A FOUR-YEAR FOLLOWUP SURVEY OF CHAGASIC CARDIOPATHY IN CHILE[1]

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INTRODUCTION

The natural history of Chagasic cardiopathy is still not well-known, mainly because innumerable clinical pictures develop without symptoms, and the cases seen at hospitals are merely the most overtly serious. This circumstance may tend to create a false impression that this cardiopathy is relatively benign, because of the small demand it generates for hospital beds in comparison with other pathologies. Hence, if it were possible to elucidate what happens to the great majority of asymptomatic cases, that would constitute an important forward step in understanding a disease that afflicts millions of people in the Americas.

In 1977 we launched a long-term project in Chile that was directed at investigating the epidemiologic picture of Chagas' disease in endemic areas and its cardiac implications. This study revealed that all previous assessments had underestimated both the incidence of the disease and its socioeconomic repercussions for the country (*1–6*). Responding to these findings, health authorities took up the problem and adopted a number of health measures—including periodic disinsection of accessible areas and health education at community centers and primary schools. (A simple explanatory leaflet was produced for these education campaigns that informed readers about the dangers of the disease and about ways to prevent household infestations of triatomid vectors.)

We also promoted parallel studies seeking to elucidate epidemiologic relationships between humans, associated animals, and vector insects (*7–8*); to detect different types of vectors and examine their interrelationships; and to define the structures of zymodemes in various *Trypanosoma cruzi* strains found in different endemic areas (*9–10*).

This article reports our experience with long-term field followup of cardiac pathologies observed during the first survey, specifically regarding

[1] This article will also be published in Spanish in the *Boletín de la Oficina Sanitaria Panamericana*, Volume 101, 1986. The work reported was financed by a grant from the University of Chile and by Grant No. 820599 from the UNDP/World Bank/WHO Tropical Diseases Research Program.

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changes in the subjects' clinical, serologic, and electrocardiographic pictures after a lapse of four years. It also reports findings concerning the risk that people exposed to chagasic infection but showing a normal ECG in the original survey would subsequently develop cardiopathy.

MATERIALS AND METHODS

Our original survey begun in 1977, whose data were employed in the work reported here, involved 2,938 subjects who were given serologic tests and ECGs. Nearly two-thirds of these subjects (1,932) yielded serologic results negative for chagasic infection. Four hundred and two (22%) of these 1,932 showed significant ECG alterations, and these 402 were considered to constitute a control group hereafter referred to as "Group A." The other 1,006 subjects yielded serologic results positive for chagasic infection. Three hundred and ninety-one (39%) of these 1,006 showed significant ECG alterations, and 298 of the latter yielded findings suggesting chagasic cardiopathy (*6,11*). These 298 constituted a group designated "Group B." As the foregoing implies, 615 (61%) of the 1,006 subjects with positive serologic findings had normal ECGs; these 615 were considered to be at risk of contracting chagasic cardiopathy at any time. For purposes of our study, 67 of these 615 were selected at random, designated "Group C," and subjected to further examination. These three groups were selected in 1981 when we began the followup work reported here.

All members of these three groups were given serologic tests for *T. cruzi* antibodies at the beginning of the original study and again after four years (*12–15*). On both occasions each serum sample was tested by two of three serologic methods, the three being indirect hemagglutination (IHA), complement fixation (CF), and indirect immunofluorescence (IIF). IHA titers above 1:16, CF titers above 1:5, and IFF titers above 1:20 were considered positive.

During the fourth year after the initial survey, the year depending upon when the first survey had been carried out, a clinical study was conducted of 481 people in the three groups; this study was similar to that conducted during the original survey. In addition, these subjects were given a twelve-lead ECG with an extended II lead for the study of arrhythmias. These ECGs were analyzed independently of the serologic results according to the following parameters: spatial P, QRS, and T axes; PR, RR, RS, and QT intervals; amplitude of R in V_1 and V_6; intrinsecoid deflection in V_1 and V_6; ST-T segment; and T-wave items (Sokolow index). The electrocardiographic diagnoses developed in this manner were grouped according to the guidelines proposed by Maguire and colleagues (*15*), and a statistical analysis was made of the differences between the groups. In addition, the diagnoses were analyzed according to the age and sex of the persons surveyed in the three groups during the initial ECG. When no significant differences were found, we used the method of diagnosis employed in the original work (*5*), to which Student's t test was applied.

We also studied the trend of ECG abnormalities in groups A and B by means of time-correlation graphs, and in this manner evaluated the origins of new abnormalities. By definition, there were initially no normal ECGs in groups A

and B, and normalization of an abnormality that had been recorded on the initial ECG was regarded as a change for purposes of statistical analysis. However, because we were dealing with multiple abnormalities in many ECGs, normalization of a specific condition did not necessarily constitute normalization of the whole tracing.

All of the studies reported here—performed in 1981, 1982, 1983, and 1984—were carried out in the 36 villages where the original sample survey was conducted. For reasons to be discussed, by the end of four years Group A had been reduced to 216 subjects and Group B to 198 subjects, and so it was these subjects who provided the basis for the comparison reported here.

The members of all three groups lived in rural, mostly semi-desert areas of northern Chile. All were engaged in farming arable land found along the courses of small rivers flowing down from the Andes Mountains, and in general all had very similar working conditions. Apart from a few people over 80 years of age who were excluded from Group B in order to eliminate arteriosclerotic pathologies (*11*), the age distribution of subjects in Group A and Group B was similar. The members of Group C shared essentially the same socioeconomic conditions as members of the other two groups, but they tended to be somewhat younger. The ages of the different subjects correspond to those recorded in the years mentioned above (1981–1984), so that the recorded ages of all subjects were four years greater than those recorded at the time of the original study.

Results

Followup of Groups A and B

Table 1 shows the reasons for reduction in the numbers of subjects in groups A and B during the study period. Of the 402 original Group A subjects (people with negative serology but abnormal ECGs), nine (2.2%) died from causes indicated below; 168 (41.8%) moved to other areas in search of better financial prospects; seven (1.7%) declined to be surveyed; and two (0.5%) showed a serologic conversion from negative to positive for *T. cruzi* antibodies.

Of the 298 original Group B subjects (people with positive serology, abnormal ECGs, and findings suggesting Chagas' disease), 22 (7.4%) died of chagasic cardiopathy; one (0.3%) died of stomach cancer; 48 (16.1%) moved to other areas; and 29 were eliminated for the following reasons: Four were hospitalized in other areas at the time of the survey; one was away in the mountains looking after livestock; four underwent serologic conversion from positive to negative; two exhibited symptoms of aortic insufficiency; one showed symptoms of obstructive cardiomyopathy; 12 had diastolic pressure readings over 100 mmHg; and five had been over 80 years old when initially surveyed.

Causes of death. All deaths in Chile must be certified by the responsible physician of the main provincial hospital. Because of this requirement, we were able to obtain reliable data about all of the study subjects who died during the study period. Four of the nine Group A fatalities (see Table 1) were caused by bronchopneumonial conditions, one by stomach cancer, one by a cerebrovascular accident, and three by refractory cardiac insufficiency. In contrast, nearly all the Group B fatalities appeared attributable

TABLE 1. Changes in the sizes of groups A and B over the four-year study period.

