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International Meeting on Surveillance and Prevention of Chagas Disease in the Amazon Region

(Manaus, Amazonas State, Brazil, 19–22 September 2004)



Implementation of the Intergovernmental Initiative for Surveillance and Control of Chagas Disease in the Amazon Region (AMCHA)

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Introduction

Official delegates of the Amazon countries, and a panel of specialists in various aspects of research, prevention and control of Chagas disease met at the Leonidas and Maria Deane Research Center, at the Amazon branch of FIOCRUZ, with the Pan American Health Organization as Secretariat, with additional support from the ECLAT-CDIA project of the European Community. The delegates developed a series of recommendations and directives in relation to four main themes:

- A. Evaluation of the risks of Chagas disease in the Amazon region.
- B. Research necessary for surveillance and prevention of Chagas disease in the Amazon region.
- C. Methods of surveillance and prevention of Chagas disease in the Amazon region.
- D. Development of a proposal for international cooperation for surveillance and prevention of Chagas disease in the Amazon region (AMCHA).

A. Evaluation of the Risks of Chagas Disease in the Amazon Region

Human infection with *Trypanosoma cruzi* has now been reported in all countries of the Amazon basin, together with infections in *Triatominae* and in animal reservoirs. Even though the presence of this parasite in the region was mentioned by Carlos Chagas at the time of his historic work on this disease, the problem has received little attention and is rarely reported by the regional health services. Knowledge of the occurrence of Chagas disease in the Amazon region remains limited, although there is increasing evidence that the problem may be much more serious than previously thought.

Transmission Patterns

1. Transmission in Rural and Periurban Zones due to Sylvatic Vectors

Transmission in rural and periurban zones is mainly due to *Rhodnius robustus* and *R. pictipes*, which invade houses without colonizing, and *Panstrongylus geniculatus* which has been encountered in peridomestic colonies. This is a warning of the potential for transmission by these species.

In the Ecuadorian Amazon and in the Rio Negro region of Brazil, epidemiological patterns have been observed that indicate a cumulative risk of transmission in relation to age group, and provide evidence of continuous transmission since several decades. Similar situations involving other vectors have been described for Peru and Colombia, and it is possible that similar patterns occur in other areas of the Amazon.

2. *TRIATOMINAE* that Colonize Domestic Habitats

2.1. The situation with *Triatoma maculata*

T. maculata is recognized in Venezuela as a secondary vector of importance in regions bounding the Amazon; it is being captured with increasing frequency in domestic habitats in Roraima, Brazil.

2.2. *P. herreri* and *R. ecuadoriensis* in Peru

P. herreri and *R. ecuadoriensis* are the main intradomestic vectors in northern Peru, and both species have been found infected with *T. cruzi* and *T. rangeli*.

3. Particular Transmission Patterns

3.1. Focal outbreaks

Focal outbreaks of transmission have been described, that are probably due to oral transmission—especially associated with contamination of fruit juice made from the *açaí* plant (*Euterpe catinga*). No other satisfactory explanation has been found.

It is suggested that that infected *Triatominae*, or their feces, contaminate some phase of the processing this fruit juice, and that transmission occurs when the juice is consumed. Up to 1998, 17 such outbreaks were reported, involving 85 human cases. These were mainly from the State of Para, with some in Amapa and more recently also in Acre and the Amazon.

This form of transmission via contaminated foodstuffs opens a new line of investigation and technical cooperation with INPPAZ (the Pan American Institute for Zoonoses and Food Protection) of the Pan American Health Organization.

3.2. Exploitation of *Piassaba fibre*

In the northern Rio Negro, Brazil, transmission of *T. cruzi* has been reported in association with extraction of fibers from the piassaba palm (*Leopoldina piassaba*), affecting families that are in contact with this natural ecotope of the vector *R. brethesi*.

3.3. Cultural Practices

In Colombia, consumption of blood from armadillos and opossums is a common feature of the traditional medicine of some indigenous groups of the Amazon region. This offers a risk for transmission of *T. cruzi*, which may also be transmitted by eating the meat of these animal reservoirs that has been undercooked or just smoked.

