffected by the outbreak. This demonstrates the ability of measles virus to seek out susceptible individuals, even in areas which have achieved and maintained high levels of population immunity.

The source of the outbreak remains unknown, but the genomic analysis of measles virus isolated from the outbreak investigation suggests that measles virus may have been imported into Santa Catarina from Europe. This finding underscores the ability of measles virus to readily travel between continents and to cause outbreaks in areas which had previously interrupted measles virus circulation. The recent report of an outbreak in the Philippines is a cogent example of the dangers that measles poses.

Since early January 1997, 59 children have died from measles in the Philippines, with most cases and deaths occurring in the Manila metropolitan area. All deaths occurred in infants and children 5 years of age and younger. Furthermore, over 1,000 children were hospitalized in the Manila area and about 200 children in other parts of the country due to complications of measles infection.

As long as measles virus is circulating anywhere in the world, Brazil and the other countries of the Americas will remain at risk for importations of measles virus. The only effective way to totally prevent importations into measles-free countries will be through the ultimate global eradication of measles. As other regions of the world learn from PAHO's measles eradication experience, global measles eradication will increasingly be seen as being an attainable goal.

Laboratory Diagnosis of Viral Hepatitis

The following article is the first of three covering the subject of laboratory diagnosis of viral hepatitis. This first article deals with general diagnostic aspects of viral hepatitis. In the April 1997 issue of the ***EPI Newsletter****, hepatitis B and hepatitis Delta will be covered, and the June issue will discuss Hepatitis A, C and E.*

Etiological Agents

Hepatitis of viral origin can be caused by different etiological agents, of which five viruses have already been identified. Although they are hepatotropic and produce hepatitis as a result of cellular infection, they present quite different morphological and molecular characteristics, as well as different transmission mechanisms, development and clinical consequences[1-4,15] (Table 1). Based on epidemiological characteristics, it was felt that viral hepatitis was caused by only two viruses: one with enteric transmission and the other with parenteral transmission; these were later identified as Hepatitis A Virus (HAV) and Hepatitis B Virus (HBV) respectively. However, during the 1970s, there were cases of post-transfusion hepatitis whose agent was neither HAV or HBV. These types of hepatitis were then called non-A, non-B hepatitis (HNANB).[5] Later in the same decade, Rizzetto identified a parenteral transmission agent, which he only managed to replicate in the presence of HBV; this defective virus was called Hepatitis Delta Virus (HDV). Finally, in the 1980s, Hepatitis C Virus (HCV)[6] and Hepatitis E Virus (HEV)[7] were identified. Nonetheless, there is still evidence of the existence of other viruses causing hepatitis in man and there is doubtless much left to be clarified regarding the non A-E types of viral hepatitis.[8-10]

Laboratory Diagnosis of Viral Hepatitis

Biochemical Diagnosis

As only some cases of viral hepatitis are initially symptomatic, laboratory diagnosis of hepatitis was based on biochemical tests of liver function. These tests involve dosages of enzymes whose concentration increase in serum during episodes of hepatocellular injury or necrosis, resulting from viral infection caused by any of the Hepatitis viruses. The tests currently used consist of levels of transaminase (alanine aminotransferase - ALT and aspartate aminotransferase - AST) and bilirubin.

In acute hepatitis, the aminotransferase begins to rise about 7 to 10 days before the onset of symptoms and can reach serum concentrations 10 to 50 times higher than normal (40 IU). However, in hepatitis C, the average peak tends to be low (200-600 IU/l), as can be seen in Table 2.