	Group A		Group B	
	No.	%	No.	%
Size of original group	*402*	*(100)*	*298*	*(100)*
Deaths due to chagasic cardiopathy	0	(0)[a]	22	(7.4)[a]
Deaths due to other causes	9	(2.2)[a]	1	(0.3)[a]
Left the area	168	(41.8)	48	(16.1)
Other status	9	(2.2)	29	(9.7)
Size after four years	*216*	*(53.7)*	*198*	*(66.4)*

[a] The difference in overall mortality (2.2% in Group A, 7.7% in Group B) is highly significant ($P < 0.001$).

to chagasic cardiomyopathy. Specifically, 12 Group B subjects suffered "instantaneous death" (two of these people were wearing pacemakers to counteract total auriculoventricular block), 10 died of congestive cardiac insufficiency, and only one died of another cause (stomach cancer).

These four-year data show that the Group B subjects (with chagasic cardiopathy) had an appreciably higher annual risk of dying than did the control subjects with abnormal ECGs in Group A, the annual risks being 0.6% in Group A and 1.9% in Group B. The difference between these mortality figures was found to be highly significant ($P < 0.001$).

Age and sex of the decedents. Regarding age and sex, Table 2 shows that most of the Group A fatalities occurred among women, while most of the Group B fatalities occurred among men. The specific ages of the nine Group A subjects at the time of death were as follows: men—63, 78, and 82 years; women—50, 67, 72, 77, 80, and 80 years. The specific ages of the 22 Group B subjects apparently dying of Chagas' disease were as follows: men—45, 46, 54, 56, 58, 59, 60(2), 61, 62(2), 63, 65, and 76 years; women—47, 48, 50, 55, 56(2), 58, and 65 years. As these figures show, most of the Group A fatalities occurred after age 60, while most of the Chagas'-related Group B fatalities occurred in younger subjects.

TABLE 2. Sex and age of the nine Group A subjects dying of all causes and the 22 Group B subjects apparently dying of Chagas' disease during the four-year study period.

Age at death (in years)	Group A			Group B		
	Women	Men	Total	Women	Men	Total
41–50	1	—	1	3	2	5
51–60	—	—	—	4	6	10
61–70	1	1	2	1	5	6
71–80	4	1	5	—	1	1
81–90	—	1	1	—	—	—
Total	6	3	9	8	14	22

Electrocardiographic findings (decedents). As Table 3 indicates, the Group B decedents with chagasic cardiopathy showed more auriculoventricular and intraventricular conduction disorders than did the Group A (control group) decedents.

Specifically, the nine Group A decedents exhibited no A-V or bifascicular block. Two Group A women (72 and 77 years old) exhibited arrhythmias (1 auricular extrasystole and 1 ventricular extrasystole). Two Group A men (63 and 78 years old) exhibited left anterior hemiblock, and a Group A woman (80 years old) exhibited complete left branch block. Left ventricular hypertrophy was observed in two Group A women 50 and 67 years old. An image indicating necrosis of the diaphragmatic wall of the myocardium was found in one Group A woman 80 years old, and another indicating necrosis of the anterior wall was found in one Group A man 82 years old.

In Group B, the four cases of arrhythmia included two cases of polyfocal ventricular extrasystole (one in a man of 56 and the other in a woman of 47) and two of auricular extrasystole (in men of 54 and 58). First degree A-V block was found in a woman of 50, and two cases of total A-V block corrected by fixed-rate pacemakers were observed in men of 60 and 76.

The eight cases of unifascicular block included four complete right branch blocks (in two women of 48 and 65 and two men of 61 and 63). There were also three cases of left anterior hemiblock (in three men of 62, 62, and 65) and one case of left posterior hemiblock (in a man of 46).

The four cases of bifascicular block involved left anterior hemiblock associated with complete right branch block (in two men of 59 and 60 and two women of 56 and 58).

One case of anterior-face ischemia occurred in a man of 45, and two cases with an inactivation or QS image of the anterior wall were observed in two women of 55 and 56.

TABLE 3. ECG abnormalities observed in the nine Group A and 22 Group B decedents.

Conditions	Group A	Group B
Arrhythmias	2	4
A-V block, first degree	0	1
A-V block, third degree	0	2
Unifascicular block	3	8
Bifascicular block	0	4
Ischemia	0	1
QS image	2	2
Cavity hypertrophy	2	0
Total	9	22

Analysis of Followup Data on Groups A, B, and C

The distribution by age and sex of all subjects remaining in the three study groups after four years is shown in Table 4. As may be seen, women predominated in all three groups, presumably because the survey was conducted on week-days during hours when the male head of the household was generally at work. The age distribution of Group A and Group B subjects was generally similar; it should be noted, however, that five Group B subjects over 81 years old were excluded from the study in order to reduce arteriosclerosis as a factor in assessing chagasic cardiopathy.

Clinical Cardiopathic Findings

In the original survey it was noted that both the Group A and Group B subjects showed few clinical symptoms, and the same circumstance prevailed in the survey reported here.

TABLE 4. Distribution by age and sex of all Group A, B, and C subjects remaining in their respective study groups four years after the initial survey.

Age group (in years)	Group A			Group B			Group C		
	Men	Women	Total	Men	Women	Total	Men	Women	Total
11–20	10	9	19	2	3	5	4	1	5
21–30	14	23	37	9	11	20	4	6	10
31–40	13	26	39	9	28	37	4	16	20
41–50	15	24	39	19	31	50	7	24	31
51–60	13	16	29	10	24	34	—	1	1
61–70	10	18	28	14	20	34	—	—	—
71–80	9	9	18	9	9	18	—	—	—
81–90	2	5	7	0	0	0	—	—	—
Total	86	130	216	72	126	198	19	48	67

Group A clinical histories revealed symptoms of congestive cardiac insufficiency in 10 subjects (4.6%). These included six men 52 to 89 years old and four women 52 to 80 years old. (The ECGs showed previous necrosis in five of the 10 cases—in three men of 52, 62, and 89 and two women of 55 and 63.)

Group B clinical histories revealed symptoms of chagasic cardiopathy in 21 subjects (10.8%), seven of these having multiple complaints. Nine subjects presented with irregular precordial palpitations and sharp precordial pain, the latter most often located on the left side. (The subjects involved were four men of 23 to 40 and five women of 19 to 50; three of these also exhibited cases of Adams-Stokes crisis.)

In all, there were 10 Group B subjects with Adams-Stokes crisis, but only one of these (a man of 60) had third-degree A-V block. Of the other nine, three women of 38, 39, and 42 showed wandering of the auricular pacemaker; one man of 38 had auricular tachycardia; three men of 49, 53, and 65 and a woman of 52 exhibited bifascicular block (left anterior hemiblock plus complete right branch block), while one man of 33 showed another type of bifascicular block (left posterior hemiblock plus complete right branch block).

Also, 10 Group B subjects exhibited symptoms of congestive cardiac insufficiency. (Four were among those with bifascicular block and Adams-Stokes syndrome.) The ECGs of three women of 45, 48, and 50 showed alteration of ventricular repolarization, while those of the other three subjects (two women of 60 and 62 and a man of 63) showed ischemia images. Neither acute-phase antecedents nor portal of entry (Romaña's sign) antecedents were observed in any members of the group.

