

# Clinical and Epidemiologic Studies of Chagas' Disease in Rural Communities of Oaxaca, Mexico, and an Eight-year Followup: II. Chila<sup>1</sup>

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*A seroepidemiologic survey conducted in 1971 in the rural Pacific coastal community of Chila in the Mexican state of Oaxaca showed an unusually high prevalence of antibody against the Chagas' disease agent Trypanosoma cruzi. Further studies were undertaken in 1973 and 1981 to (1) determine the pathologic impact of T. cruzi infection in humans, (2) investigate the natural history of the disease, (3) confirm that serologically positive persons were parasitologically positive, and (4) evaluate whether T. cruzi transmission continued into the next decade. This article reports results derived from those studies.*

**A** serosurvey in the community of Chila, situated on the south coast of the Mexican state of Oaxaca, revealed an unusually high chagasic antibody prevalence. Electrocardiographic evaluation demonstrated significant abnormalities in seropositive as compared to

seronegative people, and some of these abnormalities progressed during an eight-year followup period.

Until fairly recently, Chagas' disease was not thought to occur commonly in Mexico or to cause significant cardiac pathology. Antibody prevalences to *Trypanosoma cruzi* reported from several communities have ranged from 7% to 13% (1-6). Salazar Schettino et al. reported an overall seroprevalence of 6% for serum samples from about 6,600 persons that were collected between 1949 and 1985 in several states of southern and central Mexico (3). In 1986, Tay et al. reported that 88% of 52 schoolchildren tested, all from the town of Miahuatlan, Oaxaca, were seropositive (7).

Our 1971 seroepidemiologic surveys in 60 rural communities on the Pacific side of Oaxaca State found unusually high *T. cruzi* infection rates; in particular, three communities (Cerro del Aire, Tataltepec, and Chila) exhibited prevalences among adults ranging from 51% to 76% (8, 9).

This article, which supplements our previous report from Cerro del Aire (10),

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presents clinical, electrocardiographic, serologic, and parasitologic findings derived from a cross-sectional study and an eight-year longitudinal study conducted in Chila. The objectives of these two studies were (1) to determine the pathologic impact of *T. cruzi* infection in humans from this area, (2) to investigate the natural history of the disease, (3) to confirm that serologically positive persons were parasitologically positive, and (4) to find out whether *T. cruzi* transmission was continuing. Within this context, it should be noted that although many community-based cross-sectional studies of Chagas' disease have been reported (10–13), relatively few longitudinal community-based studies have been performed (13–28); such longitudinal studies are needed, particularly to obtain

information about the natural history of the disease (20, 29).

