

# REPORT

## **Third Meeting of the Surveillance Networks for Emerging Infectious Diseases in the Amazon and Southern Cone Regions**

**15-16 July 2000  
Atlanta, Georgia**





**REPORT  
THIRD MEETING OF THE SURVEILLANCE  
NETWORKS FOR EMERGING INFECTIOUS  
DISEASES IN THE AMAZON AND SOUTHERN CONE  
REGIONS**

**Atlanta, Georgia, U.S.A.  
15-16 July 2000**

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## TABLE OF CONTENTS

<b>I.</b>	<b>EXECUTIVE SUMMARY .....</b>	<b>3</b>
<b>II.</b>	<b>WELCOMING REMARKS .....</b>	<b>3</b>
<b>III.</b>	<b>ELECTION OF CHAIRMAN/RAPPORTEUR.....</b>	<b>4</b>
<b>IV.</b>	<b>INTRODUCTION AND OBJECTIVES .....</b>	<b>4</b>
<b>V.</b>	<b>RECOMMENDATIONS OF THE TARAPOTO AND BRASILIA MEETINGS.....</b>	<b>5</b>
<b>VI.</b>	<b>COUNTRY REPORTS.....</b>	<b>5</b>
	Argentina.....	5
	Bolivia.....	7
	Brazil .....	10
	Chile.....	15
	Colombia.....	17
<b>VII.</b>	<b>STATUS OF THE IMPLEMENTATION OF SURVEILLANCE FOR EID.....</b>	<b>26</b>
	Viral Surveillance in the Amazon.....	28
<b>VIII.</b>	<b>GLOBAL AND SUBREGIONAL SURVEILLANCE .....</b>	<b>32</b>
	WHO Global Alert and Response.....	32
	The Global Emerging Infections System (GEIS) Program.....	36
	Global Surveillance for Influenza and Selection of Vaccine Viruses.....	41
<b>IX.</b>	<b>SURVEILLANCE OF SELECTED DISEASES/SYNDROMES.....</b>	<b>42</b>
<b>X.</b>	<b>CONCLUSIONS AND RECOMMENDATIONS .....</b>	<b>50</b>
	Influenza Surveillance.....	50
	HUS Surveillance .....	50
	Hantavirus Pulmonary Syndrome .....	51
	Southern Cone Network .....	51
	Syndromic Surveillance .....	52
	<b>LIST OF PARTICIPANTS.....</b>	<b>54</b>

## **I. EXECUTIVE SUMMARY**

The aim of this meeting was to promote the enhancement of Emerging Infectious Diseases (EID) Surveillance Networks of the Amazon and Southern Cone (SC) regions. Participants of this meeting represented their respective countries' epidemiology and laboratory units of their disease surveillance system. Thus, promoting coordination and collaboration among them. The integration of epidemiology and laboratory diagnosis is critical for the strengthening of each region's disease surveillance network. For the first time, a representative from the Caribbean Epidemiology Center (CAREC) attended a meeting of this kind.

The specific objectives of this meeting were to:

- present the current situation of EID within the Amazon and SC regions, particularly key events observed during 1999-2000;
- describe activities undertaken by the countries;
- identify constraints or needs in order to better implement the activities;
- make recommendations on the implementation of future activities.

Several countries of the Amazon region network presented data obtained from syndromic surveillance conducted in sentinel sites. Most examined patients exhibited undifferentiated febrile syndromes where the majority of them were diagnosed with malaria. The remaining cases were attributed to dengue, leptospirosis and viral hepatitis. A significant number of cases however, remained without diagnoses. Cases of febrile icteric syndrome were also associated with malaria, leptospirosis and viral hepatitis.

Surveillance conducted in the SC identified an increasing number of cases of Hantavirus Pulmonary Syndrome (HPS) including some outbreaks where HPS had not previously been recognized. Certain countries have continued to strengthen their influenza surveillance. In addition, two countries have established laboratories to provide influenza diagnostic support. Efforts are also being made to improve or initiate Hemolytic Uremic Syndrome (HUS) surveillance.

As a result of the recommendations made during the second SC meeting in Brasilia, three regional workshops on Influenza, HUS and HPS took place (Buenos Aires). Each workshop dedicated one day to discuss aspects of strengthening disease surveillance epidemiologists and laboratory specialists. In addition, training for laboratory diagnosis of Influenza, HPS and HUS were offered. Proposals prepared per country for the implementation of HUS surveillance were developed as a consequence to this meeting.

During the third meeting in Atlanta, numerous recommendations and needs were identified by work groups (see Section X). No major changes were proposed to the Plans of Action approved in Tarapoto and Brasilia. In addition to previously selected disease syndromes for surveillance, it was suggested to include surveillance of environmental factors, food-borne pathogens and anti-malarial drug resistance. The participants reiterated the need for integration between laboratory and epidemiology and for strengthening of epidemiologic surveillance. It was also stressed that syndromic surveillance should be considered as a component of general surveillance and that it should be conducted in sentinel sites. The syndrome definitions and the algorithms for testing the samples should be adapted according to the epidemiological characteristics of each area. It was considered essential to develop mechanisms for dissemination of information and communication among the members of the network. On several occasions the need for standardized reagents, training and quality control programs was stressed. It was also recommended to include Ecuador, Suriname and Guyana in the Amazon Region network.

Finally, it was recommended that the two networks should continue to meet and that the next meeting should take place in Asuncion, Paraguay during the year 2001.

## **II. WELCOMING REMARKS**

Dr. James Leduc, Associate Director for the Office of Global Health, Centers for Disease Control and Prevention, welcomed the participants and stated that CDC is especially honored in organizing this meeting prior to the International Conference of Emerging Infectious Diseases to be held in Atlanta, Georgia.

Dr. Stephen Corber, Director of the Division of Disease Prevention and Control of Pan American Health Organization, also welcomed the participants and remarked the importance of having both networks working together at this meeting.

Dr. Steven Blount, Director of the Office of Global Health, also welcomed the participants to Atlanta, on behalf of Dr. James Hughes from CDC.

Dr. Marlo Libel, Regional Advisor for Communicable Diseases Program, Division of Disease Prevention and Control of PAHO, especially thanked Dr. Ray Arthur for his participation and stressed the important linkage between the networks' and WHO's activities. He also welcomed everyone to speak in their native language and thanked everyone for sending their reports ahead of time so that they could be translated and distributed as handouts.

### **III. ELECTION OF CHAIRMAN/RAPPORTEUR**

Dr. Robert Tesh, Professor of Dept. of Pathology for the University of Texas Medical Branch, was elected as the Chairman of the Meeting and Dr. Delia Enria, Director of the National Institute for Hemorrhagic Viral Diseases, Argentina (NIHVD), as the Rapporteur.

### **IV. INTRODUCTION AND OBJECTIVES**

The rise in population mobility and increase in food/animal commerce has created complexities in the dynamics of biological and ecological interactions thus creating or fostering the presence of new and old pathogens. With the emergence and reemergence of infectious diseases, networks of epidemiologists and laboratory personnel have formed to study disease trends and implement control interventions. The collaboration of both fields will serve as a way to reduce duplication of efforts and address those diseases that are most threatening to the under-served and poor.

In this meeting, two regions are being joined, the Amazon and Southern Cone regions, which requires a high degree of commitment to assume additional tasks. The participants were informed about other networks being organized in a similar manner: such as the Asian Pacific communities, the Plague network and the Influenza network. Other meetings were taking place at the same time as this Third Meeting. Also, the World Bank has taken some of the issues discussed by these networks before and is providing funding to Argentina and Brazil. Similarly, USAID-Washington office providing funds to CDC for surveillance projects, and the USAID Office in Peru funding surveillance and research on emerging diseases. The U.S. government considers infectious emerging disease an important global health policy issue at a time in which U.S. agencies are revising their plans for future assistance.

The network consists of experts in epidemiological surveillance and laboratory diagnosis and is multi-institutional; staff from several institutions, from the Ministries of Health and local Academic institutions, to CDC, USA and PAHO/WHO, collaborate to provide technical advise and various resources. The network will provide information for international public health action, standardize training and evaluation and ensure scientific quality studies.

The primary aim of the network is to generate relevant public health information. In addition the network is to train and cooperate with other countries in joint collaborative activities providing valuable laboratory information allowing for the sharing of resources, quality control mechanisms and threat recognition.

The goal of this third meeting is to continue efforts in creating a functional emerging infection surveillance network of laboratories and epidemiologists by integrating the actions already pursued in the Amazon and Southern Cone Regions, including Argentina, Bolivia, Bolivia, Brazil, Chile, Colombia, Paraguay, Peru, Uruguay, Venezuela, and The Caribbean.

The specific objectives are as follows:

- Review the status of emerging infectious diseases and updates on surveillance
- Describe activities undertaken
- Recommend adjustments, improvements or expansion of the networks.
- Identify constraints and/or needs and agree on future activities

## V. RECOMMENDATIONS OF THE TARAPOTO AND BRASILIA MEETINGS

During 1999 Tarapoto and Brasilia meetings, the Plan of Action originally developed in Manaus, 1998 was endorsed and modified such that it included a revision of case definitions of the diseases syndromes. In addition, the Plan of Action also served as a basis for the Plan of Action of the network. The five disease syndromes selected for surveillance in the original Plan included undifferentiated febrile syndrome; hemorrhagic fever syndrome; febrile icteric syndrome; acute respiratory distress syndrome and sudden unexplained death syndrome. The network added infectious neurologic syndrome and enteric syndrome during their first meeting, held in Buenos Aires in 1998. In Tarapoto, it was also recommended that: 1) each country decide the appropriate algorithm to use in testing, depending upon the knowledge of the frequency of various infectious diseases in their region and the more important disease agents common to each country; 2) In terms of priority for initial surveillance and diagnostic testing the following diseases were selected in addition to the five syndromes: **Malaria, dengue, viral hepatitis, yellow fever, leptospirosis and influenza**. During the Brasilia meeting the group developed and approved protocols for the surveillance of HUS, Influenza and HPS. In accordance with these protocols, workshops were held for each of these disease syndromes with the participation of epidemiologists and laboratory scientists from countries of the SC (Argentina, Bolivia, Brazil, Chile, Paraguay and Uruguay). Pediatricians from three countries attended the HUS workshop. All three workshops were held in Buenos Aires and their objectives included surveillance approaches and training on the laboratory diagnosis of infectious agents associated with those health problems. Moreover, each country prepared projects for the implementation of HUS surveillance. The group in Brasilia reiterated the four disease syndromes recommended in the first meeting of the SC network for initial surveillance: 1) Influenza; 2) acute diarrhea, especially bloody diarrhea leading to HUS; 3) HPS and Hantaviral disease and 4) antimicrobial resistance, especially *M. tuberculosis*.

Most importantly, both groups that met in Tarapoto and Brasilia strongly recommended the integration of epidemiologists and laboratory personnel to undertake the surveillance of these disease syndromes and jointly attend all future meetings. Also, the network was renamed to reflect this recommendation "Surveillance network for EID".

## VI. COUNTRY REPORTS

The situation on emerging/reemerging diseases and the activities undertaken on the subject in the countries of the subregions were as follows.

### **Argentina**

The National Epidemiological Surveillance System (SINAVE) is in the process of updating and reviewing its standards with the participation of laboratories, orienting activities toward the implementation of sentinel units closely linked to the laboratory network for the surveillance of highly prevalent pathologies.

The national reference laboratories working on hantavirus, influenza, and hemolytic uremic syndrome (HUS) have the capacity to act as regional reference centers since reagents production, special isolation techniques, diagnoses, characterization and sub-typing of etiologic agents, and quality control are executed. Training, technology transfer, and reagents were provided for the national network of laboratories working on those subjects.

Support for the emerging disease surveillance was provided by the Ministry of Health, in part with funding provided with a World Bank loan. External support was given by DEC, USA, the Laboratory Centers for Disease Control, Canada, and PAHO.

## **Bacterial Diseases**

**Antimicrobial resistance.** For years, an increase in antimicrobial resistance of microorganisms has been observed. Laboratory surveillance offers an opportunity to adapt strategies for antibiotic use and to attempt to control the level of resistances or changes in profiles. There is a network of 31 laboratories throughout the country reporting on antimicrobial resistance of different microorganisms: from Salmonella and Shigella to Pneumococci.

The multiresistance to tuberculosis drugs in TB patients with AIDS as a result of nosocomial transmission was detected in great numbers in 1994 (19%). Data are being updated this year.

**Cholera.** By law is a disease that requires laboratory diagnostic confirmation through the identification of *Vibrio cholerae* in feces and/or vomit, to be reported to the National System. Epidemiological and laboratory surveillance of diarrheal diseases has been conducted systematically since February 1992, when the first cases of *V. cholera* were reported. To date, 4,835 cases and 72 deaths have been reported in the seven outbreaks during the aforementioned period.

Laboratory surveillance has yielded very important findings for SINAVE. The majority of non-toxigenic *Vibrio cholerae* O1 cases linked to diarrheal cases were concentrated in one province (Tucuman). Further analysis determined that these cases constituted a new clone of a pathogenic strain, resulting in recommendations for policy such as certifying whether a new etiologic agent for choleraform diarrheal diseases is involved, and determining the characteristics of its toxicity.

Another important finding came from the last reported case, isolated in the province of Santa Fe, in 1999. It showed the close relationship to other strains found in the same province in 1998. The recommendation issued was a search for a reservoir in that province.

## **Viral Diseases**

**Dengue.** The vector is present in most of center and northern Argentina. Indigenous or imported cases of dengue have been described in the northern provinces. At a local level, cases are reported as suspicion by clinics and the participants in the laboratory networks label them as probable through ELISA.

To date, 1,633 suspected cases have been reported and among these, 515 were probable. Through viral surveillance, it was reported that the types of viruses belonging to indigenous cases correspond to dengue type I in the provinces of Formosa, Misiones, and Jujuy, and dengue type II in the Province of Salta.

**Hantavirus.** Has been subject to intensified surveillance in the country since 1995. Cases are reported to the SINAVE and confirmed by laboratory diagnosis. From 1995 through week 24 of 2000, 271 cases have been reported from 12 provinces. The number of cases has been increasing yearly, due to intensified search. The case-fatality rate has shown a continuous decline due to earlier diagnoses and more adequate medical care. The transfer of technology to the provincial laboratories was achieved.

**Influenza.** At the end of 1999, the data contributed by the SINAVE from reporting on influenza syndrome were compared with those contributed by laboratory diagnostic surveillance. The peak of case reporting coincides with the peak of viral detection. During 2000, the onset of increased viral activity was detected to begin in week 22, with a peak starting in the month of June. Epidemiological surveillance through overall reporting is not significant, since the reporting units are behind in their information. The surveillance of influenza is increasing in the country as a result of the sentinel centers, which contribute updated data weekly.

## Other Epidemiological Events/Investigations

In 1999 surveillance of *Hemolytic Uremic Syndrome (HUS)* was implemented on the basis of reporting to SINAVE and the shipment of samples and isolates to the reference laboratory. A total of 111 cases were reported to SINAVE from 8 provinces during that year, predominantly in patients under 4, with 85% of cases reported during the first six months of the year. Fifty-four percent of 111 cases were considered true positives. On the other hand, the Argentinean Society of Pediatrics received information on 308 cases from 22 centers for the same period. Thus showing that there is a significant under reporting to SINAVE. Genetic diversity studies have shown a high clonal relationship (greater than 80%) among isolates of human, animal, and food origin.

HUS persistence in different geographical areas over time most likely demonstrates the existence of reservoirs explaining the endemicity of the disease. Thus this makes it necessary to confirm this inference with case-control studies on risk factors.

## Bolivia

Support and collaboration for the activities performed were provided by the Centers For Disease Control, USA, Instituto Evandro Chagas, Brazil, Instituto Malbrán, Argentina, the Pan American Health Organization, the U.S. Naval Medical Research Center Detachment, NMRCDC, Lima, Peru, and the University of Texas at Galveston.

## Bacterial Diseases

**Antimicrobial resistance.** An updated course on antimicrobial agents, susceptibility testing, and quality control was provided to the entire laboratory network in April 2000. This was essential in order to have confidence in the results of the routine work that serve as the base of the surveillance.

*Vibrio cholerae* did not show resistance to the recommended antimicrobials. Thirty two percent of 34 strains of *Salmonella* sp. isolated during 1999 showed combined resistance to: Ampicillin, Chloramphenicol and Cotrimoxazole. In one case, resistance to Ampicillin was observed among ten strains of *Salmonella typhi*. Confirmation by Minimum Inhibitory Concentration or MIC (E-test) was performed in all cases. The same year 82% of *Shigella* isolates, mostly *S. flexneri*, were shown to be resistant to Ampicillin, 42% to Chloramphenicol and 42% to Cotrimoxazole.

A study that was conducted with 400 asymptomatic carriers of *Streptococcus pneumoniae* in children less than 5 years old, 65 strains were isolated, 6 of which (9.2%) showed resistance to Penicillin and 1 showed intermediate resistance to Cefotaxime.

Currently, 50% of strains of *Neisseria gonorrhoeae* are penicillin and tetracycline resistant. Thirty six percent of the resistant strains were confirmed as penicillinase producers but all strains were shown to be susceptible to Ciprofloxacin. On the other hand surveillance of drug resistance *Mycobacterium tuberculosis* needs to be developed further.

***Hemolytic Uremic Syndrome (HUS) - Shiga-Like Toxin Producing Escherichia Coli (STEC)*.** Bolivia's Epidemiology Directorate and a pediatric nephrologist participated in the workshop for the standardization of identification of *E. coli* O157 H7 and STEC promoted by the Southern Cone Surveillance Network. This training was essential for Bolivia to participate in surveillance activities in HUS.

## Viral Diseases

**Influenza.** Argentina provided technical cooperation for the standardization of immuno-fluorescence assays and viral isolation in cell cultures. Hospital installations and professional staff were identified for the collection of samples in La Paz, Santa Cruz, Cochabamba and Sucre. Supplies were distributed for sample collection at these sites.

A pilot study on acute respiratory infections among children <12 years old was done in La Paz. Twenty-four out of 100 samples tested positive to various respiratory viruses. Eight (33%) tested positive for the RSV and

another 8 tested positive for Influenza; 5 (21%) tested positive for Parainfluenza Virus, and 3 to Adenovirus.

**HTLV-I associated paraparesis.** During 1999 and 2000, new cases have been reported. Currently, a program for the surveillance of HTLV does not exist. However, with the collaboration of the University of Kagoshima, Japan (MONBUSHO), studies were carried out that allowed to get information for developing geographical distribution maps for the Andean region of Bolivia. INLASA is the only laboratory in Bolivia that performs detection and confirmation tests by PCR. Reagents used in these tests are needed to launch a study in blood banks aimed at showing whether changes in blood transfusion policies are needed.

**HIV/AIDS.** HIV continues to undergo epidemiological surveillance in blood donors. Tests are also conducted for patients and female sex workers. In coordination with NMRC, a study is being carried out on the genotyping of HIV. The National Program of Sexually Transmitted Infections/AIDS is coordinating these activities. The planning for re-establishing epidemiological surveillance through sentinel centers is nearly finished. This entails the collaboration of NMRC, USAID and the Ministry of Health and Hygiene.

**Hepatitis B.** A surveillance program has not been established yet, although mandatory notification continues; Sero-epidemiological studies have been conducted on female sex workers and other high risk groups.

**Hepatitis C.** Screening is not routinely done in all blood donors.

#### Other Epidemiological Events/Investigations

Following the recommendations made at the first meeting to establish a network of laboratories in the Amazon Region (Manaus, 1998), a study was implemented with two sentinel centers in El Torno and Jorochito, in order to learn more about pathogens causing febrile syndromes in these areas.

This study was carried out at the National Center of Tropical Diseases (CENETROP), a clinic that overlooks the health of sub-populations of the city and rural sites of Santa Cruz. Approximately 100 patients with non-specific febrile syndrome are seen monthly at CENETROP, 40% of them remained without etiological diagnoses.

Patients seeking medical care in the first week of each month for febrile illnesses were enrolled in the study. The following table shows the distribution of the study population by age group and gender.

**Table 1. Febrile syndrome cases distribution by age group and sex, Bolivia**

Age Group	Sex		Total
	Males	Females	
05 to 10	11	11	22
11 to 20	22	12	34
21 to 30	15	15	30
31 to 40	14	9	23
41 to 50	11	3	14
51 to 60	11	9	20
> 60	10	2	12
<b>Total</b>	<b>94</b>	<b>61</b>	<b>155</b>

The inclusion criteria in the study were: axillary temperature equal to or higher than 38°C; absence of evident septic foci; duration of the febrile syndrome not over 7 days; older than 5 years old; and informed consent to participate in the study. The signs and symptoms of the patients are shown in Table 2.