Physical examinations revealed arrhythmias in five Group A and nine Group B subjects. Mesosystolic murmurs without an organic character were observed in three Group A subjects (two men 45 and 70 years old and a woman of 72) and in six Group B subjects (three men 35, 48, and 56 years old and three women of 56, 60, and 65). This latter finding did not coincide with symptomatic Chagas' disease cases.

Electrocardiogram Results

Table 5 shows the changes found in the control group (A) and the chagasic group (B) when the first ECGs were compared with those obtained four years later. As may be seen, there was a higher proportion of ECG abnormalities per tracing among the chagasic group on both occasions. Initially, by definition, there were no normal ECGs in either group. A considerable number of these abnormalities (28.4% in the control group, 31.7% in the chagasic group) were found to have normalized themselves as of the final tracing. However, because some subjects had multiple abnormalities, the number of abnormalities normalized was greater than the number of ECGs normalized. Overall, 51 Group A final tracings (23%) were found to be normal, as were 16 Group B final tracings (8%). The number of abnormalities that became normalized were 99 in Group A and 137 in Group B.

Table 5 also shows that the prevalences of observed abnormalities in the two groups were fairly similar in most cases, and that there were only a few instances when the Group A and Group B data showed differences that were statistically very significant ($P < 0.01$). More specifically, initial abnormalities very significantly more prevalent in Group B than Group A ($P < 0.01$) included bifascicular block, subepicardial damage (which was not found in Group A), and the presence of a prolonged QT interval on the initial tracing. The greater frequency of QS images in Group A related to coronary cardiopathy (a history of in-

TABLE 5. ECG abnormalities found in the 216 Group A and 198 Group B study subjects.

	Group A				Group B			
	Initial ECG		Final ECG		Initial ECG		Final ECG	
Abnormal ECG findings	No.	(%)	No.	(%)	No.	(%)	No.	(%)
1. Normalized	0	(0)	99	(28.4)	0	(0)	137	(31.7)
2. Auricular arrhythmia	69	(27.3)	47	(13.5)	46	(14.3)	55	(12.7)
3. Ventricular arrhythmia	12	(4.7)	8	(2.3)	17	(5.3)	19	(4.4)[b]
4. A-V block, 1st degree	8	(3.2)	4	(1.1)	11	(3.4)	10	(2.3)
5. A-V block, 2nd degree	0	(0)	0	(0)	0	(0)	0	(0)
6. A-V block, 3rd degree	1	(0.4)	2	(0.6)	1	(0.3)	3	(0.7)
7. Unifascicular block	76	(30.0)	70	(20.1)	70	(21.7)	62	(14.4)
8. Bifascicular block	9	(3.6)	14	(4.0)	38	(11.8)[a]	47	(10.9)[a]
9. Ischemia image	10	(4.0)	13	(3.7)	18	(5.6)	10	(2.3)
10. Subepicardial damage	0	(0)	0	(0)	7	(2.2)[a]	4	(0.9)[b]
11. Subendocardial damage	4	(1.6)	2	(0.6)	15	(4.7)[b]	19	(4.4)[a]
12. QS image	7	(2.8)	12	(3.4)	3	(0.9)	6	(1.4)
13. Repolarization change	29	(11.5)	17	(4.9)	28	(8.7)	20	(4.6)
14. Cavity hypertrophy	27	(10.7)	32	(9.2)	23	(7.1)	21	(4.9)
15. Prolonged QT	1	(0.4)	29	(8.3)	45	(14.0)[a]	19	(4.4)
Total No. of abnormalities	253	(100)	349	(100)	322	(100)	432	(100)
Total No. of ECGs	216		216		198		198	

[a] Difference between data for Group A (initial) and Group B (initial) or between Group A (final) and Group B (final) is highly significant ($P < 0.01$)
[b] Difference between data for Group A (initial) and Group B (initial) or between Group A (final) and Group B (final) is not highly significant ($P > 0.01$).

farct) in seven Group A subjects. In contrast, the three Group B subjects initially showing QS images had no history of angina. Regarding the final ECGs, the only abnormalities very significantly more frequent in Group B than Group A ($P < 0.01$) were bifascicular block and subendocardial damage.

Auricular arrhythmias. Table 6 provides more information about the observed cases of auricular arrhythmia in the two groups. In general, it shows a higher proportion of functional abnormalities (especially short PR syndrome and bradycardia associated with simple A-V block among miners working at high altitudes) in the Group A subjects. Although auricular fibrillation was initially more common in the Group B (chagasic) subjects, the final ECGs showed it in about equal proportions of both groups. Initial abnormalities observed much more frequently ($P < 0.01$) in the Group B subjects included wandering of the auricular pacemaker, auricular tachycardia, and auricular fibrillation. Of these, the only one sufficiently more frequent in Group B than Group A on both the initial and final ECGs to register a highly significant difference ($P < 0.01$) was auricular tachycardia. Many of the Group B abnormalities were consistent with possible sick sinus syndrome. The difference between the numbers of auricular arrhythmias observed in the two groups was not very significant ($P < 0.01$).

Sex and age data. Table 7 provides data on the sex and age of Group A and Group B subjects whose initial ECGs yielded abnormal findings. While most

TABLE 6. ECG abnormalities associated with arrhythmias observed in the 216 Group A and 198 Group B study subjects.

	Group A				Group B			
	Initial ECG		Final ECG		Initial ECG		Final ECG	
Abnormalities	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Short PR syndrome	28	(40.6)	33	(70.2)	13	(28.3)	14	(25.5)
Wolff-Parkinson-White syndrome	4	(5.8)	0	(0)	0	(0)	0	(0)
Wandering auricular pacemaker	2	(2.9)	0	(0)	9	(19.6)[a]	1	(1.8)[b]
Auricular extrasystole	17	(24.6)	6	(12.8)	8	(17.4)	13	(23.6)[b]
Auricular tachycardia	1	(1.4)	0	(0)	6	(13.0)[a]	10	(18.2)[a]
Auricular bradycardia	8	(11.6)	1	(2.1)	0	(0)	5	(9.1)
Auricular fibrillation	1	(1.4)	5	(10.6)	6	(13.0)[a]	5	(9.1)[b]
Pulmonary P wave	3	(4.3)	0	(0)	0	(0)	0	(0)
Nodal rhythm	1	(1.4)	0	(0)	2	(4.3)	2	(3.6)
Isorhythmic A-V dissociation	1	(1.4)	1	(2.1)	0	(0)	2	(3.6)
Nodal tachycardia	1	(1.4)	0	(0)	0	(0)	0	(0)
Sick sinus syndrome	0	(0)	0	(0)	1	(2.2)	1	(1.8)
Nodal extrasystole	1	(1.4)	0	(0)	0	(0)	0	(0)
Sinus arrest	0	(0)	1	(2.1)	0	(0)	1	(1.8)
2/1 flutter	1	(1.4)	0	(0)	0	(0)	0	(0)
Left auricular rhythm	0	(0)	0	(0)	0	(0)	1	(1.8)
Pacemaker defect with arrhythmia	0	(0)	0	(0)	1	(2.2)	0	(0)
Total	69	(100)	47	(100)	46	(100)	55	(100)

[a] Difference between data for Group A (initial) and Group B (initial) or between Group A (final) and Group B (final) is highly significant ($P < 0.01$)
[b] Difference between data for Group A (initial) and Group B (initial) or between Group A (final) and Group B (final) is not highly significant ($P > 0.01$)

categories of findings reflected the female predominance seen previously in the two study groups, there were more Group A men than women with first degree A-V block, and about equal numbers of Group A men and women with unifascicular block and bifascicular block, as well as more Group B men than women with cavity hypertrophy and about equal numbers of Group B men and women with ventricular arrhythmia, first degree A-V block, bifascicular block, and ischemia image. Aside from the fact that the Group B (chagasic) subjects with repolarization disorders tended to be younger, no highly significant age differences were found. More specifically, no highly significant age differences were observed between Group A and Group B subjects with auriculoventricular block.