Activities that May Increase the Risk of Transmission

- Destruction of forest for:
 - Urban expansion.
 - Establishment of new pastures.
 - Plantations of *açai* and *pupuna* that substitute the primary forest.
 - Forest exploitation such as collection of Brazil nuts in Bolivia.
- Excessive increase of the human population.
- Mining and other local work without adequate measures of protection.
- Eco-tourism without adequate measures of protection.

Risk Factors in Domestic Habitats

- Houses constructed in the forest, surrounded by trees—especially palms.
- Persons with high risk of encountering *Triatominae*.
- Conditions suitable for the presence of domestic vectors and reservoir hosts in the houses.
- Houses constructed of natural materials from the ecotopes of *Triatominae*.
- Light from open houses that may attract *Triatominae*.

Epidemiological Patterns

- Risk of contact with *Triatominae* is widespread in the Amazon region.
- It is probable that lack of reports of domestic triatomine colonization in the Amazon has led to the idea that Chagas disease is not a problem for the region.
- Transmission can occur at different intensities related to different human activities.
- The classical form of vectoral transmission known in other endemic regions,
- Due to domestic colonization by vector species of *Triatominae*, appears not to have yet been established to a significant degree. This may have delayed adequate understanding of the epidemiology of Chagas disease in the Amazon.
- Epidemiological information is currently insufficient to determine the real situation, so that it is not yet possible to propose all measures of prevention and control.
- The lack of data about Chagas disease in the Amazon is mainly due to insufficient capacity of the health services in the region for epidemiological and entomological surveillance.

Research Needs

- Develop and strengthen the capacity for clinical and laboratory diagnosis, including evaluation of cross reactions, and defining a standard serological protocol.
- Determine which reservoirs may be implicated in transmission of *T. cruzi* in the Amazon.

- Extend sero-epidemiological studies in periurban areas and zones where transmission has been reported.
- Confirm the transmission route for those outbreaks already described.
- Determine the clinical characteristics of Chagas disease in the Amazon region.

B. Research Necessary for Surveillance and Prevention of Chagas Disease in the Amazon Region

In general terms, the group acknowledges that there has been some progress in understanding Chagas disease in the Amazon region. Available information, updated with country reports during this meeting, reinforce the consensus emerging amongst investigators in terms of two main aspects:

- American trypanosomiasis occurs as a widespread zoonosis throughout the Amazon, presenting characteristics that would favor its expansion as a human disease.
- Development of a system for surveillance and prevention of the disease is considered timely, since acute and chronic human cases have been detected in all countries of the region, together with a range of vector species and animal reservoirs naturally infected with *T. cruzi*.

Nevertheless, the group also acknowledges that this trypanosomiasis presents particular characteristics in the Amazon region, substantially different from the usual patterns of Chagas disease described in the Southern Cone. Similarly, the group recognizes serious deficits in the information available about several aspects of the disease – particularly in relation to ecological aspects and the extension of human involvement. To this can be added special operational difficulties especially in transport, a rapidly changing environment, and geopolitical factors that complicate an adequate description of the epidemiology, and discourage the usual methods of control. This adds urgency to the research component of this initiative which the current meeting is proposing to the countries of the region.

The basic form of this research involves studies of feasibility in relation to the various factors involved with surveillance and research in the Amazon region, with the aim that such research will be in collaboration with all countries of the initiative. To sustain such research, the group recommends that it should become part of the agenda and regular budget of the governments involved, and should also be given some priority by international agencies such as TDR, JICA, EC, and others.