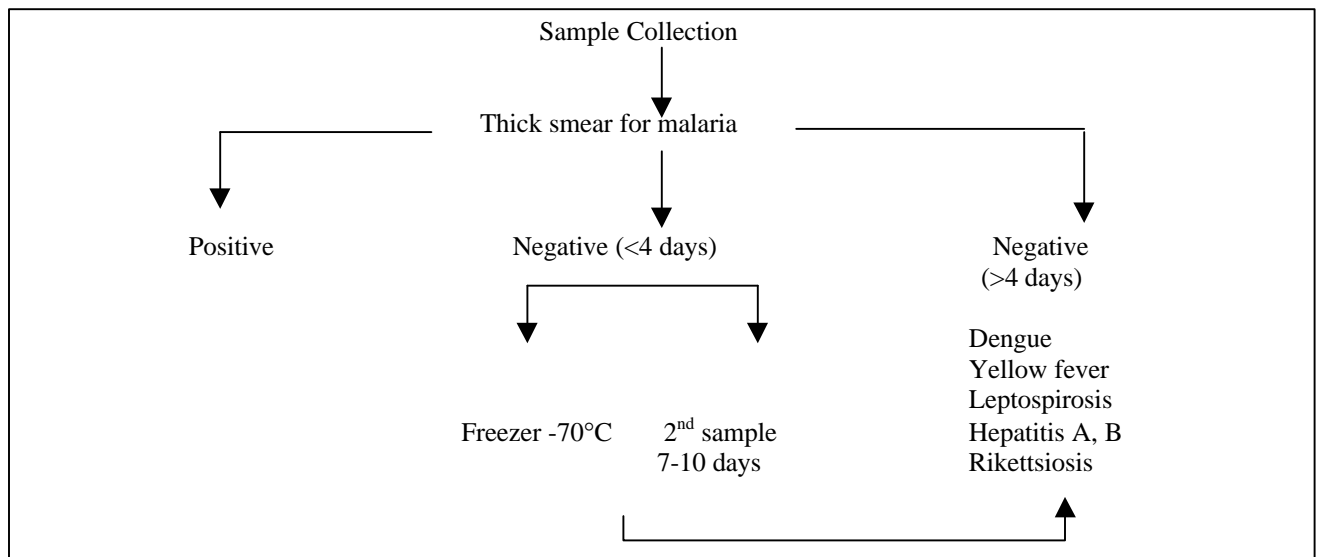
**Table 2 Febrile syndrome cases by signs and symptoms observed**

Signs/symptoms	n	%
Headache	149	96.1
Myalgia	144	92.9
Arthralgia	135	87.1
Chills	130	83.9
Nausea	112	72.3
Ocular pain	108	69.7
Jaundice	57	36.8
Rash	10	6.5

The algorithm used for diagnosis is shown in Figure 1. First, using a thick smear, plasmodium was sought to rule out malaria. If thick smear was negative for malaria and the onset of symptoms is longer than 4 days, then, laboratory tests were carried out to detect IgM antibodies, first for dengue and next for yellow fever. If the above tests are negative, then additional tests for presence of hepatitis A, B antibodies, leptospira, and rickettsia were performed.

When the sample was taken before the fourth day from the onset of symptoms during a house visit, a second sample was taken seven to ten days from the onset of symptoms. If the second sample was positive for IgM dengue or yellow fever, then the sample was cultured in C6/36 cells for the identification of dengue serotypes. Later, viral yellow fever genotyping studies were to be conducted at the Laboratory of the University of Galveston, Texas. If hantavirus infection was suspected or respiratory distress observed, an ELISA for hantavirus was performed.

**Figure 1. Algorithm used for the testing the samples.**



**Table 3. Laboratory diagnosis of inespecific febrile syndrome**

Etiologic Agent	n	%
Malaria(vivax)	73/155	47.1
Dengue	4/82	4.9
Leptospirosis	3/78	3.8
Hepatitis A	82/82	100.0
Hepatitis B(Ags)	1/82	1.2
Hepatitis B(anticore)	14/82	17.1

The clinical manifestations were classified into mild and moderate. No fatal cases were observed. The study indicated that the etiology of febrile syndrome in that area were by far malaria, followed by dengue, and leptospirosis. It must be noted however that Acute Respiratory Infections and Acute Diarrheal Diseases were not taken into consideration.

Rural yellow fever outbreak in the Department of Santa Cruz occurred between January and April 1999. Out of the 170 samples tested at CENETROP 42 had a positive serology by ELISA (IgM), 1 by isolation of the virus in cell culture, 1 by PCR, and 7 by liver necropsy. A total of 30 deaths were reported.

An outbreak of Bolivian Hemorrhagic Fever in Beni was responsible of 1 fatality serologically confirmed.

An outbreak of Hantavirus in Bermejo was responsible of 3 cases, 2 of whom died.

## **Brazil**

To improve the capability to detect and research emerging and re-emerging diseases is one of the priorities of the National Center of Epidemiology of the Ministry of Health (CENEPI). The country has made efforts in the structuring and improvement of surveillance of communicable diseases. The following initiatives are highlighted as major accomplishments.

The VIGISUS Project, a 7-year funded agreement of \$600 million dollars with the World Bank has been initiated. Its main objectives are to implement the law that establishes the national epidemiological surveillance system, develop a national information network for fast and efficient decision making, create a new communication system between municipal, state and federal institutions. In addition to this project, a portion of funds of another World Bank loan, REFORSUS, has become available for investment in the public health laboratory network. As part of the VIGISUS Project, 12 border laboratories will be established, five of them in the Amazon region, and seven in the Southern Cone borders. This project is now being implemented.

Decentralization of disease surveillance and control was implemented. States and county offices followed the definition of decentralized action funding, through Integrated Agreed Programming of Epidemiology and Disease Control (PPI/ECD). This sets forth funding parameters for actions related to indicators, surveillance goals and disease control. In order to strengthen local capabilities, a Basic Epidemiological Surveillance Course (CBV) was available at the State and Municipality level.

This course is a personnel-training course for epidemiological surveillance developed by national health officials. It is designed for professionals at a technical or academic levels and is aimed to introduce epidemiology and epidemiological surveillance. This course was taught by national health officials to state epidemiologists such that state epidemiologists were able to train their local epidemiologists. In some cases, national health officials provided additional support to state epidemiologists by training directly local epidemiologists. In addition, several training sessions were provided for surveillance, laboratory diagnosis and control of diseases, as in tegumentary leishmaniasis, Trachoma, Diphtheria, Whooping Cough, Influenza, exanthematic diseases, meningitis, malaria, tetanus, neonatal tetanus, flaccid paralysis, food transmitted diseases, cholera and acute diarrheal diseases and human anti-rabies treatment. Under an agreement with the CDC, a Biosafety Course for laboratory professionals and Field Epidemiology Training Program (FETP) will start in 2000.

Brazil has made progress in integrating disease surveillance and control with bordering countries. Starting in 1998, eight quarterly meetings of the SC surveillance have been held. Chile has begun participating. In addition to standardizing definitions, surveillance and disease control guidelines and joint research projects are also being defined. One of the first topics to be studied will be bat-transmitted rabies. Also, bi-lateral and tri-lateral specific cooperation projects in monitoring disease surveillance and control with Uruguay, Argentina, Paraguay Colombia and Venezuela are in progress.

Syndromic surveillance is being successfully used throughout the country for the surveillance of exanthematic diseases. The states of Roraima, Tocantins, Goias and the Federal District states made use of the surveillance of febrile icteric/hemorrhagic syndromes during the yellow fever epidemic of 1999 through 2000. However, the

syndromic surveillance component to epidemiological surveillance has not been incorporated in all states.

Another drawback was the limited development of the country surveillance on antimicrobial resistance at national level, in spite of the existence in Brazil of centers of excellence on the subject. Insufficient supplies and of a varieties of reagents have been identified as limiting factors in improving and increasing surveillance and research opportunities of emerging and re-emerging. In the 1999-2000 period, difficulties in the supply of diagnostic reagents for exanthematic diseases became critical. In addition difficulties were faced in the supply of reagents for dengue, measles, rubella, parvovirus B19, herpesvirus 6, leptospirosis, and visceral leishmaniasis.

### **Bacterial Diseases**

***Cholera.*** The large epidemic peak of 1993-1994, the occurrence of cholera in Brazil has been contained to the Northeastern Region of the country. Limited coverage of the basic health networks along with the lengthy draught led to a decrease in case detection in 1999. In May 1999, a large cholera outbreak of 467 confirmed cases was verified in the city of Paranagua in southern Brazil. Previously, there were no reported cases of this disease. The outbreak was related to the consumption of raw seafood, an eating habit in that region and was controlled rapidly. In 2000, the occurrence of the disease has been contained in two states: Pernambuco and Alagoas.

***Hemolytic Uremic Syndrome (HUS) and Food Borne Diseases (FBD).*** Since 1999, Brazil has implemented the epidemiological surveillance system for food borne diseases (FBD). Training sessions for epidemiological surveillance teams and laboratory personnel in the states and main municipal counties of Brazil, and manuals for epidemiological surveillance and training have been developed.. These initiatives have stimulated an increase in the detection of FBD and typhoid fever outbreaks. In the last quarter of 1999, 249 FBD outbreaks were notified in 9 states that had already implemented FBD surveillance covering over 3000 individuals. In the State of Sao Paulo, a national reference center for botulism was established.

CENEPI prepared a project for the implementation of the surveillance of Hemolytic Uremic Syndrome (HUS) surveillance, with the establishment of five sentinel sites in the States of Sao Paulo, Parana, Rio Grande do Sul, Ceara and Federal District. The Sao Paulo project is already being implemented. A workshop will be conducted in September 2000 in the above-mentioned states for training and standardization of equipment and procedures.

Leptospirosis. The number of leptospirosis cases notified in the Amazon region during 1990-1999 was 6,142. The State, of Para reported the most, with 3,374 cases (54.93%), followed by Amapa with 1,832. Both states comprise 84.69% of the total number of reported cases. a total of 148 cases were reported from 1995 to 1999 in Manaus, where there is an increase in the number of cases in the rainy season (December through June). There are always related with squatter areas where garbage accumulates. All the cases that occurred in January 1999 were workers of a small open market. No epidemics or deaths had been reported in 1998 or 1999.

### **Viral Diseases**

***Dengue.*** Dengue re-emerged in Brazil in 1982 causing an epidemic in the state of Roraima. After a three-year period of silence, it re-appeared in the city of Rio de Janeiro in the summer of 1985 and 1986. Following this, the disease spread throughout almost the entire country. Three epidemic peaks were identified in 1987, 1991 and 1995. In 1995 the epidemic reached its maximum peak in 1998, with more than 500,000 reported cases. Transmission has been observed in 23 out of 27 Brazilian states. The number of cases reported represents only a small proportion of disease occurrence. Seroepidemiological studies carried out in large Brazilian cities have demonstrated that the seroprevalence is almost universal for both circulating serotypes. Currently, epidemics are being reported in the northeastern and northern regions, namely, Paraiba, Ceara, and Para. So far, there is no report about the circulation of other serotypes besides DEN-1 and DEN-2.

In the Amazon Region Dengue transmission was first detected in Amazonas State in 1994. Cases increased from 56,621 in 1994 to 297,328 in 1999 with a peak of 570,148 cases in 1998. To date, 1,401,434 cases have been registered in the last 6 years, that is, 10.3% of the cases in the country. Para, Mato Grosso, Amazonas and Maranhão are the states with the highest number of notified cases. There is no report of dengue hemorrhagic

fever in the Amazon region although both serotypes 1 and 2 have been found circulating.

*Aedes aegypti*. was detected in Manaus in 1996. The areas surrounding the port of Manaus were supposed to be the most infested areas of mosquitoes and maintained a constant traffic of ships, and eastern and western populations from the state of Amazonas.

Autochthonous dengue cases were serologically confirmed in March 1998. Dengue 1 virus probably arrived to Amazonas state by river from the east. The index case was a patient from Parintins, which was in Belem, Para on vacation and upon feeling ill, came to Manaus for medication. The epidemic peaked in April 1998 with 4,664 probable cases. At the beginning of the epidemic, men were the most affected. As the epidemic spread to other neighborhoods in the city, the number of ill women increased. During 1998 and 1999, the total number of clinical cases diagnosed was 29,033 and 9,613 cases respectively. Upon further analysis of variables/factors that determine increases or decreases in the number of cases, a relationship was found between levels of monthly rainfalls with the magnitude of the number of cases.

**Exanthematic diseases.** After the severe measles epidemic in 1997, Brazil has reinforced surveillance and control activities of exanthematic diseases in order to achieve the goal of interrupting measles transmission until the end of the year. Thus far, only 33 cases have been confirmed with a prevalence of 0.34% of positive serology. Almost all cases occurred in two Brazilian states, Acre and the Western Amazon, where an outbreak related to Bolivian border epidemic occurred. In the latter, it must be noted that cases were confirmed in children under 1 year old in intervals higher than one month after vaccination with MMR, as well as positive serologies in individuals without a compatible clinical presentation. In some of the children under 1 year old, the laboratory tests after the neutralization of anti-measles antibody reaction identified herpes virus type 6 or parvovirus B19. With the increased number of suspected cases studied, a higher detection of other exanthematic diseases is observed (parvovirus B19, sudden exanthema, etc). Also, there is an increasing concern for the positive predictive value of the serology also increases.

The main problem in conducting the measles eradication plan has been keeping a regular supply of reagents for serology testing which has led to an accumulation of suspected cases without an etiological diagnosis, mainly among those suspected of rubella.

**Hantavirus Pulmonary Syndrome (HPS).** It has been an increase in the sensitivity of the epidemiological surveillance during 1999 and 2000. The number of suspected cases has significantly increased since 1995-1998 where 340 samples of suspected cases were received by the Institute Adolpho Lutz, Sao Paulo, while 779 samples were received from 1998 to June 2000. Most of the suspected cases came from the State of Sao Paulo (64.6%), although the case detection in other states had been on the rise. Out of the 48 confirmed cases from Brazil, 26 (54%) were detected in 1999. Cases were confirmed in eight Brazilian states. Most of the cases occurred in agricultural workers. Fatality remains high (51.6%) for the 1999-2000 period but low when compared to the 1993-1998 period when the fatality was 83%.

On July 2000, CENEPI received laboratory confirmation of an acute HPS case that resulted in death in the State of Maranhao (IgM and IgG positive). Out of 36 other samples collected on site, 26 were IgG positive. An index case from another outbreak was also confirmed in the State of Mato Grosso. In this outbreak, 10 out of 11 samples collected were IgG positive. Studies show that the Andes serotype was circulating during these outbreaks.

The geographical dissemination of cases, outbreaks detected, and the high fatality rate of HPS, suggest that its surveillance has limited sensitivity and only severe or secondary cases are detected.

**Hepatitis.** In 1992, viral hepatitis was included in the group of diseases of mandatory notification in Brazil. Hepatitis A is considered endemic in the entire country, with the sporadic occurrence of epidemics and outbreaks in enclosed populations (schools, day-care, apartment buildings, etc). Some regions in the country, such as the Amazon region and some areas of the southern and southeastern regions are known as areas of high hepatitis B endemicity. The distribution of hepatitis C is not well known in Brazil. In the period of 1993-1998, most of the notified hepatitis cases were classified as "non-specific hepatitis". More than 50% of an average of 50,000 cases notified annually did not report an etiological diagnosis. The prevalence of HbsAg and Anti-HCV antibodies among blood donors has ranged around 1% of approximately 2.5 million collections/year in the last

few years.

Since 1990, vaccination against hepatitis B was added to the basic immunization scheme for the first year of life in the hyper-endemic areas. Starting in 1998, the vaccine was included in the immunization calendar for the entire country. In June 2000, the Ministry of Health made anti-viral treatment for hepatitis C carriers available free of charge. A proportion of the “non-specific hepatitis” among cases reported is on the downward trend.

Hepatitis B information in the Brazilian Amazon region is extensive. From 1993 to 1999, 41,250 hepatitis B cases were notified in Brazil of which 4,750 cases (11.51%) were from the Amazon region; 1,047 and 1,031 cases were reported in 1995 and 1997 respectively. The States of Rondonia , Para, and Mato Grosso were among the states with the highest number of notifications.

During 1998, 1,101 cases of acute hepatitis were diagnosed at the Institute of Tropical Medicine in Manaus (IMT-AM). Seven hundred fifty one cases (68.2%) were Hepatitis A, 89 cases (8.1%) were Hepatitis B, and 261 (23.7%) were other types of hepatitis. From five years of age and on, Hepatitis A incidence tends to increase.. In 1999, 838 acute hepatitis cases were diagnosed, 473 (56.44%) were due to Hepatitis A, 106 cases (12.64%) were Hepatitis B, 2 cases (0.23%) were Hepatitis B and D and 257(30.66%) were other type of hepatitis.

The number of patients with chronic hepatitis was 439 in 1998 and 304 in 1999. The etiology of those cases when confirmation was available is shown in table 4.

**Table 4 Chronic Hepatopathies in 1998/1999**

Diagnosis	B	B+C	B+C+D	B+D	C	Negatives
Cirrhosis	25/18	0/2	1/0	5/14	1/10	13
Chronic hepatitis	91/83	1/7	0/1	26/49	47/52	55
Chronic Hepatocarcinoma	2/0	0/0	0/0	0/0	0/0	0
Chronic Renal Insufficiency	1/0	0/0	0/0	0/0	1/0	0
Carrier	87/13	0/0	0/0	4/8	0/0	0

Since 1991, the Brazilian Ministry of Health and the Health Secretariat of the State of Amazonas maintain a vaccination campaign against Hepatitis B.

**Influenza.** In 1999, Brazil began to implement the national project for the surveillance of acute viral respiratory infections. The project involves three strategies. The first strategy is virological surveillance integrating existing initiatives and including new study sites for determining the circulation of viruses in Brazil. The second strategy is the surveillance of sentinel services that allows to estimate the occurrence and incidence of acute respiratory infections. Finally, the third strategy is the analysis of secondary data of mortality and hospitalization data, supporting the ongoing trends and validating the impact of interventions, such as influenza vaccination that targets the aging population, which started in 1999 and has reached high immunization coverage.

The three national reference centers for influenza have an extensive background on research and detection of viruses circulating in Brazil. In addition, they have contributed to the selection of strains for the production and distribution of vaccines in the southern hemisphere. The Belem center is conducting an immunogenicity study of a vaccine in a population of 60 years old or older from three Brazilian states. This center has also worked jointly with the states and municipal counties of the Amazon region and the central-western Region in outbreak research.

In 2000, the circulation of A/New Caledonia/20/99 (H1N1), A/Sydney/05/97 (H3N2) and B/Iamanashi/166/98 strains were identified in Brazil. With regard to the circulation of influenza virus A/Nova Caledonia H1N1 in Brazil, this strain was first identified in March 2000 as a result of an outbreak in the city of Belem, State of Para, in the Amazon region.

There are strong indications that influenza season occurs more prematurely in the Amazon region than in other parts of the country. An analysis of viral isolation, hospitalization and death peaks shows a less marked seasonality in that region. Preliminary information from a study on the impact influenza vaccination of on a

population over 65 years old shows a decrease in the number hospitalizations due to influenza in 1999. Research on Respiratory Sincitial Viruses (RSV) is also important because the effects of RSV infections in children are indistinguishable from those of influenza. In May this year an outbreak of RSV was studied in Manaus while at the beginning of July another was notified in Belem do Para, where RSV was identified in all samples from ten children with acute respiratory infections.

**Malaria.** The total number of malaria cases reported in Brazil was 632,813, in 1999, an increase from 160,921 cases in 1998. *Plasmodium falciparum* cases were 19.6% of the total and have increased in 14,854 cases for the entire country. Also, mixed infections have increased by 69%. The percentages of *P. vivax* cases have also increased in 146,010 cases and the *P. malariae* infections have increased by 0.3%.

The Brazilian Amazon area is responsible for 99.7% of all the cases reported for the country. The highest increase in absolute numbers were observed in the States of Para (68,671 cases), Amazonas (52,794 cases), Roraima (15,033) and Maranhão (25,524). The total number of malaria cases reported in the State of Amazonas in 1999 was 167,722, showing an increase of 46.2% from 1998. *P. falciparum* infections totaled 30,649, increasing by 6,645 cases. *P. vivax* totaled 136,324, increasing by 46,351 cases.

In the city of Manaus, Malaria cases in 1999 totaled 19,723. The increase was by 5,866 cases since 1998. An increase of 1530 cases of *P. falciparum* and 4,234 in *P. vivax* cases. Manaus is a portal city of infected individuals. In 1999, 9,954 cases were detected in nine municipal counties in the vicinity of Manaus and 946 cases more in other municipal counties. This totals to 10,900 individuals in Manaus as having been diagnosed with autochthonous malaria from other municipal counties.

**Meningitis.** The Amazon region, during the period of 1997 through 1999, reported 9,137 cases of meningitis, 2,357 of them were reported considered as of non-specific etiology demonstrating the difficulty in obtaining an etiological diagnosis. Nine hundred forty two cases (10.30%) were classified as Meningococcal Disease, mostly by Meningococcus type B. The highest number of cases was in Amazonas (358), followed by Para (283), Mato Grosso (137) and Maranhão (104). In Amazonas, 93.2% of the cases were reported by the FMT. It must be noted that.

**Oropouche.** Since 1961, this arboviral disease has been described in the Brazilian Amazon region with several epidemics occurring in the States of Para, Amazonas and Rondonia. Sporadic cases were detected in Belem, Para State during the year 2000.

**Typhoid fever.** Data on typhoid fever in the Amazon region indicate that 4,317 cases were notified in the period of 1990-1999, while 16,399 cases were reported for the entire country. The Amazon region is responsible for most cases of 1,339 or 26.3%, followed by Acre (1,147), Para (987) and Maranhão with 417.

**Yellow fever.** Sharp increase in the occurrence of sylvatic yellow fever has been observed during 1998-2000. Two important outbreaks were verified in 1998, one in the State of Roraima, Northern border of Brazil and the other in the Island of Marajo, Amazon River delta. The latter extended until the first months of 1999 and had more than 50 confirmed cases. During 1999 and the first quarter of 2000, autochthonous cases were reported in the States of Tocantins, Goias, Sao Paulo, Minas Gerais and Bahia. The States of Sao Paulo and Bahia had not reported autochthonous sylvatic yellow fever cases for close to 50 years.

The occurrence of an outbreak where the transmission occurred at a national park close to Brasilia affecting tourists of various Brazilian cities made a great impact on the media and contributed to increasing the surveillance system's sensitivity, mainly in the detection and study of secondary cases. Improved surveillance was evident in that fatality decreased in 1998 and 1999. In 2000, the fatality increased again, perhaps due to depleted field research capabilities of the states Goias, which accounted for 63% of the year's cases. The increase in sensitivity and the intensification of field research led to the identification of other emerging diseases, such as Oropouche virus in the State of Tocantins.

