Clinical and Epidemiological Study of Chronic Heart Involvement in Chagas' Disease *

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It has been estimated that, in vast areas of the American continent, there is a high prevalence of human infection by Trypanosoma cruzi. *Such infection can lead to a variety of heart diseases, predominantly with involvement of the myocardium. The aim of the present work was to determine the prevalence of heart disease in two rural areas of Venezuela with a high endemicity of Chagas' disease and to try to determine the natural history of the disease. It is shown that a form of chronic myocardial disease in patients with positive specific serology and good functional capacity is highly prevalent. Electrocardiographic patterns typical of the initial and developing stages of the disease, as well as early abnormalities of the cardiac rhythm, are described and illustrated. The present work forms part of a longitudinal study still in progress.*

In Venezuela, as in other Latin American countries, Chagas' disease, in its chronic cardiac form, constitutes a sizable public health problem. In Central and South America the number of people exposed to the risk of infection by *Trypanosoma cruzi*—the causative agent of the disease—has been estimated at 35 million, of whom 7 million are probably actually infected (WHO Study Group on Chagas' Disease, 1960).

Surveys carried out in Venezuela have shown that, on average, 20% of the rural population must be considered to be infected by *T. cruzi*. Of a rural population of 2 800 000 exposed to infection, 560 000 suffer from Chagas' disease, half of whom have shown electrocardiographic evidence of myocardial damage in various degrees (280 000 cases of chronic heart involvement in Chagas' disease) (Pifano & Guerrero, 1963). It has been established that, in Venezuela, *Rhodnius prolixus* is the vector of Chagas'

disease with the greatest epidemiological importance (Tejera, 1919a, 1919b; Torrealba, 1933).

The immediate purpose of the present work was to study the prevalence of heart disease in Venezuelan rural areas where Chagas' disease is known to be highly endemic. In addition, a start has been made in the study of the natural history of the chronic cardiac form of Chagas' disease, particularly in its initial and evolutive stages, and longitudinal studies on the rural population have been initiated.

MATERIALS AND METHODS

Sites of study

Two different Venezuelan rural zones were chosen for this study—Belén (Central zone) and Eneal (Western zone)—in both of which the indices of house infestation (Belén, 75.5%; Eneal, 52.6%) and of infestation of *Rhodnius prolixus* by *T. cruzi* (Belén, 25.8%; Eneal, 9.1%) had previously been determined.

Belén zone. Belén is a small village with a population of 2016 (National Population Census, 26 February 1961, the date on which our investigations began), most of whom are farmers. Children aged 0-4 years were excluded from the survey (17.8%), reducing to 1656 the total sample to be studied. Of these, 1210 subjects of different age-groups were examined; the age and sex distribution is shown in Table 1. The sample, chosen at random, contained

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TABLE 1
AGE AND SEX DISTRIBUTION OF SAMPLES UNDER STUDY

Age-group (years)	Belén (1961)			Eneal (1964)		
	Males	Females	Total	Males	Females	Total
Number of subjects in each age-group						
5-9	82	116	198	24	25	49
10-14	102	123	225	49	54	103
15-19	72	51	123	15	28	43
20-24	73	56	129	10	19	29
25-29	50	56	106	5	15	20
30-34	54	39	93	10	21	31
35-39	42	49	91	9	16	25
40-44	45	34	79	9	17	26
45-49	23	24	47	14	15	29
50-54	21	21	42	4	10	14
55-59	16	12	28	7	6	13
60-64	19	11	30	1	5	6
65+	12	7	19	2	5	7
Total	611	599	1 210	159	236	395
Percentage of subjects in each age-group						
5-9	13.4	19.4	16.3	15.1	10.6	12.4
10-14	16.7	20.5	18.5	30.8	22.9	26.1
15-19	11.8	8.5	10.2	9.4	11.9	10.9
20-24	11.9	9.3	10.7	6.3	8.0	7.3
25-29	8.2	9.3	8.8	3.1	6.4	5.1
30-34	8.8	6.5	7.7	6.3	8.9	7.8
35-39	6.9	8.2	7.5	5.7	6.8	6.3
40-44	7.4	5.7	6.5	5.7	7.2	6.6
45-49	3.8	4.0	3.9	8.8	6.4	7.3
50-54	3.4	3.5	3.5	2.5	4.2	3.5
55-59	2.6	2.0	2.3	4.4	2.5	3.3
60-64	3.1	1.8	2.5	0.6	2.1	1.5
65+	2.0	1.2	1.6	1.3	2.1	1.8
Total	100.0	100.0	100.0	100.0	100.0	100.0

approximately the same number of males and females. Although all age-groups were represented in the random sample, no prior stratification by age was made.

A permanent field unit was installed in order to perform longitudinal studies.

Clinical studies and fluoroscopic examinations were made, and electrocardiograms and, occasionally, teleradiographs and kymograms were obtained. Routine laboratory tests were also carried out, in particular determinations of haemoglobin, haematocrit readings, and plasma protein, the serological

reaction for syphilis and faecal tests for parasites. Photofluorograms of 945 subjects were taken and the results interpreted by two observers acting independently. Two other observers, also acting separately, were engaged in analysing the electro-cardiograms. Whenever there was a discrepancy in the interpretation of the tracings, the opinion of a third observer was obtained.

Blood samples were taken and refrigerated until the serological study (specific complement-fixation test for Chagas' disease) was complete. This study covered 1153 subjects, definite serological results being obtained for 1110. Serological tests were performed using a specially prepared antigen (Maekelt & López, 1956; Maekelt, 1959, 1960). Cardiac viscerotomy was practised on five patients and two were autopsied.

