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Chagas' Disease

Introduction

Chagas' disease, or American trypanosomiasis, is a parasitic disease caused by the hemoflagellate *Trypanosoma (Schizotrypanum) cruzi,* which is transmitted to man and other mammals mainly by hematophagous insects of the sub-family *Triatominae.* The disease occurs exclusively in the Americas, and is distributed in rural areas from Mexico to the northern part of Argentina, wherever the ecological conditions permit the vectors to come in contact with human dwellings (Fig. 1).

The Parasite and its Biological Cycle

T. cruzi evolves in invertebrate hosts (triatomine bugs commonly called "kissing bugs," "barbeiros," "chinches," "chipos") and in vertebrate hosts (man, dogs, cats, rodents, and other domestic and wild mammals). The triatomine bugs become infected by ingesting blood with circulating trypanosomes from infected mammals. These blood forms evolve to metacyclic trypanosomes in eight to 10 days while in the digestive tract of the insects. These infective forms are then eliminated in the feces. The biological cycle in the vertebrate host starts with the penetration of the infective form through the skin or the ocular conjunctiva and other mucous membranes. The parasite rapidly invades fibroblasts and adipose cells underneath the skin as well as several organs and tissues: spleen, liver, bone marrow, kidneys, nervous tissue, lymph nodes, and striated muscle (heart).

Modes of Infection

In man, *T. cruzi* is transmitted by "contamination" with the triatomine bug feces. The transmission of the parasite can be through blood transfusion, the placenta (congenital) or through accidental contact with the blood of infected animals.

The penetration of the parasite through the ocular conjunctiva usually provokes a local inflammatory reaction characterized by painful unilateral edema of both eyelids, enlargement of the lacrimal sac without mucous secretion, and enlargement of the pre-auricular lymph nodes. This sign, called "ocular sign" or "Romaña's sign," is characteristic of the acute stage of the disease. The penetration of the parasite in other parts of the body causes a local in-

IN THIS ISSUE ...

Figure 1. Geographic distribution of Chagas' disease.

flammatory reaction called "Chagoma of inoculation." Both inflammatory reactions are due to the multiplication of the parasite in the underlying cells.

Blood transfusion is apparently the second most important way of transmission, since 1 to 15 per cent of serologic reactors have been detected among groups of blood donors examined in several Latin American countries *(1)*.

Vectors and Epidemiology

More than 50 species of triatomine bugs have been reported to be naturally infected with *T. cruzi,* and about a dozen are epidemiologically important as vectors. *Triatoma infestans, Rhodnius prolixus,* and *Triatoma dimidiata* are well adapted to the human dwelling and represent the principal vectors *(2)*.

The public health impact of Chagas' disease is not clearly defined in most countries. Reliability of statistical data is questionable since notification of the disease is not compulsory. Despite the phenomenon of migration of the rural population into urban areas and the consequent "urbanization" of the disease in some countries, it remains basically a rural problem associated with poor socioeconomic conditions in the population, and the domestic nature of the vector.

It is estimated that at least 20 million persons in rural and urban areas are infected with *T. cruzi.* Argentina, Brazil, Chile, Uruguay, and Venezuela are the countries where the disease has been more widely studied, and national or provincial programs to control the disease are underway.

Three types of transmission cycles of *T. cruzi* are considered: the *domestic cycle,* which is maintained by man, domestic animals (dogs, cats) and domestic triatomine bugs; *the wild cycle,* which involves rodents, marsupialia, and other wild mammals and the wild triatomine bugs, and *the peridomestic cycle,* which can be considered as a link between the other two cycles. The last cycle is integrated by the mammals (domestic rodents, marsupialia,guinea pigs, dogs, and cats) that move back and forth from the field into the human habitation, and by the wild triatomine bugs that invade the houses attracted by light or blood sources *(3)*.

The domestic cycle is undoubtedly the most important cycle in maintaining the Chagas' infection in rural and semirural areas in Latin America, since man and animal reservoirs live together in the house. Primitive houses still existing in such areas, with walls made of adobe or bahareque and covered with thatched roofs, constitute an excellent habitat for the vectors. They live and multiply in cracks in the walls, in beds, roofs, behind pictures, and in boxes where people keep and transport clothes and other personal effects from house to house when they move *(2)*.

Chagas recognized the role of rural housing and the environment in the epidemiology of the disease. Products used in the construction of dwellings and wood piled for cooking have been found to have a possible role in linking the parasite to man. One such example is the common use of palm tree leaves as material to build roofs and walls of houses and outbuildings. Certain vectors, such as *R. prolixus,* glue their eggs to the leaves, allowing for colonization to develop in the building. On the other hand, *T. dimidiata* has been known to inhabit wood used for cooking, and *T. infestans* can be found in cactus and wood in corrals.

The importance of the peridomestic and wild cycles is still under careful investigation. *T. cruzi* isolates of known human origin, and *T. cruzi*-like trypanosomes isolated from animals and triatomine bugs need to be studied and typed in order to better define the epidemiology of Chagas' disease. The existence of trypanosomes in domestic and wild animals which are morphologically similar to *T. cruzi* is well known, but their human infectivity and pathogenicity has not been clarified satisfactorily. Several research laboratories are currently studying the structural, biochemical, and immunopathologic characteristics of freshly isolated trypanosomes of different origins *(4)*.

Clinical Manifestations

The clinical manifestations of *T. cruzi* infection in man are affected primarily by intraspecific variations of the parasite, and the immune response of the host *(5)*. The

amount of the inoculum, the number of infections, and the age and nutritional state of the host are under investigation.

The prepatent period is about five days, and the incubation period lasts from five to 10 days. The infection usually evolves into acute and chronic stages of the disease.

The *acute stage* occurs more often in the first years of life, and lasts for one to three months. Continuous moderate fever (37.5-38.5°C) and the ophthalmoglandular syndrome (Romaña's sign) are the principal symptoms reported in children and young adults. Sometimes local edema of the face is seen, especially when Romaña's sign is present, or generalized edema in infants. Splenomegaly and hepatomegaly are reported, as well as enlargement of the lymph nodes particularly in the pre-auricular and submaxillar regions. Leucocytosis is moderate, with increase of the monocytes and lymphocytes. Severe infections in children may be accompanied by tachycardia, decreased blood pressure, gallop rhythm, and electrocardiographic changes. Severe myocarditis or acute meningoencephalitis are the terminal stages in fatal cases.

The *chronic stage* of Chagas' disease manifests itself 10 to 15 years after the infection through slowly evolving heart damage, which includes cardiac enlargement. There is an asymptomatic or latent period between the acute and chronic stages, which is usually evidenced only by transient parasitemias and serologic reactivity of the patients affected.