Unifascicular blocks. Table 8 provides information about the unifascicular intraventricular blocks observed in Group A and Group B subjects. As may be seen, the initial ECG showed complete right branch block to be three times as prevalent in the Group B (chagasic) subjects ($P < 0.01$), but this difference diminished markedly in data from the final ECG. Incomplete right branch block was far more prevalent among Group A subjects than among those in Group B.

Regarding the sex and age ranges of affected subjects, the data in Table 9 indicate that about equal numbers of Group A men and women initially exhibited the various types of unifascicular blocks encountered, while in Group B there was a greater (though not statistically very significant) predominance of women with complete right branch block and left anterior hemi-

TABLE 7. Abnormal initial ECG findings among the 216 Group A and 198 Group B subjects, showing the numbers and age ranges of the affected subjects, by sex.

	Group A					Group B				
	Men		Women			Men		Women		
Abnormal ECG findings	No.	Age range (years)	No.	Age range (years)	Total	No.	Age range (years)	No.	Age range (years)	Total
1. Normalized	0	0	0	0	0	0	0	0	0	0
2. Auricular arrhythmia	26	11–82	43	16–70	69	23	24–73	23	19–73	46
3. Ventricular arrhythmia	4	20–82	8	11–86	12	8	23–76	9	36–80	17
4. A-V block, 1st degree	6	32–59	2	30–63	8	5	24–49	6	34–49	11
5. A-V block, 2nd degree	0	0	0	0	0	0	0	0	0	0
6. A-V block, 3rd degree	1	65	0	0	1	1	60	0	0	1
7. Unifascicular block	39	11–83	37	15–86	76	30	20–30	40	11–80	70
8. Bifascicular block	5	15–83	4	24–64	9	21	21–80	17	22–68	38
9. Ischemia image	1	53	9	43–71	10	10	32–80	8	22–67	18
10. Subepicardial damage	0	0	0	0	0	2	32–48	5	25–63	7
11. Subendocardial damage	0	0	4	30–63	4	2	65–71	13	33–49	15
12. QS image	4	41–89	3	52–63	7	2	56–76	1	73	3
13. Repolarization change	5	23–63	24	32–83	29	4	27–56	24	30–73	28
14. Cavity hypertrophy	12	22–73	15	16–78	27	20	24–80	3	22–60	23
15. Prolonged QT	1	67	0	0	1	14	23–80	31	23–80	45
Total No. of abnormalities	104		149		253	142		180		322

TABLE 8. Unifascicular blocks observed in the 216 Group A and 198 Group B study subjects.

Type of unifascicular block	Initial ECG				Final ECG			
	Group A		Group B		Group A		Group B	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Incomplete right branch block	30	(39.5)	7	(10.0)	30	(42.9)	10	(16.1)
Complete right branch block	7	(9.2)	21	(30.0)[a]	6	(8.6)	16	(25.8)[b]
Left anterior hemiblock	29	(38.2)	36	(51.4)[a]	26	(37.1)	32	(51.6)[b]
Left posterior hemiblock	8	(10.5)	4	(5.7)	4	(5.7)	2	(3.2)
Complete left branch block	2	(2.6)	2	(2.9)	4	(5.7)	2	(3.2)
Total	76	(100)	70	(100)	70	(100)	62	(100)

[a] Difference between data for Group A and Group B (initial) is highly significant ($P < 0.01$).
[b] Difference between data for Group A and Group B (final) is not highly significant ($P > 0.01$).

TABLE 9. Numbers and age ranges of the 216 Group A and 198 Group B subjects whose initial ECGs showed unifascicular blocks, by sex.

Type of unifascicular block	Group A					Group B				
	Men		Women			Men		Women		
	No.	Age range (years)	No.	Age range (years)	Total	No.	Age range (years)	No.	Age range (years)	Total
Incomplete right branch block	15	11–77	15	21–58	30	3	20–47	4	19–65	7
Complete right branch block	4	34–83	3	31–62	7	8	26–57	13	21–81	21
Left anterior hemiblock	16	15–74	13	15–75	29	16	23–80	20	29–75	36
Left posterior hemiblock	4	30–47	4	18–43	8	2	42–49	2	11–34	4
Complete left branch block	0	0	2	42–54	2	1	65	1	61	2
Total	39		37		76	30		40		70

block. Regarding the ages of subjects with unifascicular blocks, it is worth noting that in Group B both incomplete and complete right branch block was found to occur predominantly in younger men.

Bifascicular blocks. Table 10 shows data on bifascicular blocks found in both initial and final ECGs of Group A and Group B subjects. The quantitative differences involved demonstrate that these blocks predominated among Group B (chagasic) subjects. Regarding distribution of the various types of blocks within Group A and Group B, however, statistical analysis failed to reveal any very significant ($P < 0.01$) differences in the distribution of particular types of bifascicular blocks within the groups. This suggests that a quantitative rather than a qualitative difference is involved.

Regarding distribution of bifascicular blocks by sex, the data in Table 11 show that roughly equal numbers of Group B men and women experienced blocks of the types found. The numbers

TABLE 10. Bifascicular blocks observed in the 216 Group A and 198 Group B study subjects.

Type of bifascicular block[a]	Initial ECG				Final ECG			
	Group A		Group B		Group A		Group B	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
LAHB + IRBB	2	(22)	9	(24)	8	(57)	10	(21)
LAHB + CRBB	4	(44)	18	(47)[b]	4	(29)	24	(51)[b]
LPHB + IRBB	2	(22)	1	(3)	0	(0)	2	(4)
LPHB + CRBB	1	(11)	10	(26)[b]	2	(14)	11	(23)[b]
Total	9	(100)	38	(100)	14	(100)	47	(100)

[a] LAHB = left anterior hemiblock; LPHB = left posterior hemiblock; IRBB = incomplete right branch block, and CRBB = complete right branch block

[b] Differences between the indicated Group A and Group B data are not highly significant (P > 0 01)

TABLE 11. Numbers and age ranges of Group A and Group B subjects whose initial ECGs showed bifascicular blocks, by sex.