Eneal zone. This second zone included six villages in the neighbourhood of Eneal with a total population of 898 (1961 National Population Census), mostly farmers. A temporary field unit was installed at Eneal for the transverse study of the population.

A census of the population to be studied was carried out by the authors in 1964, before selecting the sample, which was formed by 704 subjects after excluding those aged 0-4 years (21.1%). In sampling, 50% or more of the population was chosen at random, without discrimination of age or sex. In all, 395 subjects were studied as described above, conclusive serological results being obtained for 302 of them. The distribution of the sample, according to age and sex, is shown in Table 1.

Uncooperative subjects

Information was obtained solely from the chosen subjects in the two zones. However, some of those originally selected were unwilling to submit to tests. Efforts were made to persuade them to take part, but where these were unsuccessful, no substitute subjects were chosen.

Interpretation of electrocardiograms

The following criteria were used in the interpretation of electrocardiograms.

Ventricular repolarization disorders. These were considered to be indicated by an alteration of the T wave, a low-voltage T wave or inversion of the waves, particularly in leads LI, aVL, V5 and V6, which reflect the left-ventricle potential. A slight positive or negative displacement of the S-T segment, of the order of 0.5 mm-1 mm, was considered as an S-T segment alteration.

Cardiac rhythm disorders (increased automatism). Multifocal ventricular extrasystolic arrhythmia was considered as additional evidence of myocardial involvement.

Disorders of intraventricular conduction. According to the classical concept, it was considered that complete right bundle branch block occurred when the QRS complex lasted 0.12 second or more and the intrinsicoid deflection was of 0.09 second or more in the presence of supraventricular or sinus rhythm. Incomplete right bundle branch block was diagnosed when the duration of the QRS complex varied between 0.10 and 0.12 second, but this by itself did not indicate the presence of heart disease. It is evident, however, that incomplete right bundle branch block can be considered as a sign of heart disease when a series of tracings shows that this disorder of conduction is progressively increasing. It was considered important to determine the position of the Â QRS F in right bundle branch block, since the association of the latter with Â QRS F deviation towards the left is frequently found in chronic Chagas' disease (Dias et al., 1945; Laranja et al., 1946, 1951, 1956; Pileggi et al., 1961; Hernández, 1961).

QRS voltage alterations, AV conduction disorders and P and Q wave alterations. The criteria used were those established in *Diseases of the heart and blood vessels: nomenclature and criteria for diagnosis* (New York Heart Association, 1964).

Ventricular hypertrophy. The criteria of Sokolow & Lyon (1949) were adopted.

Incomplete left bundle branch block. Sodi-Pallares' definition was followed (initial slurring of R in the presence or absence of Q) (Sodi-Pallares, 1964).

Unclassified intraventricular block. Such blocks—e.g., arborization block, focal block, Purkinje-Purkinje block and muscle fibre muscle block—were considered to exist when there was a QRS complex lasting 0.12 second or more, a very aberrant morphology and a delay of intrinsicoid deflection in both right and left precordial leads (New York Heart Association, 1964; Sodi-Pallares, 1964).

RESULTS

Serological

The results of the serological survey (Table 2) allowed the population examined to be divided

TABLE 2
AGE AND SEX DISTRIBUTION OF SEROPOSITIVE SUBJECTS

Age-group (years)	Seropositive males		Seropositive females		Total seropositive	
	Number	% [a]	Number	% [a]	Number	% [a]
Belén [b]						
5-9	12	14.6	20	17.2	32	16.2
10-14	40	39.2	33	26.8	73	32.4
15-19	29	40.3	18	35.3	47	38.2
20-24	41	56.2	31	55.4	72	55.8
25-29	30	60.0	30	53.6	60	56.6
30-34	30	55.6	29	74.4	59	63.4
35-39	28	66.7	32	65.3	60	65.9
40-44	35	77.8	20	58.8	55	69.6
45-49	13	56.5	17	70.8	30	63.8
50-54	14	66.7	16	76.1	30	71.4
55-59	10	62.5	9	75.0	19	67.9
60-64	14	63.7	7	63.6	21	70.0
65+	9	75.0	5	71.4	14	73.7
Total	305	49.9	267	44.6	572	47.3
Eneal [c]						
5-9	5	20.8	6	24.0	11	22.4
10-14	14	28.6	16	29.6	30	29.1
15-19	6	40.0	11	39.3	17	39.5
20-24	6	60.0	8	42.1	14	48.3
25-29	2	40.0	3	20.0	5	25.0
30-34	5	50.0	12	57.1	17	54.8
35-39	4	44.4	7	43.8	11	44.0
40-44	4	44.4	11	64.7	15	57.7
45-49	7	50.0	9	60.0	16	55.2
50-54	1	25.0	3	30.0	4	28.6
55-59	4	57.1	3	50.0	7	53.8
60-64	1	100.0	3	60.0	4	66.7
65+	2	100.0	4	80.0	6	85.7
Total	61	38.4	96	40.7	157	39.7

[a] Based on total number of subjects in each age-group (Table 1).
[b] 17 doubtful results excluded.
[c] 27 doubtful results excluded.

into two major groups: seropositive (Belén, 572 (47.3%); Eneal, 157 (39.7%)) and seronegative. These figures indicate the prevalence rate of human infection by *T. cruzi* in these two zones. In both zones, the percentage of seropositive subjects increased with age.

TABLE 3
RESULTS OF CARDIOVASCULAR STUDY

Diagnosis	Belén		Eneal	
	Number	%	Number	%
No heart disease	915	75.6	333	84.3
Definite heart disease	209	17.3	51	12.9
Doubtful heart disease	86	7.1	11	2.8
Total	1 210	100.0	395	100.0

Cardiovascular study

The population can be divided into three groups—namely,

(a) those with no evidence of heart disease,

(b) those with definite heart disease,

(c) those with doubtful heart disease (electro-cardiograms with slight anomalies).

