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## Re-emergence of Dengue in the Americas

### Introduction

Clinically, dengue fever has been recognized for more than 200 years and a disease similar to dengue hemorrhagic fever (DHF) was first described in northern Australia at the end of the past century (1). Although several dengue epidemics or pandemics have been described in previous centuries and in the first half of this century, a remarkable increase their incidence has been noted since the 1950s. A main concern was the appearance of epidemic DHF in the Philippines in 1954 which rapidly spread to Thailand, Vietnam, Indonesia and to other Asian and Pacific countries, becoming endemic and epidemic in several of them (1). The first DHF epidemic in the Americas occurred in Cuba in 1981 (2); subsequently, 24 other countries in the Region have reported DHF. Of great concern has been the occurrence of several pandemics and countless epidemics of dengue fever over the past 40 years causing considerable health, social and economic impact.

### Present situation

About two-thirds of the world's population live in areas infested with dengue vectors, mainly *Aedes aegypti*. All four dengue viruses are circulating, sometimes simultaneously, in most of these areas. It is estimated that up to 80 million persons become infected annually although marked underreporting results in the notification of much smaller figures (3).

Currently dengue is endemic in all continents except Europe and epidemic DHF occurs in Asia and in the Americas. The incidence of DHF is greater by far in the Asian countries than in the Americas. In the Americas, the emergence of epidemic DHF occurred in 1981 almost 30 years after its appearance in Asia and its incidence is showing a marked upward trend.

### The re-emergence of dengue and the emergence of DHF in the Americas

#### Historical overview

The first description of a dengue-like disease in the Americas relates to an outbreak that occurred in Philadelphia, United States, in 1780 (1). In the following century four large epidemics affected Caribbean countries and the southern United States which occurred during the periods 1827-28, 1850-51, 1879-1880 and 1897-1899 (5). Interestingly, small-joint arthritis including swelling, which are commonly found in infections associated with the arboviruses *Chikungunya* and *Mayaro*, were among the clinical manifestations observed during the dengue outbreaks between 1827-1880 but not since this period. In the first half of this century four epidemics were reported in the same countries, the last one being during the period 1941-1946 which affected cities in the Texas Gulf, several Caribbean islands including Cuba, Puerto Rico and

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Bermuda, Mexico, Panama and Venezuela. (5). In Brazil epidemics of dengue were recorded during 1846-1848 and 1851-1853. From then until 1982 only two outbreaks were reported, in 1916 and 1923 (6,7). Peru reported cases of dengue during the 1950s but not in the following three decades (8). In 1953 a dengue virus which was identified as serotype 2 was isolated for the first time in the Americas in Trinidad. Several isolates of dengue-2 were obtained from persons in that country during 1953-1954. Interestingly, no outbreaks were reported in this period in Trinidad nor in any other Caribbean islands (9).

### **Re-emergence of dengue**

During the 1960s two extensive pandemics of dengue affected the Caribbean and Venezuela. The first one which broke out in 1963 was due to dengue-3 and swept the Caribbean after almost 20 years of silence. Jamaica, Puerto Rico, islands of the Lesser Antilles and Venezuela were among the countries affected but Cuba, Hispaniola and Trinidad were spared in this outbreak. The second epidemic occurred in the Caribbean and Venezuela during 1968-1969 and although dengue-2 was predominantly isolated, dengue-3 was also recovered from persons in some islands (5). During the 1970s these two serotypes caused extensive epidemics in Colombia where dengue had not been recognized since 1952 (10). The first epidemic occurred during 1971-1972 and was due to dengue-2 whereas the 1975-1977 epidemic was associated with dengue-3. It was estimated that more than half a million persons became infected. Both outbreaks occurred "silently" for the most part or were confused with other illnesses and did not draw much attention from the health authorities.

A milestone in the re-emergence of dengue in the Americas was the introduction of dengue-1 in 1977. This was followed by a devastating pandemic that lasted until 1980 (11). The virus was initially detected in Jamaica, possibly having been imported from Africa, and from there the epidemic spread to virtually every island of the Caribbean. The epidemic in South America began in 1978, affecting Venezuela, Colombia, Guyana, Suriname and French Guiana. The epidemic in Central America was also detected in 1978 affecting Honduras initially and

subsequently El Salvador, Guatemala and Belize. Spreading to the north, the epidemic reached Mexico at the end of 1978 and during 1979-1980 continued to affect other Mexican states, and arrived in the state of Texas in the second half of 1980. About 702,000 cases were reported to the Pan American Health Organization (PAHO) for the period 1977-1980, but the incidence was much higher since estimates from Colombia, Cuba and Venezuela alone indicated that over 5 million persons became infected. In 1981 dengue-4 strain probably imported from Pacific islands emerged in the Americas causing a series of outbreaks in the Caribbean, northern South America, Central America and Mexico; with some exceptions dengue-4 infection has generally been associated with mild disease (11).

During the 1980s five countries in South America namely Brazil, Bolivia, Paraguay, Ecuador and Peru, that had not experienced dengue before or had been free of the disease for several decades were affected by explosive epidemics caused by serotype 1 (11); in the epidemic in Peru serotype 4 was also isolated (12). The first epidemic which occurred in northern Brazil in 1982 was associated with serotypes 1 and 4 (13); vector control measures were implemented and since then no dengue activity has been reported in this area. In 1986 dengue 1 was introduced in Rio de Janeiro, Brazil, causing major outbreaks (14). It was subsequently disseminated to most states in Brazil. Following its introduction in those countries, dengue-1 virus has continued to cause major epidemics in Brazil, Ecuador and Peru in subsequent years.

During 1993 Costa Rica and Panama, the last two tropical Latin American countries which had been free of dengue for several decades, reported indigenous transmission of dengue; the serotype was dengue-1 and its introduction in Costa Rica was associated with severe outbreaks in this year and in subsequent years (15). In 1994 dengue-3 was reintroduced in the Americas after an absence since 1978 when was last isolated in Puerto Rico (16). This serotype was initially detected in Panama and Nicaragua and in the following year it spread to other Central American countries and to Mexico, causing numerous epidemics of dengue. In Nicaragua, in 1994, the introduction of dengue 3 was associated with a country-

wide epidemic of dengue/DHF but dengue-1 was also present. The introduction of dengue-3 in Mexico in 1995 coincided with an increased number of DHF cases, however only dengue-1 and particularly dengue-2 were associated with DHF (17). It should be noted that this dengue-3 virus belongs to the a genotype that has caused major epidemics of DHF in Sri Lanka and India (16). As of June 1997 dengue-3 has not been isolated outside Central America and Mexico. Over 250,000 cases of dengue were reported in the Region in both 1995 and 1996.