The group has tried to list research priorities in relation to different risk scenarios, following from intense discussion of the main components already identified or suggested from previous research in the region, as well as necessities and problems encountered by researchers studying Chagas disease in the Amazon. The topics listed below have been generically summarized in terms of requirements and research proposals, although this is seen as introductory and requires development during the course of the initiative by the

different research groups involved. What follows are the summary discussions of each theme:

1. Vectors

In spite of significant advances, there is still much to be done on this topic, especially in terms of which vectors are present, which are those most involved with transmission to humans, what the distribution of species is, and what the factors are that influence this distribution. It is generally accepted that the majority of Amazon vectors are sylvatic with little tendency for domestication, although this could change and merits adequate monitoring. There is a wide range of micro habitats in the Amazon region, and still little basic information about which factors influence dispersal and distribution of those species so far registered. In practical terms, two priority themes are proposed:

- a. assess the current capacity in each country for collecting and identifying vector species, as well as biological studies relevant to surveillance and prevention of Chagas disease.
- b. the initiative should encourage and support the development and publication of updated species lists for vectors encountered in the Amazon, together with available distribution data, ecotopes, domestic infestation rates, colonization, and natural infection rates with *T. cruzi*. This should serve as a basis for reference, and for systematic revision as additional data becomes available, as well as a way to monitor changes.

For the short to medium term, it is important that the countries designate national centers of reference for vector studies, that should be networked together and with other centers of excellence in the region and elsewhere, following the ECLAT¹ system which has been one of the main proponents of this and other initiatives against Chagas disease.

For surveillance and regular collection of material, as proposed by Bolivia, Colombia, and Ecuador, agents of the national and regional malaria programs should participate in active searching in houses, as well as promoting local community participation in vector surveillance.

In this respect, it is of fundamental importance to identify ecological and socio-cultural factors that may bear on the interaction between people and *Triatominae* in the diverse landscapes of the Amazon, including the investigation of specific situations of transmission by *Triatominae* that enter houses but do not colonize (Ecuador) and family outbreaks that may be due to oral transmission, probably as a result of contamination of foodstuffs by infected bugs (Brazil).

In terms of research on species and sylvatic habitats, the group recognized both the importance and practical difficulties that need to be addressed by groups and specialist projects, with initial priority to areas close to human settlements—especially where cases of

¹ ECLAT – Latin American Network for Research on the Biology and Control of *Triatominae*:
<http://ECLAT.fcien.edu.uy/>

disease transmission and/or invasion or domestication by the vectors has been detected. In general, research would focus on palm trees (preferred habitat of most species of the most important genus, *Rhodnius*), through dissection of palm trees or by use of available traps².

Ideally, a standard protocol should be developed for these studies, in terms of sampling, strategies, indicators and methods, which would allow comparability between different studies.

Identified research points include the following (list to be revised and amplified):

- Specific studies on *R. prolixus* and *R. robustus*, designed to provide a better understanding of the relationships between them, their potential for natural hybridization, the potential of *R. robustus* to become domesticated, markers for differential taxonomic identification³, etc.
- Specific studies on the expansion of ‘pre-domestic’ *P. geniculatus* in areas of Para (Brazil) and other countries of the region.
- Comparative studies on the morphology and vectoral capacity of *P. herreri* and *P. lignarius* in different regions, acknowledging that some authors consider these as a single species.
- Comparative and analytical studies on *R. ecuadoriensis* in Ecuador (basically sylvatic) and Peru (always domestic).
- Aggregate studies on species distribution in relation to micro and macro climatic factors, with the aim of developing geographical predictors of distribution.
- Support and follow up the entomological studies planned by the Bolivian program through regional malaria laboratories and control personnel.
- Consider the possibility of developing ‘sentinel site’ studies for monitoring *Triatominae* in specific regions.
- Evaluate the possible influence on *Triatominae* of chemical control interventions carried out by the malaria control programs, both in terms of repellence and possible development of insecticide resistance.
- Improve surveillance of *Triatominae* in area adjacent to foci of human disease.
- Evaluate possible serological indicators for contact with *Triatominae*.
- Comparative studies of physical parameters of dwellings where *Triatominae* are encountered, with a view to defining risk factors.
- Special attention to surveillance in regions of immigration and new settlement, in view of the possible introduction of triatomine species from other areas.