Table1. Characteristics of the Etiological Agents of Viral Hepatitis

Characteristics	HAV Hepatitis A	HBV Hepatitis B	HCV Hepatitis C	HDV Hepatitis Delta	HEV Hepatitis E
Identification	Feinstone,1973	Blumberg, 1964 Dane, 1970	Choo, 1989	Rizetto, 1977	Balayan, 1983
Family	Picornaviridae	Hepadnaviridae	Flaviviridae	-	Caliciviridae
Genus	Hepatovirus	Hapadnavirus	Hepacavirus	Deltavirus	Hepevirus
Virion	icosahedral 7 nm	spherical 42 nm (Dane) 22 nm*	spherical 30-60 nm	spherical 35 nm	spherical particle with spikelets and projections 27-34 nm
Envelope	no	yes	yes	yes	no
Nucleic Acid	Single stranded RNA positive polarity 7480 basess	Circular partially double-stranded DNA 3.2 Kb	Simple-standed RNA positive polarity 10 Kb	Circular simple-stranded RNA 1.7 Kb	RNA 7.5 Kb
Major Transmission Route	enteric	parenteral, sexual	parenteral	parenteral	water-borne
Fulminant Hepatitis	0.1-0.2%	1-4%	rare	<5% coinfection 10% superinfection	20% pregnant woman
Chronic Hepatitis	no	5-10% adults 90% neo-natal	>50%	<5% coinfection 80% superinfection	?
Viral Proteins	VP1, VP2, VP3, VP4	HBsAg, HBcAg, HbeAg,HBxAg	core, E1(gp31-35), E2/NS1(gp68-72), NS2(23Kd), NS3(72Kd), NS4a(8-10Kd), NS4b(27Kd), NS5a(46-58Kd), NS5b(68-10Kd)	HDAg; 24Kd and 27kd	proteins coded by ORF1: polymerase, helicase ORF2: capsid proteins ORF3:

*incomplete particles 22nm in diameter, spherical or tubular, comprised of HBsAg.
Adapted from Melnick & Howard, 1994

With the evolution of the illness to the convalescent phase, after reaching their maximum levels, ALT and AST gradually decline to normal levels within weeks or months (2-3 months).[11,12,15]

In chronic HCV infection, approximately 60% of patients show elevated ALT for more than 1 year. A biochemical pattern characteristic of acute or chronic Hepatitis C is fluctuation of the serum levels of aminotransferase, which vary from normal or near-normal levels to elevated levels. This profile can last for weeks or months. Such fluctuations can be significant, with increases on the order of 10-15 times or may be recurrent, although their magnitude decreases over time. There is sometimes a rapid increase in ALT levels followed by a decline to normal values, suggesting recovery. However, ALT reappears as altered some months or years later in association with clinical symptoms of cirrhosis. Nonetheless, in Hepatitis C, ALT is not a good prognostic marker for resolution of the infection.[12]

Another important test is the determination of serum levels of bilirubin. In jaundice, total bilirubin exceeds values of 2-3 mg per 100 ml, progressively rising over the next 10-14 days until reaching its maximum value of 10 mg per 100 ml. Both direct and indirect bilirubin contribute to the elevation of total bilirubin, but in the large majority of patients, direct bilirubin predominates. Once having reached maximum values, serum bilirubin proceeds to fall slowly, taking 2-8 weeks to return to normal.[11]

Table 2. Levels of Serum Transaminase in Acute Viral Hepatitis

Hepatitis	Transaminase
Hepatitis A*	+++
Hepatitis B*	+++
Hepatitis C**	+
Hepatitis D*	+++
Hepatitis E	++

* increase 20-50 times
** increase up to 200-600 IU/l

Etiological Diagnosis of Viral Hepatitis

From a clinical point of view, the different types of viral hepatitis present a similar set of symptoms. The etiological diagnosis consists of identifying the causative agents of the infection and can be achieved through serological, immunohistochemical or molecular techniques, where we study serological, tissue and viral nucleic acid markers respectively.[13,15]

1. Serological Diagnosis of Hepatitis Virus

Serological techniques such as enzyme immunoassays are being effectively used to define the etiology of hepatitis cases, through the analysis of antibodies and/or antigens specific to the different viruses present in the acute and chronic phases of infection. Currently, there are various commercial kits available on the market, allowing for rapid, sensitive, specific and correct diagnosis for this purpose, together with ease in handling and screening a large number of specimens.

1.1 Acute Hepatitis

In order to establish the serological and etiological diagnosis of acute viral hepatitis, we utilize a diagnostic strategy based on the analysis of antigens and/or IgM antibodies, as the latter constitute the first antibodies to appear in the course of the immune response. The serological markers indicative of acute infection and the interpretation of the serological profile obtained from the study of the different agents are described in Tables 3 and 4.