### **The Emergence of DHF**

In 1981 Cuba reported the first major outbreak of DHF in the Americas (2). Prior to this event, suspected cases of DHF or fatal dengue cases had been reported by Venezuela, Jamaica, Honduras, Curacao and Puerto Rico, but only a few of them fulfilled the WHO criteria for diagnosis of dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS) and most were not laboratory confirmed (11). During the Cuban epidemic a total of 344, 203 cases of dengue were notified, of which 10,312 were classified as severe cases (WHO grades II-IV) and 158 were fatal; a total of 116,143 patients were hospitalized, the majority of them during a three-month period (2). The DHF Cuban epidemic was associated with a strain of dengue-2 virus and it occurred four years after dengue-1 had been introduced in the island causing epidemics of dengue fever and infecting almost half of the country's population.

The outbreak of DHF/DSS in Cuba is the most important event in the history of dengue in the Americas. Subsequent to it, in every year except 1983, confirmed or suspected cases of DHF have been reported in the Americas. A marked increase in the annual incidence occurred in 1989 which was due to a countrywide epidemic in Venezuela. This was the second major DHF epidemic in the Americas with 3,108 cases and 73 deaths being reported between December 1989 and April 1990. Dengue-2 was the predominant serotype isolated from cases but serotypes 1 and 4 were also recovered from patients; although no isolate were obtained from fatal cases, immunohistochemical analysis performed with formalin-fixed paraffin-embedded tissues of fatal cases revealed the

presence of dengue-2 antigen in the liver of four of them (18). The epidemic recurred in the second half of 1990 and since then Venezuela has suffered epidemics of DHF every year.

Between 1981 and 1996 a total of 42,171 cases of DHF and 581 deaths were reported by 25 countries in the Americas. The distribution of cases by country it can be observed that 22,170 (53%) of the reports originated in Venezuela. It can also be seen that excluding Cuba and Venezuela, the number of cases by country varies from 1 to 3,740 cases. Colombia, Nicaragua and Mexico have each reported over 1,000 cases, most of them during the period 1992-1996. About 74% of the Colombian cases were notified during 1995-1996 whereas 97% of the Mexican cases were reported during 1995-1996. In Brazil four fatal cases which exhibited fever, hemorrhages and shock occurred during 1986-1987 and were associated with dengue-1 virus; confirmation was obtained by virus isolation or by antigen detection (11). In 1990-1991 an outbreak of DHF was recorded in Rio de Janeiro, Brazil (19) and 24 cases with 11 deaths occurred in the Brazilian State of Ceara in 1984 (20).

Studies of DHF cases in the Americas (21, 18, 22, 23) revealed similarities to the clinical manifestations exhibited by DHF patients in Asia. However, the incidence of gastrointestinal hemorrhages observed in Cuba and Puerto Rico seem to be higher than that seen in Thai children (24). Liver necrosis, was described in 70% of the 72 children who died of DHF in Cuba in 1981 (24). Severe neurological manifestations, renal failure and myocarditis have been occasionally reported in the Americas (20, 25, 26).

The age distribution of DHF cases in the Americas is different from that observed in Asia. In the outbreaks in Cuba and Venezuela the disease has occurred in all age groups, although children under 15 years of age have comprised about two-thirds of the fatalities. Studies of DHF cases that fulfilled WHO's criteria done in Brazil (24) showed a modal age range of 31-45 years.

Observations made in Puerto Rico showed distinct age distribution patterns of cases that fulfilled WHO's criteria: in 1986 two-thirds of the cases were under 15 years of age but during 1990-91 the mean age of patients was 38 years

(26, 22). This age distribution pattern is different from that found in South-East Asia where young children are affected predominantly. It should be noted, however, that a marked increase in the number of DHF cases in people over 15 years old has been observed in the Philippines and Malaysia during recent years (27). Regarding the sex distribution, Cuba reported no significant female predominance a finding that is in contrast with observations from Asia.

The epidemics in Cuba and Brazil were clearly associated with dengue-2 virus. In both countries dengue-1 had been introduced four years earlier, after a period of several decades of absence of dengue virus circulation. However, Cuba suffered a major epidemic while only relatively small outbreaks have been observed in Brazil. Other countries such as Peru and Ecuador have experienced a similar sequence of dengue infections with these serotypes, but no DHF epidemics were recorded. A distinct epidemiological pattern was observed in Venezuela and in French Guiana where dengue was endemic for over 20 years before the emergence of their first epidemics of DHF in 1989-1990 and 1990-1991 respectively: Dengue-2 was predominant in Venezuela (18) and in French Guiana (28) and the only serotype found in the tissues of fatal cases in Venezuela (18). Interestingly in French Guiana the dengue-2 strains isolated during the DHF outbreak and during an outbreak of dengue fever that occurred in 1986 were genetically similar and belonged to the Jamaican genotype which in turn has a genome sequence very close to dengue-2 strains from Vietnam where DHF is highly endemic (28). These findings illustrate the complexity of the factors responsible for triggering DHF. Studies in Cuba suggested that individual risk factors for DHF include chronic diseases such as bronchial asthma, diabetes mellitus and sickle cell anemia, and that race seems also to be important, since DHF/DSS was more prevalent in white than in black persons (29).

Overall, the case-fatality rate (CFR) of DHF in the Americas is 1.4%. However, a marked variation has been observed among countries. In 1995 the CFR ranged from 8.3% in Puerto Rico to 0.8% in Venezuela. This variation could be due to several factors such as reporting criteria,

viral strain, case management, host genetic factors and possibly other causes.