Digestive manifestations of *T. cruzi* infections, mainly megacolon and megaesophagus, have been reported principally in central Brazil. The prevalence and severity of chagasic myocardiopathy and digestive changes vary with the geographic region. The factors involved in this variation are under investigation *(4)*.

In the acute stage of the disease, the interstitial edema and the inflammatory reactions produced by the multiplication of the parasite damage the contractibility of the heart muscle. In the chronic stage, these lesions are replaced by fibrosis and the damage becomes irreversible. Aneurysmal dilation of the ventricular wall or the apex may occur. Sudden death can happen due to paroxysmal tachycardia and ventricular fibrilation.

Immunopathogenesis

The lack of relationship among parasitic nests and heart tissue lesions found in individuals with chronic chagasic myocardiopathy had suggested that an allergic reaction could be involved in the pathogenesis of the chagasic myocarditis (Reviewed in *6,7*). One possibility would be that cell mediated immunity is involved in the origin of lesions. In fact, lymphocytes from rabbits experimentally infected with *T. cruzi* or inoculated with fractions of dead parasites were able in vitro to destroy allogenic infected or non-infected rabbit heart cells. Moreover, the inoculation of the parasite fractions in this host induced heart lesions that histologically may resemble what could be found in infected humans. Similarly, lymphocytes from infected humans were able to react in vitro with non-infected mouse heart cells but not liver cells, and with infected and non-infected fetal human heart cells. Therefore, it seems reasonable to think that there are common antigens among *T. cruzi* and heart tissue, and that lymphocytes that would react against heart tissue are present in chagasic individuals (Rev. in *7*). However, it is not yet known whether this sensitization is the origin of the lesion or a consequence of it.

In recent years, immunoglobulins (Igs) which react with the hosts' tissue have been found in patients with different clinical forms of Chagas' disease. These antibodies react against endocardium, vascular structures, and interstitium of striated muscle (Rev. in *7,8*).

These antibodies have the following characteristics (Rev. in *7-9*):

- They are more commonly found in sera from cases of Chagas' disease than any other parasitic diseases or pathological conditions.
- In adults with Chagas' disease, they are more prevalent in cases with cardiac symptomatology than in asymptomatic ones.
- Their discovery, in some cases, was associated with the presence of skeletal muscle lesions, and intracellular myocardial alterations. In addition, biopsies of the cardiac and skeletal muscle of infected humans showed the existence of Ig deposits in the plasma membrane of these tissue cells.
- They have induced morphological and functional alterations in rat myocardial cells in vitro, apparently through modifications of the β adrenergic receptors.
- They may have in vitro influence on the postsynaptic sites of the plasma membrane of pacemaker cells, possibly acting as a partial β agonist.

Antibodies reacting against neurons and Schwann cells of peripheral nerves have also been found in the serum of acute and chronic cases (Rev. in *10*). Since it has been suggested that the lesion of the autonomic nervous system in the cardiac muscle and digestive tract may be the pathological mechanism for the lesions, these antibodies may play an important role in the pathogeny of Chagas' disease (Rev. in *10,11*).

Absorption experiments have suggested that these antibodies cross-react with antigens shared by the parasite and the human host (Rev. in *7,8*). Recently it has been shown that the host antibody is in the laminin, a glycoprotein from the basement membrane, and that a laminin-like molecule is present in the parasite *(12)*. On the other hand, the use of monoclonal antibodies against the dorsal

root ganglia membrane has also defined antigenic determinants which are common to *T. cruzi,* neurons, and cardiac muscle cells *(13).*

These findings suggested that host tissue-reacting Igs may be the origin of the cardiac lesion found in chronic Chagas' disease, which would support the earlier assumptions that pathogenesis of the disease was linked to an immunologic reaction of the host *(6-8).* Moreover, detection of these tissue-reacting antibodies may be a useful prognostic tool for the infection. However, later reports based on samples obtained from cases from other geographic areas confirmed the presence of tissue-reacting immunoglobulins but not their relationship between their presence and the existence of symptoms or their severity *(10,14, 15).* Identification of common antigens against the parasite and its human host may nevertheless provide useful information on the host-parasite interaction. In the event that vaccination attempts are made, the production of antigenic preparations that will not cross-react with human tissue components may be carried out.

Diagnosis

The diagnosis of Chagas' disease is based on the presence of *T. cruzi* in the blood. Xenodiagnosis, blood culture in agar, blood concentration by centrifugation, and direct fresh blood examination between slip and coverslip are the parasitologic techniques used to detect *T. cruzi* in both acute and chronic human infections.

There are also four serologic techniques which coincide in sensitivity and specificity: (a) the complement fixation test (CFT) or Guerreiro-Machado's reaction; (b) the indirect hemagglutination test (IHA); (c) the immunofluorescent test (IFA); and (d) the direct agglutination test (DA). The IHA, IFA, and DA become reactive earlier than the CFT, usually within three months after the infection; the CFT requires at least three months to become reactive. A new technique, the enzyme-linked immunosorbent assay (ELISA) is under intensive study with promising results.

A presumptive diagnosis can be established by taking into account the clinical manifestations (especially those related to chronic heart damage), reactive serologic tests (preferably two of them), and a history of having lived in an endemic area. In patients under 20 years or over 50 years of age, rheumatic heart disease and coronary atherosclerosis have to be ruled out, respectively. In endemic areas, Chagas' heart disease has to be differentiated from other myocardiopathies, and efforts to establish a parasitologic diagnosis is highly recommended.

Treatment

Many chemical compounds have been subject to extensive studies in Chagas' disease, but at the moment only two have shown some activity against the *T. cruzi.* They are: Nifurtimox, which has a 5-nitrofur furylidene derivative (Lampit, Bayer 2502)* and Benznidazole (RO 7-1051, Radanil, Rodragen) which is a 2-nitroimidazole derivative. The drug Nifurtimox has shown experimentally in laboratory animals and in clinical trials that it is effective in the acute stage of the disease. A cure rate between 75 to 90 per cent of patients treated has been reported by several South American investigators. In the chronic stage of the disease, definite results are still under evaluation since the parasitemia disappears but the serologic reactivity remains for years after treatment. It has been observed, however, that the heart damage remains apparently stationary in patients under treatment with evolutive heart disease. The problem with this drug is its toxicity, which causes collateral symptoms such as anorexia, weight loss, nausea, vomiting, convulsions, headache, vertigo, and insomnia, which appear 15 to 20 days after the initiation of treatment, especially in adults. Children tolerate the drug very well. The dosis of Nifurtimox actually recommended is between 8.5 to 12.5 mg per kg of weight, per day, during 90 to 120 days.

Benznidazole is also under careful investigation in the treatment of acute and chronic infections of the disease.