Table 3. Serological Markers of Acute Viral Hepatitis

Hepatitis	Markers
Hepatitis A	Anti-HAV IgM
Hepatitis B	HBsAg Anti-HBc IgM
Hepatitis C	Anti-HCV**
Hepatitis D*	Coinfection: Anti-HBc IgM and Anti-HD IgM Superinfection: Anti-HBc IgG and Anti-HD IgM
Hepatitis E	Anti-HEV IgM

* Only test HBsAg(+) individuals
**Late antibodies, difficult to detect in initial acute phase

Table 4. Interpreting the Serological Profile of Acute Viral Hepatitis

Interpretation	Anti-HAV IgM	HBs Ag	Anti-HBc IgM	Anti-HCV	Anti-HD IgM	Anti-HEV IgM
Susceptible individual	-	-	-	-	-	-
Recent acute Hepatitis A	+	-	-	-	-	-
Acute Hepatitis B	-	+	+	-	-	-
Acute Hepatitis B, initial	-	+	-	-	-	-
or recent	-	-	+	-		
Hepatitis Delta						
Superinfection	-	+	-	-	+	-
Coinfection	-	+	+	-	+	+
Hepatitis C	-	-	-	+	-	-
Hepatitis E	-	-	-	-	-	+

1.2 Chronic Hepatitis

Chronic viral hepatitis is defined by the persistence of the agent for more than 6 months. Chronic cases of viral hepatitis are associated with the HBV, HCV and HDV viruses. The search for serological markers in chronic hepatitis is based on the detection of antigens and/or IgG antibodies as described in Table 5.

Table 5. Serological Markers of Chronic Viral Hepatitis

Hepatitis	Markers
Chronic Hepatitis B	HBsAg and anti-HBc IgG
Chronic Hepatitis D	HBsAg and anti-HD IgG
Chronic Hepatitis C	anti-HCV IgG anti-HCV IgG + anti-HCV IgM (+) or (-)*

* Anti-HCV IgG quantitative tests

2. Molecular Diagnosis of Hepatitis Virus

Utilizing techniques from molecular biology such as the polymerase chain reaction and hybridization with specific probes, it is possible to detect viral genome sequences in serum or tissue samples. Recently, a variation of this technique is also permitting the detection of the replicative

intermediate of HCV and HEV (viral RNA strands, with negative polarity), the most precise indicator of viral replication.[14] These techniques make the direct study of the virus possible, and thus they are highly useful, especially when there is difficulty in detecting the respective antigens through conventional serological tests.

Applications

- to resolve doubts in diagnosis
- molecular epidemiology
- genome typing, genetic variability, follow-up studies during treatment

Advantages

- allow for direct study of viral presence
- marker of viral replication
- highly sensitive

Disadvantages

- high cost
- complicated to conduct
- false-positives
- not appropriate for routine diagnostic procedures

Source: Oliveira, M.L.A., Yoshida, C.F.T., Schatzmayr, H.G. "Diagnóstico Laboratorial das Hepatitis Virais" Virology Department, Oswaldo Cruz Foundation, Rio de Janeiro, December 1995.

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Polio Surveillance

The Region of the Americas begins its sixth year since the last case of indigenous wild poliovirus was isolated. A prominent issue last year was the evidence of deficiencies in surveillance for acute flaccid paralysis (AFP) found in some countries, and the lack of rigorous compliance with the indicators measuring 80% of cases with one adequate stool sample taken and AFP rate ≥ 1:100,000 in children < 15 years. Countries in the Americas are constantly being reminded about the danger of falling into a state of complacency, especially with the existence of the polio virus worldwide. The re-sensitization of clinicians and public health staff about the importance of reporting and investigation remains a critical issue. Furthermore, the response to the indicator measuring the percentage of reporting units in each country which notify the presence or absence of AFP each week *should not* become automatic. Compliance with this indicator is nearly complete in the Americas, however, the quality of this indicator must be continually assessed to ensure that surveillance is active, rather than passive. As we near the target for global polio eradication, the need for sensitive surveillance systems will increase. Additional training for health workers and supervisory visits may be required.