### **Causes of the emergence/re-emergence**

In 1947 PAHO was entrusted by its Directing Council to organize a hemispheric campaign to eradicate the mosquito *Aedes aegypti*. By 1962, 18 continental countries and several Caribbean islands had successfully achieved eradication. Unfortunately after 1962 only three new countries eliminated the vector. Even more serious, however, was that the countries that had achieved eradication, became re-infested with the vector in the 1960s and in subsequent decades. Countries still infested (the United States, Cuba and some other Caribbean islands, Venezuela) became sources of reinfestation for those that had eradicated the vector. Other reasons for the program failure include reduced political support for the programs, resulting in inadequate management and scarcity of trained technical personnel; resistance of *A. aegypti* to chlorinated insecticides and high cost of materials, equipment and wages. There was progressive dissemination of the vector so that by 1997 with the exception of Canada, Chile and Bermuda, all countries in the Americas are infested. The practice of water storage in domestic settings due to the problems of water supply and the exponential growth of containers than can hold water (tires, disposable containers) greatly contribute to the increase of vector densities favoring virus transmission. Other factors contributing to the emergence/re-emergence of dengue/DHF include the rapid growth and urbanization of populations in Latin America and the Caribbean, and increased travel of persons which facilitates dissemination of dengue viruses. Presently all four dengue serotypes are circulating in the Americas, thus increasing the risk for DHF in this Region.

### **Prevention and control**

The high number of dengue and DHF cases, the presence of all 4 dengue virus serotypes in the Region, and the extensive range of the vector make it necessary to intensify disease prevention and control activities.

Unfortunately, a vaccine against dengue is presently not available. A live attenuated tetravalent vaccine developed in Thailand looks promising but field efficacy

trials have not yet been undertaken. In parallel, efforts are being made to develop a genetically engineered dengue vaccine. Different approaches are being explored such as chimeric infectious clone using dengue-2 attenuated or 17D yellow fever strains as backbones, and a DNA naked vaccine. Despite these efforts it may take 5 to 10 years to have available a safe and efficacious vaccine for the immunization of children.

Therefore vector control is at present the only approach to combat dengue/DHF. Recent discussions concerning a new effort to eradicate the vector from the Americas have not been well received by countries due to its high cost, and the need for hemispheric commitment and implementation and several operational obstacles, such as difficulties in establishing a vertical program and problems of access to certain slum areas due to safety reasons. At a meeting in Caracas, Venezuela, in April 1997, experts recommended a 5-step approach beginning with control programs and leading to eventual eradication.

PAHO has developed guidelines (24) for the prevention and control of dengue/DHF and *A. aegypti* which includes several components that should be implemented together. These components are as follows: 1) Epidemiologic surveillance (active, with laboratory support); 2) Education of the medical community to recognize and properly treat dengue/DHF cases; 3) Entomological surveillance; 4) Vector control with emphasis on source reduction utilizing environmental management (improvement of water supply, adequate solid waste management, naturalistic methods), chemical methods and biologic control; 5) Community participation with efforts oriented towards the elimination or proper handling of potential breeding sites, physical protection of water storage areas and clean up campaigns; and 6) Emergency plans to cope with epidemics of dengue/DHF.

There is a lack of well organized and effective control programs at present as evidenced by the frequent outbreaks epidemics of dengue fever and the increase of DHF in several countries. Emergency measures to combat the epidemics have had limited impact. A reliance on emergency as the basis for response to this disease cannot be successful. Rather, countries must dedicate themselves to coordinated

prevention and control programs in order to be effective.

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**Source:** Division of Disease Prevention and Control, Communicable Diseases Program, HCP/HCT, PAHO.

# Dengue in Cuba

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The Ministry of Public Health officially reported that recent infection by dengue was confirmed in a total of 826 people, with 3 deaths, in the city of Santiago de Cuba, located in the southernmost region of the island, through an active search for cases and serological confirmation IgM using immuno-enzyme methods. The affected area is 36.5 km<sup>2</sup> with a population of 168,000; the total area of the city is 184 km<sup>2</sup> with a population of 465,000. Study of the first cases indicated that initial transmission occurred during the last two weeks of December 1996.

Through viral isolation and PCR, serotype 2 was identified as the etiologic agent of the outbreak. Molecular studies of the strain indicated that it belonged to the Jamaica genotype, which is widely spread in the area and closely related to the occurrence of cases of dengue hemorrhagic fever (DHF) in several countries of the Region.

The predominant clinical symptoms have been that of classical dengue (fever, retro-orbital headache, general discomfort, arthralgia, myalgias and rash). Evolution has been positive, although some patients showed thrombocytopenia and hemoconcentration with hemorrhagic manifestations. Only three cases were classified as presenting of Grade III DHF and the rest as Grade I and II. No cases have been presented in children; they have occurred only in adults.

Preliminary studies of the deceased patients indicated the presence of IgM antibodies in the serum and

anatomical/pathological studies suggested severe symptoms of the disease.

The remaining provinces of the country continue to be free of the disease and vector control measures and epidemiological surveillance were increased in those areas where the vector was detected. Community participation and specific medical care for severe cases of the disease were strengthened.

Dengue was confirmed by the *Pedro Kouri Institute* of Tropical Medicine, Collaborating Center of PAHO/WHO for the study of viral diseases. This represents the first outbreak of dengue in Cuba since 1981, when there were 344,203 cases and 158 deaths, 101 of them in children under age 15.

The presence of dengue in Cuba was confirmed for the first time in 1943, although it may have been the cause of an epidemic in 1902. In 1977, serotype 1 was introduced in the eastern part of Cuba, spreading rapidly throughout the entire country. During that epidemic, which lasted until 1978, were reported 553,132 cases. Since 1992, slow and gradual reinfestation by *Aedes aegypti* found in imported tires has been reported.

**Source:** Ministry of Public Health of Cuba, Weekly Epidemiological Record of the World Health Organization (WHO-WER) and Epidemiological Bulletin of PAHO, Vol. 3, No. 1, 1982.

## Inhibition ELISA : an alternative in the serological study of cases of dengue

In recent years, dengue fever (DF) and dengue hemorrhagic fever (DHF) have emerged as a health problem in the tropics and subtropics and they are now considered the most important arbovirus disease in terms of morbidity and mortality.