Control

Since *T. cruzi* infection depends on the distribution of domestic *Triatominae,* control measures are, fundamentally, directed to eliminate these insects from the human environment. Insecticides and housing improvement have been the most common and successfully used control measures. Health education of the population in endemic areas is also an important aspect of control.

The most commonly used insecticides with residual action are: benzene hexachloride (BHC, HCH, gammoxane), dieldrin, and a methylcarbamate (OMS-33, Baygon, propoxur). Problems have arisen concerning the high cost of these insecticides as well as the resistance shown by some of the vectors in certain areas.

The construction or repair of human dwellings seems to be a very promising and permanent control measure to eliminate or importantly reduce the *T. cruzi* transmission to man. In 1943, Dias began the first construction project in Brazil, which pioneered the concept of house improvement as a preventive measure in the control of Chagas' disease.

Since 1960 Venezuela has progressively reduced the infestation of houses by *R. prolixus* through periodical insecticide spraying and the substitution of palm roofs with tin ones in rural houses in endemic areas. The effect of such combined control measures on the transmission of *T. cruzi* has been shown by reduced seropositivity in adult and children population samples surveyed in the state of Lara

*Use of trade names and commercial sources is for identification only.

in 1980-1981 (13.1 per cent), in comparison with surveys performed in 1959-1968 (44.4 per cent) when the control was established. In children 0-9 years old, the seropositivity dropped to 1.3 from 20.5 per cent in the same period *(16)*.

In 1979, with assistance from PAHO and the Edna McConnell Clark Foundation, the Government of Venezuela began a pilot project aimed at defining the role of rural housing in the continued transmission of *T. cruzi*. The study area selected was in the State of Trujillo where the Government was in the process of modifying rural housing.

The initial construction phases of the project did not include community participation or other socioeconomic considerations. Houses were either improved or new ones built depending on the cost of repair. No modification took place unless the criteria of land ownership or property agreements were met. Improvements consisted of plastering mud walls, cementing floors, and adding zinc roofs. The new houses used a standard design with cement block walls, zinc roofs, and cement floors.

Evaluations included preconstruction and routine postconstruction, entomologic searches for vectors, xenodiagnostic examination of dogs, cats, and some domestic rodents, and serologic and electrocardiologic examination of the occupants. Similar evaluations were made in a check area in Portuguesa State receiving periodical insecticide treatment.

The housing improvement was found to significantly reduce infestation indices (from 62.4 per cent at preconstruction to 18.8, 5.2, and 2.8 per cent at, respectively, 8, 18, and 24 months postconstruction). Initially some of the modified and new houses were infested with *R. prolixus*. This was due to returning infested personal belongings to the houses. Although the study is not complete, it does demonstrate that house improvement can make houses virtually vector free for a period of time.

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(Source: Parasitic Diseases and Vector Control, Division of Disease Prevention and Control, and Research Promotion and Coordination, Division of Human Resources and Research, PAHO.)

Diseases Subject to the International Health Regulations

Cholera, yellow fever, and plague cases and deaths reported in the Region of the Americas as of 30 June 1982.

Country and administrative subdivision	Cholera cases	Yellow fever		Plague cases
		Cases	Deaths	
BOLIVIA	–	*92*	*34*	*1*
Beni	–	1	–	–
Cochabamba	–	2	–	–
La Paz	–	2	2	1
Santa Cruz	–	87	32	–
BRAZIL	–	*16*	*16*	*30*
Ceará	–	–	–	26
Maranhão	–	1	1	–
Mato Grosso	–	1	1	–
Mato Grosso do Sul	–	13	13	–
Pará	–	1	1	–
Pernambuco	–	–	–	4
PERU	–	*4*	*4*	–
Loreto	–	3	3	–
Madre de Dios	–	1	1	–
UNITED STATES	–	–	–	*4*
Arizona	–	–	–	2
New Mexico	–	–	–	1
Texas	–	–	–	1

– None.

Operational Aspects of Leprosy Control Programs[1]

Leprosy control strategy is based on the early detection of cases and the administration of adequate chemotherapy to interrupt transmission, cure the patient, and prevent the development of disabilities.

The study group convened by WHO in 1981 recommended the application of a combined treatment regimen that uses intermittent supervised administration of drugs and is shorter than the traditional treatment. This schedule, duly adapted to local conditions and resources, should be tested in the field. Follow-up of the patients that have completed treatment will make it possible to discover relapses and thus again administer treatment and evaluate whether the length of treatment adopted is sufficient to cure most of the cases.

It is recommended that a triple drug combined treatment be administered to all multibacillary patients: new previously untreated patients, those that have responded satisfactorily to prior dapsone monotherapy, those that have suffered clinical relapses after receiving dapsone monotherapy, and those with clinical relapses and with resistance confirmed in mouse footpads.

[1]This article continues the discussion begun in Vol. 3, No. 2 (1982) of the *Epidemiological Bulletin*, "Drug Resistance in the Treatment of Leprosy."

The schedule should be applied until the patient is rendered bacteriologically negative for a period of not less than two years. Its component drugs are as follows:

- Rifampicin (600 mg once-monthly, supervised administration).
- Dapsone (100 mg daily, self-administered).
- Clofazimine (300 mg once-monthly, supervised administration, and 50 mg daily, self-administered).

In paucibacillary patients it is recommended that two drugs be applied for a period of six months:

- Rifampicin (600 mg once a month, supervised administration).
- Dapsone (100 mg daily, self-administered).

The control services staff should promptly identify persons with skin lesions as presumed symptomatic patients. Reports received from the general health services, community leaders, and the patients themselves should be investigated. Contacts, especially children living with infectious cases, should also be examined and contacts of cases with open lesions should be examined annually.

In all new cases (suspected or confirmed) a bacteriological examination of the border of active lesions, the ear lobe, and the nasal mucosa is recommended. The bacteriological index continues to be the most sensitive and practical method for field work in the programs.

New knowledge of resistance to drugs used in the treatment of leprosy has led to the incorporation of more potent drug combinations in the treatment of multibacillary and paucibacillary patients and to a review of the operational aspects of leprosy programs.

The intermittent combined treatment regimen calls for uninterrupted and continued supervision by the health services staff. The use of these regimens is full of uncertainties because of irregularity in the ingestion of the drugs and the high frequency of abandonment of treatment (whether due to the negligent and inhuman treatment received by the patient, the services' inconvenient working hours, lack of access to institutions, limited supply of drugs, patients' low educational levels, etc.).

If the program is to be successful, previous measures should be taken to train and guide personnel. The highest priority should be assigned to treatment within the program, and the development of operations research that will provide new knowledge of the problem and permit it to be applied in each situation should be encouraged.