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
Chile				
Colombia				
Cuba				
Ecuador				
Guatemala				
Honduras				
Nicaragua				
Paraguay				
Peru				
Venezuela				
Bolivia				
Dominican Republic				
El Salvador				
Mexico				
Brazil				
Costa Rica				
Haiti				
Panama				
Argentina				
Uruguay				

Meet criteria

* Data as of 28 December 1996

Source: SVI/PAHO (PESS)

Vaccination During Pregnancy

In light of outbreaks of diphtheria in Ecuador (1994) and in Eastern Europe, it has been recommended that Td (diphtheria-tetanus) vaccine replace TT for the vaccination of women of childbearing age in high-risk areas. As a result, concerns have been raised as to the safety of this vaccine for pregnant women. The following two excerpts, one from the CDC's Morbidity and Mortality Weekly Report (MMWR)[1] and the other from the American College of Obstetricians and Gynecologists (ACOG)[2], provide guidelines for vaccinating women during pregnancy.

MMWR Recommendations

Risk from vaccination during pregnancy is largely theoretical. The benefit of vaccination among pregnant women usually outweighs the potential risk when a) the risk for disease exposure is high, b) infection would pose a special risk to the mother or fetus, and c) the vaccine is unlikely to cause harm.

Combined tetanus and diphtheria toxoids are the only immunobiologic agents routinely indicated for susceptible pregnant women. Previously vaccinated pregnant women who have not received a Td vaccination within the last 10 years should receive a booster dose. Pregnant women who are unimmunized or only partially immunized against tetanus should complete the primary series. Depending on when a woman seeks prenatal care and the required interval between doses, one or two doses of Td can be administered before delivery. Women for whom the vaccine is indicated but who have not completed the required three-dose series during pregnancy should be followed up after delivery to assure they receive the doses necessary for protection.

There is no convincing evidence of risk from vaccinating pregnant women with other inactivated virus or bacteria vaccines or toxoids. Hepatitis B vaccine is recommended for women at risk for hepatitis B infection, and influenza and pneumococcal vaccines are recommended for women at risk for infection and for complications of influenza and pneumococcal disease.

ACOG Recommendations

Immunization may be indicated when the risk for exposure is high, infection poses a special risk to the mother or fetus, and the vaccine is not likely to cause harm.

Although new information continues to confirm the safety of vaccines inadvertently given during pregnancy, current information is subject to change because the effects of many diseases and vaccines on the pregnant woman or her fetus may be rare and infrequently reported.

A systematic approach to vaccinating women of childbearing age is needed in order to ensure that every pregnant woman and her fetus are protected from preventable, serious diseases as well as from the possible risks that may accompany vaccination. Several factors should be weighed by the health care provider who is considering immunization for any adult female. Whenever possible, pregnant women should be immune to the diseases that pose the greatest and most common risks during pregnancy and for which there are effective vaccines. Accepted criteria for defining immunity vary by disease, and careful attention should be paid to prior illnesses, previous vaccination, and the results of past serologic tests.

In the United States, the only immunobiologic agents that are recommended for routine administration during pregnancy are tetanus and diphtheria toxoids.

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2. The American College for Obstetricians and Gynecologists. Immunization During Pregnancy. *ACOG Technical Bulletin.* No. 160—October 1991.

Editorial Note: Following the recent outbreaks of diphtheria, SVI/PAHO now recommends the use of Td in place of TT for all women of childbearing age, including pregnant women. Even though this procedure will not have a dramatic impact on the frequency of the disease, as long as the remaining adults are unvaccinated, it presents an opportunity to increase protection against a re-emerging disease.

However, these changes have raised concerns about the potential deleterious effect of diphtheria toxoid to the fetus. Given that the recommendation for vaccinating women of childbearing age and pregnant women with Td is recent, there have not been sufficient opportunities for long-term studies that demonstrate its safety, as opposed to the tetanus toxoid vaccine (see *EPI Newsletter,* August 1996 issue). Despite the lack of adequate data on this subject, as mentioned in both the MMWR and the ACOG recommendations, there is no evidence that diphtheria toxoid causes harm to the fetus. It should be reiterated that it is important for health care workers/providers to evaluate the risk of disease against the possible risks from vaccination. In this context, SVI/PAHO strongly recommends that all women of childbearing age in high risk areas be vaccinated with Td vaccine.