The publication *Dengue and Dengue Hemorrhagic Fever in the Americas: Guidelines for Prevention and*

*Control* (Scientific Publication No. 548, PAHO, 1994) summarizes the experiences of a group of experts in the subject and provide guidelines for better control of this disease. The Guidelines suggest the need to strengthen and develop active surveillance systems with a significant laboratory component. In addition to the IgM-capture ELISA for detection of dengue-specific IgM antibodies,

which has been recommended as a very useful tool in serological surveillance, the hemoagglutination-inhibition (HI) technique, which detects total immunoglobulin and utilizes paired serum samples, continues to be applicable as a serological technique capable of confirming the presence of dengue infection, or to classify a case suspected to be dengue from a clinical standpoint as probable, when high titers of antibodies are detected in a single serum sample. HI also makes it possible to determine the presence of a primary or secondary infection.

At the International Dengue Seminar, 1st. Rio Dengue Session which took place from 6 to 9 October, 1996 in Rio de Janeiro, there was discussion of the need to utilize easily attainable immuno-enzymatic methods in diagnostic laboratories in order to be able to replace HI and provide similar results.

The Virology Department of the *Pedro Kouri Institute* of Tropical Medicine, in Havana developed an ELISA Inhibition Method (EIM) which adds the dengue antigen (sucrose acetone) at a dilution of 1:40 to polystyrene plates previously sensitized for 18 hours at 4°C with anti-dengue human immunoglobulin at a concentration of 10 µg/ml and then blocked with bovine albumin at 1%. The next step is to add the sera to be tested in double dilutions from 1:20, incubating for 1 hour and finally adding the peridoxase antidengue conjugate, developing the reaction with orthophenylenediamine (OPD) and hydrogen peroxide. Between each step the corresponding washings are carried out utilizing PBS-Tween20, and incubations are done at 37°C. The antibody titer for each serum is considered to be that at which a % of inhibition  $\geq 50\%$  in comparison with the average DO value of the negative control sera is observed. A test is considered valid if the  $-/+$  ratio of the controls is greater than or equal to 5 (1). The EIM showed a sensitivity, specificity, and coincidence of 100%, 83%, and 93% respectively when compared to HI in a study with single serum samples.

This system has been used satisfactorily since 1987 in the study of sera received through the Dengue Surveillance which has been carried out in Cuba since the

epidemic of 1981; a total of 2,878 serum pairs have been processed as of 1995. It has also been used in the sero-epidemiological surveys carried out in Ecuador (1988) (2) and Panama (1994) to determine the prevalence of antibodies to this agent, using blood samples taken on filter paper (3).

Finally, in a comparative study with HI using 182 sera, it showed a satisfactory correlation ( $r=0.93$   $p<0.001$  and  $r^2=0.86$ ) and made it possible through simple linear regression to determine the expected values for EIM that correspond to different values of HI. This latter analysis made it possible to know that sera with HI antibody titers of 1:1280 (classified as probable dengue cases using HI) correspond to EIM titers of 1:120 and that sera with HI antibody titers of 1:2560 (classified as cases of secondary infection) correspond to EIM titers of 1:240 (4).

The results obtained for several years in the application of this system to the serological study of dengue allow us to recommend it as an easily used diagnostic alternative in the Region's laboratories, which would make it possible to conduct sero-epidemiological studies to define the prevalence of dengue antibodies within an area or country.

If applied in the study of samples received for sero-epidemiological monitoring in each country, it would, based on the antibody titers observed, make it possible to classify cases as primary or secondary dengue infection as well as identify probable cases of infection.

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**Source:** Virology Department of the *Pedro Kouri Institute* of Tropical Medicine, Collaborating Center of PAHO/WHO for the Study of Viral Diseases, Havana, Cuba.



## Serological Proficiency Tests for Dengue

Over the last 15 to 20 years, a gradual increase in cases and epidemics of dengue and of dengue hemorrhagic fever (DHF) has been observed in the Americas. This is primarily due to: (1) geographical expansion and increase in densities of the *Aedes aegypti* mosquito; (2) circulation of several serotypes; (3) deterioration of vector control programs; and (4) insufficient water supply and other significant factors.

Considering the above, the countries, following the lead of the Pan American Health Organization (PAHO), have worked on developing active surveillance systems, which are based on laboratory studies, making it possible to detect outbreaks, the introduction of new serotypes, and to confirm cases of DHF, as well as other important aspects.

Currently, most countries have at least one laboratory where serological diagnosis of the disease is carried out (detection of IgM antibodies through IgM-capture ELISA, detection of total immunoglobulin through hemoagglutination inhibition (HI), and ELISA detection

of IgG). Some countries have even developed laboratory networks. Several countries also have the capacity to isolate and detect dengue, and the utilization of the polymerase chain reaction (PCR) technique is gradually being introduced as a rapid and relatively simple method for detecting the nucleic acid of the agent.

Due to expansion of the diagnosis of dengue, it has become necessary to periodically conduct proficiency tests in order to determine the quality of the diagnosis and to take the necessary measures for those cases that require them.

During 1996 and early 1997, the Virology Department of the *Pedro Kouri* Institute of Tropical Medicine, Collaborating Center of PAHO/WHO for the Study of Viral Diseases, was responsible, in coordination with PAHO, for organizing and developing the Serological Proficiency Tests for Dengue. To carry out the tests, initially panels of sera were prepared and sent to those

**Table 1**  
**Serological Proficiency Tests for Dengue**

<b>Institution</b>	<b>Country</b>
<i>Dr. Julio I. Maiztegui</i> National Institute of Human Viral Diseases	Argentina
Tropical Diseases National Center (CENETROP)	Bolivia
<i>Departmental Laboratory of Public Health, Antioquía</i>	Colombia
Costa Rican Research and Teaching Institute in Nutrition and Health (INCIENSA)	Costa Rica
<i>Dr. Defillo</i> National Laboratory of Public Health	Dominican Republic
<i>Leopoldo Izquieta Pérez</i> National Institute of Hygiene and Tropical Medicine	Ecuador
National Institute of Epidemiological Diagnosis and Reference (INDRE)	Mexico
National Center for Diagnosis and Reference (CNDR)	Nicaragua
Gorgas Commemorative Center for Health Research and Information	Panama
National Institute of Health	Peru
Caribbean Epidemiology Centre (CAREC)	Trinidad and Tobago
Regional Laboratory for Diagnosis and Research on Dengue and other Viral Diseases (LARDIDEV)	Venezuela

laboratories in the region that had agreed to participate in the study.