Since 1997, the country has intensified yellow fever immunization. In this period, more than 40 million people were immunized. Two fatal adverse events occurred resulting in deaths in areas where circulation of yellow fever virus was not detected

Sylvatic yellow fever transmission is predominant in the Amazon region. Between 1990 and 1999, 262 cases were notified with 102 deaths; 233 cases and 88 deaths (88.93%) of the country's cases were in the Amazon region. Cases peaked in 1993 with 83 cases and 1999 with 65 cases. During the period of 1990-1999, Maranhão reported 90 cases, Para 72, Amazonas 25, and Roraima 21. Of the 72 cases that the State of Para reported, 36(50%) were reported for 1999.

Due to the number of cases in 1996, 14 cases with 12 deaths, in the State of Amazonas, the Health Secretariat carried out a special effort to vaccinate all inhabitants. The goal was to immunize 100% of the population of Manaus and the capital cities of all the municipal counties where *Aedes aegypti* had been found. As a result of this effort, no cases were diagnosed in 1997. In 1998, there were three cases and five in 1999.

### **Other Epidemiological Events/Investigations**

During 1999-2000, the network of epidemiological surveillance and public health laboratories of Brazil studied the following:

An outbreak of cowpox in the State of Rio de Janeiro, with laboratory confirmation of Ortopoxvirus in 23 human cases, in addition to animal viral confirmation.

Outbreaks of acute toxoplasmosis in the State of Sao Paulo. Two of them related to the consumption of bovine meat ("steaks") resulting in 35 cases and the other with 115 confirmed symptomatic cases at a university campus, possibly related to food intake in two of the campus' cafeterias.

The presence of vancomycin-resistant *Enterococcus* (*E. faecalis* and *E. faecium*) was reported in Sao Paulo. In 1999, 21.5% of 956 samples tested were vancomycin resistant. In 2000, 47.7% of 218 samples tested were resistant to this antibiotic.

An outbreak of maculous fever was studied in the State of Minas Gerais, with 15 confirmed cases in June 2000.

An outbreak of flaccid paralysis was reported in June among adults in the State of Piaui with 5 cases and 2 deaths. Paralysis was reported also among bovines. No etiological agent has been found responsible for this outbreak yet.

### **Chile**

The surveillance system for communicable diseases in Chile is based on three information sub-systems; morbidity surveillance, which involves the universal reporting of specific pathologies and sentinel systems; laboratory surveillance, requiring compulsory reporting of the detection of a list of specific agents and establishing antimicrobial resistance surveillance; and environmental surveillance which involves reservoirs, vectors, and control of water, air, soil, and food conditions.

Although WHO included Chile in the list of cholera-free countries. active surveillance continues, at both environmental and clinical levels. There have been no reported indigenous cases of dengue (serology was done in samples negative for measles or Hantavirus from the northern area of the country) malaria, or yellow fever in 1999. The active surveillance for vectors has been established in areas of greatest risk.

In response to the country's epidemiological situation and the organizational culture of the Chilean health system, it has been decided that the surveillance of syndromes will be established only for acute respiratory distress syndrome, with an initial search for hantavirus and subsequently leptospirosis, and with the possible addition of the search for psittacosis, legionella, and Q fever, depending on the diagnostic capacity. At the same time, a laboratory surveillance system complementary to morbidity surveillance is being developed and incorporated into the regulations governing the compulsory reporting of communicable disease. Under the new regulation, published April 2000, the following causative disease agents are considered to be subject to laboratory surveillance (Table 5):

**Table 5. Microorganisms subject of laboratory surveillance**

- Verocytotoxin-producing *Escherichia coli* (O157 and others)
- *Mycoplasma pneumoniae*
- *Chlamydia psittaci*
- *Leptospire* sp.
- *Coxiella burnetii*
- *Trypanosoma cruzi*
- *Treponema pallidum*
- *Beta streptococcus haemolyticus* Group A (invasive disease)
- Enteropathogens: *Vibrio parahaemolyticus*, *Vibrio cholerae*, *Campylobacter* sp., *Yersinia* sp., *Salmonella* sp., *Shigella* sp.
- *Hepatitis B* and *C*
- *HIV*
- *Legionella pneumophila*
- *Ehrlichia* sp.
- *Streptococcus pneumoniae* (invasive disease)

Whenever any of the above-cited agents are identified, the laboratory (public or private) will be required to inform the national reference laboratory (Public Health Institute (PHI)) and send to it isolates or samples within a specific time period. In addition, the PHI must report to the Ministry periodically on the results of this surveillance. To this end, the PHI is preparing standards to facilitate and regulate the operation of the system. These standards should define the algorithms for the search for and ruling out of agents included in the standards.

The monitoring of antimicrobial resistance in all public and private hospital where microbial isolation is performed is compulsory. The PHI currently carries out regular surveillance activities for the agents included in Table 6.

**Table 6. Bacteria species for which antimicrobial resistance monitoring is compulsory**

- *Streptococcus pneumoniae*
- *Mycobacterium tuberculosis*
- *Shigella* sp.
- *Salmonella* sp.
- *Haemophilus influenzae* type b
- *Staphylococcus aureus*
- *Neisseria meningitides*
- *Neisseria gonorrhoeae*
- Isolated nosocomial infectious agents, according to provisions of the existing technical standards

Collaboration for implementations of monitoring activities were provided by CDC, USA, Center for Vaccine Development, USA, Malbran Institute, Argentina, PAHO, USA and Rhoda-Merieux, Chile.

The status on the major pathologies considered emerging and reemerging included in the surveillance with results considered important for 1999 are described below.

### **Viral Diseases**

***Hantavirus Pulmonary Syndrome (HPS)***. This year, 18 new cases of HPS have been confirmed, with a total of 118 cases produced in the country since 1993. It presents as a disease of low endemicity, predominantly affecting young males (73.7% of cases), with an average age of 29.1 years (2-75 range), who reside in the southern region of the country. The average case-fatality for the period is 50%, although it has decreased in the last two years.

HPS monitoring includes the immediate compulsory reporting to regional epidemiologists and the Ministry of Health of all suspected cases, along with shipment of samples to the laboratory. The regional Service then conducts a visit to evaluate the epidemiological and environmental conditions of the alleged place of infection. The information is compiled and analyzed by the Department of Epidemiology and disseminated continuously on the Department's Web page, which is updated whenever the national reference laboratory (ISP) confirms a case.

**Influenza.** There are seasonal epidemics that occur during the winter months. Surveillance has a morbidity and laboratory components, which is the responsibility of the Ministry of Health. The latter includes weekly compulsory reporting of total cases using a specific case definition. The information is compiled and analyzed by the Ministry's Department of Epidemiology and disseminated weekly through the Department's Web page. Laboratory surveillance involves the detection of the virus in clinical case samples processed in 11 centers throughout Chile. For the most part, samples correspond to hospitalized pediatric cases for ARI. The ISP consolidates the results and prepares a weekly report posted in the epidemiology web page of the Ministry of Health's home page. The new surveillance model implies a change from a morbidity surveillance modality to a sentinel system, linked to the etiological investigation of respiratory viruses in outpatient centers.

### **Influenza in Chile, 1999.**

- 1999 epidemic, 4 times the number of expected cases
- Began in May, peaking during the first two weeks of June
- H3N2 virus homologous to the Sydney virus and sporadic cases of B.
- 239,000 reported cases (rate = 134.6/100,000 in peak week)
- 131 dead (0.87/100,000), 89% of dead were >65 years old
- 2000 Isolates: Influenza A (H1N1), with co-circulation of strains A/Bayern/07/95 and A/New Caledonia/20/99 and Influenza B.

**Rabies.** A domestic cat from Region VI was diagnosed with rabies on May 1999. Although the infective variant was found to be bat rabies virus, it was neither variant 1 (canine) nor variant 4 (the common bat). Sequencing studies for further identification of the variant are being made at CDC, USA.

### **Bacterial Diseases**

**Vancomycin-Resistant *Enterococcus*.** Two cases of vancomycin-resistant enterococcus have been isolated from hospitalized patients in two centers in the Metropolitan Region.

**Legionella.** A clinical suspicion was confirmed in a 5-year old patient by a positive serological test for *Legionella pneumophila* during 1999. Although the sisters of the patient were serologically positive, her parents were not. Possible sources of infection were investigated in the residence of the patient, with none determined. There was no evidence of travel abroad, stay in hotels, or recent hospitalization.

### **Other Epidemiological Events/Investigations**

An Outbreak of Q Fever of occupational origin originated from livestock imported from Spain was investigated. It was also detected an outbreak of *Canis ehrlichiosis* in dogs of the Metropolitan Region In 1998.

### **Colombia**

The existence of different structural development factors in certain regions and social groups make the morbidity and mortality pattern in Colombia unique. The epidemiological profile is one with the predominance of chronic, non-transmittable diseases and violence. However, infectious diseases continue to contribute to the country's disease burden. According to health statistics by the Ministry of Health, the highest outpatient and inpatient morbidity burden between 1990 and 1999 was composed not only by chronic diseases but also by infectious diseases moving in an upward trend. In fact, the progressive decrease of infectious diseases observed until a decade ago has started to recede. Today, infectious diseases are one of the most important national public health problems. Especially of concern are the reappearance of malaria, dengue and tuberculosis and the introduction of emerging infectious diseases, such as cholera and Venezuelan equine encephalitis. Emerging and re-emerging infectious diseases have also spread to new geographic areas while diseases such as malaria and tuberculosis show increased drug resistance. This situation increased the need for expanding surveillance activities and the strengthening of specific syndromic surveillance based on the Colombian National Laboratory Network (LabNet).

## Bacterial Diseases

**Cholera.** After the cholera epidemic peak in Colombia during 1991 and 1992, cholera incidence for the following years ranged from 1 to 11 per 100,000 inhabitants and the highest incidence rate was observed in 1996. In 1999, however, a marked decrease in the incidence was reported, resulting in only 20 cases. A similar behavior was observed in cholera mortality, with national rates under 0.2 per 100,000 inhabitants, whereas the fatality rate is still under 1%. The isolated serotype is 01 El Tor.

**Leptospirosis.** Several regions of the country are endemic for leptospirosis, with 15% to 20% seropositivity among the human population. *Leptospira icterohaemorrhagiae* is the predominate species. Epidemics appear in the Atlantic coast in 1995, which coincided with floods that affected that area. Information about medical consultation and hospital discharges in the entire country reveal an increased number of reported cases from 100 in 1990 to approximately 200 in 1999.

**Tuberculosis.** Although tuberculosis incidence in Colombia has been on the downward trend from 58.6 per 100,000 inhabitants in 1970 (12,522 cases) to 25.1 per 100,000 in 1999 (10,428 cases), tuberculosis currently represents one of the most severe re-emerging problems in Colombia. An average 10,000 new tuberculosis cases are being diagnosed. However, it is estimated that there is a 25% underreporting of cases due to the lack of active surveillance. Ninety-two percent of the total numbers of cases reported in 1999 were pulmonary forms and 7% were in children under 15 years old. Tuberculosis mortality is close to 4 per 100,000 inhabitants.

**Malaria.** Sixty-five percent of the Colombian population inhabits areas below 1,800 meters where environmental factors guarantee the reproduction of anopheline vectors. Colombia has reported 41 species of Anopheles which have been incriminated as the main vector species: *An. albimanus*, *An. nuneztovari* and *An. Darlingi* are predominant in the Pacific, Central and Orinoco-Amazonian regions, respectively. There are also other co-existing circumstances that enhance malaria transmission such as forced displacement of populations from malarial areas toward areas free of malaria where favorable ecological conditions for new transmissions continue to occur.

The malaria trend in Colombia shows an upward secular tendency with the highest incidence in the last few years, along with a marked increase of malaria transmission areas. *P. falciparum* infection has acquired particular relevance. It has increased since 1996 and 1998 and it has reached the highest incidence rate of the last two decades. The high number of cases due to *P. falciparum* may explain the increased malaria incidence since there have been simultaneous reports of increased resistance of this species to first generation anti-malarial medications used in the country. During 1997 and 1998, 180,910 and 194,178 new malaria cases have been reported respectively, for an average rate of 7.5 per 100,000 inhabitants of malaria risk areas. It must be highlighted that 70% of all notified cases correspond to the Pacific region of the country.

In 1999, 71,715 malaria cases have been reported with the surprising marked decrease in the number of cases of the Pacific endemic region. Toward the end of 1999 and beginning of 2000, a large outbreak occurred in Guajira. Until June 2000, 36,904 malaria cases have been notified in the country, where 63% are due to *P. vivax* and the rest due to *P. falciparum*.

## Viral Diseases

**Acute Viral Respiratory Syndrome.** Colombia faced a nationwide epidemic of influenza/Wuhan (H3N2) in September of 1996, which affected more than 6 million people and caused at least 600 deaths. After the epidemic, a respiratory infection surveillance system was implemented at two regular sentinel centers and five other centers. Nasopharyngeal samples (swabs and washes) are taken on the same day each week from people seeking medical care at the collaborating centers. All samples are processed for virus isolation and immunofluorescence (IFA) assay over a cell smear using a panel of monoclonal antibodies against influenza (Flu) A, B, parainfluenza 1,2,3, Adenovirus and Respiratory Syncytial Virus (RSV). Positive Flu samples by IFA and virus isolation are identified additionally by Hemagglutination Inhibition test using the WHO influenza reagent kit.

Between March 1997 and June 2000, 1,388 samples were processed. Influenza A was detected in 164 (12%) and Influenza B in 9 (0.6%) during 1997. Influenza/Wuhan(H3N2) was identified in 1996 and influenza/A/Sydney H3N2 in 1997 and 1998. Typing of all influenza strains in 2000 is pending. By IFA, RSV has been identified in 218 samples, adenovirus in 26, and parainfluenza in 14. Influenza and RSV are seasonal in Colombia and its circulation is heavily influenced by the amount of rainfall.

**Dengue.** Classic dengue (CD) and Dengue Hemorrhagic Fever (DHF) reports show an upward trend during 1990-1999, especially DHF with an incidence of 0.01 in 1990 and 13.9 per 100,000 inhabitants. During this same time, higher frequency of more severe cases was reported. In 1998, the epidemic peaked to 57,956 cases of CD and 5,171 cases of DHF. It must be noted that major epidemic outbreaks have been chronologically associated with viral isolations of serotype 2. The number of municipal counties that had presented DHF cases had increased from 168 (16%) in 1997 to 302 (28%) in 1998. A decrease in the number of cases was reported for the entire country, with 20,322 probable cases of CD and 1,136 cases of DHF.

In 1999, the decrease was even observed in the departments that showed a stable endemic level throughout the year. Incidence number of over 1,000 cases per 100,000 occurred persistently among urban inhabitants from seven capital municipal counties in Colombia. As for year 2000, until the second week of June, 9,564 cases of CD and 758 cases of DHF/DSS have been reported.

**Hantavirus.** Eighteen (22%) out of 83 samples from adult female Amerindians from the Leticia Area, Amazonas Department, were positive when tested by ELISA. Samples from Amerindians from additional regions in the Amazon, Orinoco and Sierra Nevada de Santa Marta, will be tested in the near future.

**Hepatitis.** The national incidence rate is 3.5 cases per 100,000 inhabitants. Areas of predominantly indigenous populations report the highest rates range of 5 and 50 per 100,000 inhabitants. The hepatitis tendency assessment based on data from the weekly notification system (SIVIGILA) for 1995-1999 shows an upward tendency but seasonality or cyclic behavior was not observed.

The information gathered for Hepatitis C from blood banks during 1993-1999 has shown a prevalence among blood donors ranging from 0.7 to 1%.

**HIV/AIDS.** During 1990 and 1999, incidence rates were 2.1 per 100,000 among women and 15.2 per 100,000 among men. Eighty-seven per cent of the HIV infected cases are in the 14 to 49 age group. Among the cases reported, 97% were infected by sexual transmission, which correlates well with the associated risk due to sexual behavior.

The epidemiological behavior pattern has currently changed, heterosexual transmission is considered higher than homosexual transmission. This implies a risk for increased HIV/AIDS among women, which is also shown in man to woman ratio. In 1986, the ratio for infection was 47 men to 1 woman. Currently, the ratio is 7 men per 1 woman. Therefore, in the near future, an increase in the mother-child transmission will be observed.

**Rabies.** naturally infected areas of rabies decreased from 28 departments in 1980 to 7 in 1999. However Animal and Human Rabies control has deteriorated since 1994 with low anti-rabies vaccine coverage for canines of fewer than 70%. Consequently, there has been an increase in the number of animal cases from 72 confirmed canine cases in 1994 to 168 in 1999, and from one human case in 1994 to 7 in 1998.

Most of the canine rabies cases have mainly occurred on the Atlantic Coast with an epidemic peak in 1998. In 1999, a tendency to spread toward the interior of the country was observed by the presence of urban animal rabies outbreaks, associated to human rabies cases in the Colombian-Ecuadorian border. The occurrence of human rabies has been related with the higher number of canine rabies cases that occurred in endemic areas. It has been also noticeable increase in the number of cases of bovine rabies. These cases were transmitted by the hematophagous species and are not associated to exposure cases or human rabies.

**Venezuelan equine encephalitis (VEE).** Various strains of VEE have caused periodic epidemics among humans and equines in Latin America since 1920. The largest epidemic since 1973 occurred in 1995 in

Colombia and was caused by subtype I variant C-D. It affected an estimate of 75,000 to 100,000 individuals, 3,000 of them suffered neurological complications, 300 fatal human cases in la Guajira and 50,000 equines were affected with an 8% mortality rate. The virus introduced from Venezuela coincided with a high density of the vector, *Aedes taeniorhynchus*. The epidemic had an attack rate of 30%.

During epidemiologic week 13 of year 2000, two probable VEE cases occurred in children under 5 years old in the Department of La Guajira. Serological testing however, showed that IgM for VEE was negative.

**Yellow Fever.** Colombia has not seen urban yellow fever, in spite of the re-introduction and spread of the *Aedes aegypti* since 1929. In total twenty one cases have been reported in the last 5 years, all of them were of the sylvatic form, where vaccine coverage has been hard to maintain.

### **Status of Diseases or Major Investigations During 1999-2000**

**Undifferentiated febrile syndrome/Hemorrhagic fever syndrome.** Blood samples were screened by ELISA for IgM-Dengue(D) and IgM-Yellow Fever (YF). Virus isolation (VI) was attempted in C6/36 cells, while viral Identification, the four dengue serotypes and yellow fever, was done by indirect Fluorescent Antibody Assay. From February to November 1999, 305 samples were obtained from the Currillo, Florencia, and San Vicente del Caguan municipalities of Caqueta Department. Patients' age distribution was 5-95 years of age (median 23 years) and 56% were females. From the 159 samples tested none was positive for flavivirus. Thirty-seven samples (12%) were positive for the IgM-D test, 69 samples (23%) were positive for IgM-YF test and negative for the IgM-D test. Among these samples, 15 patients say that did not receive the 17D vaccination that was administered massively in Caqueta during 1998. However there is no way to assure the confidence of the negative information concerning YF immunization. In addition the test used for detection of YF was not considered highly specific. In any case syndromic surveillance was reasonable useful for identifying cases of dengue.

The IgM-YF assay is performed only at the Instituto Nacional de Salud but LabNet performs IgM-D assays for 31 out of 33 departments. LabNet will strengthen its capability for detection of YF and Dengue. The latter also in three new sentinel surveillance centers implemented in Puerto Asis (Putumayo), Tumaco (Nariño) and Buenaventura (Valle).

### **Paraguay**

Regulations for surveillance were reviewed and updated by the Ministry of Health. The General Directorate for Health Surveillance and the Division of Emerging and Re-Emerging Diseases has been created within the Ministry of Health.

To improve and strengthen surveillance a linkage for surveillance of Dengue and Hantavirus has been established between the Ministry of Health and the National University. On the other hand, still there is lack of efficient participation in surveillance activities of other institutions that are part of the health sector, such as the Social Security, the Military and the private sector. National support for monitoring emerging/reemerging diseases was provided by the Ministry of Health and the National University of Asuncion. At the international level support was provided by the CDC, USA, FIOCRUZ, Brazil, Institute Carlos Malbran, Argentina, and PAHO.

### **Bacterial Diseases**

**Leptospirosis.** Four cases of leptospirosis were detected in 1999 and 1 case thus far in year 2000. Three of the four cases in 1999 originated from the Department of Cordillera, 56 kilometers northwest of the capital city of Paraguay. diagnosis was made by the microagglutination method at Central Public Health Laboratory (CPHL) and by the macroagglutination test (Laboratory of the Ministry of Agriculture and Livestock). The case reported in year 2000 was in the Department of Paraguari, which is bordering the Department of Cordillera. It was confirmed by laboratory tests and occurred in an adult patient who died under suspicion of dengue hemorrhagic fever.

**Tuberculosis.** The number of new tuberculosis cases, in all of its forms, remains high with an average of 1765 cases annually in 5 years (incidence of 35 per 100,000 inhabitants). Ninety-seven percent (97%) of these cases have a pulmonary location and 45% of these have a positive bacilloscopy. The health regions of Boqueron, Alto Paraguay and Presidente Hayes have incidence rates 10 times higher than the national average. Samples are processed and analyzed at the CPHL.

**Malaria.** After a decline in the number of cases within the last decade, a sudden increase was observed in 1999 where an epidemic of 9,943 cases was reported. The incidence rate in areas with evidence of transmission was 412 cases per 100,000 inhabitants where as in 1997 the incidence rate was only 23 per 100,000. The foci are geographically limited to three departments: Caaguazu, Alto Parana and Canindeyu, where approximately 92% of all the cases occur. Ninety-nine percent (99%) of the malaria cases in Paraguay are due to Plasmodium vivax.

### **Viral Diseases**

**Dengue.** The dengue epidemic in 1999 stretched from February through June and the most affected regions were Asuncion, Central, Alto Parana and Amambay. The number of cases notified reached 1564 cases – confirmed by laboratory. However, the number of cases that occurred is estimated at several thousands. In the months of November-December, another outbreak took place in the region of Concepcion and later in the district of Luque in the Central region, spreading with disperse foci throughout other districts, Asuncion and Alto Parana.