Regional Update

VI Conference of Wives of Heads of State and Government of the Americas - December, 1996

In their final communiqué, the *Declaration of La Paz*, the First Ladies corroborated their commitment to promote and support policies and strategies for sustainable human development that seek complete and fair participation from all sectors of society, especially women and children.

Paragraph 12 from the Declaration of La Paz related to PAHO's measles eradication initiative:

"We reaffirm our commitment to mobilize national efforts to protect children from measles and to eradicate this illness from the Americas. We applaud the efforts and successes attained by all our countries in the fight against this illness and all those illnesses that can be prevented through immunization. We will continue to support actions in order to maintain the high coverage of immunization so that the goal of eradicating measles can be met by the year 2000."

Reported Cases of Selected Diseases

Number of reported cases of measles, poliomyelitis, tetanus, diphtheria, and whooping cough, from 1 January 1996 to date of last report, and the same epidemiological period in 1995, by country.

Country/Territory	Date of last report	Measles				Polio		Tetanus				Diphtheria		Whooping Cough	
		Confirmed 1996			Confirmed*			Non Neonatal		Neonatal					
		Laboratory	Clinically	Total	1995	1996	1995	1996	1995	1996	1995	1996	1995	1996	1995
Anguilla	28 Dec	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Antigua & Barbuda	28 Dec	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Argentina	28 Sep	0	38	38	655	0	0	36	13	3	3	0	4	315	844
Bahamas	28 Dec	0	0	0	0	0	0	1	0	0	0	0	0	1	1
Barbados	28 Dec	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Belize	28 Dec	0	0	0	4	0	0	0	0	0	0	0	0	0	0
Bermuda	28 Dec	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Bolivia	28 Dec	0	4	4	76	0	0	22	28	14	20	1	5	14	36
Brazil	28 Dec	24	273	297	793	0	0	500	779	51	85	108	165	805	2,807
British Virgin Islands	28 Dec	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Canada	28 Dec	325	—	325	2,357	0	0	0	4	...	...	...	2	1,333	7,758
Cayman Islands	28 Dec	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Chile	28 Dec	0	0	0	0	0	0	1	11	0	0	1	2	583	424
Colombia	28 Dec	4	36	40	410	0	0	...	57	27	35	0	6	17	1,137
Costa Rica	28 Dec	4	3	7	35	0	0	3	6	0	0	...	0	18	21
Cuba	28 Dec	0	0	0	1	0	0	...	5	...	...	...	...	...	...
Dominica	28 Dec	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dominican Republic	28 Dec	0	0	0	0	0	0	21	37	0	0	6	13	2	0
Ecuador	28 Dec	0	30	30	919	0	0	63	158	34	50	17	130	81	163
El Salvador	28 Dec	1	0	1	0	0	0	10	3	5	3	0	0	3	4
French Guiana	...	...	...	...	...	0	0	...	...	...	...	...	...	...	...
Grenada	28 Dec	0	0	0	3	0	0	0	0	0	0	0	0	0	0
Guadeloupe	28 Dec	12	1	13	0	0	0	...	...	...	...	...	...	...	...
Guatemala	28 Dec	0	0	0	23	0	0	7	8	12	9	0	0	66	34
Guyana	28 Dec	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Haiti	...	...	...	...	...	0	0	...	...	...	...	...	...	...	...
Honduras	28 Dec	0	3	3	0	0	0	15	7	4	3	0	0	193	0
Jamaica	28 Dec	0	0	0	15	0	0	0	9	0	0	4	0	22	7
Martinique	...	...	...	...	...	0	0	...	0	...	0	...	0	...	0
Mexico	28 Dec	2	102	104	244	0	0	156	128	60	67	0	0	21	15
Montserrat	28 Dec	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Netherlands Antilles	...	...	...	...	...	0	0	...	...	...	...	...	...	...	...
Nicaragua	28 Dec	0	0	0	5	0	0	10	8	1	4	0	0	14	8
Panama	28 Dec	0	0	0	19	0	0	3	2	0	1	0	0	44	3
Paraguay	05 Oct	0	5	5	73	0	0	16	42	8	16	0	1	22	13
Peru	28 Dec	2	66	68	353	0	0	57	70	46	97	4	4	355	832
Puerto Rico	28 Dec	8	—	8	11	0	0	...	...	...	...	...	...	...	...
St Vincent/Grenadines	28 Dec	0	0	0	0	0	0	0	0	0	0	0	0	0	0
St. Kitts/Nevis	28 Dec	0	0	0	1	0	0	0	0	0	0	0	0	0	0
St. Lucia	28 Dec	0	0	0	2	0	0	0	0	0	0	0	0	0	0
Suriname	28 Dec	0	0	0	0	0	0	1	3	1	0	0	0	0	0
Trinidad & Tobago	28 Dec	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Turks & Caicos	28 Dec	0	0	0	4	0	0	0	0	0	0	0	0	0	0
United States	28 Dec	488	—	488	309	0	0	...	34	...	...	...	0	775	4,315
Uruguay	10 Aug	0	0	0	5	0	0	1	2	0	0	0	0	0	69
Venezuela	28 Dec	4	32	36	172	0	0	...	56	12	17	0	0	362	375
TOTAL		**874**	**593**	**1,467**	**6,489**	**0**	**0**	**923**	**1,470**	**278**	**410**	**141**	**332**	**5,046**	**18,866**