The approach emphasizes the need to organize health education systems aimed at community leaders, schoolteachers, and rural health workers so they can adopt a sensible attitude to the disease and actively cooperate in supervising its treatment. The principal purpose of health education is to provide a knowledge of the characteristics of the disease and its lengthy course, combined treatment regimens, possible resistance due to monotherapy or inadequate therapy and the serious disabilities caused by the disease, as well as rehabilitation activities.

Every leprosy control program should have a data collection, recording, analysis, and distribution system that will make it possible to plan and evaluate all control measures, especially strategies for combined treatment regimens. Without systematic evaluation it is impossible to know whether the program is operating properly and achieving the objectives proposed, or whether changes and adjustments are required.

WHO has proposed a leprosy epidemiological information system that will permit evaluative comparisons of the control measures applied. The system will measure the efficiency and effectiveness of the programs against well-defined standards and strategies and will cover individual (clinical, administrative, socioeconomic aspects), operational (case detection, treatment, relapses, and coverage rates) and epidemiological (incidence and prevalence) information. Table 1 shows the operational indicators proposed for evaluating leprosy control programs.

To adopt combined treatment regimens, sufficient amounts of the three drugs recommended (rifampicin, dapsone, and clofazimine) must be available. An adequate supply calls for budgets that will ensure their prompt and continuous delivery to the services.

In addition to including the combined treatment regimens into the technical and operational elements of the program, it will be necessary to retrain the personnel to use it. Indeed, control services personnel should be trained to find alternatives in the administration of the treatment. Leprosy control manuals should include information on the organization and supervision of the treatment and the combinations, delivery, and possible side-effects to the drugs. The learning process needs to be continuous and should therefore be incorporated into the existing general health structures.

Likewise, research in new areas will be necessary. For example, more information must be obtained about clofazimine and ethionamide/protionamide. The optimum dosage of clofazimine for monthly intermittent administration or its relationship to skin pigmentation is still not known with certainty. Nor is sufficient information available about the bacteriostatic effect of ethionamide and protionamide on *Mycobacterium leprae* when administered intermittently. The minimum daily dosage of these toxic and expensive drugs is the same as that used against tuberculosis (500 mg); the basis for this dosage is that *M. leprae* is more susceptible to the drug than is *M. tuberculosis*. The development of new bactericidal drugs that use different attack mechanisms should be promoted.

Since the treatment regimens recommended for the control programs have not yet been used, it would be advisable to investigate their practicality and acceptance by the patients. Furthermore, the continuation of research aimed at the preparation of an effective vaccine is of worldwide interest.

Table 1. Operational indicators for the evaluation of leprosy control programs.

Activities	Indicators	Information
Case detection	Case detection coverage rate	Population served/population covered
	Annual incidence rate	Number of reported cases/population
	Proportion of lepromatous cases	Number of lepromatous cases/total cases
	Proportion of contacts examined	Number of contacts examined/contacts registered
	Age of cases	Number of new cases in children and adults/cases detected
Prevention of disabilities	Proportion of new cases with disabilities	Number of cases with disabilities/cases detected
Treatment completed	Treatment completion rate	Number of cases that completed treatment/cases reported
Regular treatment	Treatment attendance rate	Number of cases regularly treated/cases registered
	Annual treatment abandonment rate	Number of cases than abandon treatment/cases under treatment
	Proportion of patients recovered for control	Number of cases that resumed treatment/patients that abandoned treatment
Adequate treatment	Annual bacteriological negativization rate	Number of bacteriologically inactive cases/positive cases per year
	Patient discharge rate	Number of cases out of treatment/cases treated per year
Number of relapses	Annual reactivation rate	Number of relapses/cases out of treatment and under surveillance

Finally, to provide patients with comprehensive care, the program should include a disability prevention component. The need to find practical solutions to the problem of disabilities calls for active participation at the primary level of all the pertinent elements so as to ensure that the activity is carefully planned and adapted to the conditions in each country, to the environment, and to the patients' aptitudes and skills. The early prevention of disabilities is a real problem in Latin America, in particular because of socioeconomic and cultural factors.

(*Source:* Leprosy Control Program, Division of Disease Prevention and Control, PAHO.)

Dengue in Puerto Rico

Epidemic dengue type 1 occurred in Puerto Rico during the summer and fall of 1978 as part of the pandemic which affected most of the Caribbean region between 1977 and 1980. During 1979, 1980, and the first months of 1981, dengue transmission was sporadic with only a few confirmed cases occurring each month. All viruses isolated during that time were dengue 1. Beginning in late July and early August 1981, the number of reported cases of dengue-like illness began to increase, and by early September it was clear that an outbreak of dengue was in progress. The number of cases increased dramatically in September, peaked in October, and began to decline in November 1981 (Fig. 1). By December, few cases were being reported. Approximately 70 paired sera per week were tested for dengue infection by HI, with an average of 48 per cent confirmation. Cases were reported from all over the island, but the area of highest transmission was the southwest coast.

Figure 1. Reported dengue cases in Puerto Rico by week of onset, 1981.

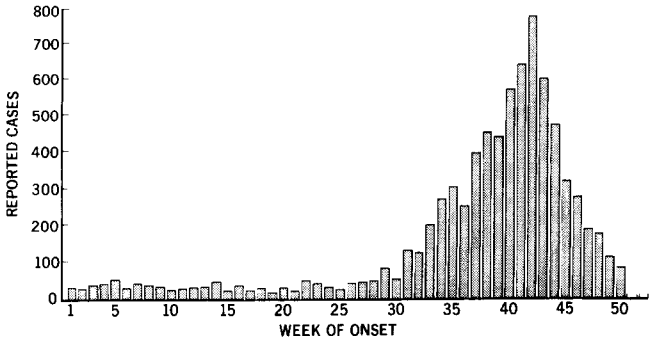
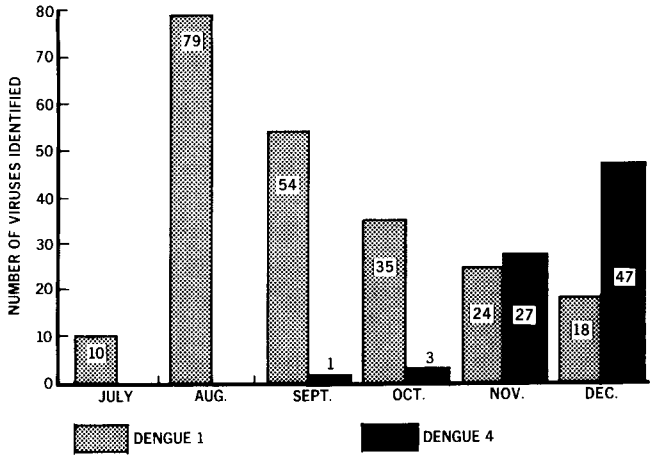


Figure 2. Dengue viruses isolated and identified in Puerto Rico, July-December 1981.