Until February 2000, the epidemic had spread throughout the entire national territory. A total of 988 cases were confirmed by laboratory methods and more than 7,000 cases were clinically diagnosed, bearing in mind the significant amount of under reporting, we could have confronted a large magnitude epidemic. Serotype 1 was the virus involved.

**HIV/AIDS.** The 1998 and 1999 incidence rates of AIDS were 1 to 0.9 cases per 100,000 inhabitants respectively, and have decreased to 2 cases per 100,000 inhabitants in 2000. This might be due to the delay in between the time a case is detected and when it is reported.

Using the total accumulated figure from 1985 to 1999, the age group with the highest incidence rate is the 30 to 34 year-olds. Groups, which have showed highest increases in incidence rates, are 25 to 29, 30 to 34, and 20 to 24 in order of magnitude. The group between 25 to 29 year olds has shown a 19-fold increase in its incidence rate in the previous 10 years.

For women, the risk factors associated with acquiring the disease are heterosexual intercourse (73.2%), and blood transfusions 10.9%. For men, since 1995, heterosexuality is the most frequent risk factor in contrast to previous years, when the disease was predominant among homosexuals. For males, no cases showed blood transfusion as a risk factor.

**Hantavirus.** Hantavirus Pulmonary Syndrome (HPS) is an endemic pathology for the Chaco Central Region. Starting in 1995 until January 2000, 44 cases had been reported, mostly males between 13-52 years old. No secondary cases among relatives, neighbors or health care personnel have been reported. Almost all cases have been confirmed clinically and by the laboratory (36 cases were IgM and IgG positive and 6 retrospective cases with IgG positive; 1 was positive by the immunohistochemical test). One had a HPS confirmation by clinical and epidemiological criteria. The cases come from the Chaco Central area, departments of Boqueron and Presidente Hayes. The first 23 cases were centered in a surrounding 100-kilometer area, with the epicenter in the city of Philadelphia. The current tendency is to spread in a circular pattern, with a radius over 200 kilometers. The most affected areas were Philadelphia and Loma Plata. The occurrence curve of all notified cases presented a bi-modal tendency where a small peak occurred in April-June and then another one occurred in August. Individuals who live in rural areas are identified as the risk group and the risk behavior is related to agricultural type of activities where contact with wild rodents' feces, urine or saliva is possible. Serological diagnosis is made by the CPHL and confirmation of results is performed at the Institute Carlos G. Malbran, Argentina.

## URUGUAY

The activities coordinated between the Department of Laboratories and the Department of Epidemiological Surveillance, from the Ministry of Health, have been markedly strengthened. Staff from the Ministry has been trained in influenza, hantavirus and HUS. External support was provided by CDC, USA, and reference laboratories from Argentina, and PAHO. However, limitations in the infrastructure, human resources and budget constraints, prevent full materialization of the syndromic approach for surveillance.

### Bacterial Diseases

**Foodborne transmitted diseases.** Analysis of the data from 1999 shows that the tendency from previous years remains the same, *Salmonella* is the main causative agent of Food borne Disease. In particular eggs not cooked thoroughly or at all are the most frequent source of infections. Homes were the place where lack of hygiene was the origin of most problems.

### Viral Diseases

**Dengue.** In 1997, after 39 years of its elimination, *Aedes aegypti* larvae were detected in a Department bordering with Argentina. A contingency plan was prepared against *Aedes aegypti*. During 1997-2000, new foci were detected in different Departments. In 1999, a peak was observed in the months of May and June with a total of 6 positive Departments, the same has been observed this year.

Serological studies carried out indicated that the antibody findings in normal population represent cross-reaction with other flavivirus, especially with the Saint Louis Encephalitis virus. No autochthonous cases have been reported, although the presence of imported cases has been registered; two Dengue cases were imported last year, one from Paraguay and the other from Bolivia. Joint activities for epidemiological surveillance are planned in a sentinel study of febrile syndromes to monitor influenza and dengue activities in areas bordering with Argentina.

**Hantavirus.** Hantavirus Pulmonary Syndrome (HPS) was detected for the first time in 1997 and since then, an annual increase in the incidence and a decrease in fatality have been observed.

Diagnostic activities for Hantavirus have continued to increase as a consequence of acquiring more knowledge of the disease by medical personnel. The most important clinical characteristics of the disease and its unique geographic distribution in Uruguay have been determined. Through 2000 a total of 24 HPS have been registered. The virus reservoir has not been established, although partial data may point to *O. flavescens* as one of the Hantavirus reservoirs in Uruguay.

**Influenza.** During the cold season of 1999, influenza surveillance activities were intensified by increasing the number of sentinel posts and samples tested. The addition of rapid tests for diagnosis has allowed for the generation of earlier epidemiological information and a weekly feedback system to health professionals. Currently, data regarding work absentees for the capital of the country are available. Also, molecular biology techniques have been added to allow for better epidemiological surveillance. In Uruguay, one can observe a progressive awareness by the medical personnel of the anti-flu vaccination. The Ministry of Public Health has distributed 300,000 doses for the cold season of 2000.

## VENEZUELA

Venezuela has highly qualified human resources and solid health infrastructure with 1869 health care centers [Outpatient: Urban-Rural and Hospitals types I, II, III and IV] that make up the notification network. It also has a solid epidemiological information system, with over 80% of mandatory notification reporting diseases over 80% and general morbidity of 100%. And, there is available a network of public health laboratories in 23 out of 24 States, and qualified reference laboratories. In addition, the government has undertaken a significant effort to strengthen a national diagnostic support network for public health; develop of a syndromic surveillance system (ictero-hemorrhagic febrile syndrome); and prepare epidemiological surveillance manuals for: Leptospirosis, Yellow Fever, and syndromic diagnosis. Still the main weakness of the system is the lack of stability of the

staff, not using the laboratory to its full potential, and budget constraints to send samples.

National support for surveillance activities was provided by the Ministry of Health. The Institute Hygiene receives funding from the national government and also generates its own income. Due to ministerial resolution delegating duties, the Institute has recently started to coordinate the national diagnostic support network of public health. For that purpose, 23 laboratories have been established and this number can be increased with the 16 laboratories existing since 1995. International support has been provided by the CDC, USA, the Dutch Government, Institute Pasteur, France, PAHO, the National Institutes of Health, USDA, the Rockefeller Foundations, and the United Nations Development Fund.

## **BACTERIAL DISEASES**

***Antimicrobial Resistance.*** In 1988, the Venezuelan Societies of Microbiology, Infectology and Pharmacology initiated a network for the surveillance of bacterial resistance to antimicrobial agents. At first, 9 hospitals participated and by the year 2000, 29 Microbiology laboratories in various areas of the country are now members of the surveillance system. The National Center operates at the Microbiology Laboratory of the Hospital Vargas in Caracas. Data processing is performed using the WHONET software. Since 1997, a network of laboratories for establishing antimicrobial resistance on Enterobacteria (*Salmonella*, *Shigella* and *Vibrio cholerae*) is also functioning. A total of 37 laboratories currently take part in this network at national level. Some of the results obtained through those networks are described below.

***Neisseria meningitidis type C.*** Responsible agent for an outbreak in the city of Caracas during the first three months of 1994, which was later confined to small outbreaks in the military base of Caracas (Tiuna Fort 1997) and the Naval Base of Carupano, in 1999. In all three episodes, the agent had a decreased sensitivity to Penicillin (minimum inhibitory concentration higher or equal to 0.1 ug/ml).

***Streptococcus pneumoniae.*** Its sensitivity to Penicillin has gradually decreased and to date, the percentage of resistance is close to 35%.

***Neisseria gonorrhoea.*** Data shows resistance to Penicillin above 25%, at least in the cities of Caracas and Maracaibo.

***Escherichia coli.*** It has a high percentage of resistance to several antibiotics administered orally.

***Shigella sp.*** Agent shows a high resistance to antibiotics, especially *Shigella flexneri*.  
*V. cholerae.* It has been shown resistant to Thrimethropin Sulpha and Ampicillin.

***Cholera.*** In 1996, after two years without detecting the presence of Cholera, it was detected the presence of imported cases from Colombia. The outbreak spread out and toward the end of 1997, it had reached 14 states, with a total of 2557 cases; morbidity rate was 11.14 per 100,000 inhabitants, with a fatality rate of 2.30%. The most affected age groups correspond to both ends of the life span. During this epidemic, 68% of the cases reported were detected by active surveillance. Also, 55% of the cases were confirmed by laboratory tests, whereas the rest met the clinical and epidemiological criteria. A total of 61% of the deaths had laboratory confirmation. In the middle of 1998, isolated Limited outbreaks were notified in the states of Zulia and Delta Amacuro. Later on an explosive outbreak was reported in the state of Delta Amacuro which started spreading to the neighboring states. By 1999, the states of Sucre, Monagas, and Nueva Esparta had already been involved. At the end of that year, an isolated outbreak was reported in the State of Miranda and one case in the State of Anzoategui, with persistent foci in the eastern states. During 1998-2000, a total of 840 cases and 27 deaths have been reported. The circulating serotype was Inaba 01.

The epidemic is characterized by presenting multiple foci and is food and water borne, but other factors are involved in the persistence of the disease transmission. Such as: socioeconomic conditions, lifestyles, personal hygienic and eating habits, high population movement from areas with active foci of the disease to disease-free areas, persistence of asymptomatic carriers, hygienic practices in food handling and weak regulation of food commercialization activities, environmental health conditions, proper disposal of fecal matter, and finally, availability/quality of water. The epidemic that started in 1998 in the eastern states progressed and was

enhanced by the rainy season and flooding affecting the eastern part of the country; severe problems in environmental health, disposal of fecal matter, treatment of sewage water and supply of intra-domicile potable water; scarce participation of government and non government institutions from other sectors; life conditions and styles of the population; budget constraints for health education through the media; and Increased number of food vendors on the streets.

**Leptospirosis.** It is currently subject to epidemiological surveillance. In this study period, 960 samples were processed using microagglutination techniques in plates and 270 (28.13 %) were positive distributed throughout the 21 states. The diagnosis is only performed at reference laboratories in only 9 states.

**Streptococcus pneumoniae and Haemophilus influenzae type b.** In 1999, the surveillance of pneumonias and meningitis was initiated for these agents with 6 sentinel posts at a national level that were capable of isolating these micro-organisms. The results obtained from 43 strains processed for *S. pneumoniae*, 40 were typed and the most frequent serotypes were 14 (10 strains), 6B (7 strains), 23F (3 strains) and 1 (3 strains), and 17 strains of other serotypes. In the case of *H. influenzae*, 45 strains were isolated with predominance of serotype b.

**Tuberculosis.** In 1999, the incidence rate for all forms was 26.1 per 100,000 inhabitants. The highest rates are those where the indigenous population lives or large cities with high population density of low socioeconomic level. The highest rate in the country occurs in Delta Amacuro: 93.2 x 100,000 inhabitants; the Federal District: 49.8 x 100,000 inhabitants; Portuguesa: 47.8 x 100,000 inhabitants; and Amazonas: 47.4 x 100,000 inhabitants. Much lower rates are found in Falcon: 9.6 x 100,000 inhabitants, Mérida: 12.3 x 100,000 inhabitants, and Nueva Esparta: 13.0 x 100,000 inhabitants. Out of the 6,187 new cases reported in the country during 1999, 85% are pulmonary and 3,517 are bacilliferous, patients are older than 15 years of age. The number of cases reported as tuberculosis meningitis reached 22 and only 3 of these are in children under 5 years of age (rate of 0.03 x 100,000 inhabitants). However, the tendency to decrease mortality remains the same in spite of the peaks observed in 1990, 1991 and 1992. The last available figure corresponds to 1997 where 736 deaths due to tuberculosis were reported in country, which corresponds to a rate of 3.1 x 100,000 inhabitants.

**Malaria.** In 1999-2000 were reported malaria 38,384 cases. By the time this report was prepared, for year 2000, a total of 16,669 cases had been notified. This doubled the number of cases reported for the same period in 1999. In the current year, three states present 95% of the malaria originated in Venezuela (Bolívar, Sucre and Amazonas). *P. vivax* predominates, *P. falciparum* at a lesser frequency, and mixed forms have also been reported.

## **Viral Diseases**

**Dengue.** *Aedes aegypti* is widely spread in the country. Its main rearing sites are barrels, rubber tires and tanks. The highest dengue morbidity rate was reached in 1998 (161.7/100,000 inhabitants). Between 1999 and June 3, 2000, a total of 34,925 cases have been reported, 3644 of which correspond to the hemorrhagic form with 17 deaths (provisional data). Throughout 1999-2000, a total of 4352 samples were processed with a seropositivity rate of 34.1 % (1485 samples) and 882 samples with 69 isolations. The serotypes in circulation were Dengue type 1, 2 and 4. There is evidence of the virus circulating throughout the entire national territory during the above mentioned period although its incidence has decreased in the last year. Viral genotyping studies continue to be performed, currently in collaboration with the Instituto Venezolano de Investigaciones Científica (IVIC) for serotypes 1 and 4. Preliminary results indicate the circulation of a genotype of Dengue 1 phylogenetically related with Dengue 1 from Singapur, Nigeria, Burma and the Caribbean Islands and only 1 genotype of Dengue 4 related to the Dengue 4 viruses from Latin America, Indonesia and the Pacific Islands. Diagnosis is performed in 23 of the 24 states.

**Hantavirus.** In the middle of 1999, one isolated case of Hantavirus Pulmonary Syndrome was detected and confirmed by laboratory in an individual from the State of Anzoátegui. The field study collected 18 samples from residents of the area and they all tested negative. The retrospective review of the morbidity in the area showed no evidence of compatible cases. Currently in progress are rodent collection and exposure of sentinel hamsters in the area to determine viral circulation.

**HIV/AIDS.** In spite of its under-reporting estimated to be 75 to 80%, Venezuela used to be considered as a country at a low epidemic level. During 1982-1999, a total of 8,047 cases have been reported, 89.3% are males; 5313 deaths, 91.26% were males. The most affected age group, for males as well as for females is the 20-44 range where 81.04% of the cases are reported. The transmission mechanism is known only in 62.97% of the cases. Sexual transmission was the most common (90.25%). Homosexual intercourse is the most frequent means for infection, 2101 cases (41.46%). Blood transmission represents 4.3% of the cases; drug use 1.9%; and perinatal transmission is 3.1%. At a national level, all the regions are affected, particularly the Federal District (capital region) with 3730 cases with a rate of 163.5/100,000 inhabitants. The State of Aragua is in second place with a rate of 35.36 (495 cases). The State of Nueva Esparta is in third place with 33.22 (116 cases), State of Merida is in fourth place with 26.31 (186 cases) and the State of Anzoategui is in fifth place with a rate of 22.18 (239 cases). These regions have rather significant characteristics: Aragua has productive centers, Nueva Esparta and Merida are tourist areas and all are student sites. At the "Rafael Rangel" National Institute of Health (RR NIH) and in public health laboratories, laboratory testing was performed for 4,217 cases and 218 were confirmed. Serological and confirmatory diagnosis is currently performed in the 24 states whereas isolation, viral load and genotyping studies are carried out at reference laboratories.

**Respiratory viruses.** Epidemiological surveillance started in 1988 with sentinel posts at the Federal District and periodic sampling at a national level. All laboratory tests are carried out at the reference laboratory. Through the surveillance efforts, a total of 353 samples were tested by ELISA and/or viral isolation in 1999. Sixteen samples were positive for Influenza A (H3N2), 4 Influenza B and 13 for Parainfluenza.

**Venezuelan Equine Encephalitis (VEE).** At the end of 1992, an outbreak was reported at Costa Sur del Lago de Maracaibo, State of Trujillo, and later extended to the Perija Municipal County, State of Zulia. In the same year, the circulation of the VEE virus was confirmed, reporting a total of 38 cases and no deaths. The 1995 outbreak showed an incidence higher than that reported in the previous outbreaks, with the exception of the outbreak in 1963-1965, which resulted in a total of 12,317 cases. However, the fatality rate of the disease was the lowest ever observed (0.2%). From then on, no new cases in humans have been reported. During the present year, but 3 foci of the disease were detected in equines, 2 in the State of Barinas and 1 in the State of Carabobo. no serological evidence of infection, nor virus isolation, was obtained when 262 samples from the surveillance were tested. The field studies of sentinel hamsters and/or collection of smaller mammals, suggest the enzootic circulation of the virus in the Araurima region, State of Falcon in mid April 1999. diagnosis of VEE is only carried out at the reference laboratory.

**Venezuelan Hemorrhagic Fever.** it emerged as a public health problem in 1989, simultaneously with dengue hemorrhagic fever and mostly affected farmers from the Guanarito municipal county (State of Portuguesa). From its start and until 1999, a total of 269 cases have been detected with 74 deaths showing a fatality rate of 27.5% for that period. The behavior is cyclic with epidemic stages every 4 or 5 years, followed by inter-epidemic stages of low incidence. Two epidemic periods have been reported in all. The first one was between 1989-1991 (94 cases) and the second one was between 1995 and January 1998 with a total of 116 cases. The highest number of cases was detected at the end of the rainy season (highest agriculture and livestock industry activity). The affected municipal counties were Guanarito and Papelon as well as areas adjacent to the State of Barinas. Currently, it has been identified in the States of Portuguesa, Barinas, Apure and Lara. The most affected age group is 6-54 years old with the highest attack rate in the group over 15 years old. The infection rate in humans ranges from 0 to 10%, according to seroprevalence studies of antibodies in the municipal counties of Guanarito and Papelon. Diagnosis has been carried out only at the reference laboratory since 1999. To date, 146 serological tests have been performed, 4 were positive.

**Yellow Fever.** Three foci of Sylvatic Yellow Fever have been identified: Lago de Maracaibo, San Camilo and Guyana (including the States of Bolivar and Amazonas). Since 1980, in spite of having a Yellow Fever epizootic in 1991 and in the first months of 1992, no human cases were reported. In 1998, an outbreak was detected in the Yanomami community, located in the Parima area, Alto Orinoco Municipal County, State of Amazonas. This outbreak involved 14 cases and 3 deaths. The cases came from the areas of Parima A, Platanal and Parima B, affecting a total of 6 villages (or shabonos). A yellow fever immunization campaign was performed in the Alto Orinoco Municipal County, with a total of 177 villages where 68 of them can be accessed by air and in the rest by river. This area contains 6776 inhabitants with vaccine coverage of 86%. There was no

knowledge of any deaths among primates (araguatos) in the area and it was verified that the symptoms in the case subjects started when they came back from a migratory movement during which this time there was yellow fever activity in Brazil. In 1999, it was reported a death due to yellow fever (laboratory confirmation) of US National that was not immunized against yellow fever and who entered the Amazon jungle of the State of Bolivar.

**Other epidemiological events/investigations.** In addition to the above 1 case of *Legionellae pneumoniae* was detected in the Federal district; 2 outbreaks of , *Mycoplasma pneumoniae* with 28 and 53 cases were reported in the Federal District and Monagas State respectively; and an outbreak of 39 cases of histoplasmosis was detected in the Federal district. No deaths were reported in any of them.

## **VII. STATUS OF THE IMPLEMENTATION OF SURVEILLANCE FOR EID**

### **Surveillance in the Caribbean Epidemiology Centre (CAREC)**

The Caribbean Epidemiology Centre (CAREC) serves 21 Member Countries (CMCs) with a population of 6.5 million. The level of development of these countries varies and therefore there are diverse levels of technical support. Their economies depend on tourism of 30 million tourists annually. This has produced an increase in the risk for travelers associated health problems. CAREC has the organizational responsibility for the surveillance of communicable and non-communicable diseases.

Notifications on mortality, morbidity and occurrence of disease outbreaks reach the Epidemiology Division through different routes and continued collaboration with our CMCs. Following receipt of these reports, data are consolidated into a regional database, EPISUM, from which it is analyzed, interpreted and appropriate reports are produced.

During the period of the 1980's and first part of 1990's, morbidity of communicable diseases in the Caribbean declined as the result of the expansion of health services, implementation of Expanded Programme on Immunization, reduction in poverty and increasing educational levels. Today, the three diseases subject to global surveillance, AIDS, Tuberculosis and Malaria are of considerable concern for the sub-region.

The Caribbean region has the highest incidence rate of reported AIDS cases in the Americas and the second highest in the world after the sub-Saharan Africa. Since 1995, AIDS has become the leading cause of death among the 15-49 years old group in many of the 21 CMCs; the annual incidence increased from 854 in 1991 to 2,279 in 1998. The CAREC analysis on the HIV/AIDS epidemic in the Caribbean indicate that the changes are associated with steady increasing numbers of cases in the homosexual/heterosexual and pediatric populations.

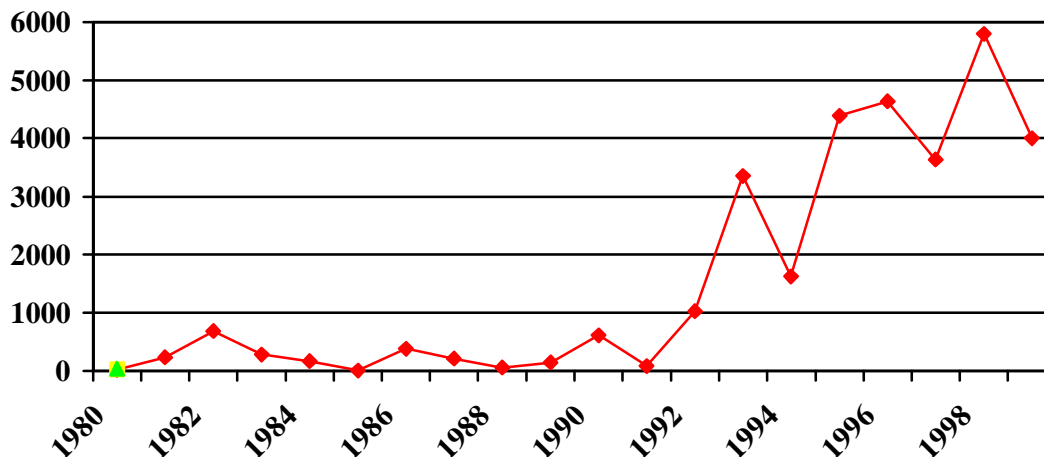
Tuberculosis has re-emerged as a major public health problem as part of the HIV/AIDS epidemic and the emergence of multiple-drug-resistant strains. As a priority problem, considerable resources have been allocated to ensure effective management and control strategies. During 1999, an emphasis was placed on the assurance that member countries adopt and utilize effective strategies to facilitate the early identification and treatment of tuberculosis.