The percentage of the sample with definite signs of heart disease was 17.3% in Belén and 12.9% in Eneal (Table 3).

Correlation of the results of the cardiovascular and serological surveys allowed a subdivision of the population into six epidemiological subgroups—namely,

(I) those with no evidence of heart disease and negative serology,

(II) those with no evidence of heart disease and positive serology,

(III) those with definite heart disease and negative serology,

(IV) those with definite heart disease and positive serology,

(V) those with doubtful heart disease and negative serology,

(VI) those with doubtful heart disease and positive serology.

The classification is shown in Table 4.

Distribution according to cardiovascular diagnosis

Studies carried out on patients with definite heart disease (Table 5) indicated a high prevalence of chronic myocardial heart disease (Belén, 193 (92.3%); Eneal, 40 (78.4%)), a high percentage being associated with positive serological results (Belén, 145 out of 171; Eneal, 23 out of 26). The prevalence of other types of heart disease was low (Table 5). The distribution of chronic seropositive myocardial heart disease by age-group and sex is shown in Table 6. Table 7 shows the estimated rates per 100 inhabitants for seropositivity and heart disease.

TABLE 4
CORRELATION OF RESULTS OF CARDIOVASCULAR AND SEROLOGICAL SURVEYS

Cardiovascular evaluation	Serological results							
	Seronegative			Seropositive			Total	
	Epidem. subgroup	No.	%	Epidem. subgroup	No.	%	No.	%
Belén								
No heart disease	I	472	90.6	II	359	62.8	831	76.1
Definite heart disease	III	29	5.6	IV	155	27.1	184	16.8
Doubtful heart disease	V	20	3.8	VI	58	10.1	78	7.1
Total		521			572		1 093	
Eneal								
No heart disease	I	109	92.4	II	121	77.1	230	83.6
Definite heart disease	III	4	3.4	IV	30	19.1	34	12.4
Doubtful heart disease	V	5	4.2	VI	6	3.8	11	4.0
Total		118			157		275	

TABLE 5

DISTRIBUTION OF HEART DISEASES
OF DIFFERENT TYPES

Heart disease	Belén		Eneal	
	No.	%	No.	%
Chronic myocardial	193	92.3	40	78.4
Chronic cor pulmonale	4	1.9	0	
Hypertensive and atherosclerotic	4	1.9	0	
Hypertensive	2	0.9	11	21.6
Congenital	2	0.9	0	
Syphilitic	1	0.5	0	
Other types	3	1.5	0	
Total	209		51	

Clinical results

One hundred and forty-five cases of chronic myocardial heart disease with specific positive serology were classified according to their functional capacity as follows: Class I, 79 (54.5%); Class II, 58 (40.0%); Class III, 2 (1.4%); Class IV, 6 (4.1%).

Ninety-five patients aged under 50 years were selected arbitrarily for further study. Of these, 32 (33.7%) were asymptomatic and 63 (66.3%) presented symptoms related to the cardiovascular system.

Asymptomatic group (32 subjects). The apical impulse was found to be normal in 19 cases, abnormal in five and not felt in eight. The abnormality consisted of an increase in the intensity and amplitude of the apical impulse. A right ventricular lift in the left sternal border was found in one case.

In eight of the cases a permanent splitting of the second sound at the pulmonary area was found. An early diastolic gallop rhythm, accompanied by a palpable phenomenon, was present in one case.

A faint murmur (I-II/IV) with little radiation was heard in 16 cases (50%). In one case, a pansystolic regurgitant murmur was heard over the tricuspid area. This murmur became louder during post-inspiratory apnoea and on fluoroscopy there was evidence of tricuspid regurgitation. In six cases the arterial pulse was found to be irregular owing to extrasystolic arrhythmia. The blood pressures were normal, except in two cases where an increase in the systolic pressure was observed.

Symptomatic group (63 patients). The apical impulse proved to be normal in 43 cases, abnormal

in 17 and not felt in three. The abnormalities of the cardiac impulse consisted of an increase in its amplitude, intensity, downward and outward displacement and, occasionally, a rocking movement at the apical area. A right ventricular lift in the left sternal border was observed in seven cases.

In 17 cases, the second heart sound was found to be constantly split. A presystolic gallop rhythm was audible in three cases, and one of early diastolic type in one case. A decrease in the intensity of the first sound was observed in two cases.

Systolic murmurs were present in 34 cases with the previously mentioned characteristics. A pansystolic regurgitant murmur at the mitral area, which radiated towards the axilla, was found in one case (mitral incompetence on fluoroscopy). In 14 cases the arterial pulse was found to be irregular owing to extrasystolic arrhythmia. Blood-pressure figures were normal. Four patients showed clinical manifestations of bilateral congestive heart failure with predominant right-sided failure.

The clinical manifestations are summarized in Tables 8 and 9.

Electrocardiograph results

The 1210 electrocardiograms were classified as normal (903; 74.6%), abnormal (198; 16.4%) or " doubtful " (109; 9.0%). Most of the electrocardiograms classified as " doubtful " showed slight alterations of the T wave.

Electrocardiographic analysis performed in 95 selected cases in patients aged under 50 years revealed the following results: normal (3; 3.3%), " doubtful " (4; 4.2%) and abnormal (88; 92.5%). The abnormalities found in the pathological group are summarized in Table 10.

The distribution by age of patients with complete right bundle branch block is shown in Fig. 1. A gradual increase in the incidence of right bundle branch block with age was observed over the age-band 10-50 years.