A total of 298 dengue viruses were isolated from patients with onset of illness between 1 July and 31 December 1981. Most (220) were identified by complement fixation and/or monoclonal antibody as dengue 1. The distribution of these isolates was islandwide, but as might be expected, the majority were from the southwest coast.

Dengue 4 was first isolated in Puerto Rico from a patient with onset in September, although serologic evidence suggested it was on the island as early as August 1981. Transmission of this serotype remained sporadic during October, increased in November, and by December, was the dominant virus isolated in Puerto Rico (Fig. 2). Dengue was reported as increasing again during the first two months of 1982. Nearly 50 per cent of these cases were from the San Juan metropolitan area and most of the new transmission appeared to be dengue type 4.

Dengue Virus Isolation

The use of specific monoclonal antibodies greatly facilitated the identification of dengue viruses. Although this technique can be used to identify dengue viral antigen in mosquito brain squashes, it requires a minimum of six and preferably 12 known positive mosquitoes. This means that most isolates must be passed in mosquitoes at least once after isolation and thus delays the identification process, whether by monoclonal antibody or complement fixation. Although less sensitive, the use of mosquito cell lines to isolate dengue viruses and the subsequent use of monoclonal antibodies to type the viruses requires much less labor and allows processing of larger numbers of samples.

These procedures were initiated during the 1981 dengue epidemic in Puerto Rico. As a part of this transition, three mosquito cell lines, Igarashi's clone C6/36 of *Aedes albopictus*, *A. pseudoscutellaris* (AP-61), and *Toxorhynchites amboinensis* (TRA-284) were compared for sensitivity to dengue virus and ease of handling. Cells were grown in either disposable tubes (16 x 125 mm) or in plastic flasks (25 cm^2) and simultaneously inoculated with 0.05 ml each of undiluted sera collected from patients in acute phase of dengue-like illness. After a 10-day incubation period at 28°C, the cells were spotted on slides, fixed with cold acetone, and processed for virus isolation and identification using a direct fluorescent antibody test (DFA) for screening and indirect (IFA) with monoclonal antibodies for identification.

The results obtained with 83 sera are shown in Table 1. The AP-61 and TRA-284 lines were most sensitive with 31 and 29 isolates, respectively. Only 25 isolates were obtained with the C6/36 cells. It will be noted that some of the viruses isolated in C6/36 and AP-61 cells could not be typed. This was due to the small number of cells infected and the small amount of antigen detectable by DFA but not by the monoclonal IFA. These sera have been inoculated into mosquitoes for confirmation.

In addition to virus isolation rate, the three cell lines were compared with respect to the following criteria: (1) ease of handling and cultivation; (2) brightness of fluorescence; (3) resistance of sera to toxicity; (4) growth rate in different types of culture vessels; and (5) cost/culture/specimen. While ease of cultivation was nearly the same for all three cell lines, *A. albopictus* cells were the best in terms of uniform dispersal of cells (without clumping) on

Table 1. Comparative sensitivity of three mosquito cell lines for isolation of dengue viruses in Puerto Rico.

Cell line	No. sera inoculated	Number and types of dengue isolates			
		D1	D4	Unknown	Total
C6/36	83	5	16	4	25
AP-61	83	8	21	2	31
TRA-284	83	9	20	0	29
All cell lines	83	9	26	2	37

spot slides. Intensity of fluorescence was similar for all cell lines, but easier to read in C6/36 because the cells were never disrupted. TRA-284 and AP-61 cells were generally more resistant to serum toxicity than *A. albopictus* cells. While both *A. albopictus* and AP-61 cells grew well on glass as well as on plastic surface, TRA-284 cells did not grow well on glass tubes. The cost of tube culture was far less expensive than that of plastic culture. These advantages and disadvantages will be evaluated for the selection of a cell line for routine dengue virus isolation/identification.

(*Source:* San Juan Laboratories, Center for Infectious Diseases, Centers for Disease Control, San Juan, Puerto Rico, U.S.A.)

Diarrheal Diseases

An Overview of the Situation in the Americas

Diarrheal disease constitutes a clinical syndrome of varied etiology which includes specific infectious diseases such as shigellosis, salmonellosis, amebiasis, as well as other diseases caused by bacteria, protozoa, viruses, and helminths.

In Latin America, these diseases constitute a major public health problem, especially among children under 5 years of age. However, in most countries, it is difficult to determine the extent of the problem accurately. In both urban and rural areas, current clinical and laboratory services are not always adequate to identify these infectious agents and the etiologies of reported diarrhea episodes are often unknown. Furthermore, the number of cases and deaths reported does not reflect the magnitude of the problem caused by the diseases due to limitations of surveillance systems. More specifically, reliable morbidity data for diarrheal diseases are difficult to collect because of reporting constraints characteristic of many national health systems. The coverage and quality of case reporting varies from country to country and by geographic regions within the same country. Other factors which influence the data include the extent to which various populations receive health care services and the completeness of disease surveillance by those services.

Mortality data offer more opportunities for analysis, but similar shortcomings may exist. For example, infant deaths may be underreported and the cause of death may be unknown, inaccurate, or nonspecific. Nevertheless, available mortality data provide some insight into the seriousness of the problem. In interpreting the significance of mortality data in Tables 1 and 2, it is necessary to consider the wide variations in data compilation and reporting.

Around 1978, diarrheal diseases[1] were among the first and second causes of all deaths in children less than 1 year of age in 20 of 31 countries reporting figures for children between 1 and 4 years of age.

As shown in Table 1, around 1970 for 20 selected Latin American countries, 69,591 of the 108,627 deaths due to diarrheal diseases[2] recorded in children less than 5 years of age were in children under 1, yielding age-specific death rates of 1,346.07 and 456.0 per 100,000 population, respectively.

In Table 2 for the same countries, around 1978, of 80,307 diarrheal deaths reported in children under 5 years of age, 55,672 occurred in the under 1 age group, producing age-specific death rates of 290.2 and 934.0, respectively. These figures indicate a 26 per cent decrease in the overall age-specific mortality rate due to diarrheal diseases in children under 5 years of age over an eight year period. This decrease in mortality has declined by annual proportions in 18 out of the 20 countries reporting detailed information.

Although the 1978 age-specific diarrheal mortality rate in children under 5 was only 5.0 per 100,000 population in North America, the problem was much more acute in the Caribbean and in Central and South America, where

[1] Codes 008 (Enteritis) and 009 (Other diarrheal diseases) of the *International Classification of Diseases* (Ninth Revision, 1975). Geneva, World Health Organization, 1977.