Malaria had been virtually eliminated from the Caribbean islands of the CMC's. In the last 5 years, there have been malaria-imported cases from travelers and since all countries possess the vector species, the presumption of autochthonous transmission can occur. This stresses the need for health authorities to continue surveillance and for physicians to include malaria in the differential diagnosis in cases of undifferentiated fever. However, in the mainland countries of Suriname, Guyana and Belize, malaria continues to be highly prevalent. In the Guyanese shield the Annual Parasitic Index (API) and the Annual Falciparum Index (AFI) were more than 100 and 70 respectively during 1998. These values indicate that 4.4% of the new cases in the Americas are occurring on this area where the population is less than 1 and 1/2 million, 36.6% of the new cases are reported in Brazil. These values also indicate a clear link between the malaria hyper endemic areas and the indigenous population living in the rain forest. The increase in morbidity and mortality is associated with dramatic changes in the rain forest ecosystems, related to illegal gold mining and the rapid spread of chloroquine resistant P. falciparum strains.

Although Malaria is the most important vector borne disease at a global level, dengue is of special interest for the Caribbean. The incidence of dengue has been constantly increasing over the last decade (Figure 2).

**Figure 2. Reported cases of Dengue in the CAREC Member Countries. 1980-1999.**

This has been caused by the increased frequency of epidemic activity in some of the Caribbean countries:



Barbados, Belize, Suriname, Trinidad and Jamaica. For example, the annual incidence rate was as high as 800-cases/100,000 population in Barbados during the 1995 epidemic. In other countries the epidemiological pattern has been cluster outbreaks with the incidence rates from 1.4- 73-cases/100,000.

The French overseeing Departments of Martinique, Guadeloupe and French Guyana, (non CAREC Member Countries), report similar epidemiological patterns to those of the neighboring Caribbean countries. In contrast, annual incidence rates of 1,880 suspected cases/100,000 inhabitants have been recorded in French Guyana during 1998.

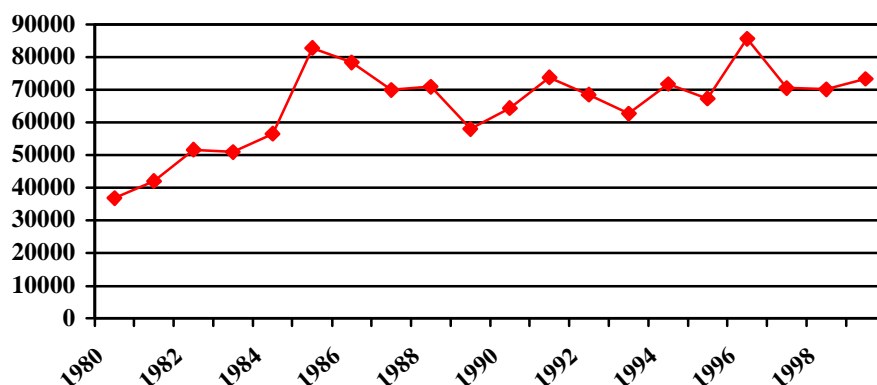
A review of the virus isolation profile during the last 20 years indicated that all four-dengue serotypes were circulating in the sub-region as follows:.

- Den-1 produced cluster outbreaks in Barbados and Trinidad during 1990-1991, but severe epidemics occurred during 1995-1996; this serotype circulated in Suriname during 1981 and 1992 and 1998.
- Den-2 circulated in Barbados and Trinidad during 1987 to 1990 producing cluster outbreaks, but it produced important epidemics during 1998. Since then Den-1 and Den-2 became endemic in both countries. Den-2 dengue produced outbreaks in Suriname during 1987 but significant epidemics during 1993 and 1999-2000.
- Den-3 reappeared in the Americas 1994, and caused an extensive epidemic in Jamaica during 1998. Thereafter cluster outbreaks were registered in Barbados, Grenada, Aruba, Belize Martinique and French Guyana.
- Den-4 has been present in the Caribbean since 1980 however the only important epidemic was in the Bahamas during 1998 with an incidence rate of 116.7/100.000.

Dengue hemorrhagic fever (DHF) is becoming an increasing problem in several countries like Trinidad and Tobago, Suriname, Jamaica and Barbados. One hundred and forty-nine (149) and 69 suspected or confirmed cases of DHF have been recorded in Trinidad and Tobago during 1998 and 1999 respectively.

Another relevant public health problem in the Caribbean is influenza and other respiratory illnesses. Increase influenza morbidity is recorded regularly every year (Figure #3). Because of intense traveling it is unlikely that any country can escape from the introduction of different influenza variants. It is also true that this activity also contributes to the rapid dissemination of new variants to the rest of the world.

**Figure 3. Reported cases of Influenza in CAREC Member Countries, 1980-1999.**



Although the seasonal occurrence of influenza in the tropics is not well defined, the pattern in the Caribbean is linked to the influx of tourist from areas such as Europe, USA and South America where influenza epidemics are actively occurring and which also impacts on the local population. Sixteen thousand (16,864) cases of influenza were notified during the fourth quarter of 1999 as compared to (11,055) for the corresponding period in 1998.

Among the diseases subjected to international health regulation, yellow fever and cholera are of concern for this region. No cases of yellow fever have been notified from any CMCs and the last activity occurred in Trinidad during 1988/89 but no human cases were reported.

Historically, CAREC and its predecessor the Trinidad Regional Virus Laboratory (TRVL) conducted extensive research on the arbovirus ecology and their association with human and animal diseases. Hundreds of viruses were made and new human pathogens such as Marayo, Oropuche were discovered; St. Louis Encephalitis, and Ilheus were also detected during these investigations. Because of the changing ecology due to urbanization, industrialization and agricultural practices, the effect of these viruses on the population is not fully known.

Today the Laboratory Division at CAREC is committed to providing technical support to its CMCs to predict, detect, investigate and monitor the epidemiological behavior of viral diseases. However, our human resources are limited and need to be strategically assigned to cover the priorities such as outbreak investigations and disaster responses.

The major challenges for the CMCs is the increasing morbidity of vector and food borne diseases, influenza and other infectious as well as chronic diseases and conditions. Therefore, a short term research framework has to be implemented and establishing infrastructures locally and in the member-countries for early warning and rapid response to public health problems are a necessity.

### **Viral Surveillance in the Amazon**

During the past 50 years, dengue and dengue hemorrhagic fever have emerged as a major public health problem throughout the tropics. It is estimated that from 50 to 100 million people are infected with dengue viruses each year, and it is generally acknowledged that dengue fever is now the most common and important arthropod-borne viral disease worldwide. The factors responsible for the global resurgence of dengue and its increased pathogenesis have been discussed in detail by others. The subject of this presentation will be the inaccuracy of current dengue surveillance and reporting and the need for a laboratory-based surveillance system.

With the re-infestation of much of Central and South America with *Aedes aegypti* and the reintroduction of multiple dengue virus serotypes into most countries of the region, dengue has become the great "umbrella disease" in tropical America. Because of its extensive distribution and presumed frequency in the region, a wide

variety of acute febrile illnesses with and without hemorrhagic manifestations are now being clinically diagnosed as dengue fever or dengue hemorrhagic fever, in the absence of laboratory confirmation. In most countries of the region, dengue surveillance is passive in nature and depends upon case reporting. But dengue is a protean disease; it is not easily diagnosed clinically. Infection with dengue virus can result in a variety of outcomes including asymptomatic infection, a mild undifferentiated febrile illness, classical dengue fever, dengue fever with hemorrhagic manifestations, and frank hemorrhagic fever with or without shock. Thus it can mimic a number of other viral, bacterial and protozoal infections that also are endemic in tropical America. This is the danger of the current clinically-based dengue surveillance and reporting system. Many other important infectious diseases go unrecognized or are mistreated because they are mistaken for dengue.

Support this hypothesis three types of evidence. First, there are some examples of recent well-publicized outbreaks of other diseases that were reported initially as dengue or dengue hemorrhagic fever based on clinical diagnoses. In 1989, physicians in Portuguesa State in central Venezuela began to report an increased number of cases of dengue hemorrhagic fever, with a mortality rate of about 50%. Subsequent investigation of the outbreak demonstrated that it was a new disease, designated "Venezuelan hemorrhagic fever", that was caused by a novel arenavirus. Even after Venezuelan hemorrhagic fever and its mode of transmission had been identified and local health authorities had widely publicized this information in the affected communities, physicians in the endemic region still had difficulty differentiating the disease from dengue.

In 1995, following heavy rains and flooding, an outbreak of acute febrile illness with pulmonary hemorrhage occurred in Nicaragua. The outbreak was initially reported as dengue hemorrhagic fever, and it was not until a pathologist at the CDC demonstrated leptospirae in tissue samples of some of the fatal cases that the true etiology of the outbreak was identified. Retrospective studies indicated that approximately 2,259 clinical cases of leptospirosis had occurred during this epidemic, with 15 deaths.

In 1995, a major epidemic of Venezuelan Equine Encephalitis (VEE) occurred in northern Venezuela and adjacent areas of Colombia, affecting an estimated 100,000 people. Many of these cases were initially reported by physicians and local health authorities as dengue fever. This erroneous information was disseminated by the local press and by ProMED. Subsequent laboratory studies confirmed that the outbreak was due to VEE virus. In 1997, dengue reemerged in Cuba after an absence of 15 years. Cuban health authorities carried out active, laboratory-based surveillance during the epidemic in Santiago. Based on their clinical presentation, a total of 17,114 febrile patients were initially considered compatible with dengue. However, retrospective serologic testing (IgM ELISA) of 10,024 of these patients confirmed dengue in only about 29%. Some of the dengue-seronegative cases were subsequently shown to be due to influenza, adenovirus infections and leptospirosis.

In each of the aforementioned examples, outbreaks of febrile illness were initially diagnosed by physicians as dengue fever or dengue hemorrhagic fever, and the true etiology was identified only after laboratory-based epidemiologic investigation. Although somewhat anecdotal, these 4 examples illustrate the inaccuracy of dengue surveillance systems based on clinically diagnosed case reports or outbreaks of suspected febrile illnesses.

An evaluation of a clinically based dengue surveillance system was carried out by CDC and PAHO personnel during a dengue I virus outbreak in Rio de Janeiro, Brazil in 1986. In that study, the sensitivity of dengue surveillance, using a clinical case definition of the disease, was compared with laboratory-confirmation. The case definition system had a sensitivity of only 64% and a false-positive rate of 57%. In other words, for every 100 laboratory-confirmed dengue infections, 230 clinically diagnosed cases of the disease were made.

The second evidence, surge from the official reports of dengue from countries of the Americas; total number of reported cases of dengue and dengue hemorrhagic fever from six selected countries for the years 1995 and 1996. These figures were taken from the WHO Weekly Epidemiologic Record and the data presumably were provided by Ministries of Health of each respective country. There are several evidences suggesting the unreliability of the data. For example, it was indicated that there were only 107 cases of dengue in Colombia in 1995 and that 100% of them were dengue hemorrhagic fever. In contrast, the following year there were 7,787 cases reported, and 22.6% of these were dengue hemorrhagic fever. Similarly high rates of dengue hemorrhagic fever were reported from Venezuela in 1995 and 1996, and from the Dominican Republic in 1996. In contrast, Brazil, Mexico and Nicaragua all reported much lower rates of dengue hemorrhagic fever. These latter figures

are more credible and are similar to the frequency of DHF observed in dengue-endemic countries of Southeast Asia. However, the total number of dengue cases reported for Brazil, Mexico and the Dominican Republic are rather low considering the size of their respective human populations. On the other hand, Haiti did not report any cases of dengue during this two-year period. Yet it is well known from other studies that dengue is highly endemic in Haiti. So official reports of the incidence of dengue from most countries of the Americas are also extremely inaccurate including the United States.

A third illustration of the inaccuracy of the clinical diagnosis of dengue and the importance of laboratory confirmation, is based on some data from an ongoing prospective study of acute, non-specific febrile illness in Iquitos, Peru. This study is a collaborative effort between the U.S. Naval Medical Research Center Detachment in Lima, the Peruvian Ministry of Health in Iquitos, the Instituto Nacional de Salud in Lima, and the University of Texas Medical Branch in Galveston. The study was started in October 1994 following a dengue outbreak in Iquitos; its primary objective has been to determine the frequency of dengue and other arboviral diseases among persons with acute, undifferentiated febrile illnesses in Iquitos.

Iquitos is a city of about 300,000 people; it is located about 120 meters above sea level in the northeastern region of Peru, on the banks of the Amazon River. The climate is tropical with an average temperature of 27.5°C and a mean annual precipitation of 2.7 meters. Iquitos is relatively isolated; there are no roads into the city from Lima or other major Peruvian cities. Access to the city is by air or via the River. The majority of the native population is of Spanish and Indian ancestry. However, Iquitos is also a tourist center, and many European and North American visitors come to the city annually. There are also many smaller communities, located along the banks of the Amazon River and its tributaries, within a few hours by boat from Iquitos. People living in these villages are mainly involved in subsistence agriculture and fishing, but many come to Iquitos for their medical care.

The study population includes civilians and Peruvian military personnel living in and around Iquitos and attending local hospital or outpatient clinics with acute, undifferentiated febrile illnesses. Criteria for enrollment in the study are fever (oral or axillary temperature of  $> 38.0^{\circ}\text{C}$ ) of not more than 5 days duration, accompanied by headache, myalgia and other non-specific signs and symptoms of an acute dengue-like illness. After completion of a standardized questionnaire with demographic and clinical data, an acute-phase blood sample is obtained from each subject for virus isolation attempts and for serological studies, and a blood smear is made to examine for malaria parasites. When possible, a convalescent-phase serum sample is obtained from each patient 2-4 weeks later.

Primary virus isolation is attempted on acute phase sera of all patients. Sera are inoculated into cultures of African green monkey kidney (Vero) and mosquito (C6/36) cells, and occasionally into newborn mice for virus isolation. Paired acute and convalescent sera are also tested by IgM and IgG antibody-capture ELISA against a variety of arboviral antigens. The initial laboratory work is done at the Naval Medical Research Center Detachment in Lima. Confirmation of most of the virus isolates was done at the University of Texas Medical Branch. Thick and thin blood smears were also done on most of the patients by malaria control personnel of the Peruvian Ministry of Health; those were examined on-site in Iquitos.

Between October 1994 and April 2000, a total of 7,195 febrile cases, meeting our clinical criteria of an acute dengue-like illness, were enrolled in the study. From these patients, 11 different arbovirus types were isolated. Dengue, VEE, Mayaro and Oropouche were the most commonly isolated viruses and will be discussed separately. The other six viruses were less commonly encountered, although it is interesting that yellow fever virus was isolated from one patient who appeared at a clinic with an acute febrile illness and without jaundice or other symptoms suggestive of yellow fever.

Of the 7,195 febrile cases examined, 569 or 7.9% were confirmed as dengue virus infection. The actual number of dengue cases may have been slightly higher, since convalescent serum samples were obtained from only about 60% of the subjects, consequently some seroconversions could have been missed. But even allowing for this underestimate, it seems unlikely that more than 10% of the febrile illnesses in this patient population were due to dengue virus infection. Two different dengue virus serotypes (types 1 and 2) were isolated from febrile patients at various times during the study. Virologic and/or serologic confirmation was also made of VEE in 133 or 1.8% of the subjects; Oropouche virus infection in 55 or 0.8% of the patients; and Mayaro virus infection

in 22 people, or 0.3% of the total.

Malaria was the most common infection associated with acute, non-specific febrile illness in the Iquitos population. Malaria smears were done on only 4,528 of the febrile cases, but 23.1% of the smears were positive. Both *P. vivax* and *P. falciparum* were detected; the ratio of the two parasites among the study population was about 70:30, respectively. In the case of malaria, it is uncertain how many infections were acute and the cause of the febrile illness and how many were chronic asymptomatic infections. Malaria is hyperendemic in rural communities around Iquitos; in a survey done in 1997, up to 30% of people with positive smears in some villages were found to have asymptomatic malaria infections. In our study, 105 subjects were found co-infected with malaria and an arbovirus. Twenty-four patients with dengue infections had positive malaria smears.

The monthly distribution of febrile cases that were sampled between October 1994 and April 2000 increases. This increase during the last 3.5 years is partly a reflection of increased sampling during that period. However, the jump in febrile cases during 1997 also reflects a marked increase in malaria cases that occurred during that year. 1997 was an El Niño year and the Amazon was quite dry. In that year, there was a marked increase in malaria transmission and an estimated 40,000 new cases of malaria were diagnosed in and around Iquitos. There was also a large outbreak of influenza in this part of South America in 1977 and that epidemic probably accounted for additional febrile cases.

The monthly distribution of confirmed dengue cases among the study population is as follows. In August of 1995 a total of 52 dengue cases were diagnosed; this number represented about 30% of all febrile cases seen that month. Although the data suggest that dengue is endemic in Iquitos; there were two clear epidemic periods. The outbreak in 1995 was due to dengue 2 virus and the epidemic peak in 1998 and early 1999 was due largely to dengue I virus. As noted before, 569 cases of dengue were diagnosed during this period; that represented about 8% of all febrile cases.

The distribution of Venezuelan equine encephalitis cases during the 5.5 period shows that VEE also is endemic in the area around Iquitos, and 131 cases were diagnosed. All of the virus isolates that we have sequenced were of the VEE ID variety, which is an endemic form. Cases occurred in almost every month; the preponderance of cases after January 1997 probably reflects increased sampling during that period, rather a change in VEE virus activity. Overall, VEE represented less than 2% of the total febrile cases seen; however, in a few months, it accounted for as many as 6 to 8% of all febrile cases seen

A total of 26 cases of Mayaro fever were diagnosed. As with VEE and dengue, Mayaro virus also appears to be endemic in forested areas around Iquitos. Clinically, this disease cannot be differentiated from dengue.

A total of 55 cases of Oropouche were diagnosed during the 5.5 year period. The data suggest that this disease is also endemic in the Iquitos area. On the other hand other viruses were isolated too infrequently to allow meaningful analyses.

Now, the important question is "can these other viral infections be differentiated from dengue?" The signs and symptoms of dengue, Mayaro, Oropouche and VEE are very similar. It would be very difficult for a clinician to differentiate these diseases. In the case of Oropouche fever and VEE, patients usually do not have a rash. However, among the patients with confirmed dengue and Mayaro fever infections, only 31% and 21%, respectively had a rash. Many of these patients were seen during the first few days of their illness before the characteristic rash appeared. If the patient is seen once by a physician, the rash may not be observed. Also not all patients with dengue or Mayaro virus infection developed a visible rash.

More males than females were infected with dengue, VEE, Mayaro and Oropouche virus infections such that the ratio was about 2:1 in favor of males. The age distribution for dengue, VEE and Mayaro were not very different; most of the cases occurred among persons in the 10-39 year age range. The Oropouche fever cases had a slightly more even age distribution.

In summary, the results from the Iquitos fever study indicate that a number of different viral illnesses are endemic in this region of the Peruvian Amazon. While dengue is the most common virus infection, it accounted for less than 10% of all acute febrile illnesses. More important, it cannot be differentiated clinically from many

other viral diseases or other causes of non-specific febrile illness that are endemic in the region. This is the danger of the current dengue reporting system, which is largely based on clinical diagnoses. If another clinically similar disease like yellow fever, VEE or the next arenaviral hemorrhagic fever is introduced into a community in tropical America, the initial cases will probably be diagnosed as dengue or dengue hemorrhagic fever. The dangers of such an erroneous diagnosis and of the resulting delay in the appropriate public health response are obvious. Thus the improvement of existing laboratory facilities and establishment of a laboratory-based dengue surveillance system seems imperative.

## **VIII. GLOBAL AND SUBREGIONAL SURVEILLANCE**

### **WHO Global Alert and Response**

#### **Components of outbreak response**

There are generally two outbreak scenarios. The first is where the etiology and epidemiology is known and the steps that must be taken to control the outbreak are straightforward, e.g., cholera. The second situation is where either the cause of the outbreak or the epidemiology, or both, is not known. This requires the development of hypotheses and research. Recommendations are the product of this type investigation and must be conveyed to, and accepted by, local health authorities and then implemented. An example is the recent Nipah virus outbreak in Malaysia. There can also be situations where control measures can be implemented quickly, yet the outbreak provides the opportunity to answer important research questions. The ongoing Marburg epidemic in the Democratic Republic of Congo is an example as it is the rare occasion to search for the natural reservoir of this filovirus.