Each laboratory received two panels, one for determining the presence of IgM antibodies and one for determining the titer of the hemoagglutination inhibiting antibodies. Each panel held 20 sera. To analyze the results obtained in each laboratory, the McNemar and Kappa tests were applied.

Of the twelve laboratories that participated in the study, six showed maximum concordance with regard to detection of IgM antibodies. Five showed variable but acceptable levels of concordance and only one showed unacceptable levels. Eight of the twelve participating laboratories carried out HI titration of antibodies to one or more dengue antigens in the corresponding panel of sera. Upon application of the Kappa test, only one laboratory showed poor concordance, and the others showed good to excellent concordance depending on the antigen processed.

The principal problem observed in the IgM-capture ELISA was detection of false negatives; the principal problem with HI was potentially inadequate titration of antigens. Most of the laboratories utilize antigens prepared

in suckling mouse brain and extracted through the sucrose acetone method, usually obtained from one of the Collaborating Centers of PAHO/WHO in the Region.

Each laboratory was informed of its results, and pertinent recommendations were carried out where necessary.

The results obtained in the Serological Proficiency Tests suggest that for the most part serological diagnosis in the laboratories evaluated is of adequate quality. This type of study should serve as an incentive for other laboratories to take part in the Serological Proficiency Tests as a method of quality control for the diagnosis of dengue in the region and should be carried out periodically.

Table 1 shows the laboratories and countries participating in the study. As can be seen, participants included laboratories from countries with variable degrees of endemic dengue and from different areas in the region.

**Source:** Virology Department, *Pedro Kouri* Institute of Tropical Medicine, Collaborating Center of PAHO/WHO for the Study of Viral Diseases.

## Health Crisis and the INTERNET

### *An International Meeting on Harnessing the Internet for Disasters and Epidemics*

Santa Fe de Bogotá, Colombia - 18 - 21 November 1997

The objective of this meeting is to encourage participants to exchange information and make recommendations on using the Internet for preparedness planning, strategic decision making, and operational coordination of health crisis.

**For more information:**

Pan American Health Organization  
Emergency Preparedness Program  
525 Twenty-third Street N.W.  
Washington, D.C. 20037, U.S.A.

**Fax:** (202) 775-4578

**E-mail:** crisis-internet@paho.org

**Web:** <http://www.paho.org/spanish/disaster.htm>

## A Profile of the Health Conditions of Older Persons of Latin America and the Caribbean

The formal dynamics of fertility, mortality, and age structure implies that the trajectory of vital rates of countries in Latin America over the past forty years will systematically and inexorably lead towards the aging of the population in the continent. This heritage from past trends cannot be tinkered with, halted, or modified in any way, except through unlikely sudden events or bizarre population policies. The die have been already cast.

By the end of 1995, in only five countries: Argentina, Barbados, Cuba, Martinique and Uruguay, the proportion of the population older than 65 approximated or exceeded 10 percent, a level slightly below those attained in Canada and the United States (about 12 percent). However, the bulk of other countries in South and Central America and the Caribbean will attain or exceed such levels very soon, almost surely within the next ten or twenty years. Current projections indicate that for the year 2025, more than half of the countries in the continent will be on their way toward substantial aging of their age structure. Of course, the path toward aging will appear more accelerated if we define more inclusively the older population as the subset aged 60 and above.

The aging of population in the continent will not follow a unique, homogeneous course. Indeed, there will be substantial intercountry heterogeneity in the timing, levels, and other characteristics of the aging process. The timing and speed of past fertility declines will largely determine the timing and speed with which the aging of the age structure is occurring or will occur. Thus, for example, Brazil and Mexico will age later but in a more compressed period of time than Chile and Costa Rica or Uruguay and Argentina. An essentially equivalent, but less dominant, role will be played by the widespread survival improvements in infancy and early childhood that took place during the post-World War II period. Finally, prospective changes in adult and old age mortality will shape the age distribution of the older population, particularly the relative sizes of the youngest old (aged

between 65 and 84) and the oldest-old (aged 85+), and thus determine a most central characteristics of the aging process.

The aging process has a sizable and formidable impact on a number of dimensions that affect the normal functioning of societies and the relative well-being not just of elders but also of the younger generations. The most important among these dimensions are pension and retirement systems, composition of the labor force, family and household arrangements, intergenerational intra-family transfers, and health status and health conditions of elders. The relative importance of each one of these aspects is of course variable and dependent on peculiarities of the demographic regimes and the institutional idiosyncrasy of countries. But, as the experience in Europe and North America plainly demonstrates, none of them is likely to be as paramount and influential as the health status and health conditions of older persons.

The gradual impairment of physical and mental health conditions that accompany the individual aging process the resulting reduction in the expected years of active and healthy life expectancy, the reduction or complete cessation of participation in the labor force and the increased dependency on income transfers from various public and private sources, all dictate that the growth of the older population should lead to mounting demand for health care and health services. Since the most relevant health conditions of older persons are chronic rather than acute and progressive rather than regressive, this demand could also entail steep escalation of health care costs. As the case of the United States, England and most Western European countries attest, these costs can attain formidable magnitudes. Moreover, as the sad experience of Eastern European countries also shows, inability to confront these problems leads to rapid deterioration of the health status of elders and to the shocking loss of years of life expectancy.

The health problem associated with the growth of the

older population also involves important equity issues. First of all, there will be class differentials since members of different social classes will experience sharply different health profiles. Similarly, the ability to access and use comprehensive and high quality health care will differ substantially across social strata. Unless properly addressed, the aging process in these societies will result in sharp increases in inequality in the quality of life and well being of members of different social classes.