[2] Defined according to categories of the Eighth Revision of the *International Classification of Diseases*, including other salmonella infections (003), bacillary dysentery (004), amebiasis (006), enteritis (008), and other diarrheal diseases (009).

Table 1. Total diarrheal diseases,[a] around 1970. Number of deaths and age-specific rates per 100,000 population for selected countries.

Country	Year	< 1		1 - 4		< 5	
		Number	Rate	Number	Rate	Number	Rate
Argentina	70	4,561	880.5	722	38.5	5,283	220.8
Belize	70	39	823.6	15	86.7	54	245.1
Chile	70	3,853	1,418.1	422	46.7	4,275	363.8
Costa Rica	70	845	1,509.5	271	108.1	1,116	363.9
Cuba	71	1,313	564.7	82	8.6	1,395	118.2
Dominica	70	25	984.6	13	127.1	38	297.7
Dominican Republic	70	1,642	1,177.9	612	111.1	2,254	326.6
Ecuador	70	2,382	968.9	1,691	194.4	4,073	365.1
El Salvador	70	2,245	1,457.7	2,055	386.2	4,300	626.8
Guatemala	70	3,643	1,817.8	5,749	807.6	9,392	1,029.5
Honduras	70	880	792.7	1,166	299.5	2,046	409.0
Martinique	70	63	598.4	20	47.9	83	158.8
Mexico	70	37,197	1,802.1	20,464	274.0	57,661	605.0
Nicaragua	75	984	1,224.8	316	109.1	1,300	351.5
Panama	70	275	588.6	209	112.5	484	208.2
Peru	70	5,501	1,037.3	3,798	209.1	9,299	396.3
St. Vincent	70	47	1,080.4	16	118.6	63	353.1
Trinidad and Tobago	70	169	710.0	28	25.5	197	147.4
Uruguay	70	254	479.2	14	6.4	268	98.8
Venezuela	70	3,673	874.7	1,373	94.2	5,046	268.7
Total		69,591	1,346.3	39,036	209.2	108,627	456.0

[a]Other salmonella infections, bacillary dysentery, amebiasis, enteritis, other diarrheal diseases.

Table 2. Total diarrheal diseases, around 1978. Number of deaths and age-specific rates per 100,000 population for selected countries.

Country	Year	< 1		1 - 4		< 5	
		Number	Rate	Number	Rate	Number	Rate
Argentina	78	2,641	463.3	420	20.0	3,061	114.9
Belize	79	45	762.7	9	41.2	54	194.9
Chile	79	705	264.9	85	8.6	790	63.4
Costa Rica	79	136	195.3	24	11.2	160	56.6
Cuba	78	237	122.7	41	4.3	278	24.3
Dominica	78	5	178.5	3	25.4	8	54.7
Dominican Republic	78	949	538.8	321	46.1	1,270	145.7
Ecuador	78	3,667	1,144.1	2,605	231.0	6,272	433.2
El Salvador	74	2,035	1,345.0	1,002	184.1	3,037	436.6
Guatemala	78	3,934	1,311.3	3,864	424.1	7,798	643.9
Honduras	78	926	873.5	624	112.4	1,550	234.4
Martinique	75	39	390.0	2	4.7	41	78.8
Mexico	76	30,806	1,258.8	11,393	127.2	42,199	370.1
Nicaragua	77	1,215	1,409.5	326	104.9	1,541	388.4
Panama	74	158	305.9	158	77.2	316	123.4
Peru	78	4,872	751.8	3,058	144.6	7,930	287.1
St. Vincent	79	23	403.5	8	45.9	31	134.1
Trinidad and Tobago	77	159	676.0	43	43.1	202	163.9
Uruguay	78	284	521.1	15	7.1	299	113.6
Venezuela	78	2,836	600.8	634	38.2	3,470	162.9
Total		55,672	934.0	24,635	113.4	80,307	290.2

the rates were 82.1, 379.4, and 207.6, respectively. Comparing the rates for the year 1970 and 1978, reported diarrheal disease age-specific rates in children under 5 years of age decreased 54 per cent in the Caribbean and about 25 per cent in both Central and South America.

Diarrheal mortality rates (age-specific) varied considerably throughout the countries of the Americas. In 1978 relatively high diarrheal death rates for the under 1 age group were reported in Nicaragua (1,409.5), El Salvador (1,345.0), Guatemala (1,311.3), and Mexico (1,258.8). Together these four countries accounted for approximately 68 per cent of all diarrheal deaths registered that year among children under 1 year of age. If a reduction of mortality in this age group is to occur, improved maternal and child nutrition activities, especially the promotion of breastfeeding and proper preparation of food during the weaning period, and the early introduction of oral rehydration therapy treatment will be necessary. In 1978 the lowest reported age-specific mortality rates for diarrheal diseases in the Latin American region for the under 1 age group were in Cuba (122.7) and Dominica (178.5).

With a reported rate (age-specific) of 424.1 per 100,000 population in 1978, diarrheal mortality in children ages 1-4 years was highest in Guatemala. Nevertheless, this represents a 52 per cent decrease from the 1970 rate of 807.6 per 100,000 population in the 1-4 age group.

As health program coverage extends to scattered rural populations, the number of reported diarrheal cases and deaths is expected to increase. Rather than an actual increase in incidence or severity, this increase will more likely reflect better information and reporting systems. Treatment and prevention of diarrheal diseases should be an integral part of overall health care services and should incorporate multidisciplinary, preventive strategies such as health education, maternal and child health, water and sanitation, breastfeeding, and nutrition. When such measures, coupled with aggressive oral rehydration therapy, are effectively introduced in developing countries, a substantial decrease in the number of diarrheal cases and deaths can be anticipated.

Research in Diarrheal Diseases

Funds are available in 1982 for support of health services (operational, field-oriented) research in diarrheal disease control. Funds are also available for research being carried out in support of national diarrheal disease control activities and which is aimed at developing more effective ways of implementing control strategies.

A Regional Scientific Working Group composed of public health officials and scientists who are experts in the area of diarrheal disease control has outlined priorities for research within the Region of the Americas. These include: studies of different methods for the preparation and packaging of oral rehydration salts (ORS); investigations of different approaches for delivery of oral rehydration therapy at the village and community level; studies to determine optimal ways of promoting breastfeeding and preparation of safe, locally available weaning foods; and studies of traditional beliefs and practices regarding diarrheal disease, and evaluation of health education approaches to modify those that are harmful.

Interested persons should first send a letter of intent (1 to 2 pages) outlining the proposed project to: Regional CDD Program, Division of Disease Prevention and Control, Pan American Health Organization, 525 23rd Street, N.W., Washington, D.C., 20037, U.S.A. A standard application form and additional information will then be sent if the project is considered to fall within the priorities of the program.