Type of bifascicular block[a]	Group A					Group B				
	Men		Women			Men		Women		
	No.	Age range (years)	No.	Age range (years)	Total	No.	Age range (years)	No.	Age range (years)	Total
LAHB + IRBB	1	15	1	64	2	5	37–62	4	32–63	9
LAHB + CRBB	3	26–83	1	65	4	10	29–80	8	22–69	18
LPHB + IRBB	0	0	2	24–28	2	1	54	0	0	1
LPHB + CRBB	1	38	0	0	1	5	21–80	5	42–54	10
Total	5		4		9	21		17		38

[a] LAHB = left anterior hemiblock; LPHB = left posterior hemiblock; IRBB = incomplete right branch block, and CRBB = complete right branch block

of Group A subjects with such blocks were too small for conclusions to be drawn.

ECG changes. So far we have examined numerical data that establish certain differences between the two groups studied but do not express the variation in ECG abnormalities over time. To assess this variation we have used cross-indexed tables in which the 15 ECG abnormalities diagnosed from the first tracing are listed vertically, and the same abnormalities diagnosed from the second tracing are listed horizontally by number. The place where the two listings for a given abnormality cross shows the number of cases in which that abnormality appeared on both ECGs, while other entries on the same horizontal line show the number of cases in which the initial abnormality became normalized or in which it was associated on the later ECG with other abnormalities. For example, Table 12 shows that of 12 subjects with ventricular arrhythmia on the initial ECG, nine did not show this abnormality four years later; three did show it; and the final ECGs of these 12 subjects also showed unifascicular block (in one case),

QS image (in one case), repolarization change (in one case), and cavity hypertrophy (in three cases). In addition, looking down column three it may be seen that five other subjects (for a total of eight) exhibited ventricular arrhythmia on the final ECG.

Table 12, which lists only data for Group A (the control group), shows that 99 of the 253 abnormalities found in the initial 216 ECGs had normalized on the final ECG. Those abnormalities that disappeared were as follows:

(a) 32 auricular arrhythmias—four cases of Wolff-Parkinson-White syndrome (in men given the final ECG when they were 35 to 54 years old), two cases of wandering auricular pacemaker (in women of 23 and 35), one case of auricular tachycardia (in a woman of 25), 11 cases of auricular extrasystole (in five men 16 to 54 and six women 17 to 68), seven cases of auricular bradycardia (in four men 28 to 35 and three women 18 to 40), three cases of pulmonary P wave (in women 27 to 49), one case of nodal tachycardia (in a woman of 27), one case of nodal extrasystole (in a woman of 70), one case of nodal rhythm (in a man of 35), and one case of 2:1 auricular flutter (in a man of 61);
(b) nine ventricular arrhythmias (all of ventricular extrasystole in three men 20 to 82 years old and six women 38 to 61 years old);
(c) five cases of first-degree A-V block (in four men 32 to 59 and one woman of 30);
(d) 13 cases of unifascicular block—six cases of incomplete right branch block (in three men 31 to 42 and three women 21 to 39), four cases of left posterior hemiblock (in two men 35 and 56 and two women 30 and 43), and three cases of left anterior hemiblock (in two males 15 and 24 and a girl of 15);
(e) six ischemia images (in women 43 to 71 years old);
(f) all four images indicating subendocardial damage (in women 30 to 50);
(g) 19 cases of repolarization alterations (in four men 23 to 55 and 15 women 17 to 68);
(h) 11 images of cavity hypertrophy (in three men 45 to 56 and eight women 17 to 76).

The remaining Group A abnormalities persisted over time. In this regard, it should be noted that all seven of the initial QS image abnormalities associated with myocardial necrosis appeared on the final ECG. In addition, 105 new abnormalities appeared on the final ECG, these being as follows:

(a) 10 new auricular arrhythmias—five cases of short P-R syndrome (in men 17 to 54), four cases of auricular fibrillation (in women 70 to 78), and one case of sinus arrest (in a woman of 58);
(b) five new cases of ventricular arrhythmia (all of ventricular extrasystole in men 54 to 73);
(c) one new case of first-degree A-V block (in a man of 68 whose ECG also showed a picture of left ventricular hypertrophy);
(d) one new case of third-degree A-V block (in a man of 68 with an image indicating subendocardial damage);
(e) 13 new cases of unifascicular block—three cases in which a bifascicular block had reverted to a unifascicular form (left posterior hemiblock plus incomplete right branch block becoming left posterior hemiblock in a woman of 38; left anterior hemiblock plus incomplete right branch block becoming incomplete right branch block in a boy of 15; and left anterior hemiblock plus complete right branch block becoming complete right branch block in a woman of 21); five cases of incomplete right branch block (in three men 15 to 56 and two women 36 and 47); three cases of complete left branch block (in two men 54 and 79 and one woman of 70); and two cases of left anterior hemiblock (in men 56 and 75);
(f) eight new cases of bifascicular block, six of which developed in subjects whose initial ECGs showed unifascicular blocks (three cases of incomplete right branch block changed to left anterior hemiblock plus complete right branch block in men of 22, 37, and 57, and three other cases of incomplete right branch block changed to left anterior hemiblock plus incomplete right branch block in women of 29, 39, and 47); in addition, two new cases of left anterior hemiblock plus incomplete right branch block appeared in women of 48 and 74;
(g) two new cases of subendocardial damage (in a man of 50 and a woman of 63);

TABLE 12. Group A abnormalities found by analysis of the initial and final ECGs of the 216 Group A study subjects. The numbers of abnormalities found initially, by type, are shown in column 2. The numbers of subjects with particular abnormalities found on the final ECG, by type, are shown at the bottom of the table (e.g., four subjects showed first-degree A-V block on their final ECGs). The numbers of subjects in whom the initially observed abnormality persisted are shown by the dark numbers running diagonally through the table. And the numbers of subjects who initially had a particular abnormality that disappeared on the final ECG or who showed other abnormalities on the final ECG may be seen by reading horizontally across the table (e.g., of eight subjects with first-degree A-V block on the initial ECG, five did not show this abnormality on the final ECG, three did show it, and one showed another abnormality, prolonged QT).

Initial ECG findings (1–15)	Total No. of initial abnormalities observed	Final ECG findings (1–15)														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. Abnormality normalized	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
2. Auricular arrhythmia	69	32	**37**	1	—	—	—	2	—	3	—	—	1	—	2	6
3. Ventricular arrhythmia	12	9	—	**3**	—	—	—	1	—	—	—	—	1	1	3	—
4. A-V block, 1st degree	8	5	—	—	**3**	—	—	—	—	—	—	—	—	—	—	1
5. A-V block, 2nd degree	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
6. A-V block, 3rd degree	1	—	—	—	—	—	**1**	—	—	—	—	—	—	—	—	—
7. Unifascicular block	76	13	1	1	—	—	—	**49**	6	4	—	—	2	3	5	9
8. Bifascicular block	9	—	—	—	—	—	—	3	**6**	—	—	—	—	—	1	3
9. Ischemia image	10	6	—	1	—	—	—	1	—	**4**	—	—	—	1	1	1
10. Subepicardial damage	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
11. Subendocardial damage	4	4	—	—	—	—	1	—	—	1	—	—	—	1	—	—
12. QS image	7	—	4	—	—	—	—	1	—	—	—	—	**7**	1	—	—
13. Repolarization change	29	19	—	1	—	—	—	2	1	—	—	1	1	**10**	4	5
14. Cavity hypertrophy	27	11	5	1	1	—	—	3	1	1	—	1	—	—	**16**	3
15. Prolonged QT	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	**1**
Total abnormalities or normalized events observed on final ECG		99	47	8	4	—	2	62	14	13	—	2	12	17	32	29

(h) five new images of myocardial necrosis—QS image (in two men of 53 and 82 and three women of 29, 61, and 68, the last two being associated with left anterior hemiblock; the woman of 29 had no history of angina);
(i) seven new cases of repolarization alterations (in two men of 31 and 82 and five women of 38 to 62);
(j) 16 new images of cavity hypertrophy—three cases of hypertrophy of the left auricle (in a man of 47 and two women of 67 and 74) and 13 cases of left ventricular hypertrophy (in five men of 55 to 82 and eight women of 58 to 78);
(k) 28 new cases of prolonged QT (in seven men of 43 to 83 and 21 women of 21 to 66).