Most outbreaks are managed at the state or national level, but some outbreaks exceed the capacity of the country and require international assistance. There are many common elements of an international response irrespective of the etiology and include the following:

1. **Building the team:** The team must be comprised of an adequate number of persons with the appropriate skills and credentials, such as epidemiologists, clinicians, laboratorians, disease specialists, and scientists in other disciplines, e.g., entomology. In addition to technical experts, support staff including logisticians, other administrative staff and a press officer may be needed to facilitate operations. It is desirable that all persons have field experience and language skills appropriate for the environment in which they will be working.
2. **Obtaining access to the affected area:** Local authorities must cooperate and grant permission to gain access to the site of the outbreak, and to local institutions and personnel who can provide expertise or important information about the disease event. Prospective team members must have valid passports and subsequently obtain visas to be able to travel as quickly as possible. International travel arrangements are easily made, but if the outbreak area is at a remote site or a place inaccessible due to natural disasters, special assistance is needed from someone who has knowledge of what transport is available locally and can make the appropriate arrangements.
3. **Provision of equipment and supplies:** Depending on the location, the team must have the appropriate communication equipment such as satellite or cellular phones. Portable computers with appropriate software are required for data analysis. Specimen collection devices, and the necessary equipment and supplies for processing and transporting samples must accompany the team. If laboratory testing is to be established on-site, appropriate reagents, equipment and disposable supplies must be available. When appropriate, medical supplies for treating patients must also be available. The team should have basic personal protective equipment, e.g., gloves and eye protection. Management of viral hemorrhagic fevers requires additional protective clothing. And finally, the team must take their personal items. These may be limited if the site is at a remote location that must be accessed by private air charter or on foot.
4. **Support for the team while on-site:** Once on-site, the team will require operation and communication centers and an appropriate location to process specimens or to perform laboratory tests. Staff resources must be dedicated to arranging transportation for personnel and transporting samples, and obtaining or replenishing supplies. If the team is at a remote site, arrangements for food and accommodations must be made.

5. Recommendation and implementation of control measures: Implementation of control measures must be accepted by local health authorities, and the team, in conjunction with local authorities, must establish criteria for monitoring and evaluating the effectiveness of the intervention. Lessons learned from the current event should be institutionalized in a program of preparedness.

### **Criteria for effective response**

The following criteria can be used for measuring the effectiveness of the response to a communicable disease event. 1) The response must be timely. The faster that control measures can be put in place, the greater probability that the disease burden will be reduced. Obviously, responses that require an investigation have inherent delays. 2) The control measures must prevent infections via reduction in transmission or must reduce morbidity and mortality by improved case management of those already infected. 3) The intervention must provide the opportunity for training local authorities in controlling the specific disease and sensitize them regarding the need to maintain preparedness to control the disease should it occur again.

### **Response mechanisms**

The effectiveness of the response is determined by resources that can be mobilized to control an outbreak and coordination for best utilizing these resources; to repeat, the key factors are resources and coordination.

There are three response models that are used most frequently in outbreak response.

1. The first response mechanism is bilateral where the affected country invites an institution in another country to respond. The number of persons with the needed skills and the amount of financial resources available to support the response are dependent on the capabilities of the institution. Coordination is usually good since only one institution is involved and efforts focus primarily on coordination with host country institutions.
2. The second model is where the country invites multiple institutions. This increases the potential for bringing more resources to manage the outbreak. However, for an effective response, strong coordination is required by either the national authorities or by the institutions themselves while they are on-site. With the multi-lateral approach there is also the potential for duplications and gaps in personnel.
3. The third mechanism also involves multiple institutions thereby garnering the maximum resources, but has the coordination component, for example, WHO, as a pre-defined part of the structure. This model has the potential to deliver global resources to the local outbreak in the best-coordinated manner and has the advantage of being able to make advance arrangements for many response components before the outbreak. Also, assessment missions can be conducted to properly gauge the required response. This is difficult to do with the multi-lateral model and too many or too few resources may be committed to the effort.

### **WHO's role in global outbreak response**

WHO promptly respond to outbreaks of international importance when invited by the member states. WHO provides immediate expertise from WHO staff, and facilitates international response by assembling teams and obtaining laboratory support from its international network of collaborating centers and other partner institutions, and provides funds to catalyze the process and fill gaps. Access to the countries is facilitated by the United Nations diplomatic passport, which often has modified visa requirements that make access easier. Local support from the WHO country office to assist with travel arrangements is also an asset. Because of its international mandate and access to information about the outbreak, WHO is well positioned to coordinate the response and often does so. This provides an element of neutrality. WHO provides technical guidelines for management of specific diseases. Outbreaks of infrequent or new disease events provide the only opportunities for research on these diseases. WHO recognizes this and facilitates appropriate research. WHO also provides guidelines and training to the country for epidemic preparedness. Finally, WHO is viewed as a credible source of accurate and timely information and provides this information to the press and general public.

On April 26-28, 2000 WHO held a meeting in Geneva on the subject of "Global Outbreak Alert and Response." Including WHO staff from Headquarters, Regional and country offices, the meeting was attended by 124

representatives from 69 key partners and institutions in epidemic surveillance and response. The purpose of the meeting was to discuss the challenge of epidemic-prone and emerging diseases, and create a global network based in existing partnerships to deal with these threats.

Participants approved a framework and tentative timetable for establishing the network. A more detailed description of the network was made at the ICEID meeting in Atlanta 18 July 2000.

### **Responses to Influenza Outbreaks**

WHO Influenza Program: The WHO Influenza Program and Network for global surveillance was described earlier by Dr. Cox. The network is comprised of 100 national laboratories in 83 countries. Four WHO Collaborating Centers (Australia, Japan, UK, and USA) are reference centers for the Network and coordinate many of the aspects of its operation. The primary functions of this network are rapid isolation and characterization of viruses throughout the world, the investigation with rapid collection/dissemination of epidemiological data about new viruses and to make semi-annual recommendations for vaccine composition. The network has accomplished this by developing and standardizing surveillance and diagnostic techniques and rapidly transferring information and viral isolates. The network assists in preparing plans for influenza pandemics by devising control methods to limit the spread, severity and consequences of a pandemic when it occurs.

A recent example that illustrates the network's global surveillance and response capability is the influenza A (H5N1) outbreak in 1997. The first case occurred in May 1997, the isolate was sent to a WHO Collaborating Centre in August where influenza A (H5N1) was confirmed. A multinational investigation, coordinated by WHO, intensified surveillance among humans and animals. Serological investigations around contacts of cases showed no clear evidence of human-to-human transmission. Chicken and other fowl were the source of the virus and 1.5 million chickens were slaughtered at the end of December. A total of 18 human cases were confirmed up to the end of 1997 and no additional cases occurred afterwards. Kits of diagnostic reagents for identifying the H5 strain were promptly developed and distributed and research was initiated to develop influenza A (H5) strains as potential vaccine candidates, should they be needed.

The international collaboration with Hong Kong health officials had many public health benefits. Case detection was strengthened in hospitals and clinics, laboratories procedures for virus isolation and identification were improved, and surveillance of influenza viruses in poultry was initiated. Health education programs and guidelines were formulated and implemented for managing this and similar events.

### **Influenza Pandemic Preparedness Plan**

It is impossible to predict when a pandemic might occur, but it is evident from past events that the morbidity and mortality would be great. Air travel would hasten the spread of a new virus, and decrease the time available for preparing interventions. Health care systems could be rapidly overburdened, economies strained, and social order disrupted. Although it is not considered feasible to halt the spread of a pandemic virus, it should be possible to minimize the consequences by having prepared for the challenge in advance. Pandemic planning must accomplish two objectives. It should make provisions for the rapid and effective assessment of risk from new viruses that appear and it should insure effective management of the risk to the general population when the new viruses have properties enabling them to spread widely and cause serious disease.

With this background, WHO and its partners have prepared the Influenza Pandemic Preparedness Plan (WHO, April 1999; <http://www.who.int/emc/diseases/flu/index.html>) to assist medical and public health leaders to better respond to future threats of pandemic influenza. It outlines the separate but complementary roles and responsibilities for the World Health Organization (WHO) and for national authorities when an influenza pandemic appears possible or actually occurs. Specific descriptions are given of the actions to be taken by WHO as it assesses the risk posed by reported new sub-types of influenza, in advance of any epidemic spread. The responsibility for management of the risk from pandemic influenza, should it actually occur, rests primarily with national authorities. WHO strongly recommends that all countries establish multidisciplinary National Pandemic Planning Committees, responsible for developing strategies appropriate for their countries in advance of the next pandemic.

In recognition of the individuality of countries, as well as the unpredictability of influenza, this document emphasizes the processes and issues appropriate for WHO and National Pandemic Planning Committees, but does not provide a "model plan". Furthermore, it is anticipated that the national committees will confront new issues, which will call for additional international dialogue. For example, more consideration is needed about how scarce supplies of vaccines can be shared, and what might be the benefit of canceling public gatherings to slow the spread of a pandemic virus among unvaccinated populations.

### **Responses to Outbreak of Viral Hemorrhagic Fevers**

Acute hemorrhagic fever syndromes can be attributable to dengue (dengue haemorrhagic fever), yellow fever, arenavirus infections (Machupo, Junin, Guanarito, Lassa), hantavirus infections (Hantaan, Dobrava, Seoul), Rift Valley fever (RVF), Crimean-Congo haemorrhagic fever (CCHF), filovirus diseases (Ebola, Marburg) and other viral, bacterial or rickettsial diseases with a potential to produce epidemics. All of these viral infections produce a spectrum of disease that include no symptoms, an uncomplicated febrile illness, fever and jaundice (yellow fever), fever and retinitis (RVF), encephalitis (RVF), and fatal multi-system disease with or without hemorrhage (CCHF, Ebola, yellow fever). Modes of transmission of hemorrhagic fever viruses include person-to-person (Ebola, Marburg, Lassa and CCHF), arthropod vectors such as mosquitoes (yellow fever, dengue, RVF) and ticks (CCHF), rodents (arenaviruses and hantaviruses) and contact with infected livestock animals (RVF, CCHF). With respect to Ebola, Marburg, Lassa and CCHF, there is a high potential of amplification of the number of cases when patients are treated in health facilities with low standards of hygiene. Mosquito-borne viruses have the potential to produce explosive epidemics. However, the proportion of hemorrhagic fever cases is low.

Surveillance of acute hemorrhagic fever syndrome is aimed at early detection of cases in order to avoid epidemics and the possible national and international spread of the disease. All cases of acute hemorrhagic fever syndrome, whether single or in clusters, should be notified immediately from peripheral to intermediate and central level without waiting for the causal agent to be identified. Laboratory testing is required to determine the etiology of hemorrhagic fevers because the viruses described above produce a similar syndrome of fever and bleeding. Blood samples and other appropriate clinical specimens must be collected and tested as rapidly as possible. Epidemiological information usually provides some indication of the most likely pathogen, but in some areas, particularly Africa, multiple viruses are present in the same geographic areas and laboratory testing is essential.

Control measures of viral hemorrhagic fever outbreaks are determined by modes of transmission or availability of effective vaccines. For example, those spread person-to-person and nosocomially are controlled by implementing barrier nursing for patient management and improving infection control practices. These procedures are particularly applicable to Ebola, Lassa, CCHF and Marburg, but should be implemented for the management of all hemorrhagic fever cases while the etiology is being investigated. Prevention of yellow fever is through immunization. Control of RVF is dependent on effective preventative programs for livestock vaccination, and public health education about risks associated with slaughtering animals during RVF epizootics. Vector control, where it can be applied effectively, reduces transmission of dengue, RVF, yellow fever and CCHF. Limiting exposure to rodents and their excreta are the key elements in preventing of hantavirus and the majority of arenavirus infections. WHO publishes a series of technical guidelines for surveillance and control of specific viral hemorrhagic fevers.

### **Network of WHO collaborating centers**

There are presently over 30 WHO collaborating centers that specialize in arboviruses and/or viral hemorrhagic fevers. These centers are distributed throughout the world, particularly in countries where viral hemorrhagic fevers frequently are found, e.g. six centers in Africa. These centers play an important role in laboratory diagnosis and provide specialized technical expertise in the investigation of disease outbreaks. Because many of the hemorrhagic fever viruses produce highly lethal infections for which there are no treatments or vaccines, diagnostic testing is restricted to specialized high-containment laboratories. Virus propagation in cells and laboratory animals and the production of inactivated virus antigens used in serological tests can only be done in these facilities, thus supplies of these reagents often have a restricted distribution.

A recent example of international collaboration involving an outbreak of viral hemorrhagic fever is Marburg hemorrhagic fever in the Democratic Republic of Congo. Cases first began in November 1998 and continue to occur today. Two missions were conducted in May and October 1999. CDC-Atlanta, NIV-South Africa, MSF Belgium and Holland, Institute Pasteur, and ITM-Antwerp participated in these WHO-coordinated missions. Protective equipment and training in barrier nursing methods were provided to the local medical staff. This is only the fourth time since the initial discovery of the virus in Europe in 1967 that naturally acquired Marburg infections have been recognized. It is the largest outbreak ever reported in Africa and has provided the rare opportunity to conduct research. Epidemiologic, ecologic and virologic studies have already produced new and important information about the natural history of this disease.

DengueNet: Dengue (DF) and dengue hemorrhagic fever (DHF) have become major international public health concerns in recent years. Dengue infections are prevalent in over 100 countries and territories and threaten the health of more than 2.5 billion people, living in urban, peri-urban and rural areas of tropical and subtropical regions. WHO currently estimates there may be 50 million cases of dengue infection worldwide every year. The spread of dengue is attributed to expanding geographic distribution of the four dengue viruses and of their mosquito vectors, the most important of which is *Aedes aegypti*. A rapid rise in population in many urban centers, lack of adequate resources for water storage and solid waste disposal (creates mosquito breeding sites) and inadequate vector control programs are bringing ever-greater numbers of people into contact with the vector mosquito.

Reporting of DF and DHF is presently not standardized throughout the world. Also, while laboratories in many countries provide information about circulating virus serotypes, a potential indicator of future DHF epidemics, epidemiological and laboratory data are often collected by different institutions and are therefore difficult to collate. Furthermore, collection and analysis of data at regional and global levels is protracted. To address these limitations, DengueNet is being created as a central data management system to collect and analyze standardized information in a timely manner, and present epidemiological trends as soon as new data are entered. DengueNet is being developed by the Institute for Medical Research and Health (INSERM Unit 444), Paris, France and is supported by WHO and the US National Aeronautics and Space Administration. Epidemiological data based on standardized case definitions for DF, DHF and deaths will be input weekly by national health officials into the DengueNet database via the Internet. Participating laboratories will report the currently circulating dengue virus serotypes. Laboratories will be encouraged to use standardized protocols, and reference materials including monoclonal antibodies, PCR primers, and virus strains. Laboratories in non-endemic countries will report confirmed imported cases.

Access to DengueNet will be unrestricted and users will be able to display maps (at the state/provincial level) of incidence data and case fatality rates, graphics of the frequency and distribution of cases and virus serotypes, and data in tabular form and as free text. Data sets can be downloaded for specific purposes (e.g., modeling). When fully operational, the system will provide early alerts of dengue epidemics at the country or regional level, target areas for training in DHF case management, and be a tool to improve the awareness of public health professionals for epidemic preparedness and control.

## **The Global Emerging Infections System (GEIS) Program**

### **Overview**

The G.E.I.S. stands for Global Emerging Infections System. It is a targeted program of the United States Department of Defense (DoD) to identify and combat emerging infectious disease threats throughout the world. The program has as its basis Presidential Decision Directive NSTC-7, of June 1996 that formally expanded the mission of the DoD to support global surveillance, training, research, and response to emerging infectious disease threats. President Clinton directed a centrally coordinated program that improved DoD epidemiological capabilities and involved US military treatment facilities and military medical research units in the United States and abroad.

Even prior to the Presidential Decision Directive and the establishment of GEIS, all branches of the DoD had a history of strong infectious disease surveillance and intervention programs. For this reason, the U.S. military

identified several emerging and resurgent infectious disease outbreaks in the 1990s. Among these were: Wuhan flu on a Navy ship operating in the South Pacific (1996); leishmaniasis among troops after a brief visit to French Guyana (1993); viscerotropic leishmaniasis among troops participating in the Persian Gulf War (1991); dengue fever and drug-resistant *P. vivax* malaria among troops sent to Somalia (1993-1994); and *P. vivax* malaria among troops stationed in Korea (1993). Against this background, U.S. military research and preventive medicine units were highly motivated to participate in the newly established GEIS program.

The principal goals of the DoD GEIS program are: **i.** surveillance; **ii.** systems research, development and integration; **iii.** response; and **iv.** training and capacity building.

The program is centrally managed from the DoD-GEIS Hub in Silver Spring, MD. Surveillance efforts within the U.S. and at DoD medical treatment facilities throughout the world are coordinated by the Navy Hub at the Naval Health Research Center, San Diego, CA and the Army Hub at the U.S. Army Center for Health Promotion and Preventive Medicine, Aberdeen Proving Ground, MD. International public health emerging disease surveillance and response is a significant and integral part of the GEIS program. These international GEIS initiatives are the responsibility of the five overseas Department of Defense (DoD) research laboratories: the : Overseas U.S. DoD Infectious Disease Research Laboratories; Navy Medical Research Unit No. 3, Cairo, Egypt; U.S. Army Medical Research Unit, Nairobi, Kenya; U.S. Army Medical Research Unit, Bangkok, Thailand; Navy Medical Research Unit No. 2, Jakarta, Indonesia; and the Navy Medical Research Center Detachment, Lima, Peru.

The primary GEIS activities of the Overseas Laboratories are: antibiotic-resistant enteric bacteria; drug-resistant malaria; influenza; and acute febrile illnesses, including Dengue. All these subjects are focus of activities of the GEIS Program at the Naval Medical Research Center Detachment (NMRCDC), Lima Peru:

This Center (NMRCDC) in Lima collaborates with host government, academic, and non-government organizations (NGOs) in the conduct of its GEIS activities. The majority of effort is focused in Peru and the adjacent countries of Bolivia and Ecuador. The following is a summary of its activities.

**Drug-resistant malaria.** In 1999 NMRCDC personnel in collaboration with Peruvian Ministry of Health counterparts conducted two therapeutic efficacy trials of sulfadoxine- pyrimethamine for *P. falciparum* malaria in the villages of Padre Cocha and Caballo Cocha in the Amazon basin. The greater than 50% RII/RIII resistance to sulfadoxine-pyrimethamine identified in these studies helped influence a change in malaria drug policy by the Peruvian MOH. Five additional efficacy trials are ongoing. The following are preliminary results from those trials:

*Chloroquine treatment of P. vivax*; Caballo Cocha – 27 enrolled, no resistance; Iquitos – 75 enrolled, 2 questionably resistant.

*CQ/SP treatment of P. falciparum*: Yurimaguas – 24 enrolled, failures in 8 of 14 CQ patients and 0 of 10 SP patients.

*Mefloquine treatment of P. falciparum*: Caballo Cocha – 13 enrolled, no resistance.

*MQ/Artesunate vs. MQ for P. falciparum*: Iquitos – 60 enrolled, no failures on either drug.

*MQ/Artesunate vs. SP for P. falciparum*: Sullana – 24 enrolled, recurrence of parasitemia in 2 SP patients and none on combination therapy.

**Drug-resistant enteric bacteria.** During 1998 and 1999 this was a collaborative effort with individual hospital laboratories in Peru and with the Center for Tropical Medicine and the National Food Institute in Santa Cruz and Sucre, Bolivia respectively. The strategy has been to perform standard disk diffusion antibiotic susceptibility testing on enteric isolates from diarrhea and dysentery patients seen at participating clinics. Starting in 2000 enteric drug resistance testing in Peru will be done in collaboration with a greater MOH diarrhea disease surveillance program. The following graphs summarize drug resistance levels for *Campylobacter*, *Shigella*, and *Salmonella* from 1998 and 1999 and compares them to the National

Figure 4 Campylobacter Drug Resistance, selected sites in Peru.

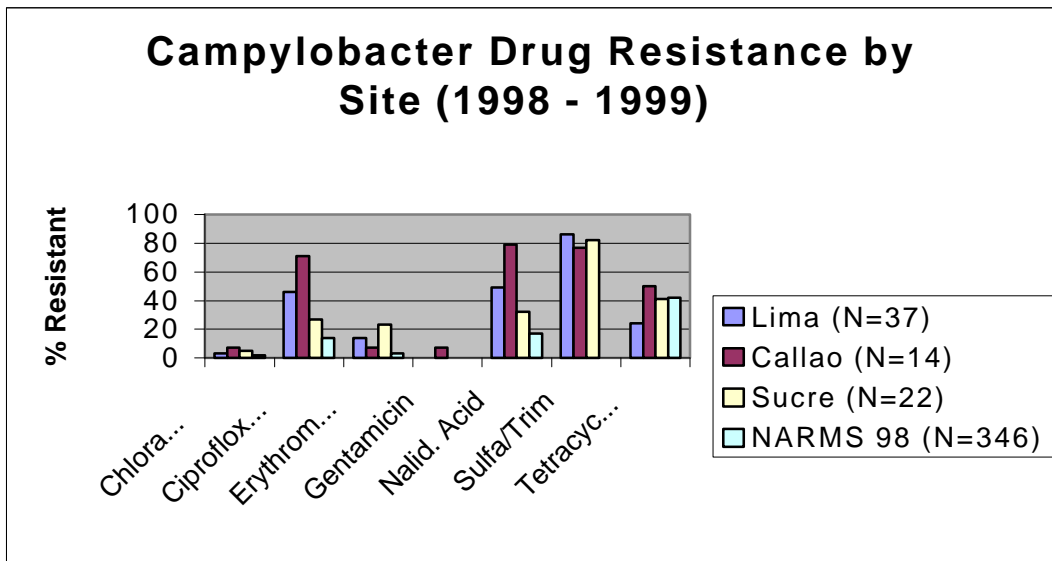


Figure 5 Shigella Drug Resistance, selected sites in Peru.