In addition, the Program is supporting basic, biomedical research aimed at developing new and better tools (drug, vaccines, diagnostic procedures) for the prevention and treatment of acute diarrheas or at further defining the global epidemiology of these diseases. For further information on support to this type of research, interested workers should write to: Program Manager, CDD Program, WHO, 1211 Geneva 22, Switzerland.

(*Source:* Enteric Disease Control Program, Communicable Diseases Control, Division of Disease Prevention and Control, PAHO.)

Information on Malaria Risk for International Travellers

The following updates information on malaria protection and drug prophylaxis and supersedes all data published earlier on this subject.

Duplication and distribution by health authorities is authorized and would greatly contribute to the dissemination of this information to those who give advice to international travellers (medical professions, travel agencies, etc.).

Protection against Malaria

Several deaths due to malaria are reported every year among international travellers. These deaths occur because:

(a) travellers are not aware of, or underestimate, the danger of contracting malaria abroad—especially when their stay in malarious areas is short—and consequently do not take the required protection measures;

(b) malaria, especially falciparum malaria (malignant tertian), can simulate a variety of diseases, hence the clinician may not make an early diagnosis and provide adequate treatment in time.

"Where have you been?" should become an essential part of the interrogation of the patient. This is particularly necessary in Asia, Oceania, Europe, and North America now that air transport enables people to cover vast distances while incubating a disease. People often regard their travel as irrelevant to their illness and will mention it only if specifically asked, whereas they should provide this information immediately to their physician when ill.

Protection against malaria consists mainly of drug prophylaxis directed against the malaria parasite. The traveller should take prophylactic antimalaria drugs at regular intervals. This prophylaxis should start at the latest on the day of arrival in the malarious area and should continue for a certain time after returning home. This single precaution, if properly taken, would undoubtedly prevent the vast majority of cases of falciparum malaria (malignant tertian); it will not always prevent the late occurrence of malaria attacks, usually of the benign type, weeks or even years after the return of the traveller.

Additional precautionary measures to prevent mosquito bites (see below) would also be useful and are to be recommended.

Drug Prophylaxis

The prospective traveller should consult his doctor who will determine the appropriate prophylactic drug and its dosage according to the area to be visited and taking into consideration any drug intolerance of the traveller. The recommended prophylactic drug for malaria protection varies according to the type of malaria present in the visited area and its drug sensitivity, the age of the traveller, the traveller's previous exposure to antimalarial drugs, the duration of stay in the malarious area, and conditions which may prejudice the use of certain drugs.

To ensure full effectiveness, active blood levels of the drug must be attained at the time of potential blood infection. With 4-aminoquinolines (chloroquine, amodiaquine), this necessitates initial loading doses which are indicated in Table 1. This table may be of assistance when giving advice on drug prophylaxis for international travellers.

Since the strength of available tablets (and other preparations such as syrup) varies considerably depending on the brand, the doses recommended are given in terms of milligrams (mg) of the active compound. Whenever possible the physician or the pharmacist should be consulted as to the number of tablets or quantity of syrup to be taken that correspond to the doses in mg indicated in the table.

For protection against malaria attacks, 4-aminoquinolines such as chloroquine and amodiaquine remain the drugs of choice except for areas affected by chloroquine-resistant malaria.

Other Protective Measures

Malaria is transmitted through the bites of certain anopheline mosquitoes. Therefore, in addition to drug prophylaxis, protection against mosquito bites is also of great importance especially after dark. This can be obtained by the following measures:

- Staying in quarters with screens on windows and other openings in order to prevent mosquitoes from entering.
- Use of "anti-fly" spray containing pyrethrum insecticides to kill any mosquitoes that may have entered in spite of screening. But the effect is rather short-lived and the spraying must be repeated frequently, should mosquitoes continue to enter.
- If the entrances to bedrooms are not screened, the use of mosquito nets around the beds at night is advisable, especially for babies and young children; it is essential to tuck in the net carefully under the mattress; the net should have no holes.
- After sunset, all persons staying in the open should wear sufficient clothing to protect the body from mosquito bites (long sleeves, long trousers, etc.). Those parts of the body not covered by clothing may be smeared with an insect repellent, such as dimethyl-phthalate. But the lasting effect of these products is only two to three hours and they must be re-applied.
- The use of long-acting sulfonamides in combination with pyrimethamine should be restricted to short-term prophylaxis in areas with confirmed *P. falciparum* resistance to 4-aminoquino-

Table 1. Malaria prophylaxis—Drugs and dosages.

Drug	Dosage	
*Chloroquine**	*Adults:*	300 mg base once a week (or 5 mg/kg body weight once a week)
Brand names: Avloclor, Aralen, Nivaquine, Resochin, etc.		
Depending on the brand, usually available in tablets of 100 mg, 150 mg and 300 mg of the base (active compound).	*Children:*	
For children, available also in tablets of: 37.5 mg, 50 mg and 75 mg of the base and in the form of syrup, one teaspoonful of syrup containing 25 mg or 50 mg of the base.	– less than 1 year:	37.5 to 50 mg base once a week
	– 1 to 4 years:	50 to 100 mg base once a week
	– 5 to 8 years:	150 to 200 mg base once a week
	– 9 to 12 years:	200 to 300 mg base once a week
N.B. To accelerate the establishment of reliably protective drug levels, it is recommended to double the above dosage the first week of prophylaxis during which chloroquine will be given the first and second day. Thereafter chloroquine will be taken once a week.		
*Amodiaquine**	*Adults:*	300 to 400 mg base once a week (or 5 mg/kg body weight once a week)
Brand names: Camoquin, Flavoquine, etc.		
Available in tablets of 150 mg and of 200 mg of the base (active compound).	*Children:*	
For children, available also in the form of a flavoured powder (to be mixed with milk, etc.), 1 teaspoonful containing 50 mg of the base.	– less than 1 year:	50 mg base once a week
	– 1 to 4 years:	50 to 100 mg base once a week
	– 5 to 8 years:	150 to 200 mg base once a week
	– 9 to 12 years:	200 to 300 mg base once a week
N.B. To accelerate the establishment of reliably protective drug levels, it is recommended to double the above dosage the first week of prophylaxis during which amodiaquine will be given the first and second day. Thereafter amodiaquine will be taken once a week.		

*International Non-proprietary Note (INN).

lines. This resistance is reported from a number of areas or countries: Americas (areas in: Brazil, Colombia, Ecuador, French Guiana, Guyana, Panama, Suriname, Venezuela), Asia (areas in: Bangladesh, Burma, China south of 25°N), India (Assam, Meghalaya, Orissa), Indonesia (Irian Jaya, Java, Kalimantan), Democratic Kampuchea, Lao People's Democratic Republic, Malaysia, Nepal (areas bordering India), Papua New Guinea, Philippines, Solomon Islands, Thailand, Vanuatu, Viet Nam, and Africa (areas in Kenya and United Republic of Tanzania).