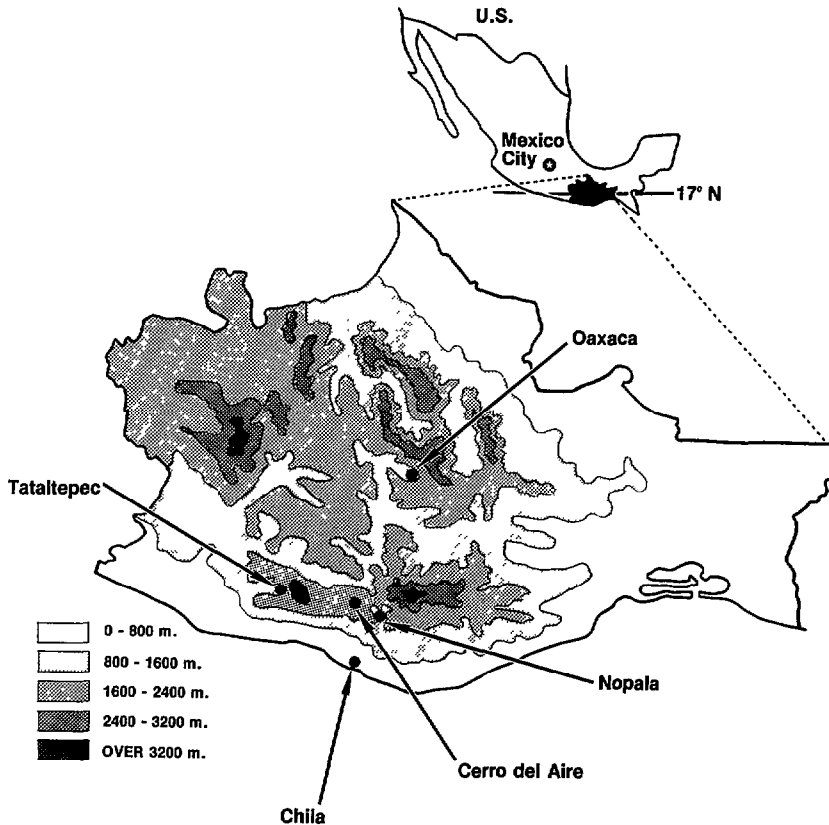
## METHODS

### Study Area

Oaxaca, one of Mexico's southernmost states, is around 17° north latitude and 96° west longitude (Figure 1). The town of Chila is a rural settlement located on the state's Pacific Coast. Chila has an annual rainfall of about 150 cm, most of which occurs between May and October.

Between 1971 and 1973 Chila had approximately 2,600 inhabitants. Thus, our sample of 238 people represented about 9% of the total population in that period

Figure 1. A map of Mexico's Oaxaca State showing the location of Chila.



(9). By 1981, however, the population had grown to approximately 3,100 people.

Homes in Chila were made from a variety of materials. Some had concrete walls, concrete or dirt floors, and tin or thatch roofs (the latter being made of palm fronds or straw); while others had wood slat and adobe walls, dirt floors, and thatched roofs.

## Field Trips to Chila

Field trips to Chila, which took place in 1971, 1973, and 1981, involved the following activities and objectives:

### *Serologic Surveys*

Our 1971 serologic survey included 238 people of all ages. The methods used in this survey have previously been described (9). In brief, Chila households were selected at random and, for the most part, all residents of the selected households were included in the survey sample.

In 1981, primarily to evaluate continued transmission of *T. cruzi* infections to humans, blood specimens obtained from 144 children under the age of 10 were tested for *T. cruzi* antibody. The subjects were "self-selected" by their parents or guardians in response to an invitation issued through the town mayor asking mothers to have their children tested.

### *Cross-sectional Clinical Study*

In 1973, we evaluated the cardiac status of 119 people from the original 1971 cohort of 238. These 119 were self-selected in response to an invitation asking cohort members to participate. The subjects' cardiac status was evaluated by reviewing their history and by means of a physical examination, electrocardiogram (ECG), and repeat serology.

In 1981, a group of 135 newly seen self-selected adults was added to the ECG

cross-sectional study; because of time limitations, histories and physical examinations were obtained from only 58 of these 135 persons. This resulted in medical history and physical examination data being obtained from a total of 177 people and ECGs being administered to 254.

### *Longitudinal Clinical Study*

In 1981 repeat ECGs, clinical evaluations, and serologic tests were obtained from 57 people who had been tested in 1973. The participants were those who continued to reside in the community and agreed to participate.

### *Xenodiagnosis*

Xenodiagnosis was performed on 40 seropositive people in 1981.

### **Methods of Blood Collection, Serology, and Xenodiagnosis**

The methods used for the collection and storage of blood (9), *T. cruzi* antigen preparation (8, 30), conduct of the indirect hemagglutination (IHA) serologic test (positive titer  $\geq 128$ ) (8), and xenodiagnosis (10) have already been described.

### **Electrocardiograms**

ECGs, recorded with either a Cambridge or Burdick portable ECG machine, included the six standard limb leads and either three or six standard precordial leads. The ECGs were evaluated by a cardiologist (LBJ) for rhythm, rate, PQRSTU contours, PR interval, and QRS axis, duration, and configuration in accordance with standard criteria but without knowledge of the patient's serologic status.

### **Statistical Analysis**

The statistical association between two dichotomous outcomes was evaluated

using the chi-square test or, when the expected number for a cell was less than 5, Fisher's exact test.