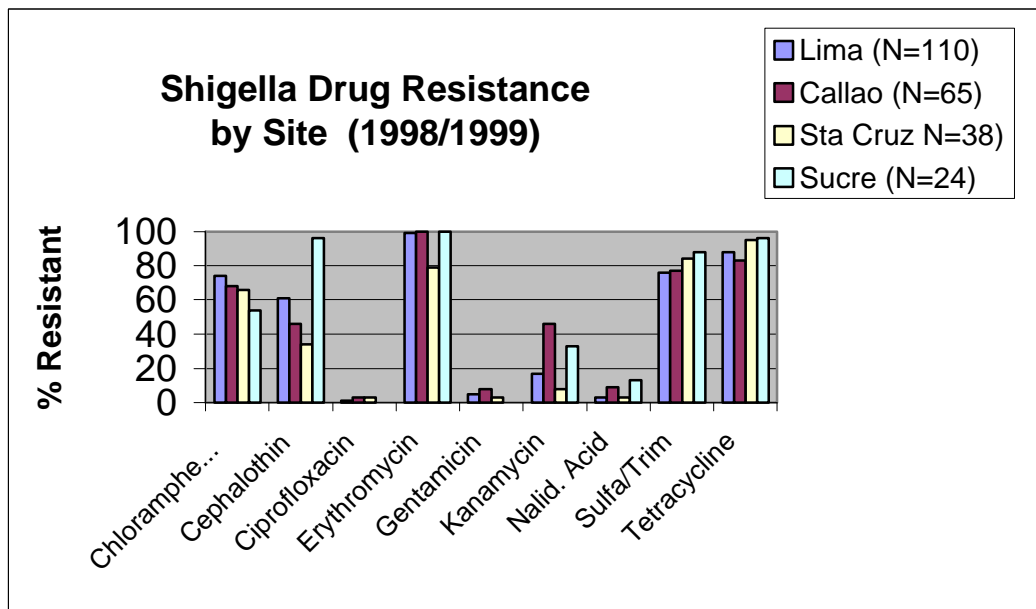
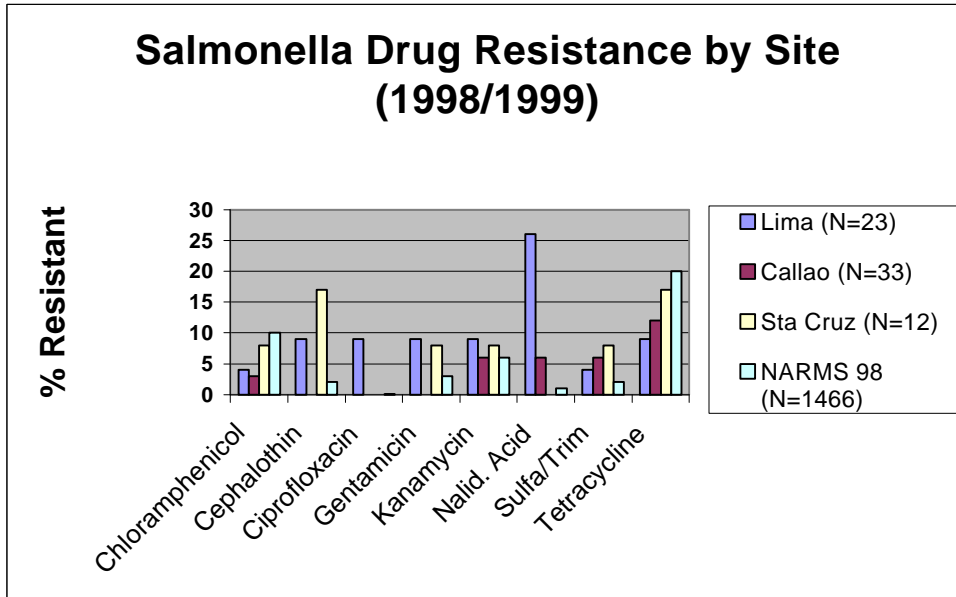


Figure 6 Salmonella Drug Resistance, selected sites in Peru.

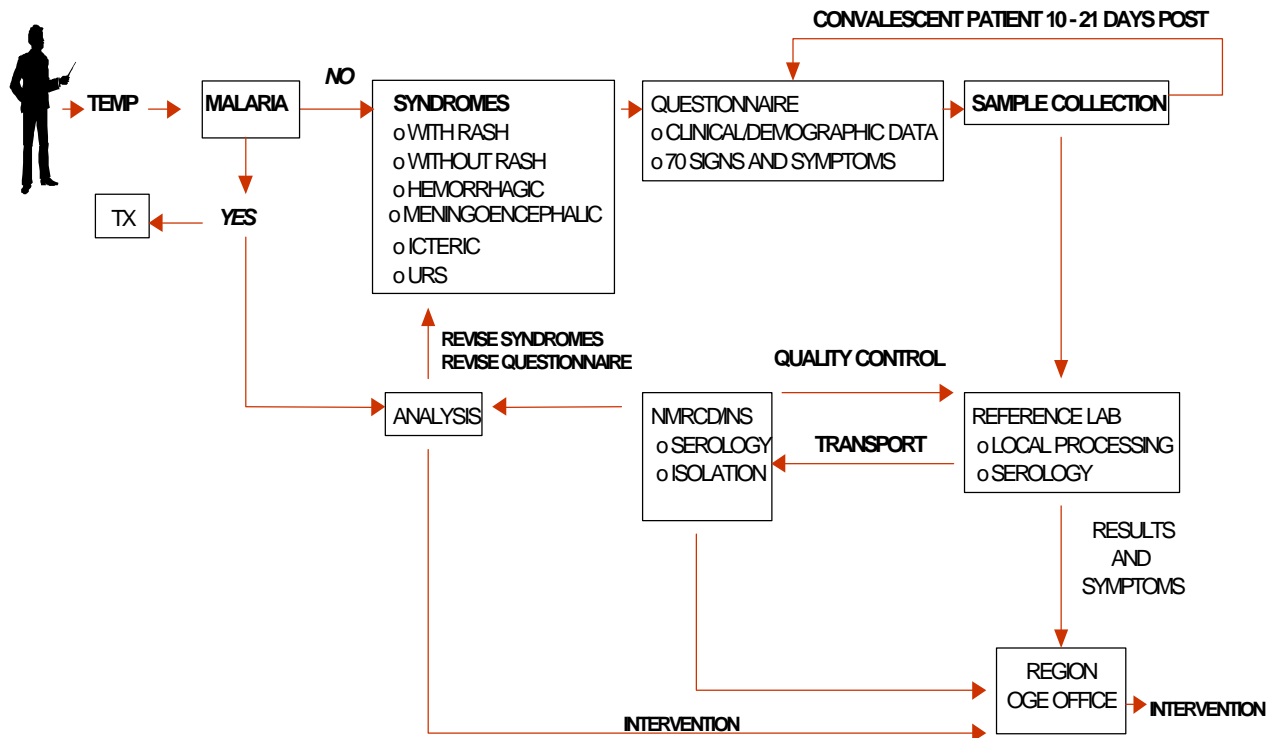


Acute Febrile Illness Surveillance: NMRCB is collaborating with the Peruvian MOH, Cayetano Heredia University, and CENETROP in Santa Cruz, Bolivia in a pilot program of syndromic surveillance for acute viral fevers. This surveillance effort should provide both the required information for public health intervention and will assist the practicing physician in the field with patient management. Feverish patients are initially assigned to syndrome categories as follows:

- Undifferentiated febrile syndrome without rash
- Undifferentiated febrile syndrome with rash
- Hemorrhagic fever syndrome
- Meningoencephalic syndrome
- Febrile icteric syndrome
- Fever with upper respiratory symptoms

These syndromic classifications will be validated or changed based on supporting extensive medical questionnaires and comprehensive laboratory testing both at the regional and reference laboratories as outlined below in Figure 7.

**Figure 7. Febrile Illness Surveillance**



This surveillance effort is just being put into place therefore there is no data to report yet.

Surveillance of Mosquito populations for Arboviruses: This is an NMRCD GEIS Program funded continuation of a successful collaboration with the Peruvian Ministry of Health, the U.S. Army Research Institute for Infectious Diseases, and the University of Texas Medical Branch, Galveston. Over the last three years this effort has identified numerous new arboviruses in a variety of mosquito species. The results of this work are being reported separately at this meeting by Dr. Tesh and Dr. Watts.

**Influenza Surveillance.** NMRCD collaborates with U.S. Embassy Medical Units and host nation institutions primarily in Peru, Ecuador and Argentina to forward respiratory specimens to the U.S. Air Force “Project Gargle” for viral isolation. Last year this effort resulted in two isolations of Influenza A (New Caledonia H1N1) a strain that has subsequently been included in the new vaccine formulation for South America. Results of Surveillance for FY2000 to date are as follows: in Peru from 45 samples collected were isolated 5 Influenza A (2 New Caledonia H1N1), 2 HSV, and 1 Adenovirus; in Ecuador from 47 samples were identified 6 Influenza A (1 Bayern H1N1; 5 H3N2) and 2 Adenovirus.

**Outbreak Investigations FY2000.** The GEIS Program personnel collaborated in the conduct of the following outbreak investigations: Hantavirus – Bermejo, Bolivia; Dengue – Guayaquil, Ecuador; Febrile Illness (Dengue) – Sullana, Peru; Dengue – Bagua, Peru; Febrile Illness – El Torno, Bolivia; and Febrile Illness – Yurimaguas, Peru.

## **Global Surveillance for Influenza and Selection of Vaccine Viruses**

Valuable insights have been gained regarding the structure, replication, epidemiology, pathogenesis, antigenic properties, molecular properties, and ecology of influenza viruses during the past six decades. However, because influenza viruses undergo relatively rapid and unpredictable antigenic variation, they have remained important viral pathogens for humans, in spite of the development and use of effective inactivated influenza vaccines. In 1948, the World Health Organization established an international surveillance network to detect variants of influenza with epidemic or pandemic potential. This network is viewed as an early warning system that functions to detect circulation of antigenic variants coincident with outbreaks of respiratory disease which may signal a need to update the strains, included in influenza vaccines. This WHO influenza surveillance program has often been cited as a model for international collaboration and rapid exchange of information.

This WHO influenza surveillance network has grown over the years to include approximately 110 laboratories in over 80 countries and four WHO Collaborating Centers for Reference and Research on Influenza located in Australia, Japan, the United Kingdom, and the United States. Use of this influenza surveillance network has made it possible to achieve a good match between circulating and vaccine strains in many recent years, a match that is necessary for optimal vaccine effectiveness. By facilitating the early detection of new antigenic variants of influenza and recommending the use of these viruses for inclusion in vaccines, this system provides the foundation for vaccination activities to prevent and control influenza in many countries.

A brief description will be provided of the purposes of influenza surveillance, established surveillance systems, the types of data required for vaccine strain selection, and developments that have contributed to achieving a good match between epidemic strains and the strains included in the vaccine during most recent years. In addition, recent improvements in surveillance and existing gaps will be described. Influenza viruses pose a constant threat to public health in the form of antigenic variants or of strains of a new subtype with pandemic potential. Although a worldwide surveillance network exists that is capable of providing an early warning for newly emerging influenza viruses, increasing international cooperation will be required to maintain and improve this system.

### **Influenza Surveillance in Argentina**

Influenza surveillance in Argentina is being done by means of a network of 24 collaborating laboratories mainly located at public hospitals in 14 provinces and in Buenos Aires. Three National Reference Centers are working with different degrees of complexities and areas.

During 1999, this network processed 19,117 samples and identified 1,140 influenza A viruses and 108 influenza B. Eventhough the number of samples processed for virological diagnosis is high, the majority of them (71%) are corresponding to hospitalized children under 5 years of age. In this population, the rate of influenza virus detected is around 5%. The best rate of influenza detection was obtained in adult groups and children consulting to the sentinel physicians with a flu-like syndrome. The detection of influenza virus in this group was 21.4% for type A and 2.5% for type B.

The collaborating laboratories in the network send samples to the National Reference Center at the INEI. We were able to isolate 33.8% of the viruses received and typify 89 of them. The results were as follows: 20.2% A (H1N1), 73.0% A (H3N2) and 6.7% influenza B. The antigenic characterization indicate that the viruses were similar to A/ Sydney/05/97 (H3N2), A/Bayern/07/95 (H1N1) and B/Beijing/184/93. Molecular characterization of Argentinean strains confirmed these results.

During the first 5 months of this year, sporadic cases of influenza A (H1N1) and B were detected. Six A strains were characterized similar to A/New Caledonia/20/99 (H1N1). From week 21 until the end of June an increased activity of influenza A was detected in numerous regions of the country.

A summary of actions implemented in the country to improve influenza surveillance include:

An increase of samples processed by the network and send to the National Reference Centers.

- The increase of isolates obtained.

- The improvement in characterization of isolates by immunological and molecular techniques.
- The adaptation of our time schedule to contribute to the Meeting of September for Southern Hemisphere Vaccine.
- The biannual bulletins with data provided by the network are published and distributed among physicians.

### **Joint actions of the Southern Cone countries**

Argentina provided training in influenza laboratory techniques to Paraguay and Bolivia. The training was done in the Laboratorio de Salud Pública de Asunción, Paraguay and in INLASA in La Paz, Bolivia. The training was to improve the laboratory rapid diagnosis of influenza, to give advice on the type of samples to be collected, conservation and utilization of reagents for the immunofluorescence test, and method of transporting samples. Viral isolation techniques in MDCK cells were standardized to obtain isolates with high titer of virus by HA. It was discussed that during the next meeting Hemagglutination inhibition should be addressed so as to be implemented and analyzed. Considerations about organizing a network of collaborating hospitals were exchanged.

A workshop on Surveillance and Laboratory Diagnosis of Influenza was held in Buenos Aires (INEI-ANLIS "Carlos G. Malbrán") with the participation of CDC staff. Twelve participants of the influenza laboratories from Brazil, Bolivia, Chile, Paraguay, Uruguay and Argentina were included. A previous meeting of epidemiologists and laboratory scientists from these countries was held to share information about surveillance and to know the each country's proposal. As a result of this meeting, it became known that all six countries were working on influenza laboratory surveillance, which did not occur previously, when countries participated in the Brasilia meeting. Each country has a key person responsible for influenza laboratory surveillance. In addition, Chile, Brazil and Argentina have laboratory networks that are collecting samples and data.

The laboratory procedures were based on those of the CDC with some modifications so as to adapt them to our flux of samples: laboratory rapid diagnosis, isolation and typing.

For the next two years it is proposed:

- To improve epidemiological data
- To establish sentinel units
- To inform weekly or monthly about influenza cases and isolates
- To exchange technical assistance and training among the laboratories
- To maintain a strong collaboration with the Reference Laboratory at the CDC
- To implement a quality control of the laboratories
- To produce a regional report of influenza activity
- To extend our activity to surrounding areas with little or no influenza surveillance

## **IX. SURVEILLANCE OF SELECTED DISEASES/SYNDROMES**

### **Antimicrobial Resistance**

The reemergence of diseases like cholera and the threat they pose to Central and South America; the recognition of infections such as those caused by the verotoxins produced by E. coli; the importance of salmonellosis and shigellosis in both the community and the food and tourism industries; the appearance of previously unknown antimicrobial resistance in some microorganisms; and an awareness of the lack of timely information on the frequency of antimicrobial resistance in the countries of the Region were the context in which PAHO, pursuant to the mandates of its Governing Bodies, considered the launching of a surveillance system for antibiotic resistance a priority. Thus, activities were sponsored to strengthen epidemiological surveillance of various diseases and study the antimicrobial resistance of certain microorganisms.

In 1996, the Program on Communicable Diseases of the Pan American Health Organization, in collaboration with Canada's Laboratory Center for Disease Control, initiated a project to strengthen surveillance of the

resistance of certain enteropathogens to antimicrobials, the general objective of which is:

To develop an epidemiological surveillance system for the antimicrobial resistance of *Salmonella*, *Shigella*, and *Vibrio cholerae* in the Region of the Americas, and to strengthen the laboratory infrastructure and the capacity for epidemiological surveillance.

The proposed mechanisms for achieving the objectives are:

- Improvement of the capacity to identify emerging serotypes and the predominant modalities of resistance to antibiotics;
- Preparation of short- and long-term training programs to strengthen epidemiological control and surveillance, as well as laboratory capacities;
- Preparation and application of protocols to improve quality assurance and evaluate the sensitivity of given enteropathogens to antibiotics.

In 1996, the project included the participation of Argentina, Brazil, Colombia, Chile, Costa Rica, Mexico, Peru, and Venezuela, as well as the LCDC. In 1997 some Caribbean countries were incorporated (Bahamas, Barbados, Saint Lucia, Jamaica, Suriname, and Trinidad and Tobago) and in 1999, Bolivia, Ecuador, Nicaragua, and Paraguay.

The data collected since the start of the Project not only constitute a baseline for analyzing the trend in antimicrobial resistance but also make it possible to detect quality problems. In addition to the creation of the database, numerous training workshops were held (workshop on the standardization of laboratory procedures and epidemiology, workshop on the production of antisera, courses on internal and external quality control, etc.), and supervisory visits to laboratories participating in the network.

### **Bolivian Hemorrhagic Fever**

There was an occasional occurrence of Bolivian hemorrhagic fever, and cases presented without a cyclical relationship that would enable us to deduce that it is transmitted during particular periods; however, it can be stated that historically, three causes have determined case occurrence:

- The indiscriminate hunting of felines in the 1960s, resulting in rapid multiplication of rodents. This, together with the growth of brush around housing areas, contributed to rodent infestations.
- Difficult-to-control floods during the rainy season.
- The burning of pastures by livestock producers in the affected area, which, in addition to polluting the environment, led to the exodus of rodents toward dwellings, increasing the risk of transmitting hemorrhagic fever to the inhabitants.

The first recorded case occurred in early 1959 in San Joaquín, Mamoré Province, in the department of Beni. In 1960, 21 cases were reported between July and December in that same locality, and 107 cases with 44 dead in Orobayaya, Iténes Province in the same department, between 1960 and 1962.

A national commission was formed which, together with MIDDLE AMERICAN RESEARCH UNITED (MARU), investigated the outbreaks.

The report of the research commission calculates the case-fatality rate in San Joaquín and Orobayaya in 1962, with 448 cases and 132 dead (30% case-fatality). As a result, until December 1962, the disease was known to exist only in these two regions; subsequently, the causative agent, Machupo virus, was isolated (the river Machupo runs through San Joaquín), and the vector was then identified: the rodent *Calomys callosus*, the only reservoir of the Machupo virus.

Between 1963 and 1964, another major outbreak occurred in San Joaquín, resulting in the hospitalization of 778 people suspected of being carriers of the disease; 336 pairs of sera were examined, of which 282 (84%) showed positive antibodies by complement fixation to the Machupo virus, leading to the belief that 653 people were

hospitalized for hemorrhagic fever; the case-fatality rate was 20% (122 and 653).

During 1963, the epidemic curve peaked during the months of March and June; in January 1964, it began to rise and reached its highest level in March until the beginning of May, when the curve fell sharply to zero at the end of July due to the control activities established.

The following were registered in later years: in 1968, 6 cases in La Cayoba, Iténez Province; in 1969, 6 cases in San Joaquín; in 1970, 12 in Magdalena and San Joaquín (100% case-fatality in all of them).

In 1971, 5 cases occurred in the city of Cochabamba because of a sick patient from the Yacuma Province (Beni), with 4 dead (2 nurses and a medical pathologist), an 80% case-fatality.

The last outbreak occurred in 1975 in San Joaquín, with 7 cases and 2 deaths (30%).

In 1982, significant spread of the vector (*Calomys callosus*) was observed because of flooding in Yacuma, Mamoré, and Iténez Provinces, which forced the reservoir to seek higher elevations in Cercado and Marbán Provinces.

In 1990, the construction of a road to Santa Cruz favored furthered its spread. It is believed that the floods of 1992 may also have contributed to the displacement of the vector to new areas.

In 1993, during the month of March, another case occurred in Bolpebra (Mamoré Province). Laboratory-confirmed, the patient died. In order to conduct epidemiological surveillance and control of Bolivian hemorrhagic fever, program activities were reinitiated.

In 1994, suspected cases occurred in March, with a death at the beginning of April and an untimely resurgence of Bolivian hemorrhagic fever beginning in July; there were 9 cases in the Iténez Province in Beni, with an index case that survived in a family with 6 dead and a case-fatality rate of 78%.

No cases have occurred since then, until February of this year, when a merchant fell ill in the environs of Huacaraje, Iténez Province, and died.

With the exception of the last case reported in Huacaraje, the cases mentioned earlier came from the endemo-epidemic area located in Iténez and Mamoré Provinces and specifically between the Machupo and Black Rivers to the west and the Itonama River to the east: Machupo and Itonama come together in the locality of La Horquilla, very near the Marquez Coast of Brazil.

There are 52 positive localities in Iténez and Mamoré Provinces, with a reservoir density that places most of them at medium- and high-risk.

The endemo-epidemic area is located in the department of Beni, at an altitude of 500 meters above sea level and with an oscillating hygroscopic range of 75% and 80%, belonging to the mezothermic plains of Bolivia, where temperatures range from 25 to 35 degrees centigrade.

The idea that contaminated food was the mode of transmission was supported until the last time; it is currently hypothesized that transmission occurs through aerosols that may be released by the rodent when it defecates, urinates, or eats. These aerosols are considered responsible for transmission of the virus to humans, without ruling out the possibility of transmission from a sick to a healthy person and through secretions such as blood, urine, feces, and saliva.

The specific treatment, under investigation, is the administration of RIBAVIRIN, which should be administered on a set schedule for 10 days.

## **Dengue in the Americas**

The campaign to eradicate *Aedes aegypti* from the Americas was initiated in the late 1940's and ended in 1962 with the elimination of this mosquito species from almost all mainland countries and from several Caribbean island nations. Despite the enormous efforts carried out, the eradication program ultimately failed and *Aedes aegypti* slowly returned. At present, all countries in the Americas have been re-infested, except for Canada, Chile and Bermuda.

Autochthonous transmission of dengue fever (DF) has now been reported from the southern United States to northern Argentina. In the Americas, Brazil has reported about 40% of all cases. In 1994, Brazil reported 56,621 DF cases; by 1998, the number had reached 570,148, an increase of more than 1000%. This increase in cases was accompanied by an increasing geographic distribution of the vector within the country. In South America, only Uruguay and Chile have not reported DF cases; in North America, Bermuda and Canada are the only countries free of autochthonous cases.