Photofluorographic examination

Of the 1210 individuals under study in Belén, 945 were examined photofluorographically. The fluorograms were classified (by two independent observers) as follows: normal (848 (89.7%); 851 (90.1%)), abnormal (43 (4.6%); 41 (4.3%)) and " doubtful " (54 (5.7%); 53 (5.6%)).

Fluoroscopic examination

Fluoroscopic examinations were carried out on all 1210 subjects in Belén, the results being: normal

TABLE 6

AGE AND SEX DISTRIBUTION OF SEROPOSITIVE SUBJECTS WITH CHRONIC
MYOCARDIAL HEART DISEASE

Age-group (years)	Seropositive males		Seropositive females		Total seropositive	
	No.	%[a]	No.	%[a]	No.	%[a]
Belén						
5-9	1	1.2			1	0.5
10-14	3	2.9			3	1.3
15-19	5	6.9			5	4.1
20-24	6	8.2	4	7.1	10	7.8
25-29	7	14.0	2	3.6	9	8.5
30-34	7	13.0	9	23.1	16	17.2
35-39	9	21.4	7	14.3	16	17.6
40-44	15	33.3	7	20.6	22	27.8
45-49	6	26.1	7	29.2	13	27.7
50-54	7	33.3	5	23.8	12	28.6
55-59	6	37.5	7	58.3	13	46.4
60-64	5	26.3	9	81.8	14	46.6
65+	7	58.3	4	57.1	11	57.9
Total	84	13.7	61	10.2	145	12.0
Eneal [b]						
30-34	2	20.0	4	19.0	6	19.4
35-39	2	22.2			2	8.0
40-44	2	22.2	1	5.9	3	11.5
45-49	1	7.1	2	13.3	3	10.3
50-54			1	10.0	1	7.1
55-59			1	16.7	1	7.7
60-64	1	100.0	2	40.0	3	50.0
65+	1	50.0	3	60.0	4	57.1
Total	9	5.7	14	5.9	23	5.8

[a] Based on total number of subjects in each age-group (Table 1).

[b] No subjects from Eneal in the age-band 5-29 years had chronic seropositive myocardial heart disease.

(1083; 89.5%), abnormal (84; 6.9%) and " doubtful " (43; 3.6%). Differentiation between categories was made on the basis of modifications in the size of the cardiac silhouette.

Of 95 selected cases (chronic seropositive myocardial heart disease in subjects under 50 years of age), 30 (31.6%) showed modifications in the size of the cardiac silhouette; 12 (12.6%) presented doubtful cardiomegaly and 53 (55.8%) did not show any evidence of cardiac enlargement. Of the 30 subjects with cardiomegaly, 12 cases were determined as slight, 9 as moderate and 9 as severe. In the 12 cases of slight cardiomegaly, the chambers involved were: left ventricle, 9; right ventricle, 2; right atrial appendage, 1. Enlargement of both ventricles was regularly observed in patients with moderate cardio-

TABLE 7

ESTIMATED RATES PER 100 INHABITANTS OF SERO-POSITIVITY AND HEART DISEASE (WITH 95 % CONFIDENCE LIMITS)

Characteristic	Rate per 100 inhabitants			
	P	δ_p	Lower limit	Upper limit
Belén				
Seropositivity	47.3	1.43	44.4	50.2
Heart disease	17.3	1.08	15.1	19.5
Seropositivity in myocardial heart disease	84.8	2.74	79.3	90.3
Eneal				
Seropositivity	39.7	2.46	34.8	44.6
Heart disease	12.9	1.69	9.5	16.3
Seropositivity in myocardial heart disease	88.5	6.25	76.0	100.0

TABLE 8

CLINICAL MANIFESTATIONS OF CHRONIC MYOCARDIAL HEART DISEASE (63 SUBJECTS)

Symptom	Subjects with symptoms	
	Number	%
Palpitations	50	79.4
Dyspnoea on effort	32	50.8
Chest pains	20	31.7
Leipothymia	7	11.1
Oedema	4	6.3

TABLE 9

CLINICAL MANIFESTATIONS (95 SUBJECTS)

| Physical characteristic	Subjects showing physical characteristic			
	Asympto-matic	Sympto-matic	Total	
			Num-ber	%
Abnormal apical impulse	5	17	22	23.2
Right ventricular lift	1	7	8	8.4
Permanent splitting of second sound at pa	8	17	25	26.3
Gallop rhythm	1	4	5	5.3
Systolic regurgitant murmur	1 [a]	1 [b]	2	2.1
Irregular arterial pulse	6	14	20	21.1
Blood pressure	normal	normal	—	—

[a] Tricuspid incompetence.   [b] Mitral incompetence.

TABLE 10

ABNORMALITIES FOUND IN ELECTROCARDIOGRAMS OF 88 SUBJECTS

Abnormality	Subjects with abnormality	
	Number	%
1. Ventricular repolarization disorders		
T-wave alterations	58	
S-T segment alterations	13	
	71	80.7
2. Intraventricular conduction disorders		
Right bundle branch block of bundle of His		
Incomplete	9	
Incomplete + Â QRS F deviation towards left	4	
	13	14.8
Complete	8	
Complete + Â QRS F deviation towards left	19	
	27	30.7
Left bundle branch block of bundle of His		
Incomplete	6	6.8
Unclassified intraventricular block	3	3.4
3. Cardiac rhythm disorders (increased automatism)		
Ventricular extrasystoles		
Multifocal	17	
Unifocal	14	
	31	35.2
Supraventricular extrasystoles	7	8.0
4. Voltage alterations		
Low voltage	16	
High voltage	12	
	28	31.8
5. Ventricular enlargements		
Left	12	13.6
Right	2	2.3
6. P-wave alterations	11	12.5
7. Inactive electrical zones		
Abnormal Q waves	6	
Absence of precordial R	3	
	9	10.2
8. AV conduction disorders		
Incomplete AV block	5	5.7