## RESULTS

### Serologic Surveys and Seroconversion

Results of the 1971 serologic survey, in which sera from 238 people were tested by IHA, are shown in Table 1, which groups the subjects by age and sex. Of the 86 children (subjects under age 16) who were tested, four (5%) were found to be seropositive. However, for all subsequent age groups from ages 16 through 39, the percentage of seropositives increased progressively—from 41% in the 16–19 year age group to 78% in the 30–39 group. Thereafter, in the older age groups, the rates either remained about the same or declined. The difference in seropositivity among females (48%) versus males (36%) was not statistically significant. Overall, of the 238 people tested, 42% were seropositive; but of the 135

people over 19 years old who were tested, 67% were seropositive.

IHA results from the 1981 serologic survey, which tested 144 children under age 10 and 135 adults over age 19, are shown in Table 2. Of the 144 children, only one was positive. Of the 135 adults, 43 (32%) were positive.

Regarding seroconversion, of 61 subjects tested in 1971 and 1973 and retested in 1981, one of 21 seronegatives converted to positive and four of 39 seropositives converted to negative.

Of the 238 persons seen in 1971, four had died by 1981, three of unknown causes.

### Cross-sectional Study of 254 Subjects

#### *Comparison of Clinical Findings among Seropositive and Seronegative Subjects*

Medical histories were provided by 177 subjects. As indicated in Table 3, differences in the frequency of signs and symptoms reported by the 83 seroposi-

**Table 1.** Age- and sex-specific indirect hemagglutination test (IHA) results for 238 people tested in the Chila serologic survey of 1971.

Age group (in years)	% of study population in each age group	% males in each age group	IHA test results (positive titer $\geq 128$ )					
			Males		Females		Total	
			No. pos.		No. pos.		No. pos.	
			No. tested	% pos.	No. tested	% pos.	No. tested	% pos.
0–3	5	69	0/9	0	0/4	0	0/13	0
4–6	8	65	0/13	0	0/7	0	0/20	0
7–9	7	44	0/7	0	2/9	22	2/16	13
10–12	9	68	2/15	13	0/7	0	2/22	9
13–15	6	73	0/11	0	0/4	0	0/15	0
16–19	7	47	4/8	50	3/9	33	7/17	41
20–29	16	41	10/15	67	13/22	59	23/37	62
30–39	11	46	10/13	77	11/14	79	21/27	78
40–49	12	32	6/9	67	13/19	68	19/28	68
50–59	10	42	8/10	80	10/14	71	18/24	75
60+	10	40	3/8	38	6/11	55	9/19	47
Total	100	50	43/118	36	58/120	48	101/238	42

**Table 2.** IHA test results for 144 children and 135 adults tested in the 1981 survey.

Age group <sup>a</sup> (in years)	Indirect hemagglutination test results <sup>b</sup>	
	No. pos. No. tested	% positive
Children		
0-3	0/41	0
4-6	0/39	0
7-9	1/64	2
Total	1/144	0.7
Adults		
20-29	4/36	11
30-39	20/46	43
40-49	7/25	28
50-59	8/17	47
60+	4/11	36
Total	43/135	31.9

<sup>a</sup>No people in the 10-19 age range were tested.

<sup>b</sup>Positive titer  $\geq 128$ .

tives and the 94 seronegatives were statistically significant ( $p < 0.05$ ) in the following instances: (1) initial bite lesions (Romaña's sign [unilateral bipalpebral

edema] or chagoma [furuncle-like skin lesion]) or edema of the face or body was recalled by four (4.8%) seropositives but no seronegatives; (2) fatigue affected eight (9.6%) of the seropositives but only two (2.1%) seronegatives; and (3) orthopnea was reported by six (7.2%) seropositives but only one seronegative.

No statistically significant differences were found in the frequencies of physical examination abnormalities among the 83 seropositives and 94 seronegatives (Table 4).

### *ECG Findings among Seropositives and Seronegatives*

Of the 254 people tested by ECG, 115 were seropositive and 139 seronegative (Table 5); the age distribution of these subjects is shown in Table 6.