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

In Memoriam: Dr. Sandra Silveira

Dr. Sandra Silveira, who had worked for the Special Program for Vaccines and Immunization since 1988, passed away unexpectedly at the age of 45, in the city of Natal, Brazil on February 9, 1997. Based at PAHO's Country Office in La Paz, Bolivia, Dr. Silveira was most recently responsible for assisting the countries of Argentina, Bolivia, Chile, and Paraguay in programming and evaluating national plans of action and strategies for national immunization programs, and for implementing PAHO's measles eradication strategies in the Southern Cone. Dr. Silveira was one of the pioneers in her home country of Brazil in the efforts to control and eradicate poliomyelitis. During the polio years, she worked incessantly in the state of Rio Grande do Norte, one of the areas hardest hit by the disease. In collaboration with the Ministry of Health, Dr. Silveira played an important role in the elaboration of Brazil's polio eradication plan.

Dr. Silveira studied medicine at the Federal University of Rio Grande do Norte, Brazil and obtained a degree in Public Health from the University of São Paulo. At the Oswaldo Cruz Foundation's (FIOCRUZ) National School of Public Health in Rio de Janeiro, Dr. Silveira completed a specialization in epidemiology and later a master's degree in the same subject.

Until July 1987, Dr. Silveira worked as the Coordinator of Epidemiology at the Secretariat of Public Health in the state of Rio Grande do Norte. During that year, she was invited to teach epidemiology at FIOCRUZ's National School of Public Health. Dr. Silveira initiated her work with PAHO in Ecuador in 1988, where she provided technical support to Ecuador's Expanded Program on Immunization and the eradication of polio. In 1994, Dr. Silveira also collaborated in organizing Venezuela's successful measles *catch-up* vaccination campaign. In her last assignment in Bolivia, Dr. Silveira was the PAHO/SVI focal point for the control and elimination of vaccine-preventable diseases in the Southern Cone.

Her colleagues at SVI and in the PAHO Offices of Bolivia, Ecuador and Venezuela, as well as the many health officials and staff in the countries where she worked will remember Dr. Silveira for her many achievements in the field of vaccine-preventable diseases, but they will also remember her great enthusiasm for life, her camaraderie and compassion. She is sorely missed.

The *EPI Newsletter* is published every two months, in Spanish and English by the Special Program for Vaccines and Immunization (SVI) of the Pan American Health Organization (PAHO), Regional Office for the Americas of the World Health Organization (WHO). Its purpose is to facilitate the exchange of ideas and information concerning immunization programs in the Region, in order to promote greater knowledge of the problems faced and their possible solutions.

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ISSN 0251-4729

Pan American Health Organization
Pan American Sanitary Bureau
Regional Office of the
World Health Organization

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