Second, there will be gender differentials to contend with since male and females experience very different mortality regimes and are affected by significantly different health problems. Moreover, since women have had a history of lower levels of labor force participation, their access to health care and services when they age will differ substantially from that of men. This is likely to generate important deterioration of women's well being at very old ages, where the majority of them are widowed.

Finally, the growth of the older population will be accompanied by important intercohort differentials. This will occur for two reasons. First, members of different cohorts were exposed to very different regimes of disease, behaviors, and health care during their youth. This is because, as is well known, past exposure to diseases, behavioral practices and health care all affect subsequent health of the individuals. Second, to the extent that the nature of the labor force participation and education of members of a cohort affect their ability to demand and receive resources, younger and older cohorts will experience important differentials in their access to resources in general and to medical and health care in particular.

To understand the nature and magnitude of the health problem and the equity-relevant issues associated with it, to identify the social institutions that will bear the costs, and to ensure that policies implemented in the future translate into acceptable standard of well-being among older persons without unduly eroding equity concerns, it is necessary to evaluate the health status of those who are elders now and, equally importantly, of those who will become elders in the near future.

In a recent review of the health status of elders in Latin America, the authors note with some frustration that "...the

difficulties outlined in this paper associated with the aging of the population in the region are compounded by the lack of adequate information systems which could inform decision-makers on the best course of action for specific problems.

This lack of 'quality data' also prevents the long-term evaluation of interventions: in the absence of baseline data measuring their impact, such interventions become fruitless exercises...".

Whereas in the United States, Canada, Europe and even Asia, aging was anticipated and accompanied by a surge of research into the nature and consequences of the problems associated with it, particularly on the health dimension, nothing of the sort is occurring in Latin America. A recent publication of the United States National Academy of Sciences identifies about 25 surveys, completed or in course, designed to study various aspects of aging, and about half of them are dedicated to health. Similarly, Canada and most countries in Western Europe have fielded or are in the process of fielding numerous surveys which directly or indirectly retrieve information on health status of older persons and other related aspects.

This lack of information in Latin America is worrisome not just because Latin American countries will face problems associated with aging in the very short run but because the combination of demographic regimes and institutional contexts are likely to increase the magnitude of the problems and to force their occurrence in a much more compressed period of time than ever before. This lack of information is also paradoxical for while funding for family planning continues unabated as levels of Total Fertility Rates rapidly dip below 3, only scarce resources are flowing to investigate the aging consequences of the unprecedented sudden and rapid fertility decline for which family planning programs are partly responsible.

Comparative studies on the health conditions of elders in Latin America simply do not exist. The only pertinent and most comprehensive data base ever assembled was produced through an intercountry study sponsored by PAHO. However, the results of these studies are based on protocols that are not consistent across countries and that retrieve information on only the most elementary aspects of health status of elders, necessary but insufficient

to characterize thoroughly the health profile of elders. These studies cannot be used to study the prevalence of important illnesses that are typical among older persons or to compare prevalence across countries, nor can they be utilized to support an understanding of the type of medical and health care that older persons require, demand, and effectively receive. Similarly, these data are of limited value to draw inferences about relations between behavioral aspects of risk profiles and health conditions nor to carry out a study in a comparative perspective to explain how country-specific factors affect the prevalence of physical or mental disability and disease or the extent to which the associated needs of elders are satisfied.

The information on the health status of older persons or, for that matter, any other dimension of the aging process in Latin America, consists of localized studies, most of which are highly selected and thoroughly unsuitable to draw inferences about current and future health status profiles.

In the absence of information of any sort, collection of single country data sets is useful whether or not the data sets resist tests of rigorous comparability. However, for scientific and policy purposes, it is more efficient to invest resources in comparable data sets. As stated before, past demographic trends dictate that the experience of population aging in countries of Latin America will occur at sharply different speeds and so will the societal and economic stressors generated by it. Similarly, each country offers unique social, political, and cultural conditions conforming an institutional context where aging occurs and offering the resources to deal with the problems posed by it.

The nature and magnitude of the aging problem and of all its dimensions is determined by the interaction of these two factors, the demographic regime itself and the socio-political-cultural institutional context. If so, a comparative perspective for the study of any dimension of aging is not only useful but necessary. The study of a single case is not without value—particularly for understanding the case itself—but it is hopelessly limited as a basis for making broad inferences or for drawing sweeping policy implications. Comparative studies have important return to scales and unique benefits relative to a set of unconnected single country studies.

A comparative data collection project about health status and conditions of older persons is invaluable for scientific and policy purposes. Basic research into the aspects that determine health status and conditions among elders requires at the very minimum an assessment of the status and condition among current elderly cohorts. Ideally, the project should be longitudinal and apply protocols already validated elsewhere thus enhancing comparability with the experience of other countries.

Similarly, the foundation of any health policy formulation cannot be erected without an evaluation of current health status and health conditions and an assessment of the relation between current status and conditions, on the one hand, and behavioral and social and economic determinants on the other. The latter is a crucial input for reliable and robust forecasts and projection of the short and medium run of the magnitude and nature of the health demands of older persons.

The Pan American Health Organization has proposed a study that will be carried out in the following seven urban areas: Bridgetown (Barbados); Santiago (Chile); San Jose (Costa Rica); Mexico City (Mexico); Havana (Cuba); San Paulo (Brazil); Montevideo (Uruguay). These are all large urban centers in countries representing a broad spectrum of demographic regimes and institutional contexts. Barbados, Uruguay and Cuba are countries experiencing gradual and 'early' aging in the Latin American context whereas Chile and Costa Rica will do so slightly later, and Brazil and Mexico represent examples of demographic regimes with more sudden but 'late' aging. Similarly, these countries represent a fairly broad population of 'institutional contexts', from one totally relying on the role played by central governments to those where support for the elderly is virtually all in the hands of families and private enterprise. This proposal was prepared by Alberto Palloni, Center for Demography and Ecology, University of Wisconsin-Madison and Martha Peláez, Regional Advisor, Aging and Health, with contributions by Eduardo Arriaga and Kevin Kinsella, of the U.S. Census Bureau.