Table 13, which presents the data for Group B, shows that 137 of the 322 abnormalities found in the initial 198 ECGs had normalized on the final ECG. Those abnormalities that disappeared were as follows:

(a) 10 auricular arrhythmias—eight cases of wandering auricular pacemaker (in three men of 38, 44, and 73 and five women of 46 to 73), one case of auricular fibrillation (in a woman of 65), and one case of arrhythmia in a man 68 years old with a fixed-rate pacemaker that was complicated by multiple extrasystole;
(b) nine ventricular arrhythmias (all of ventricular extrasystole in four men of 23 to 76 and five women of 36 to 63);
(c) five cases of first-degree A-V block (in four men of 26 to 49 and a woman of 34);
(d) 11 cases of unifascicular block—four cases of incomplete right branch block (in a man of 47 and three women of 19 to 38), five cases of left anterior hemiblock (in two men of 47 and 49 and three women of 29,[5] 35, and 66), one case of left posterior hemiblock (in a man of 49), and one case of complete right branch block (in a man of 30);
(e) two cases of bifascicular block (both left anterior hemiblock plus incomplete right branch block, in a man of 37 and a woman of 38);
(f) 11 cases of ischemia image (in six men of 36 to 71 and five women of 37 to 66);
(g) six images of subepicardial damage (all in the apical region, in two men of 32 and 48 and four women of 25 to 63);
(h) 11 images of subendocardial damage (in two men of 65 and 71 and nine women of 33 to 49);
(i) two cases of myocardial necrosis—QS image (in a man of 76 and a woman of 73);
(j) 21 cases of repolarization change (in two men of 51 and 56 and 19 women of 30 to 73);
(k) 13 images of cavity hypertrophy (in nine men of 29 to 77 and four women of 60 to 80);
(l) 36 cases of prolonged QT syndrome (in 12 men of 29 to 80 and 24 women of 20 to 60).

The remaining Group B abnormalities persisted over the four-year study period. In addition, 130 new abnormalities appeared on the final ECG, these being as follows:

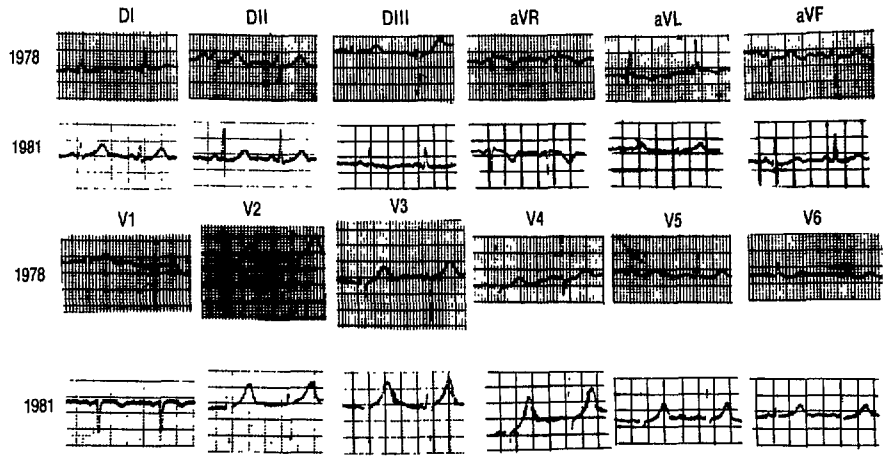
(a) 19 new auricular arrhythmias—one case of short P-R syndrome (in a man of 47), five cases of auricular extrasystole (in a man of 47 and four women of 47 to 57), four cases of auricular tachycardia (in women of 30 to 43), one case of left auricular rhythm (in a woman of 46), two cases of isorrhythmic A-V dissociation (in a man of 52 and a woman of 73), one case of sinus arrest (in a woman of 44), and five cases of sinus bradycardia (in four men of 37 to 76 and a woman of 53);
(b) 11 new cases of ventricular arrhythmia (all of ventricular extrasystole in six men of 36 to 60 and five women of 36 to 60); six of these cases were multifocal;
(c) four new cases of first-degree A-V block (in two men of 47 and 77 and two women of 39 and 61); all four were associated with intraventricular conduction blocks;
(d) two new cases of third-degree A-V block (in a man of 66 whose first ECG had shown a bifascicular block and a woman of 51 without prior evidence of an intraventricular conduction disorder);
(e) 18 new cases of unifascicular block—four cases in which a bifascicular block had reverted to a unifascicular form (left posterior hemiblock plus complete right branch block becoming complete right branch block in a man of 60; left posterior hemiblock plus incomplete right branch block becoming incomplete right branch block in a man of 54; and left anterior hemiblock plus complete right branch block

[5] ECG tracings obtained from this subject are shown in Figure 1.

TABLE 13. Group B abnormalities found by analysis of the initial and final ECGs of the 198 Group B study subjects. The numbers of abnormalities found initially, by type, are shown in column 2. The numbers of subjects with particular abnormalities found on the final ECG, by type, are shown at the bottom of the table (e.g., 10 subjects showed first-degree A-V block on their final ECGs). The numbers of subjects in whom the initially observed abnormality persisted are shown by the dark numbers running diagonally through the table. And the numbers of subjects who initially had a particular abnormality that disappeared on the final ECG or who showed other abnormalities on the final ECG may be seen by reading horizontally across the table (e.g., of 11 subjects with first-degree A-V block on the initial ECG, five did not show this abnormality on the final ECG, six did show it, and one showed another abnormality, unifascicular block).