As Table 5 indicates, a statistically significant difference ( $p < 0.005$ ) was observed between the frequency of com-

**Table 3.** Frequency of abnormalities in medical histories from 83 seropositive and 94 seronegative subjects.

Signs and symptoms reported in medical histories	Frequency of the abnormality among:				p values
	83 seropositives		94 seronegatives		
	No.	%	No.	%	
<i>History of acute illness:</i>					
Chagoma, Romaña's sign, or edema of the face or body	4	5	0	0	<0.05
<i>History of chronic illness:</i>					
Fatigue	8	10	2	2	<0.05
Weight loss	23	28	17	18	NS <sup>a</sup>
Palpitations	38	46	36	38	NS
Dyspnea on exertion	22	27	23	24	NS
Orthopnea	6	7	1	1	<0.05
Precordial pain	20	24	24	26	NS
Loss of consciousness	7	8	7	7	NS
Convulsions	0	0	2	2	NS
Peripheral edema	9	11	7	7	NS
Dysphagia (mild)	5	6	6	6	NS
Dysphagia (severe)	0	0	0	0	—
Regurgitation	10	12	10	11	NS
Constipation	8	10	4	4	NS

<sup>a</sup>NS = not significant.

**Table 4.** Frequency of physical examination abnormalities among the 83 seropositives and 94 seronegatives.

Physical examination findings	Frequency of the abnormality among:				p values
	83 seropositives		94 seronegatives		
	No.	%	No.	%	
Arrhythmias	7	8	2	2	NS <sup>a</sup>
Cardiac murmurs	44	53	35	37	NS
Gallops	11	13	8	9	NS
Cardiomegaly	1	1	1	1	NS
Cardiac insufficiency	9	11	6	6	NS
Large bowel fecal mass	0	—	0	—	—

<sup>a</sup>NS = not significant.

plete right bundle branch block (RBBB) with or without other findings in seropositive versus seronegative subjects. Overall, RBBB was found in nine (7.8%) of the seropositives but only one (0.72%) of the seronegatives.

Another significant difference ( $p < 0.05$ ) was observed with respect to premature ventricular contractions, which were found in seven (6.1%) of the seropositives as compared to two (1.4%) of the seronegatives.

#### *Demographic and Laboratory Findings for Subjects with RBBB*

Of the 10 subjects with RBBB, nine were seropositive. Of these seropositives, two were between the ages of 8 and 29 years, five were 30 to 49 years old, and two were 50 years of age or older; three of the nine were men and six were women. The one seronegative subject with RBBB was a 66-year-old man with a negative history for Chagas' disease and no abnormalities on physical examination.

#### **Longitudinal Study of 57 Subjects: ECG Changes, 1973–1981**

A total of 57 people (all over the age of 15 years in 1973) who received an ECG in 1973 and again in 1981 were included

in the longitudinal study. All 42 of the initially seropositive subjects remained seropositive over the eight-year period, and all 15 of the initially seronegative subjects likewise remained seronegative (Table 7).

Of the 57 ECG pairs, 18 showed no changes, 29 showed doubtful changes, and 10 revealed definite changes. As Table 7 indicates, most of these changes occurred among the seropositives. Specifically, nine (21.4%) of the 42 seropositive pairs showed definite changes (equivalent to 2.7% per year), as compared to only one (6.6%) of the 15 seronegatives. However, this distribution was not statistically significant ( $p > 0.05$ ).

Of the definite changes observed in the nine ECG pairs from seropositive subjects, three were changes characteristic of Chagas' disease, two involving ventricular premature beats and one involving an increase of the R:S ratio in lead V1. The other six changes were not characteristic of Chagas' disease, three involving QRS axis shifts (two rightward and one leftward, the axis always remaining within normal limits); two involving mild T contour changes; and one involving changes suggestive of an interval inferior and posterior wall myocardial infarction. The one seronegative subject with a definite change showed a change of T contour from upright to inverted in AVL. No