**Source:** Division of Health and Human Development, Research Coordination Program, HDP-HDD, PAHO.

**Number of reported cases of AIDS by year, and cumulative cases and deaths, by country and subregion,  
as of 10 June, 1997.**

SUBREGION Country or Territory	Number of cases							Cumulative total(b)	Total deaths	Date of last report
	Through 1991	1992	1993	1994	1995	1996	1997(a)			
<b>REGIONAL TOTAL</b>	<b>331,305</b>	<b>103,771</b>	<b>107,143</b>	<b>99,859</b>	<b>91,969</b>	<b>62,134</b>	<b>879</b>	<b>797,227</b>	<b>468,065</b>	
<b>LATIN AMERICA</b>	<b>61,123</b>	<b>22,943</b>	<b>26,455</b>	<b>27,743</b>	<b>27,113</b>	<b>23,143</b>	<b>839</b>	<b>189,487</b>	<b>88,420</b>	
<b>ANDEAN AREA</b>	<b>7,280</b>	<b>2,545</b>	<b>2,471</b>	<b>3,313</b>	<b>2,818</b>	<b>2,520</b>	<b>89</b>	<b>21,036</b>	<b>9,861</b>	
Bolivia	47	19	21	19	14	28	6	154	102	31/Mar/97
Colombia	2,790	931	732	1,324	897	872	...	7,546	3,149	31/Dec/96
Ecuador	198	69	90	117	69	67	...	610	432	31/Dec/96
Peru	1,766	643	659	773	1,043	998	76	5,958	2,220	31/Mar/97
Venezuela	2,479	883	969	1,080	795	555	7	6,768	3,958	31/Mar/97
<b>SOUTHERN CONE</b>	<b>2,722</b>	<b>1,456</b>	<b>1,799</b>	<b>2,468</b>	<b>2,095</b>	<b>2,561</b>	<b>355</b>	<b>13,459</b>	<b>4,877</b>	
Argentina	1,872	1,139	1,414	2,033	1,666	2,055	282	10,461	3,048	31/Mar/97
Chile	535	199	237	292	279	300	21	1,863	1,182	31/Mar/97
Paraguay	70	28	45	24	23	50	19	262	157	31/Mar/97
Uruguay	245	90	103	119	127	156	33	873	490	31/Mar/97
<b>BRAZIL c)</b>	<b>33,004</b>	<b>13,258</b>	<b>14,989</b>	<b>15,572</b>	<b>15,402</b>	<b>11,037</b>	<b>*</b>	<b>103,262</b>	<b>52,099</b>	<b>01/Mar/97</b>
<b>CENTRAL AMERICAN ISTHMUS</b>	<b>3,022</b>	<b>1,226</b>	<b>1,680</b>	<b>1,781</b>	<b>1,933</b>	<b>2,424</b>	<b>367</b>	<b>12,529</b>	<b>3,435</b>	
Belize	46	13	24	18	28	38	...	198	190	31/Dec/96
Costa Rica	324	127	127	163	205	179	...	1,133	606	31/Dec/96
El Salvador	315	114	176	387	380	417	86	1,875	276	31/Mar/97
Guatemala	277	94	178	110	141	831	152	1,787	455	31/Mar/97
Honduras	1673	751	973	878	955	698	81	6,057	1,042	31/Mar/97
Nicaragua	29	10	24	38	21	23	2	152	92	31/Mar/97
Panama	358	117	178	187	203	238	46	1,327	774	31/Mar/97
<b>MEXICO</b>	<b>9,057</b>	<b>3,210</b>	<b>5,058</b>	<b>4,111</b>	<b>4,310</b>	<b>4,216</b>	<b>...</b>	<b>29,962</b>	<b>16,636</b>	<b>31/Dec/96</b>
<b>LATIN CARIBBEAN</b>	<b>6,038</b>	<b>1,248</b>	<b>458</b>	<b>498</b>	<b>555</b>	<b>385</b>	<b>30</b>	<b>9,239</b>	<b>1,512</b>	
Cuba	109	70	82	102	114	78	...	555	381	31/Dec/96
Dominican Republic c)	1,768	372	376	396	441	307	30	3,717	834	31/Mar/97
Haiti	4,161	806	...	...	...	...	...	4,967	297	31/Dec/92
Puerto Rico d)	8,683	2,250	2,374	673	...	...	...	13,980	8,183	30/Sep/94
<b>CARIBBEAN</b>	<b>3,781</b>	<b>1,138</b>	<b>1,318</b>	<b>1,476</b>	<b>1,802</b>	<b>1,564</b>	<b>15</b>	<b>11,135</b>	<b>6,566</b>	
Anguilla	5	0	0	0	0	...	...	5	3	31/Dec/95
Antigua and Barbuda	14	14	17	16	7	13	1	82	26	31/Mar/97
Aruba	11	3	1	0	6	1	...	22	17	31/May/96
Bahamas	838	254	297	322	390	374	...	2,475	1,583	31/Dec/96
Barbados	252	78	88	119	95	130	...	762	637	31/Dec/96
Cayman Islands	11	4	0	3	0	3	1	22	18	31/Mar/97
Dominica	12	0	14	6	5	14	...	51	70	31/Dec/96
French Guiana	230	73	52	70	78	44	...	588	267	31/Dec/96
Grenada	31	4	21	7	18	18	...	99	62	31/Dec/96
Guadeloupe	311	81	77	104	104	54	...	731	226	31/Dec/96
Guyana	230	160	107	105	96	...	...	698	193	30/Jun/95
Jamaica	333	100	236	359	505	527	...	2,060	1,148	31/Dec/96
Martinique	193	44	43	49	38	35	...	402	184	31/Dec/96
Montserrat	6	0	1	0	0	0	...	7	0	30/Jun/96
Netherlands Antilles	100	10	47	0	76	...	...	233	74	31/Dec/95
Saint Kitts and Nevis	31	4	3	5	5	6	...	54	31	31/Dec/96
Saint Lucia	33	8	12	13	10	14	5	95	91	31/Mar/97
St. Vincent and the Grenadines	41	5	8	8	6	19	8	95	93	31/Mar/97
Suriname	106	28	35	20	20	...	...	209	189	30/Jun/95
Trinidad and Tobago	968	263	243	269	340	311	...	2,394	1,619	30/Sep/96
Turks and Caicos Islands	21	4	14	...	...	...	...	39	30	30/Sep/93
Virgin Islands (UK)	4	1	2	1	3	1	...	12	5	31/Dec/96
<b>NORTH AMERICA</b>	<b>266,401</b>	<b>79,690</b>	<b>79,370</b>	<b>70,640</b>	<b>63,054</b>	<b>37,427</b>	<b>23</b>	<b>596,605</b>	<b>373,079</b>	
Bermuda	191	17	15	44	48	17	8	340	238	31/Mar/97
Canada c)	7,672	1,689	1,714	1,637	1,392	717	15	14,836	10,837	31/Mar/97
United States of America d)	258,538	77,984	77,641	68,959	61,614	36,693	...	581,429	362,004	31/Dec/96