FIG. 1

FREQUENCY DISTRIBUTION OF PATIENTS WITH RIGHT
BUNDLE BRANCH BLOCK IN SAMPLE FROM BELEN
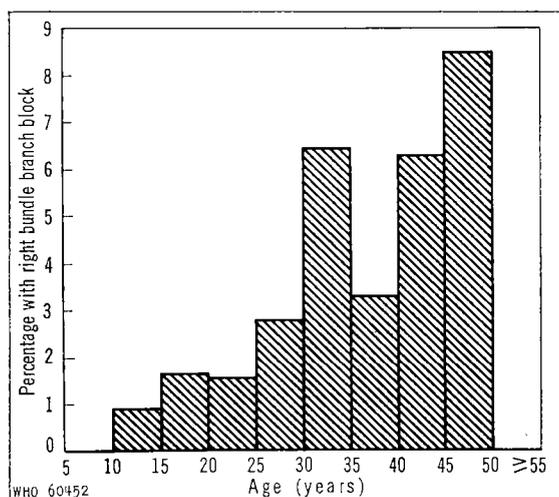
megaly, while in patients with extreme cardiomegaly all the chambers were enlarged.

Abnormalities of the cardiac pulsation were found in 14 cases. These abnormalities had been previously defined in chronic Chagas' disease (Gil Yépez et al., 1962, 1964) as follows. Diminished apical pulsations were indicated by a marked decrease in the amplitude at the apical left ventricular contour (10 cases) and paradoxical pulsations by the presence of a rocking movement (4 cases). Radiokymographic studies confirmed these cardiac pulsation abnormalities, which had previously been observed fluoroscopically (Fig. 2 and 3).[1]

Laboratory results

Specific serological tests for syphilis were performed on 835 subjects. The results were positive in 38 cases (14.5%), but in only two instances (both patients under 50 years old) was the reaction associated with chronic seropositive myocardial heart disease.

Haemoglobin and haematocrit values were normal in 832 subjects (81.3%). In six patients aged under 50 years, mild anaemia (haemoglobin values 9.8 g/100 ml to 11.6 g/100 ml) was associated with seropositive chronic myocardial heart disease.

[1] For another typical case see *Bull. Wld Hlth Org.*, 1965, **33**, 262 (Fig. 18).

Plasma protein concentrations were within normal limits in 682 subjects (93.8%). Hypoproteinaemia, with inversion of the A/G coefficient index, was observed in one patient with chronic seropositive myocardial heart disease. Coprological studies carried out on 1051 subjects showed the existence of parasitosis in 76%. Infection by *Necator americanus* was frequently found (270 subjects; 25.7%) and in 19 cases, four of which presented mild anaemia, it was associated with chronic seropositive myocardial heart disease.

Pathological findings [2]

In Belén, seven cases were studied and the pathological findings were as follows.

(1) In all cases there was an increase in the weight of the heart.

(2) In all cases there was a thinning of the wall at the apical portion. The thickness of the basal portion of the left ventricle bore no relation to that of the apical portion (" increased apicobasal discrepancy ").

(3) In all cases an apical lesion of the left ventricle was found.

(4) In all cases there was dilatation of both ventricles and auricles.

(5) Pericardial lesions were found in five cases and endocardial lesions in two.

(6) Intracardiac thrombosis, localized chiefly within the left ventricle and the right auricle, was observed in four cases.

(8) In all cases there were inflammatory lesions, an increase in the connective tissue and lesions of the myocardial fibres (fibrosis) in varying degrees.

(9) In the sections there was no evidence of *Leishmania* pseudo-cysts.

The findings are summarized in Table 11.

These pathological findings agree with those reported by other workers on chronic Chagas' heart disease (Jaffe, 1938; Andrade & Andrade, 1955; Andrade, 1956; Laranja et al., 1956; Köberle, 1957, 1958; Mignone, 1958; Bruni-Celli et al., 1959; Brass, 1960).

[2] Autopsy specimens (Belén) showing various degrees of evolution of the apical left-ventricular lesion are shown in Fig. 10 of a recently published memorandum entitled *Cardiomyopathies* (*Bull. Wld Hlth Org.*, 1965, **33**, 257).

TABLE 11
PATHOLOGICAL FINDINGS [a]

Subject	Athero-sclerosis	Heart weight (g)	Thickness LV	Thickness RV	Apical lesion LV	Dilatation LV	Dilatation RV	Dilatation LA	Dilatation RA	Pericardial lesions LV	Pericardial lesions RV	Pericardial lesions LA	Pericardial lesions RA	Endocardial lesions LV	Endocardial lesions RV	Endocardial lesions LA	Endocardial lesions RA	Thrombosis LV	Thrombosis RV	Thrombosis LA	Thrombosis RA	Inflammatory lesions LV	Inflammatory lesions RV	Inflammatory lesions LA	Inflammatory lesions RA	Increased connective tissue LV	Increased connective tissue RV	Increased connective tissue LA	Increased connective tissue RA	Fibrosis LV	Fibrosis RV	Fibrosis LA	Fibrosis RA
MP	0	528	10	2	+	+	+	+		+	0	0	0	0	0	0	0	0	+	0	0	+	+	+	+	+	+	0	0	+	+	+	+
			2	1	+	+	+	+	+	+	0	0	0						+			+				+				+			
TA	0	462	8			+	+	+	+	+	0	0	+	0	0	0	0	0	+	0	+	+	+	+	+	+	+	0	0	+	+	0	+
			2	3	+	+	+	+	+										+		+	+	+	+		+	+			+	+		
					+															+		+											
SC	+	445	8	3	+	+	+		+	+	+	0	+	0	0	0	0	0	0	0	+		+	+	+	+	+	+	+	+	+	+	+
			1		+	+	+																			+	+						
CS	0	440	8	3	+	+	+	+	+	+	+	+	+	+	0	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
			2	2	+		+	+						+				+		+	+	+	+			+	+			+			
SGC	0	300	7			+	+	+		0	0	0	0	0	0	0	0	+	0	0	0	+				+				+			
			4	3		+	+	+	+													+								+			
JAH	0	422	10	3	+	+	+	+	+	0	0	0	+	0	0	0	0	0	0	0	0	+	+	+	+	+	+	+	+	+	+	+	
			2	2	+	+	+	+														+	+			+	+						
ARP	0	382	10	3	+	+	+	+	+	+	+	0	+	+	+	0	0	+	0	0	0	+	+	+	+	+	+	+	+	+	+	0	+
			3	2	+		+			+												+				+				+			+