**Table 5.** Frequency of electrocardiographic abnormalities among 115 seropositive and 139 seronegative persons.

Electrocardiographic findings	Frequency of the abnormality among:				p values
	115 seropositives		139 seronegatives		
	No.	%	No.	%	
Intraventricular conduction delays	10	9	5	4	NS <sup>a</sup>
<i>Right bundle branch block (total)</i>	9	8	1	1	<0.005
RBBB alone	5	4	1	1	NS
RBBB with left anterior fascicular block	1	1	0	0	NS
RBBB with superior, rightward axis	1	1	0	0	NS
RBBB with right axis deviation	2	2	0	0	NS
<i>Left anterior fascicular block alone</i>	1	1	4	3	NS
Left bundle branch block	0	0	0	0	—
rS <sub>r</sub> ' in V <sub>1</sub> , QRS = 0.10 sec	0	0	0	0	—
1° Atrioventricular block	0	0	1	1	NS
Right axis deviation	1	1	2	1	NS
R > S in lead V <sub>1</sub>	3	3	0	0	NS
Left atrial abnormality	0	0	0	0	—
Myocardial infarction, probable	0	0	0	0	—
Myocardial infarction, possible	1	1	1	1	NS
Primary ST-T-U abnormalities <sup>b</sup>	17	15	22	16	NS
Premature ventricular contractions	7	6	2	1	<0.05
Premature atrial contractions	2	2	1	1	NS
Short PR interval (<0.12 sec)	0	0	1	1	NS
High voltage <sup>c</sup>	2	2	2	1	NS
Atrial fibrillation	0	0	1	1	NS
Subjects with one or more abnormalities	43	37	38	27	NS

<sup>a</sup>NS = not significant.

<sup>b</sup>ST-T-U abnormalities occurring in the presence of normal QRS complexes.

<sup>c</sup>Possibly due to left ventricular hypertrophy.

subject exhibited a new bundle branch block.

numbers of bugs positive when tested individually ranged from 2 to 23.

### Isolation of *T. cruzi* from Seropositives

Of 40 seropositive subjects tested by xenodiagnosis in 1981, seven (18%) yielded positive results. Among the batches of bugs used to test these seven people, the

### DISCUSSION

#### High Prevalence of Infection but Absence of Transmission in Chile

The 1971 serosurvey in Chile found a *T. cruzi* antibody prevalence in adults of

**Table 6.** Frequency of complete right bundle branch block (RBBB) by age group and serologic status for 254 persons on whom ECGs were conducted in 1973 and/or 1981.<sup>a</sup>

Age group (in years)	Seropositives		Seronegatives		p values
	No. with RBBB	% with RBBB	No. with RBBB	% with RBBB	
	No. tested		No. tested		
8-19	1/5	20	0/23	0	NS <sup>b</sup>
20-29	1/18	6	0/41	0	NS
30-39	3/42	7	0/28	0	NS
40-49	2/18	11	0/21	0	NS
50-59	2/21	10	0/14	0	NS
60+	0/11	0	1/12	8	NS
Total	9/115	8	1/139	1	<0.005

<sup>a</sup>If ECGs were conducted during both time periods, the subject's age was that at the first test.

<sup>b</sup>NS = not significant.

67%. This finding approximates the 76% prevalence reported in nearby Cerro del Aire (10). These are both high prevalences for Mexico; however, they are not unlike high prevalences reported from South America.

In contrast, our serosurveys of Chila children revealed a near-absence of *T. cruzi* antibody, a finding similar to those we obtained with sera from young people in Cerro del Aire and other communities in the region (9, 10).

This paucity of antibody in young children indicates a near cessation of *T. cruzi* transmission to humans in the region from approximately 1955 to 1981. This correlates with onset of residual insecticide spraying for malaria control and with disappearance of triatomine vector(s) from Chila and other communities in the Pacific coastal study region of Oaxaca (9, 10). A review of malaria campaign records through 1981 has shown that DDT was used almost exclusively for spraying within the region after 1962 (31). Initially, the insecticide was applied every four months. Beginning in 1976, the schedule was changed to twice-yearly spraying in Chila and other communities, and in some areas spraying was discontinued.

Extensive searches by us for vectors in

the region produced only rare specimens of *Rhodnius prolixus* and *Triatoma dimidiata* (12, 13). Villagers told us that they had not seen the bugs for about 10 years. We presume the indigenous vectors before onset of spraying were *T. dimidiata* and *R. prolixus* (9) and *T. mazzottii* (32).