During the 1970s, dengue hemorrhagic fever (DHF) was notified in 5 countries, and only 60 cases were reported during that decade. During the 1980s, a total of 13,235 cases of DHF were reported; by the 1990's, a total of 54,092 DHF cases were reported from 27 countries in the Region. The reported DHF case/fatality ratios in some countries are significant: Mexico (3,611 cases/137 deaths), Cuba (10,517/170), Nicaragua (3,890/26), Puerto Rico (580/57), Venezuela (36,881/299), Colombia (14,400/123) and Brazil (865/43). Venezuela alone reported almost 51% of all DHF cases in the Region. It is noteworthy that many of the reported DHF cases do not fulfill the WHO criteria, and most of them were not laboratory-confirmed. The reported case fatality rates in the Americas have ranged from 0.8% in Venezuela to 8.3% in Puerto Rico, suggesting that there are differences in the criteria for diagnosis and reporting.

Clearly the pattern of DF and DHF in the Americas is evolving into the endemic pattern seen in Southeast Asia. Factors favoring this development are: the presence of four dengue serotypes with expansion in transmission of serotypes 3 and 4, widespread distribution of the vector, inadequate water supplies that lead people to store water and provide increased vector breeding sites, structural failure of mosquito control programs in some countries, insecticide resistance in vector populations, and increased travel and better transportation which facilitate the movement of vectors and viremic people.

The surveillance of DF and DHF in the Americas should be supported by laboratory-based networks. Its main functions should include monitoring of endemicity levels, early warning of epidemics and identification of circulating serotypes. Since vaccine against dengue will not be available in the near future, a political decision and agreement among governments in the region must be made to implement better control of dengue. If not, DF will continue to cause epidemics, resulting in thousands of DHF cases with increased mortality in the American Region.

## **Argentinean Hemorrhagic Fever**

South America has experienced during the last five decades the emergence of four hemorrhagic fevers caused by arenaviruses: Argentine Hemorrhagic fever (AHF – Junin virus), Bolivian Hemorrhagic fever (Machupo virus), Venezuelan Hemorrhagic fever (Guanarito virus), and a hemorrhagic fever in Brazil (Sabia virus). Other arenaviruses not yet associated with human illnesses have also been discovered circulating in the region, particularly in the last decade.

AHF was an emerging zoonosis in the 1950's, but it is considered controllable. The disease has produced annual outbreaks without interruption, that were accompanied by a progressive extension of the endemic area (from 16,000 km<sup>2</sup> in 1958 to 150,000 km<sup>2</sup> at present), with a remarkable increase of the population at risk (from 270,00 persons to more than 5,000,000). Incidence rates as high as 140/100,000 persons and 355/100,000 adult males have been registered in some rural areas. Surveillance of AHF has been mainly directed to the early detection of cases for gaining access to the specific treatment: immune plasma. This treatment is effective in reducing the AHF case-fatality rate from 15-30% to less than 1% only when given during the first week of illness. The AHF surveillance system is addressed to the early identification of febrile syndromes of unknown etiology in the at-risk population. The AHF algorithm includes the implementation of clinical laboratory

studies, particularly white cell and platelet counts, with clinical case definitions of known sensitivity and specificity. In all notified cases, specific virologic studies are performed. Since the early 1990's, an effective live attenuated Junin virus vaccine (Candid #1) is available. Limited doses (because Candid #1 is an orphan vaccine) restricted the areas and the population targeted. Between 1991-2000, 209,912 adult persons (161,564 males and 48,348 females) coming from 209 selected counties were vaccinated. Ongoing studies continue reinforcing previous safety and immunogenicity findings. Persistence of the specific immune response has been demonstrated in >90% of the vaccinated up to 10 years after vaccination. Calculated effectiveness of Candid #1 for 1992-99 period was 98%. Impact of this selected vaccination resulted in changes in the classical epidemiologic features of the illness, with an increase in the proportion of women and children, and a lower percentage of cases with rural contact. AHF epidemic outbreaks since 1992 have been at their lowest recorded levels since the discovery of Junin virus. With sufficient supplies of Candid #1 vaccine to protect the whole population at risk (an objective that could be achieved with a full operation of the production facility at INEVH), AHF may be controlled. However, the disease can not be eradicated. Small outbreak and isolated cases may be expected, even with good vaccine coverage. For this reason, the surveillance system should continue to include the systematic study of rodent reservoirs.

AHF surveillance structure was used by NIHVD as a baseline system for the recognition of hantavirus illnesses. First hantavirus pulmonary syndrome (HPS) patients in Argentina were identified in 1993 among AHF notified cases without etiologic confirmation as acute arenavirus infections. The spectrum of clinical illnesses associated with hantavirus infection in central Argentina could be analyzed when we combined the systematic study of all notified AHF cases negative for Junin virus infections, all suspected leptospirosis cases, and all cases fulfilling HPS clinical case definition. In a group of 30 cases of serology confirmed acute hantavirus infections hospitalized at INEVH during 1987-99, 4 cases (13%) had a mild febrile syndrome; one surviving case (3%) had a febrile syndrome with renal complication; another single surviving case (3%) had a febrile syndrome followed by an encephalopathy. These cases, that represent 20% (6/30) of this series would not be usually detected by HPS surveillance. The remaining 24 patients (80%) fulfilled HPS case-definition, but with 50% (12/24) having renal complication.

In the region of the Americas, many areas endemic for arenaviral hemorrhagic fevers are at risk of HPS and other hemorrhagic syndromes, such as dengue. An integrated system of surveillance and laboratory studies could improve current sensitivity and can elicit the identification of other emerging diseases (e.g., leptospirosis, rickettsiosis) that are still lacking adequate methodology of investigation.

### **Hemolytic Uremic Syndrome**

Hemolytic Uremic Syndrome (HUS) is a serious illness characterized by acute renal injury, thrombocytopenia and microangiopathic hemolytic anemia. Years before HUS emerged as an important pediatric disease in North America, it was recognized as the major cause of acute renal failure in childhood and infancy in the Southern Cone Countries of America, being hyperendemic in Argentina and endemic in Chile.

The association between HUS and infection by Shiga toxin-producing *Escherichia coli* (STEC), particularly strains of serogroup O157, was first demonstrated in Canada in 1983-1985 and has been subsequently confirmed by numerous studies conducted in different areas, including Latin American countries.

A meeting to discuss the implementation of common surveillance protocols for HUS and bloody diarrhea in the Southern Cone Region took place in Buenos Aires on June 4, 2000. At that meeting training and methodology transfer for the diagnosis of STEC infections was also provided to laboratory personnel from: Bolivia 1; Brazil 2; Chile 1; Paraguay 1; Uruguay 1 and Argentina 17. Participants recommended development of a sentinel Hospital-based system for identification of HUS cases with laboratory confirmation in all countries. Criteria for sentinel-site selection should be: i. interest and availability to participate; ii. availability of laboratory personnel at the hospital; iii. history of HUS cases in the area; iv. likelihood of cases being admitted to the hospital; and v. selection of hospitals from different geographic areas. Laboratory surveillance of bloody and non-bloody diarrhea will be performed in the same sentinel-hospitals. Implementation of the sentinel system will begin this year.

The situation of HUS in the Southern Cone countries is as follows:

### **Argentina**

A nationwide mandatory notification system has been established since May 1999 by Health Ministry using C2 form (Medical Diagnosis) for HUS case reporting and L2 form (Laboratory Diagnosis) for Escherichia coli O157 infections. HUS is endemic and over 7,000 cases have been reported since 1965. In 1999, hospital nephrology units reported 308 new cases with an estimated annual incidence rate of 9.2 per 100,000 in children less than five years of age. Mortality rate was 2.9%. Both sexes were equally affected (45.5% male), 80% of children were under 36 months with a mean age of 22.4 months (range 4 - 96 months). The illness was distributed throughout the whole country, but cases were reported more frequently in central and southern states during warmer months from October to May.

### **Bolivia**

Post-diarrheal HUS is not a reportable disease. There is not enough information about the occurrence of HUS in Bolivia with the exception of data obtained from an intensive therapy unit of the Hospital del Niño "Dr. Ovidio Aliaga" in La Paz, that showed 24 cases occurring between 1986 - May 2000. All children were under 18 months of age, both sexes were equally affected, and cases tended to come from low socioeconomic groups. Regarding STEC infections, a study performed with diarrhea patients in three hospitals of La Paz, Cochabamba and Santa Cruz showed an isolation frequency of 3.5% in patients under 17 years old and 1.2% in patients older than 17 years olds.

### **Brazil**

HUS is not a reportable disease. Sporadic cases have been reported in Sao Paulo, Rio Grande do Sul and other States. Hospital admissions are currently registered in a National Information System (SIN). Discharge diagnosis is regularly registered using the International Disease's Classification (CID-10). Until 1999, HUS was included in the Hemolytic Anemia and not codified separately. Since 1999, HUS has its own independent code, which allowed the detection of 19 cases, including 7 deaths with a fatality rate of 36.8%.

### **Chile**

HUS is not a reportable disease. In 1996, the Health Services received general information (Form 4B/11, February 1996) about the disease in order to alert the surveillance system and inform the community. In April 2000, E. coli O157 and other STEC were incorporated into the Laboratory Surveillance System. Between 1997 and 1999, the Public Health Institute (National Reference Laboratory) received 80 strains from 41 HUS cases. STEC was identified in 22/41 (53.6%), being stx2 prevalent (63.6%). Different serogroups were detected being O6 and O157 prevalent. Most of the children were under 2 years old (72.7%), 54.5% of the patients were male and 68% of cases occurred between December and March.

### **Paraguay**

HUS is not a reportable disease. From 1992 to April 2000, 23 HUS cases were reported from the Gran Hospital Nacional de Itaguá, Hospital IPS, Hospital de Clínicas and Private Hospitals in Asunción. Eight cases were admitted to the Gran Hospital Nacional de Itaguá and one patient died. All the children were under 2 years old and belonged to low socioeconomic level. Both sexes were equally affected.

### **Uruguay**

HUS is not a reportable disease. In 1989 - 1990 and 1994 - 1996 periods, 11 and 14 HUS cases were reported, respectively. Among the 14 cases detected during 1994 - 1996, the mean age was 11.2 months and 57% were male. These children were well nourished, from middle or low income socioeconomic groups and living in urban areas. The estimated annual incidence is lower than 5.0 per 100,000 children under 5 years old. No data are available since 1996.

## **West Nile Virus in the Americas**

West Nile virus (WNV) was detected in the Western Hemisphere for the first time in September 1999, when it caused an epidemic/epizootic in New York City and surrounding counties and states. A total of 62 cases of neurologic disease and 7 deaths were reported. A serologic survey of residents in the Queens epicenter showed a 2.6% seroprevalence rate; approximately 30% of these individuals reported a febrile illness.

In addition to humans, major epizootics occurred in birds and horses. The American crow was the principal bird affected, but morbidity and/or mortality was confirmed in 26 species of birds; positive birds were detected in 4 states, New York, Connecticut, New Jersey and Maryland. The epizootic in horses occurred in the eastern part of Long Island, New York where 25 cases of clinical disease with 9 deaths were reported. A serosurvey of stable and farm mates showed a seroprevalence of about 31 horses.

West Nile virus infection in humans in the northeastern US was clinically and epidemiologically similar to St. Louis encephalitis (SLE) virus. *Culex pipiens* complex mosquitoes appeared to be the principal mosquito vector in 1999. However, WNV was also isolated from *Aedes vexans* and the epizootic in horses suggests that an alternative vector may have been involved in that area of Long Island. Since the epidemic/epizootic in 1999 occurred at the height of the southern bird migration season, it is possible that WNV was taken to southern latitudes by migratory birds.

Surveillance for WNV must be coordinated with other flaviviruses circulating or introduced in an area. As with other arboviral encephalitides that have birds as the natural reservoir host, emphasis should be placed on detecting virus activity in bird and mosquito populations before it enters the peridomestic environment and causes human and/or equine infection. Surveillance must be active, and laboratory-based to effectively detect virus activity prior to human involvement.

In the Caribbean, Central and South America, surveillance for WNV infection will be complicated by the presence of other flaviviruses, primarily dengue and yellow fever. The lack of specificity of the IgM-capture enzyme-linked immunosorbent assay (ELISA), which is used as the primary laboratory test in dengue virus surveillance, will likely allow WNV to go undetected in areas where dengue is endemic unless other laboratory methods are used to identify the IgM antibody and/or the infecting virus. Thus, laboratories will need to perform more specific serologic and/or virologic tests in order to effectively support surveillance for WNV.

## **Yellow Fever**

Yellow fever continues to be an important public health problem in the Americas. Between 1985 and 1999, Bolivia, Brazil, Colombia, Ecuador, Peru, Venezuela and French Guyana reported 2,935 cases and 1,764 deaths. During this period, more than 80% of all yellow fever reports in the American Region came from Bolivia and Peru. In 1999, Bolivia, Brazil and Peru accounted for 33%, 36% and 27% of all cases respectively. However, from January to June 2000, a total of 71 confirmed cases were reported in Brazil, which represent more than 90% of all the cases notified in the Region during this period. Reports from the Brazilian Ministry of Health show that most of those cases come from the State of Goiás and its neighboring States, where an extensive epizootic is taking place since the beginning of the year (Table 7 and 8).

All cases notified in the Region since the 1940s have been the jungle form of yellow fever transmitted by mosquitoes of the genus *Haemagogus*. However, the overwhelming spread of the *Aedes aegypti* mosquito threatens to re-urbanize the disease. The seriousness of the current yellow fever situation in the Region demands a firm commitment by the countries to a strong and effective strategy for controlling the disease. PAHO's recommendations focus on the prevention of its re-urbanization, through surveillance, vaccination and vector control.

The establishment of a sensitive surveillance system is critical for the control and prevention of yellow fever. Currently notified cases tend to be of the severe clinical form of the disease, and therefore correspond to only a fraction of the total number of yellow fever virus infections, since as much as 50% of all cases can be asymptomatic.

In order to provide immediate protection to residents in enzootic areas and to prevent the introduction of yellow fever into nearby urban areas infested with *Aedes aegypti*, high levels of vaccination should be maintained among individuals living in both areas. During its Seventh Plenary Session in 1997, PAHO's Directing Council exhorted its member states to include a yellow fever vaccine in their national immunization programs at all areas at risk of transmission of the disease. The countries and territories that have included universal children immunization against yellow fever are Trinidad and Tobago, Guyana and French Guyana. Brazil, Ecuador and Peru have given priority to the immunization of children in enzootic areas. Trinidad and Tobago and Guyana have implemented "catch-up" campaigns in all age groups in the entire country, and Brazil and Ecuador have used the same strategy for enzootic areas and regions with high risk of transmission of the disease. Peru, Bolivia, Surinam and Venezuela have developed plans to introduce the yellow fever vaccine in their children vaccination schedule, as well as the vaccination of all age groups in enzootic areas.

Present day control strategies against the urban vector *Aedes aegypti* are based primarily on the reduction of breeding sources through their elimination. Social communication, community participation and health education are fundamental elements in these strategies. Insecticides are widely used where there are high vector population densities.

**Table 7: Confirmed Cases of yellow fever in Brazil  
January-May 2000**

State	Cases	Deaths
Amazonas	1	0
Bahia	10	3
Brasilia, D.F.	1	1
Goiás	45	22
Mato Grosso	4	3
Minas Gerais	2	2
Sao Paulo	2	2
Tocantins	6	4
Total	71	37

Source: *CENEPI-FUNASA-Ministry of Health of Brazil*

**Table 8: Reported Cases and deaths from yellow fever in the Region of the Americas, by country, 1985-2000**

Country	1985-1995		1996		1997		1998		1999		2000*	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
Bolivia	424	319	30	21	63	47	57	39	68	33	7	5
Brazil	202	88	15	12	3	3	34	15	75	28	71	37
Colombia	55	47	8	4	5	4	1	0	2	2		
Ecuador	45	29	8	8	31	4	3	1	5	3		
F.Guyana	-	-	-	-	-	-	1	1	-	-		
Peru	1431	914	86	34	44	20	165	49	56	33	2	1
Venezuela	2	1	-	-	-	-	15	4	1	1		
Total	2,159	1,398	147	79	146	78	276	109	207	100	80	43

\* Provisional data

Source: PAHO Division of Vaccines and Immunization

## **X. CONCLUSIONS AND RECOMMENDATIONS**

### **Influenza Surveillance**

#### **Conclusions**

- New national laboratories have begun to perform the diagnosis of influenza, and there was a significant increase in the number of clinical samples processed by the laboratories.
- The coordination between the laboratories and epidemiology was strengthened.
- Laboratory training was conducted to improve influenza diagnosis.
- There was improvement in the dissemination of information.
- Some National Influenza Centers are implementing the use of molecular techniques.
- Chile has established a quality control program for national laboratories involved in the diagnosis of influenza.

#### **Recommendations**

- Improve the epidemiological data and information flow.
- Train personnel in the epidemiology of influenza.
- Evaluation of the vaccination programs.
- Improvement of information systems and dissemination of information on a monthly basis.
- Exchange of technical information and training among the laboratories in Latin America.
- To maintain close contact with the WHO Collaboration Center for Influenza located at the CDC, USA.
- Integration of public and private laboratories that perform the diagnosis of influenza under the coordination of a National Reference Center.
- Assurance of the provision of diagnostic reagents, and funding to support an annual meeting for the influenza network.
- To publish every six months a report on influenza activity, to begin on November 2000.

### **HUS Surveillance**

#### **Conclusions**

- There is better trained personnel.
- Active HUS surveillance with laboratory support should be conducted at sentinel sites in each of the six countries of the SC region. Activities to be developed were as follows:

*Argentina-* diarrhea surveillance with stool culture in 20 sentinel units

*Bolivia-* to conduct a study of STEC infections

*Brazil-* surveillance of bloody diarrhea in sentinel units located in five states and surveillance of STEC

*Chile-* surveillance of bloody diarrhea in sentinel areas and investigation of STEC in outbreaks due to ETA

*Uruguay-* surveillance of bloody diarrhea in a sentinel hospital

#### **Recommendations**

- Designation of a regional reference laboratory capable to perform sub-typing techniques.
- To establish a quality control program with three levels: national, regional and extra-regional.
- Provision of reagents for the national reference laboratories of the six countries.
- To establish a flow of information among the countries of the SC region.

## Hantavirus Pulmonary Syndrome

### Recommendations

- To improve HPS surveillance among the countries of the network and to extend it to Ecuador.
- In order to achieve better surveillance the medical knowledge about SPH should be disseminated, case notification should be compulsory, and data concerning the case fatality rate among cases of respiratory distress should be submitted to analysis.
- To secure funds for the preparation and distribution of serum panels for quality control and use during training.
- To implement training in serological diagnosis of HPS first, and next on the use of molecular biology.

### Amazon Region Network

#### Recommendations

- To include in the network Ecuador, Suriname and Guyana.
- To standardize the reagents used for the syndromic surveillance.
- To strength surveillance of drug resistance for *P. falciparum* and *P. vivax*.

### Southern Cone Network

#### Conclusions

It was general agreement that reagents, software and computer equipment was the area of greatest needs.

#### Recommendations

##### 1. Surveillance

- To maintain Influenza, HUS and HPS surveillance.
- To strengthen anti-microbial resistance surveillance (as agreed in Brasilia).
- To include surveillance for food-borne pathogens, and outbreak notification and investigation, as well as leptospirosis.

##### 2. Incorporation of physicians

- To involve physicians in surveillance.
- To disseminate information about EID problems.
- To contact scientific societies.
- To train health workers.
- To establish hospital committees in order to deal with nosocomial infections.

##### 3. To improve the availability of information regarding the environmental and vector factors

- study of reservoir hosts
- food control
- vector studies
- water, soil, air and food contamination

##### 4. Development of information systems

- To strengthen the development of web pages of the countries.

- To develop intranet systems.
- The use of geographic information systems.
- To conduct a training workshop on the above topics during the year 2001.

#### 5. *Strengthening of epidemiologic analysis*

- To attempt making predictions of future events by using available information.
- To initiate a process of standardizing information in order to facilitate its analysis.

#### 6. *Quality control*

- To assure the use of the recommended quality control practices.

#### 7. *Molecular Epidemiology*

- To conduct a survey in order to determine the network's current capacity to conduct molecular epidemiology.

### **Syndromic Surveillance**

#### **Conclusions**

Participants in both networks agreed on the importance of an integrated surveillance system such that clinicians, epidemiologist and laboratory staff working on a coordinated manner in order to detect and control the emergence and re-emergence of infectious diseases. The strengthening of surveillance systems will prepare the public health system to have a greater impact on early detection and control of future emerging diseases. The need for enhanced communication among participants within and between both networks by electronic means was also stressed. It was also agreed that syndromic surveillance should be considered as an integral part of general surveillance, since this is responsible for the surveillance of different events. In addition the following:

#### **Recommendations**

- To utilize sentinel sites to conduct syndromic surveillance.
- The definitions of the different syndromes and the algorithms should be adapted to the epidemiological characteristics of the area.
- Certain algorithms should consider the performance of laboratory tests only in a percentage of the samples (e.g. 1 in each 10 malaria positive cases).
- The surveillance of undifferentiated febrile syndrome is costly, therefore should be excluded.
- PAHO and other agencies should help to overcome the problems associated with the provision of reagents, including the funding aspects and purchasing.
- To stimulate the development of projects of technical cooperation among countries (TCC-PAHO) in order to transfer technology and training.
- To identify mechanisms to facilitate the transport of diagnostic samples.
- To participate in other forums (MERCOSUR, Andean Pact) to coordinate and facilitate technical cooperation among the countries of the networks.

#### **Other recommendations**

- To establish ongoing mechanisms of communication among the countries that participate in both networks.
- To assign more time for discussions of issues of the interest of the networks in future meetings.
- PAHO should provide standard models for the tabulation of data to be presented in the country reports.
- The two networks should continue to meet. The next meeting will take place in Asuncion, Paraguay, during the year 2001.

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