[a] LV = left ventricle; RV = right ventricle; LA = left auricle; RA = right auricle.

DISCUSSION

The serological survey carried out in two zones with high indices of house infestation and of infection of *Rhodnius prolixus* by *T. cruzi* indicated that the rate of human infection by *T. cruzi* was also high. Chagas' disease was highly prevalent among the population studied (Table 7).

Classification of the disease into six epidemiological subgroups, on the basis of the absence, presence, or possible presence of heart disease, coupled with either positive or negative serological results, is a feature likely to prove of great value in the longitudinal study of Chagas' disease; this aspect will therefore be further discussed.

This classification indicated a high prevalence of chronic heart disease, together with positive serological results, among people with undoubted cardiopathy (Table 7). The highest frequency was found in patients aged 30-44 years. The high prevalence of seropositive heart disease contrasts with the low prevalence of other types of heart disease (ischaemic, hypertensive, rheumatic and syphilitic). These data contrast with the results of pathological studies on atherosclerosis in urban populations,[1] which show the high prevalence and severity of this disease. Over 14 000 epidemiological records from the Venezuelan urban areas have been analysed from a clinical point of view (selected samples); the distribution according to etiological diagnosis is shown in Table 12. Although these results cannot be strictly compared with those obtained from the studies carried out in rural populations, the difference in frequency of the various types of heart disease is marked.

The purpose of the present study was not to compare the two rural areas, since the two samples did not have the same age distribution. Moreover, it was not possible to perform significance tests for each of the characteristics investigated. Therefore, the study was only concerned with determining over-all rates for the total population.

Most patients with chronic seropositive myocardial heart disease showed good functional capacity and were classified as Class I or II (94.5%). The rest (5.5%) belonged to Class III or IV. Most of the patients, males as well as females, were accustomed to stenuous physical work and did

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[1] Carbonell, L. & Suárez, J. A. (1964) *Historia natural de la ateroesclerosis en Venezuela*, unpublished paper presented at the IV Jornadas Venezolanas de Cardiología, Barcelona, Venezuela.

TABLE 12

ETIOLOGICAL ANALYSIS OF 14 070 EPIDEMIOLOGICAL RECORDS FROM VENEZUELAN URBAN AREAS [a]

Etiology	Subjects with disease	
	Number	%
Congenital heart disease	1 532	10.9
Rheumatic fever	627	4.5
Syphilis	238	1.7
Chagas' disease	678	4.9
Atherosclerosis	7 398	52.5
Arterial hypertension	2 410	17.0
Other etiologies	1 187	8.5
Total	14 070	100.0

[a] From Central Morbidity Registry; records from cardiovascular services.

not show any significant evidence of anaemia or malnutrition from a clinical or laboratory point of view.

The selection of 95 patients under 50 years old for further study was arbitrary; it is obvious that within this group the primary cardiovascular lesion was chronic myocardial heart disease related to Chagas' infection. However, the role played by an associated factor of atherosclerotic nature must not be disregarded, even though there was no clinical evidence of ischaemic heart disease.

From a clinical point of view, it was found that the patients were either asymptomatic or symptomatic. The symptoms most often observed, in decreasing order of frequency, were: palpitations, dyspnoea on effort, and chest pains with no coronary features. Only four patients showed a clinical picture of bilateral heart failure with predominant right ventricular failure. In none of these cases were symptoms of paroxysmal nocturnal dyspnoea observed.

The abnormalities most frequently observed upon physical examination were as follows.

(1) Alterations in apical impulse became more noticeable as the severity of the myocardial involvement increased. In patients with advanced myocardial heart disease, the apical impulse became more intense and increased in amplitude while being displaced downwardly and outwardly, appearing sometimes as a rocking movement. In patients in

whom this physical finding was observed, there were usually paradoxical pulsations (as observed on fluoroscopy) and marked electrocardiographic alterations. The cause was considered to be weakness of the heart-muscle wall or of the apical region related to extensive and confluent fibrotic areas localized at the myocardium. A right ventricular lift in the parasternal border related to right ventricular enlargement was more frequently observed in the symptomatic group.

(2) Permanent splitting of the second heart sound in the pulmonary area was relatively frequent and was related to the existence of a right bundle branch block of the bundle of His, as reported by other workers (Laranja et al., 1956; Morales Rojas et al., 1959).

(3) Cardiac rhythm disorders, particularly extrasystolic arrhythmia, appeared relatively frequently upon auscultation of the precordial zone or palpation of the pulse.

(4) The incidence of systolic murmurs with functional acoustic characteristics was very frequent and there was no correlation with a decrease of the haematocrit values. In two cases there was evidence of a murmur due to mitral and tricuspid incompetence of a functional nature. Murmurs of an organic nature of the type encountered in acquired valvular lesions, congenital heart disease or obstructive myocardial heart disease were not found.