### Clinical Manifestations of Chagas' Disease in Chila

Acute Chagas' disease probably occurs in Chila but is not recognized for lack of any trained medical observers in the community. However, in response to our inquiries about possible clinical findings, chagoma-like or Romaña-like lesions were reported more frequently by seropositive subjects than by seronegatives.

In the chronic myocarditis of Chagas' disease, cardiomegaly and heart failure may occur; and the conduction system may be affected, leading to a variety of arrhythmias and conduction disturbances. The histories we obtained from chronically infected subjects showed fatigue and orthopnea to be significantly more frequent among seropositives than seronegatives. However, the physical examinations showed no significant differences in findings of the sort that may



**Table 7.** Longitudinal study: Electrocardiographic changes between 1973 and 1981 for paired ECGs from 57 subjects.

	Seropositives (n = 42)	Seronegatives (n = 15)
Age range <sup>a</sup>	17–65	16–66
Median age	35	37
Mean age	37	37
% males	43	43
Number (%) with progression of ECG abnormalities	9 (21%) <sup>b</sup>	1 (7%) <sup>b</sup>

<sup>a</sup>Age in years in 1973.

<sup>b</sup> $p > 0.05$ .

occur in chronic Chagas' disease. In addition, sudden and unexpected death of young adults, a feature of the disease in some parts of South America, does not appear to occur in Chila. Although chronic infection may also result in intestinal motility disturbances or in dilatation of the esophagus, colon, or other organs in central Brazil and some other regions of South America, our history and physical examination findings do not suggest that the infection in Chila causes the digestive form of the disease.

## Electrocardiographic Findings

### *Cross-sectional Study*

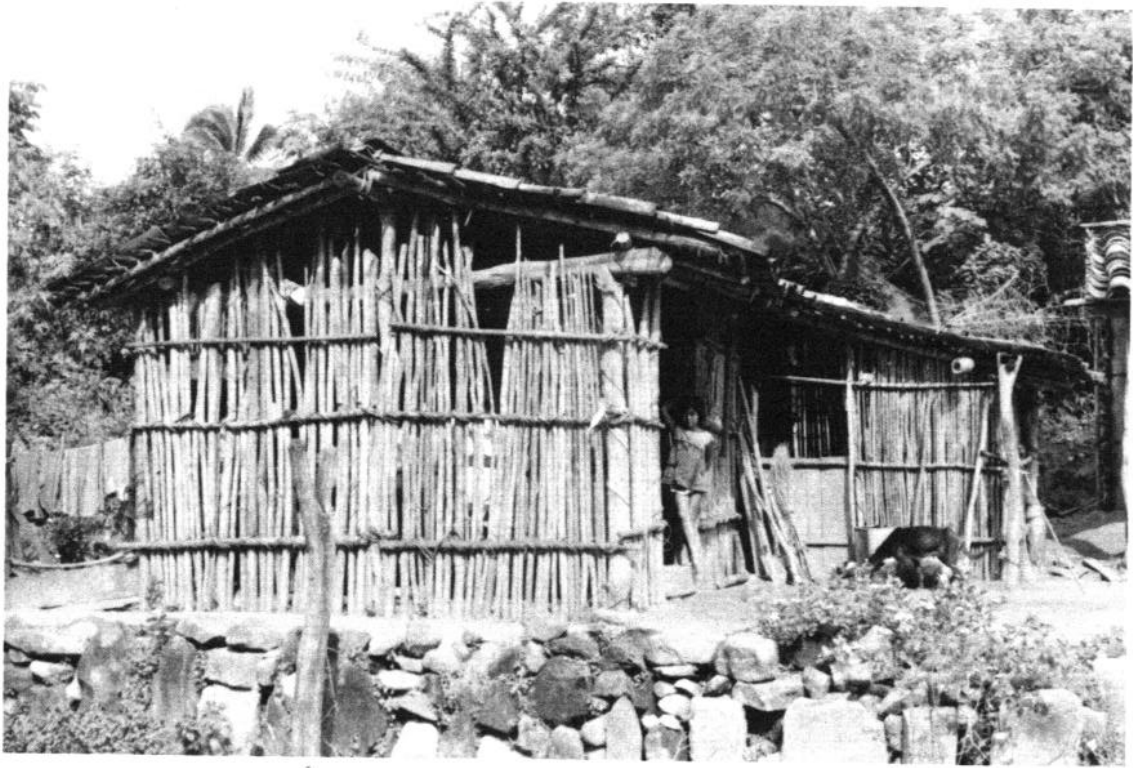
RBBB is a characteristic ECG feature of chronic Chagas' disease (13). Pinto-Dias (33) has commented that an endemic region for Chagas' disease could be recognized electrocardiographically by either one of two findings: (1) a prevalence of RBBB higher than 2% and (2) a marked disproportion in the frequency of right and left bundle branch block. In this study, the frequency of RBBB was 4% among all people tested and 8% among seropositives; while the ratio of RBBB to LBBB was 9:1 among seropositives and 1:4 among seronegatives.