2. Reservoirs

Also of high importance, in view of the associations and wide dispersal of *T. cruzi* populations already detected in the Amazon. The list of species found naturally infected is voluminous, with the last general revision carried out by Mauro Barretto (Brazil) in the

² In this respect, collaboration of entomologists with ecologists and specialists in palm trees would be important, and has already given excellent practical results in various projects.

³ The Oswaldo Cruz Institute is developing a molecular technique for distinguishing these two species, which will be offered to the laboratories of the region.

1960s. For this reason, an updated list should be developed, as basis for periodic revisions in the future. As mentioned above, standard research protocols should be developed by the Initiative, with a view to comparability of findings.

Basic prospection should be carried out using conventional parasitological methods (xenodiagnosis and hemoculture), amplified by molecular techniques and anatomic pathology when possible.

Laboratory studies may help in a better understanding of oral transmission of the parasite, between sylvatic reservoirs and, potentially, to humans.

Special attention should be given to sylvatic rodents and marsupials due to their synanthropic habits. Further studies of the development of *T. cruzi* in anal glands of marsupials would be appropriate.

Collaboration with groups specializing in the ecology and systematics of the relevant species would be recommended. In particular, it is suggested that the member countries seek to identify such centers of reference in zoological taxonomy, and facilitate national and international cooperation.

For domestic habitats, the group gives particular emphasis on investigation of infections with *T. cruzi* in dogs and cats living around the house, which can become infected in different ways - especially through oral route transmission, ingesting infected *Triatominae* or rodents. The mobility of species such as *Rattus rattus* between houses and sylvatic habitats should be considered in areas where the parasite is circulating.

3. Parasite

In general, studies of the parasite are considered complex and difficult in the Amazon region. There is a great variety of populations, especially in the sylvatic habitats, although apparently only those of lineages I and III have so far been isolated and characterized (consensus classification of 1999, *Memorias do IOC* 94, supl.1). Ideally such studies should be carried out within the region, through centers of excellence with capacity for isolating and characterizing parasite strains using biochemical and molecular markers. In the Amazon region there are many other flagellates similar to *T. cruzi*, such as *T. saimiri*, *T. rangeli*, *Phytomonas* sp. and others, which can complicate microscopical identification, and also lead to confusing serological results in humans and mammalian reservoirs.

In the case of acute phase infections in humans, diagnosis by classical direct and indirect parasitological approaches remains the method of choice, and should be carried out by diagnostic laboratories. For reference laboratories using protocols developed by FIOCRUZ, it is recommended to use PCR to increase the specificity of the diagnoses which is particularly important for the Amazon. This technique will also help in strain typing, which is more complex and requires higher stringency.

A molecular technique is available for differential diagnosis of *T. rangeli* (from *T. cruzi*) which could be implemented in laboratories in the region. To optimize parasite identification in reservoir hosts and *Triatominae*, it is better to isolate and culture the parasites, which is not always easy—especially for strains of lineage I.

All these studies have importance in terms of epidemiological surveillance, and are fundamental for mapping the infection trends in the region. In addition, it is of interest to characterize the parasite in chronic phase patients, which should be done from parasite isolates, although this has been shown to be difficult in some Amazonian studies. Maintenance of strain banks for the region is of particular relevance, and could be set up in some of the reference laboratories.

4. Diagnosis of chronic human infections

In the Southern Cone and other regions this is routinely done by conventional serology, although this can give problems of sensitivity and especially specificity in the Amazon. This would be the basic approach in sero-epidemiological studies, but requires careful checking in the region due mainly to the high rate of false positives seen. In studies in the Alto Rio Negro (Brazil), final serological characterization is generally done using Western Blot, since the conventional techniques alone are insufficient. This problem requires further investigation in the Amazon region, through development of a specific study of serology in the area involving various laboratories. In parallel, the group suggests research to improve molecular methods for complementary diagnosis of human cases in the Amazon.