(5) Arterial pressure values were within normal limits.

Thus, clinical analysis of patients with seropositive chronic myocardial heart disease with good functional capacity (I, II) established the following conclusions: absence of a history indicative of ischaemic heart disease; evidence of cardiomegaly of varying degrees; extrasystolic arrhythmia; splitting of the second sound; and absence of auscultatory findings related to valvular lesions or congenital heart disease.

Analysis of 1210 electrocardiograms showed that 16.4% of them were abnormal. Of the group of patients under 50 years of age with seropositive chronic myocardial heart disease, 92.5% had abnormal electrocardiograms, which constituted the earliest and most significant evidence of myocardial involvement. However, it was evident that consideration of the electrocardiograms in isolation could lead to erroneous interpretations; this method of examination is most valuable when an integral evaluation of the patient is made.

The electrocardiographic abnormalities most frequently observed were ventricular repolarization disorders, in particular T-wave alterations. When the latter were recorded in an isolated, slight or localized manner, the electrocardiograms were classified as " doubtful ". When such alterations were associated with other significant electrocardiographic findings, they were either marked or of a diffuse nature; the tracings were considered abnormal. Further electrocardiographic studies will be made in an attempt to determine the different types of evolution that can arise in the population studied (Fig. 4 and 5).[1] The intraventricular conduction disorder more frequently found was complete right bundle branch block associated with Â QRS F deviation towards the left (Fig. 6).

This pattern has been previously described and considered as suggestive of chronic heart involvement in Chagas' disease (Dias et al., 1945; Laranja, Dias, Duarte & Pellegrino, 1951; Laranja, Dias & Nobrega, 1951; Rosenbaum & Alvarez, 1955; Laranja et al., 1956; Hernández, 1961; Pileggi et al., 1961). The Â QRS F deviation towards the left was interpreted (Pileggi et al., 1961) as an electrical phenomenon that could be related to the pathological lesion at the left ventricular apex, with suppression of the vectorial forces in this zone and relative predominance of the basal vectors of left ventricular activation. Another possibility, which was taken into consideration for the interpretation of this finding, was the existence of an enlargement of the left ventricle, associated with the right-branch conduction disorder.

The more frequent cardiac rhythm disorders were extrasystoles, present on rest and increased by emotion or even slight physical effort. In one case the subsequent evolution led, on two occasions, to attacks of paroxysmal ventricular tachycardia.[2] In the severe form, numerous multifocal extrasystoles were observed.[3]

Most of the electrocardiograms analysed did not show voltage alterations; the numbers with either low or high voltage were the same.

The predominance of left ventricular enlargement might be explicable on the basis of the relatively early stage of heart disease in the people examined. P-wave alterations correspond, in general, to morphological modifications (notches and slurrings).

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[1] For other typical cases see *Bull. Wld Hlth Org.*, 1965, **33**, 262 (Fig. 20 and 21).

[2] See *Bull. Wld Hlth Org.*, 1965, **33**, 263 (Fig. 22).

[3] See *Bull. Wld Hlth Org.*, 1965, **33**, 263 (Fig. 23).

Abnormal apical impulse; extrasystolic arrhythmia; ECG shows multifocal extrasystoles; T wave negative in V1 through V4; lack of voltage increase of R wave in V3.

(A, B) Slight cardiomegaly.

(C) Radiokymograph: diminished amplitude of cardiac pulsations at lower portion of left contour.