In addition to being a feature of Chagas' disease etiology, RBBB can occur as an expression of coronary artery disease (generally in people over age 60), in patients with hypertension, on rare occasions as a manifestation of rheumatic heart disease, and as an isolated finding in the absence of other cardiac abnormalities. In Chila, the relatively young age of most people with RBBB and the near absence in the population of hypertension or murmurs indicative of rheumatic heart disease suggests that these other potential causes of a high RBBB frequency were not operative.

### *Longitudinal Study*

Our eight-year prospective observations of paired ECGs from 57 subjects showed electrocardiographic changes appearing among seropositives at a rate of 3% per year. These changes, although distinct, did not include new atrioventricular blocks; and some of the changes were not characteristic of Chagas' disease. For purposes of comparison, it is worth noting that we found no ECG changes in 37 people from Cerro del Aire who we followed prospectively for seven years (10).

Community-based longitudinal studies of Chagas' disease conducted in other countries have shown progression of ECG abnormalities in seropositive persons that have often included development of atrioventricular blocks (13). More specifically, in Venezuela, studies have found 3.1% yearly increases in ECG abnormalities over a seven-year followup period (15) and 0.5% yearly increases over a four-year followup period (14). In Brazil, studies have found 3.2% yearly increases over a 10-year followup period (28), 5.8% yearly increases over a six-year followup period (28), and other yearly increases of 2.6% (11, 12, 16) and less than 5% (20). In Chile, studies have found 2.3% yearly increases



Typical homes in the study area display walls of wood poles and mud with roofs of palm thatch and tile.

over a four-year followup period (19), 2.5% yearly increases over a four-year followup period (19), and yearly increases of 10% (27).

We conclude from the cross-sectional and longitudinal ECG studies in Chila and from the *T. cruzi* isolations from seropositive subjects that *T. cruzi* infection in this region of Oaxaca can induce a substantial degree of cardiac electrical abnormality. Whether the myocardial damage responsible for these abnormalities results in significant morbidity or in early death is not yet established. Our knowledge is also incomplete with regard to the frequency and severity of both acute and congenital *T. cruzi* infections.

Given the pathogenic potential of the infection in Chila, the serendipitous but effective control of *T. cruzi* transmission as a result of the malaria control program, and the reduction in the scope of that program in some regions, it is essential that monitoring designed to detect repopulation of houses by the triatomid bugs be maintained and that serologic surveillance of residents continue, particularly through serial surveys of children, in order to recognize resumption of transmission of the infection to humans.

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### *Cholera in the Americas*

As of 27 February 1992, a cumulative total of 439,839 cases of cholera had been recorded in the Americas since the epidemic began in early 1991. Nearly 49,000 of these cases have occurred in 1992, resulting in 24,000 hospitalizations and 296 deaths. To date, 18 countries have reported cases, four of them (Argentina, Belize, Costa Rica, and French Guiana) for the first time since the beginning of 1992.

Source: Pan American Health Organization, Health Situation and Trend Assessment Program.