Initial ECG findings (1–15)	Total No. of initial abnormalities observed	Final ECG findings (1–15)														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. Abnormality normalized	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
2. Auricular arrhythmia	46	10	**36**	1	—	—	1	3	—	—	—	1	—	—	—	2
3. Ventricular arrhythmia	17	9	2	**8**	—	—	—	1	—	—	1	—	—	—	1	—
4. A-V block, 1st degree	11	5	—	—	**6**	—	—	1	—	—	—	—	—	—	—	—
5. A-V block, 2nd degree	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
6. A-V block, 3rd degree	1	—	—	1	—	—	**1**	—	—	—	—	—	—	—	—	—
7. Unifascicular block	70	11	8	3	3	—	—	**44**	15	1	—	4	3	4	2	2
8. Bifascicular block	38	2	3	4	1	—	1	4	**31**	1	—	1	2	1	2	2
9. Ischemia image	18	11	1	—	—	—	—	—	—	**7**	—	3	—	2	1	1
10. Subepicardial damage	7	6	1	1	—	—	—	2	—	—	**1**	1	—	1	—	1
11. Subendocardial damage	15	11	1	—	—	—	—	2	—	—	—	**4**	—	4	—	2
12. QS image	3	2	—	—	—	—	—	—	—	—	—	—	**1**	—	—	—
13. Repolarization change	28	21	1	1	—	—	—	4	—	1	—	5	—	**7**	4	—
14. Cavity hypertrophy	23	13	1	—	—	—	—	—	—	—	1	—	—	—	**10**	—
15. Prolonged QT	45	36	1	—	—	—	—	1	1	—	1	—	—	1	1	**9**
Total abnormalities or normalized events observed on final ECG		137	55	19	10	—	3	62	47	10	4	19	6	20	21	19

FIGURE 1. In 1978 the ECG tracings of a Group B woman 25 years old revealed an evident left anterior hemiblock. About four years later the same subject yielded normal tracings with no evidence of any intraventricular conduction defect.



becoming complete right branch block in two women of 60 and 68); nine cases of left anterior hemiblock (in four men of 37 to 65 and five women of 38 to 68); one case of left posterior hemiblock (in a man of 54); two cases of complete right branch block (in two men of 47); and two cases of incomplete right branch block (in a man of 43 and a woman of 33);

(f) 16 new cases of bifascicular block, 15 of which developed in subjects whose initial ECGs showed unifascicular blocks (four cases of left anterior hemiblock changed to left anterior hemiblock plus incomplete right branch block in two men of 55 and 58 and two women of 54 and 68; another two cases of left anterior hemiblock changed to left anterior hemiblock plus complete right branch block in a man of 66 and a woman of 47; three cases of complete right branch block changed to left anterior hemiblock plus complete right branch block in two men of 57 and 66 and a woman of 51; another three cases of complete right branch block changed to left posterior hemiblock plus complete right branch block in one man of 66 and two women of 31 and 34; two cases of left posterior hemiblock changed to left posterior hemiblock plus complete right branch block in a man of 42 and a woman of 21; and a case of incomplete right branch block changed to left anterior hemiblock plus incomplete right branch block in a man of 20); the sixteenth new case of bifascicular block (left posterior hemiblock plus incomplete right branch block in a woman of 34) was associated with a prolonged QT syndrome;

(g) three new images of ischemia (in a man of 49 and two women of 36 and 66);

(h) three new images of subepicardial damage (in two men of 36 and 66 and a woman of 63);

(i) 15 new images of subendocardial damage (in two men of 49 and 67 and 13 women of 26 to 66);

(j) five new images of myocardial necrosis—QS image (in two men of 36 and 54 and three women of 44, 47, and 55); these images appeared to involve the interior wall of the left ventricle and were associated in all cases with uni- or bifascicular block;

(k) 13 new cases of repolarization alteration (in three men of 49 and 10 women, six of them under age 50, who were 32 to 67 years old);

(l) 11 new images of cavity hypertrophy—four cases of left ventricle hypertrophy (in a man of 21 and three women of 58, 67, and 73) and seven cases of left auricle hypertrophy (in two men of 23 and 60 and five women of 43 to 67);

(m) 10 cases of prolonged QT syndrome (in two men of 40 and 49 and eight females, seven under age 50, who were 11 to 73 years old).

A comparison of Tables 12 and 13 indicates that Group B (the chagasic group) exhibited more changes in its abnormalities over the four-year period between ECGs. Also, in comparison with Group A, fewer of the Group B auricular arrhythmias disappeared, while more indications of ischemia, subepicardial damage, subendocardial damage, and prolonged QT syndrome disappeared. In addition, it should be noted that in comparison to Group A, Group B exhibited larger numbers of new auricular arrhythmias (19 versus 10), ventricular arrhythmias (11 versus 5), unifascicular blocks (18 versus 13), bifascicular blocks (16 versus 8), images of subendocardial damage (15 versus 2), and repolarization alterations (13 versus 7). Also, the ages of the Group B subjects experiencing new abnormalities tended to be younger, overall, than the ages of their Group A counterparts.

Another important point is not merely that auricular and ventricular arrhythmias were associated with many Group B diagnoses, but that a relatively high proportion of them were associated with intraventricular conduction blocks. It is also clear that many of the bifascicular blocks developed from previously established unifascicular blocks.

Development of ECG Abnormalities in Infected Subjects

This matter was studied by examining the 67 Group C subjects, whose serologic responses to the initial survey had indicated chagasic infection but whose initial ECGs had shown no abnormalities. This group, comprised of 19 men and 48 women not over 60 years of age at the time of the initial survey (all but two were 50 or under), received the same final tests and examinations as groups A and B. Because this group was selected at the time of the final survey, its size was naturally unaffected by deaths or migrations during the study period. However, as Table 14 shows, the final ECGs revealed abnormalities in 26 of the 67 study subjects. These abnormalities, 28 in all, included one case of auricular arrhythmia (corresponding to a nodal rhythm problem in a woman of 48), five cases of incomplete right branch block (in two men of 16 and 26 and three women of 41, 46, and 47), one case of bifascicular block (left anterior hemiblock plus complete right branch block in a man of 37), two images of ischemia (in women of 27 and 43), three cases of repolarization change (in a man of 35 and two women of 31 and 47), and 16 cases of prolonged QT (in four men of 38 to 48 and 12 women of 37 to 47).

TABLE 14. ECG abnormalities indicated on the final ECGs of the 67 Group C subjects with chagasic infections, whose initial ECGs had shown no abnormalities.

ECG findings	No.	%
1. Abnormality normalized	N/A[a]	N/A[a]
2. Auricular arrhythmia	1	3.6
3. Ventricular arrhythmia	—	—
4. A-V block, first degree	—	—
5. A-V block, second degree	—	—
6. A-V block, third degree	—	—
7. Unifascicular block	5	17.9
8. Bifascicular block	1	3.6
9. Ischemia image	2	7.1
10. Subepicardial damage	—	—
11. Subendocardial damage	—	—
12. CS image	—	—
13. Repolarization change	3	10.7
14. Cavity hypertrophy	—	—
15. Prolonged QT	16	57.1
Total No. of abnormalities	28	100.0
Total No. of ECGs with abnormalities	26	

[a] N/A = not applicable.

The number of abnormalities arising in this group of relatively young subjects (all those afflicted were under the age of 50 at the time of their initial ECGs) is quite striking. Except for the two women with ischemia images, who complained of sharp precordial pain without the characteristics of angina, none of the Group C subjects involved showed any overt symptoms.

On the basis of these data, it appears that the risk of contracting cardiopathy for a population of persons with chagasic infections is on the order of 38.8% over a period of four years, or about 9.7% per annum.