\* Cases reported in 1997 are included in 1996.

a) 1997 data are incomplete due to delayed reporting b) May include cases for year of diagnosis unknown. c) Country has revised data d) Cumulative total number of cases and deaths for the United States of America includes data from Puerto Rico. Total number of cases and deaths reported by Puerto Rico as of 30/Sep/94 has not been included in the Latin Caribbean totals.

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## CONGRESSES

### ■ III Chilean Epidemiology Congress Santiago, Chile - 14-17 October 1997

The Chilean Society of Epidemiology is sponsoring the III Chilean Epidemiology Congress, which will be held in Santiago on 14-17 October 1997.

Pre-Congress courses will be conducted on 14-15 October. The Congress, to be held on 15-17 October, will consist of plenary sessions, round tables, work sessions, and poster design.

Papers will be presented on the following topics:

1. Environmental and occupational health: risk assessment and exposure.
2. Chronic diseases, mental health, accidents, and nutrition.
3. Communicable diseases: classical, emerging, zoonoses.
4. Health systems management: surveillance in health, equity, quality, prioritization.
5. Research and education: design, analysis, curriculum innovations, teaching techniques.

To register, contact:

Francisco Cumsille G.  
Sociedad Chilena de Epidemiología  
Casilla 52.750, Correo Central, Santiago, Chile

For additional information, telephone: 638 42 48 or 632 72 56 in Santiago, Chile.

### ■ VIII Colombian Epidemiology Congress Bucaramanga, Colombia 6 - 10 October 1997

The VIII Colombian Epidemiology Congress will be held from 6 - 10 October 1997 in Bucaramanga, Colombia. The central theme will be devoted to epidemiology of chronic diseases.

In addition to presentations and discussions of research results, five pre-congress workshops will be held on the following subjects: Clinical Epidemiology, Cases and Controls, Geographic Information Systems in Epidemiology, Epidemiology and Health Services, and Writing Scientific Articles.

For more information, please contact:

Asociación Colombiana de Epidemiología (ASOCEPI)  
Calle 74 A # 49-63. Conjunto 1, casa 94. Palmeras del Cacique  
Bucaramanga, Colombia  
E-mail: asocepi@b-manga.cetcol.net.co

### ■ I Venezuelan Congress of Epidemiology II Andean, II Latin-American and III Ibero-American Congresses of Epidemiology Caracas, Venezuela - 17 to 21 November 1997

The **central subject** of the event will be: *Epidemiology and health policies*. Conferences will be presented on: Epidemiology, health policies, and development; Health sector reform; Public health surveillance; Society, culture, and epidemiology; Evolution of paradigms in epidemiology.

**Pre-Congress courses:** Qualitative models; Environmental epidemiology; Health services evaluation; Geographic information systems in epidemiology; and Nosocomial Infections.

For more information:

**Dirección General Sectorial de Epidemiología**  
Edif. Sur Piso 8. Oficina 818. Centro *Simón Bolívar*.  
El Silencio, Caracas, Venezuela  
Sede del Ministerio de Sanidad y Asistencia Social  
Telephone: 02-482 2139; 481 7727  
Caracas, Venezuela

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# EPIDAT

## Epidemiological Analysis of Tabulated Data

### Version 2.0 for Windows - June 1997 Coming soon

*Epidat 2.0 is a software package for use by epidemiologists and other health professionals who habitually manage tabulated data. Its objectives are to complement other statistical software packages that utilize databases and to provide an instrument to facilitate and support the teaching of epidemiology.*

*This second version is a Windows® application and consists of the following modules:*

**Rate adjustment.** - This software makes it possible to introduce the data manually or import them in .DBF format. As many rates as the user desires may be adjusted simultaneously, either directly or indirectly.

**Sampling.** - It calculates the minimum sample size for estimates of prevalences and means, case-control, and cohort studies, and verification of the quality of batches. It also generates pseudorandom numbers.

**Agreement.** - It analyzes the agreement between two or more observers, with two or more classification categories. It also contrasts kappa equality hypotheses.

**Tables.** - It analyzes 2x2 tables from cross-sectional, case-control, or cohort studies in simple or stratified tables. In paired case-control studies it permits up to four controls per case. It incorporates the Bootstrap method for calculating confidence intervals. It makes specific calculations in MxN tables if the categories are ranked. It incorporates the Chandra-Sekar-Deming capture-recapture method and the Knox method for cluster detection.

**Diagnostic tests.** - It calculates the sensitivity, specificity, and predictive values of simple, serial, and parallel diagnostic

tests. In combined tests it makes the calculations if it has either the cell values or the sensitivity and specificity values of each test. It makes it possible to produce ROC curves, calculating the area under the curve and the optimal cut-off point if the prevalence and cost ratio are known.

**Inference.** - It makes it possible to contrast equality of averages and proportions hypotheses with one or two dependent or independent samples and to calculate confidence intervals.

**Prioritization.** - It proposes a simple method for the determination of health priorities (CENDES/PAHO), based on user-defined indicators and areas. Epidat 2.0 is a freely-distributed program developed by public institutions. Consequently, dissemination is not only permitted, but encouraged, together with any criticisms or observations that may help to improve future versions.

Program developed by the *Servicio de Información sobre Saúde Pública de la Consellería de Sanidade and Servicios Sociais de la Xunta de Galicia* and the Program on Health Situation Analysis (HDP/HDA) of the Pan American Health Organization, PAHO.

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