- Multiresistant *P. falciparum* failing to respond to chloroquine and sulfadoxine pyrimethamine combinations occur in certain rural areas of Thailand and adjacent countries. Travellers intending to visit these areas may contact WHO Headquarters, the WHO Regional Offices for South East Asia or for Western Pacific, or relevant institutions for appropriate advice on prophylaxis.
- In many tropical areas malaria parasites are resistant to dihydrofolate reductase inhibitors such as pyrimethamine and proguanil. These drugs alone are therefore not reliable enough for malaria prophylaxis.

(*Source: Weekly Epidemiological Record* 57 (12), 1982.)

Calendar of Courses and Meetings

Clinical Epidemiology Courses

With funding from The Rockefeller Foundation, the institutions mentioned below will offer one-year intensive courses in clinical epidemiology for junior faculty members from clinical departments of medical schools in developing countries. Participants will learn to apply the basic concepts of causation, bias, clinical measurement, natural history, and disease frequency. Supervised by a designated preceptor, the fellows will apply these skills in

completing the design of a research project to be conducted in their own country on return. The opportunity will be provided to take part in faculty research programs designed to gain experience in practical research methods.

Financial support will cover tuition, travel, and maintenance expenses. On successful completion of the course, modest research support at the participant's home institution and a visit to that institution by the preceptor to consult on the research project also may be provided.

Applications should outline past experiences, current interests and responsibilities, and future plans, and should be accompanied by a curriculum vitae and endorsing letters from the department head and dean which would include reasons for sponsoring the applicant. Correspondence should be addressed as follows:

Professor Stephen R. Leeder, Director, Asian and Pacific Centre for Clinical Epidemiology, Faculty of Medicine, The University of Newcastle, New South Wales, 2308, Australia.

Deadline for applications:
1 September 1982
(Course starts: 3 January 1983).

Professor Paul D. Stolley, Director, Clinical Epidemiology Unit, Department of Medicine, School of Medicine, Room 229L - TRINEB/S2, Philadelphia, Pennsylvania 19104, U.S.A.

Deadline for applications:
1 November 1982
(Course starts: 1 July 1983).

Professor Peter Tugwell, Chairman, Department of Clinical Epidemiology and Biostatistics, Faculty of Health Sciences, McMaster University, 1200 Main Street West, Hamilton, Ontario L8N3Z5

Deadline for applications:
1 November 1982
(Course starts: 1 July 1983).

Applied Epidemiology

The Centers for Disease Control, Atlanta, Georgia, USA, have announced this course designed to provide health professionals with the skills and knowledge necessary to perform the tasks of an epidemiological work system, from the first step (reporting of a case) to the last step (preparation of surveillance reports).

Epidemiologists, disease investigators, and other health professionals who spend at least 50 per cent of their time in the performance of epidemiological functions within the context of community-wide disease control programs, are eligible for participation.

The course will be offered at the Centers for Disease Control, 1600 Clifton Road, N.E., Atlanta, Georgia 30333, 13-22 October, 1982.

For more information, please contact: Center for Professional Development and Training, Course Number 4440-G, PFY, Room 419, Centers for Disease Control, Atlanta, Georgia 30333.

Courses in the Epidemiology and Control of Tuberculosis

The following courses, organized by the governments with PAHO collaboration, will be offered in 1982:

Argentina: 21 September-29 October
Emphasizes epidemiological and research aspects and includes observation trips to programs in the provinces.
Instituto Nacional de Tuberculosis, Casilla de Correo 106, Santa Fe (Dr. Eduardo Balestrino, Director).

Cuba: 4-30 October
Emphasizes aspects of the organization of the services and includes a seminar on the evaluation of the national program.
Ministerio de Salud Pública, Apartado Postal 9082, Zona 9, La Habana (Dr. Rodolfo Rodríguez Cruz, Programa de Tuberculosis).

Chile: 2-28 August
Includes a clinical short course and a seminar for evaluation of the national program, and highlights aspects of programming, clinical and epidemiological topics, and the control of acute respiratory infections.
Instituto Nacional de Enfermedades Respiratorias y Cirugía Torácica. Casilla de Correo 9634, Santiago (Dr. Gladio Mena Salinas).

Mexico: 2-27 August
Covers clinical aspects, epidemiology, and control of acute respiratory infections.
Dirección General de Control de Tuberculosis y Enfermedades Respiratorias, Leibnitz 32, 5° piso, México 5, D.F. (Dr. Carlos R. Pacheco).

CEPANZO: 19 October-1 December
Regional course in the bacteriology of tuberculosis.
Centro Panamericano de Zoonosis, Casilla de Correo 3092, Buenos Aires (Dra. Isabel N. de Kantor).

Regional Symposium on Human Resources for the Water Decade

Planning is underway for the regional symposium on Human Resources for the International Drinking Water Supply and Sanitation Decade, 1981-1990. It will be sponsored by PAHO and is to be held 26-30 July in Panama City, immediately prior to the XVIII Congress of the Inter-American Association of Sanitary and Environmental Engineering (AIDIS). The congress will discuss and adopt resolutions on recommendations of the symposium. Specifically, it seeks the development of persons capable of manning programs aimed at providing drinking water and sanitation services to some 150 million rural inhabi-

tants and well over twice as many city dwellers by the end of this decade.

A systematic approach will necessitate the concerted efforts to remedy the manpower problem of all those involved in supplying drinking water and sanitation—at the local, national, and subregional, as well as the regional levels. It is precisely the purpose of this regional symposium to promote such an approach.

Training in the future will have to be extended to the community at large and to the vocational and university classrooms. Projects will need to assign high priority to the active participation of community members in both the making and implementing of decisions and the operation and maintenance of systems. Education through the formal academic system and training within organizations will have to be seen as complementary activities and utilized to their fullest potential in the countries.

Participants will include national authorities in a position to influence policy-making, strategy design, and fund allocation that will result in the development of individuals trained in the water and sanitation sector. Their objective is presentation and discussion of human resource demand for the Decade and the various means that can be used to meet it.

It is anticipated that the symposium will lead to national and subregional activities that will more effectively promote both national self-reliance in terms of an awareness and development of human resources and technical cooperation among developing countries.

CORRIGENDUM

Epidemiological Bulletin, Vol. 3, No. 2, 1982

Page 7, "Surveillance and Control of *Aedes aegypti,* in Bolivia," line 7:

Delete: *Antimalaria vaccination*

Insert: *Vaccination against yellow fever*

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