5. Clinical Aspects of Human Infection

Acute Chagas disease appears similar in the Amazon region and the Southern Cone, in terms of parasitemia and fatality rate, although there are some clinical differences. It is suggested to develop a standard protocol for clinical evaluation and characterization of such cases, both for cases detected in individual febrile patients (e.g. through malaria slide examination) and for family episodes.

In particular it is important to clarify the transmission route in all such cases, in order to improve effective surveillance.

For acute cases, in terms of secondary prevention, it is vital to carry out specific treatment, which should be followed up through clinical and laboratory studies. Particularly endorsed is the recommendation of previous workshops (Santarem 2001, Palmari 2002) that the laboratory network for malaria diagnosis should actively participate in prospection for acute cases of Chagas disease, through training (and regular supervision) of slide microscopists.

For chronic cases, in parallel with the search for better specific diagnosis, follow-up protocols should be developed with the aim of improved characterization of clinical presentations, including possible identification clinical signs specific to the region.

For additional diagnosis of chronic cases, regular screening of blood banks is suggested, as well as standard verification of cause of death throughout the region.

Focal studies also suggested include investigation surveillance in municipalities with high incidence of family episodes in Para, Brazil, and experimental studies with PCR in non-acute patients with negative conventional serology.

A further suggestion is that TDR (and/or Ministries of Health or Science and Technology of the countries of the region) could consider a program of small research grants to stimulate focal projects, which could be managed by a committee set up by the Initiative, giving priority to research themes related to surveillance and prevention of Chagas disease in the Amazon.

C. Proposal for a System of Surveillance and Prevention of Chagas Disease

Introduction

It is recognized that there are common perspectives and objectives, as well as similar elements and structures relevant to the development of Chagas disease surveillance in all countries of the Amazon region.

The proposal is based on conserving the identity of the surveillance system of each country in terms of its organization and function, as well as those of the health system and system of environmental management.

Definition

It is proposed that an integrated system of Chagas disease surveillance be developed, that makes use of the existing systems for surveillance of vector-borne diseases and epidemiological surveillance, through progressive intersectoral development closely linked with national primary health care systems, in order to develop a system that is efficient, effective, and sustainable.

Objectives

The proposed objectives are:

- detection of human infection with *T. cruzi*
- identification of situations of risk for contact between people and *Triatominae*
- identification of risk situations by factors:
 - social
 - ethnic
 - economic
 - forms of production
 - cultural
 - amongst others possible

Structural Options

A. Minimum System of Surveillance

- Based on established operational definitions.
- Integrated with surveillance systems already established in the subregion: malaria, emerging diseases, and primary health care.
- With a component of active surveillance: serological surveys and investigation of foci in situations of risk.
- Development of community notification, to health authorities, of the presence of *Triatominae* in domestic habitats or in other situations of risk for man-vector contact, with special emphasis on use of the primary education system.
- With a component for control and treatment.

B. Maximum Surveillance System, with Intersectoral and Extrasectoral Integration

- Environment
- Education
- Agriculture
- Civil associations
- Ethnic associations
- Commercial projects
- Amongst others

Components

1. Epidemiological surveillance, based on: geographic information systems, diagnostics, treatment, health education and community participation.
2. Environmental surveillance, including:
 - entomological surveillance;
 - environmental indicators (climate, pollution, etc.);
 - environmental health (housing, peridomestic habitats etc.);
 - ecosystems (reservoirs, vegetation).
3. Development of a research component with feedback between surveillance and research and vice versa.
4. Chagas disease control activities within the capacity of the Primary Health Care system.
5. Training in diagnostics and entomology, relevant to existing systems and the primary health care (PHC) services, particularly:
 - malaria microscopists and health services;
 - entomological staff of the health system;
 - environmental staff of various systems;
 - PHC professionals.

The system should operate with a **national focal point** for each country (Official delegate of the Intergovernmental Commission for the Initiative, with institutional support), and a **subregional focal point** (Technical-Executive group of the Initiative) who would prepare

an annual report of activities by country and subregion in accordance with an agreed format. This report would be presented at the annual meetings of the Initiative.