DISCUSSION AND CONCLUSIONS

This longitudinal study yielded a number of findings about the natural history of chagasic cardiopathy that seem significant. To begin with, the data indicate that mortality was four times higher among infected subjects and that the disease threatens a much younger population than is threatened by nonchagasic cardiopathy. Also, it appears noteworthy that cardiopathy developed among the infected Group C subjects at a rate of 9.7% per year, and that the ECG abnormalities involved were similar to those found in Group B, the chagasic group with initial cardiopathy. This 9.7% rate is considerably higher than that cited by Puigbó (*11*) in his longitudinal study. In addition, these findings point up the fact that cases with cardiopathologic problems can be detected. This is significant, because cases in which lesions have only begun to appear lend themselves to timely treatment, and so ECG findings of the sort described could serve as criteria for selecting patients to receive therapeutic treatment (*16*).

The study also indicates that the Chagas' disease picture in Chile differs from that found in a number of other countries in the Americas. Specifically, we did not see the acute phase with characteristic myocarditis, nor did we find cases with Romaña's sign (*16–19*), or chronic cases with bradycardia (*20*). Indeed, the overt symptoms exhibited were scant, disproportionately so considering the highly abnormal ECGs obtained from many of the same subjects and the severe myocardial compromise evidenced by high mortality, including a large proportion of sudden deaths. (The fact that many of the fatalities were sudden suggests that death was caused by profound changes in myocardial rhythm and electrical conduction—*21*.)

In general, comparison of the ECG data on Group A (control subjects with cardiopathy) and Group B (chagasic subjects with cardiopathy) showed the latter to have a higher frequency of bifascicular block, subepicardial damage, and prolonged QT syndrome. This finding, which attracted our attention because it does not agree with the classical descriptions of chagasic cardiopathy (*11,17,21–23*), can be explained by two circumstances that distinguish this investigation from other epidemiologic studies. First, this study employed a control group (Group A) with nonchagasic cardiopathies residing in the same endemic area as the other study subjects. And second, findings for subjects with chagasic cardiopathies are customarily compared to results obtained with negative controls. Our data thus provided a basis for comparing chagasic and nonchagasic cardiopathies, unlike other available data, and so a different picture was obtained (*24,25*). Because of these differing cir-

cumstances, there seems no reason to doubt that if the work described here were repeated, a similar result would be obtained. Another investigation, conducted by Schenone and coworkers (*26*) and carried out on 9,990 subjects in Chile, describes ECG abnormalities in the control group that were similar but less frequent than those seen in the chagasic subjects. Unfortunately, no detailed report of these findings is available.

Another point worth noting is that for many Group B (chagasic) subjects, the abnormalities seen on the final ECG differed from those seen on the initial ECG. This is in accord with available information indicating that the electrical tracing can "blank out," i.e., pass through periods of normality, a circumstance described by Anis Rassi in reporting on his cases (*27*). As time goes by, many more changes occur, and occur in a much higher proportion of the subjects, than is true in the control group; the arrhythmias are associated with a larger number of other events and are more serious; and intraventricular blocks are much more frequent.

In our own study, if the Group B intraventricular (unifascicular and bifascicular) blocks that disappeared are added to those that did not change and to the new ones, the total obtained is 122 intraventricular blocks as compared to 89 in the control group. The number of unifascicular and bifascicular blocks disappearing in Group B was less than the number appearing, so the total apparent number increased, with many of the abnormalities appearing in relatively young subjects. In general, these findings tend to confirm the classic picture of the disease.

This longitudinal study also demonstrated that both unifascicular and bifascicular blocks appear together with repolarization alterations, ischemia images, and prolonged QT syndromes as the first manifestations of abnormality in previously normal ECGs. It is possible that the apparent disappearance of some of these abnormalities in our study subjects was only temporary, a point that requires further investigation.

Regarding our serologic findings, the low rate of conversion from negative to positive for chagasic infection (in only two of 218 Group A subjects tested in the followup study) is not consistent with the situation generally observed in endemic areas (*11*). It seems likely that this finding derives from the effectiveness of government anti-vector efforts that have reduced public exposure to triatomid bugs. The conversion in some subjects from positive to negative is harder to explain. However, the four subjects involved showed minimum positive titers to begin with, and so the results could have represented errors (false positive findings in the initial survey or false negative findings in the final survey), or else could have arisen from immunologic depression, a phenomenon observed by Breniere and coworkers that could explain periodic conversions in subjects with marginally positive or negative sera (*28, 29*).

In conclusion, our study has sought to probe the "great silent group" described by Laranja (*17*), and has obtained from it findings that represent no more than a tiny fraction of the information needed about the pathology of Chagas' disease. In the process, by selecting a control group with ECG abnormalities, we have also dealt with the broader group of pathologies described by Blackburn (*30*). As a result of this investigation, we have learned that it is relevant, indeed necessary, to study the problem of chagasic cardiopathy over an extended period of time; we have also gained a

heightened awareness of the fact that many matters remain to be resolved and that a great deal of work must still be done.

Acknowledgments

The authors wish to thank Dr. Luis Cabrera, Dr. Fernando Arab, and Dr. Ricardo Estela for assisting with the clinical work described herein.

Summary

In 1977 the authors launched a long-term investigation of the epidemiology of Chagas' disease and its cardiac implications in Chile. During this work, clinical examinations were performed, blood samples were drawn for serologic tests, and electrocardiograms were obtained using a study population of 2,938 subjects residing in rural settlements of northern Chile; and this was done again four years later with 481 study subjects remaining in the area. This article reports on the latter four-year followup study.

To begin with, the study subjects were divided into three specific groups: those with no evidence of Chagas' disease but with cardiopathy (as indicated by abnormal ECGs) were designated Group A; those with positive chagasic serology and cardiopathy were designated Group B; and 67 subjects randomly selected from those with positive chagasic serology and normal ECGs were designated Group C. At the time of the followup work, 216 subjects were retained in Group A and 198 in Group B.

Comparison of the initial and final Group A and Group B data yielded a number of results that seem significant. To begin with, they indicated that mortality was four times higher among the infected subjects and that the disease tended to threaten a much younger population than was threatened by nonchagasic cardiopathy. Also, cardiopathy appeared to develop among the infected Group C subjects at a rate of about 9.7% per year, considerably faster than indicated by a previous longitudinal study (*11*). In addition, the results point up the ability to detect developing chagasic cardiopathy on ECGs, an ability that suggests ECGs could prove useful in selecting patients to receive therapeutic treatment.

The findings also suggest that the clinical picture of Chagas' disease in Chile differs from that found in certain other parts of the Americas, in that overt symptoms are scant despite the fact that the disease gives every appearance of doing severe damage.

Another point worth mentioning is that Group B subjects exhibited higher frequencies of bifascicular blocks, images indicative of subepicardial damage, and prolonged QT syndromes than did their Group A counterparts. This finding is at variance with the classical descriptions of chagasic cardiomyopathy. It also appears that unifascicular and bifascicular blocks, together with repolarization changes, ischemia images, and prolonged QT syndromes, were the first manifestations of abnormality in previously normal ECGs. The apparent appearance and disappearance of some of these abnormalities in our study suggests some could be only temporary.

Seroconversion of four study subjects from positive to negative over the followup period is hard to explain; it could indicate immunologic depression

or erroneous (false positive or false negative) serologic findings. The seroconversion of only a few (two) study subjects from negative to positive during this period may have been due to the effectiveness of a government disinsection campaign designed to cut public exposure to the triatomid bugs that carry the disease.

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