Monthly, the national programs, through their focal points, would present notifications through a website to be specified.

D. Proposal for a System of International Cooperation for Surveillance and Prevention of Chagas disease in the Amazon Region (AMCHA)

The delegates of the countries of the Amazon region, participating in the International Workshop on Surveillance and Prevention of Chagas Disease, propose creation of an *Initiative of the Amazon Countries for Surveillance and Control of Chagas Disease (AMCHA)* to be formally constituted by decision and political agreement of the Ministers of Health of Bolivia, Brazil, Colombia, Ecuador, France, Guyana, Peru, Suriname, and Venezuela.

The AMCHA Initiative would have as **general objective** the following:

*Prevention of large-scale establishment of endemic vectoral transmission of Chagas disease in the Amazon region, through the following **specific objectives**:*

- Development and implementation of a system of regular epidemiological surveillance, integrated with and making best use of, the resources, services and health programs already available.
- Development of methods and/or techniques for control appropriate to the known mechanisms of transmission (extra-domestic vectoral transmission, intradomestic transmission without vectoral colonization, oral-route transmission).
- Development of new understanding of the epidemiology of Chagas disease in the region (following research suggestions indicated in B above).

In support of the development and implementation of these objectives, the following **support structure** is proposed:

- i) An **InterGovernmental Commission (CI)** to be constituted by express and formal delegation by the health authorities of each country, as soon as this proposal is approved by the Ministries of Health.
- ii) A **Technical Secretariat**, under the responsibility of PAHO/WHO through their representation in Brazil.
- iii) An **Executive Technical Coordination Group**, with specific responsibilities defined by the delegates of the member countries, hosted in rotation each two years. This Technical Coordination Group would be responsible to promote national efforts to implement the recommendations and mandates of the Intergovernmental Commission. In view of the research needs, it would also be appropriate that representatives of the research community should be included as advisers to the Technical Coordination Group, to assist in supervision, motivation, and coordination of the ongoing research.

This meeting has recommended that Brazil be the first host country for the Executive Technical Coordination Group of the Initiative, and that the immediate task proposed should be definition and standardization of procedures for epidemiological surveillance, with such proposals to be discussed in a future *ad hoc* meeting with specialist technical personnel designated by each member country.

Responsibility for the Executive Technical Coordination Group should be with an Institution designated by the Government of the host country, according to the requirements indicated by the Technical Secretary of the Initiative.

For implementation of the activities of the Initiative, the following are proposed:

1. Annual meetings of the CI in the host countries, by rotation, in order to analyze progress, achievements and constraints in the process of implementation of the Initiative, as well as setting specific annual goals.
2. Make use of technical cooperation projects between countries (TCCs/PAHO) especially during the initial phase because of the differing levels of national experience
3. Recognizing existing networks that could continue to benefit the Initiative, develop exchange systems between countries and institutions with capacity and interest relevant to the objectives, such as ECLAT/CDIA, OTCA, MSF, EC, etc.

Acknowledging that creation of this Initiative is not within the competence of this meeting, it is proposed that the Ministries of Health of the nine countries sharing the Amazon watershed should mutually agree creation of this Initiative as part of the agenda of the next Meeting of Ministers of Health of South America, to be held in March 2005 in Santiago de Chile, or prior to this if appropriate opportunity presents. This implies that appropriate justification be brought to the attention of the respective Governments, for which the following actions are agreed:

- To request that OTCA includes the AMCHA Initiative within its Special Commission on Public Health (CESAM), and adopts the same objectives.
- To request that PAHO appropriately circulates this report.
- To request that ORAS-CONHU and the PAHO Country Representatives take appropriate steps to bring about agreement from the Ministries of Health to include the creation of the AMCHA Initiative in the agenda of the next Ministers' Meeting in Santiago de Chile in 2005.
- The National Delegates here present take to their respective authorities the proposal for the creation of the AMCHA Initiative as a recommendation of this meeting.

Manaus, Amazonas State, Brazil, 22 September 2004

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