FIG. 3

RADIOGRAPHS OF 38-YEAR-OLD MALE PATIENT WITH POSITIVE SEROLOGICAL REACTION SPECIFIC
FOR CHAGAS' DISEASE
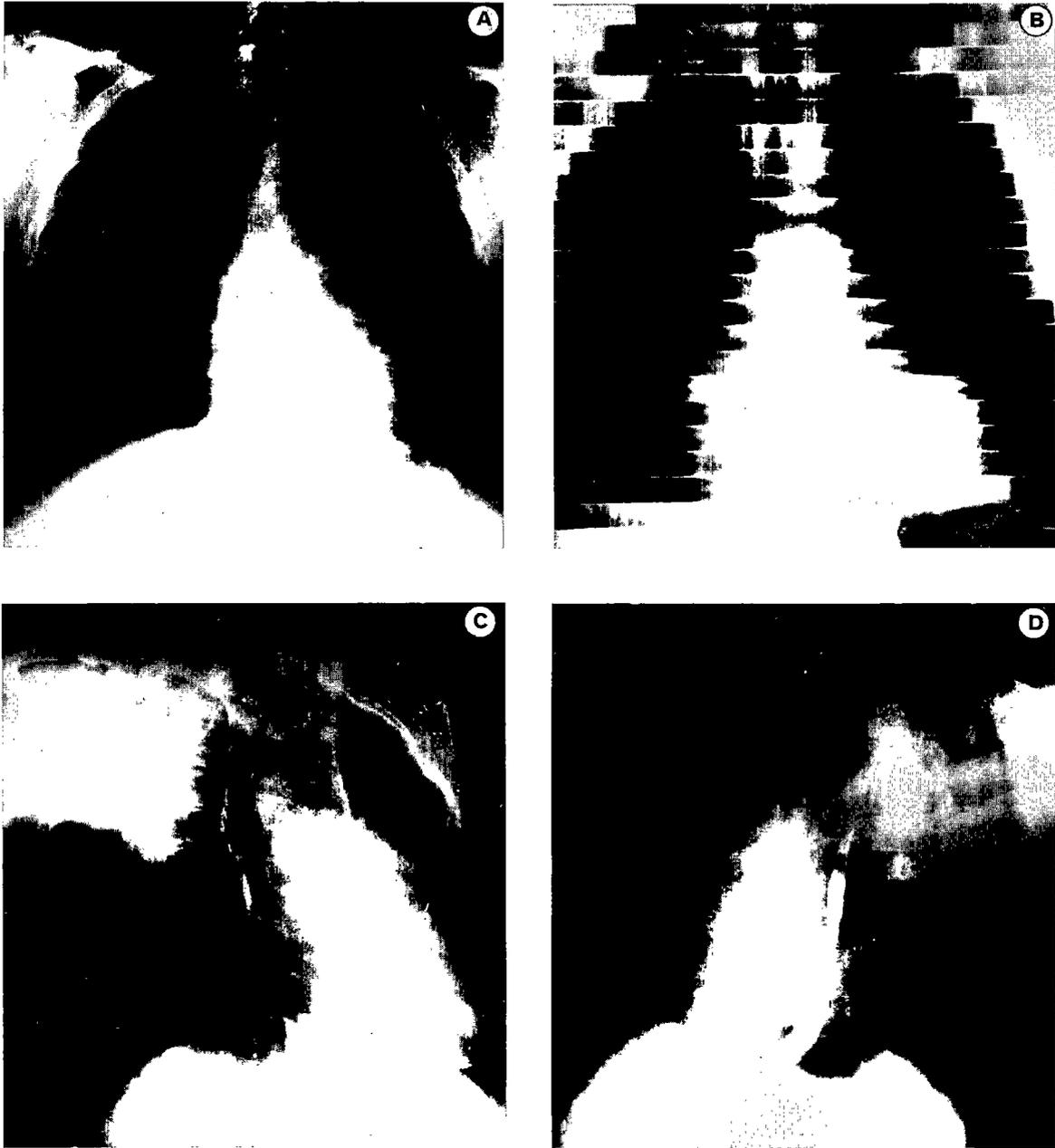
Abnormal apical impulse; ECG normal.
(A, C, D) Slight cardiomegaly.
(B) Radiokymograph: plateau-like appearance of left contour.
Paradoxical pulsations, observed on fluoroscopy.

FIG. 4
ELECTROCARDIOGRAMS OF 24-YEAR-OLD MALE PATIENT WITH POSITIVE SEROLOGICAL REACTION SPECIFIC FOR CHAGAS' DISEASE
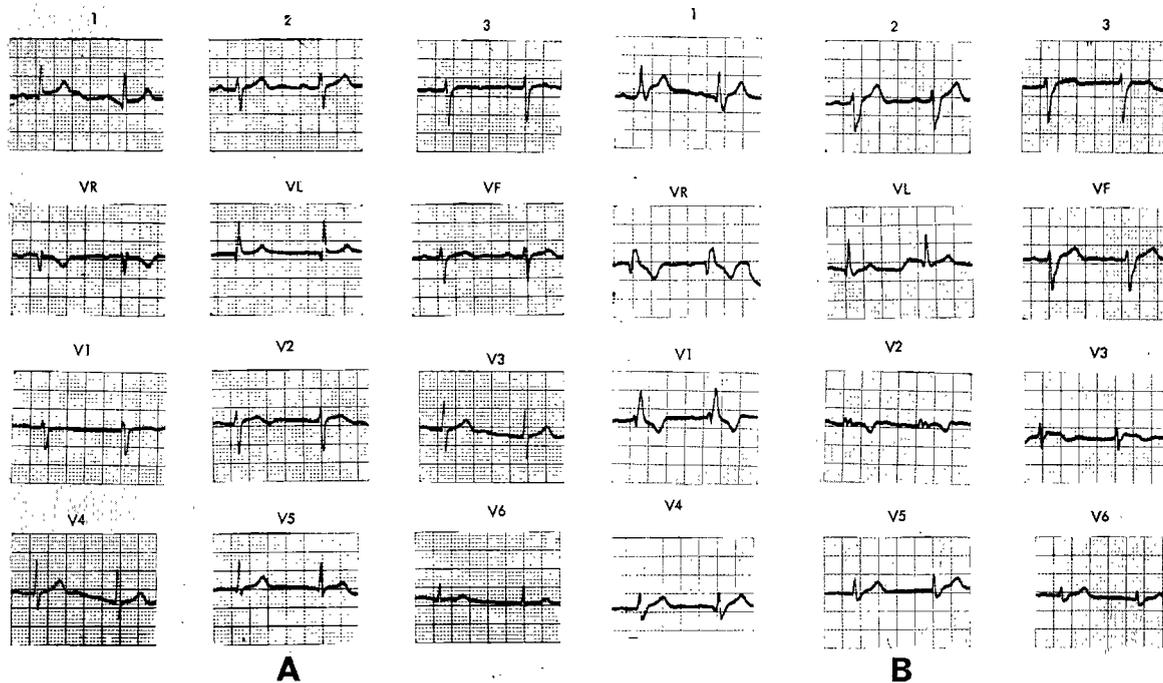
Asymptomatic; normal physical condition; normal cardiovascular shadow.

(A) Taken on 24 Sept. 1963; normal Â QRS F deviation towards left.

(B) Taken on 13 July 1964; complete right bundle branch block with important change of Â QRS F spatial position, slight positive shift of S-T segment with ± type of T wave in V3.

Evolutive pattern from apparent normality with Â QRS F deviation towards left through right bundle branch block of bundle of His.

FIG. 5

ELECTROCARDIOGRAMS OF 44-YEAR-OLD MALE PATIENT WITH POSITIVE SEROLOGICAL REACTION SPECIFIC FOR CHAGAS' DISEASE
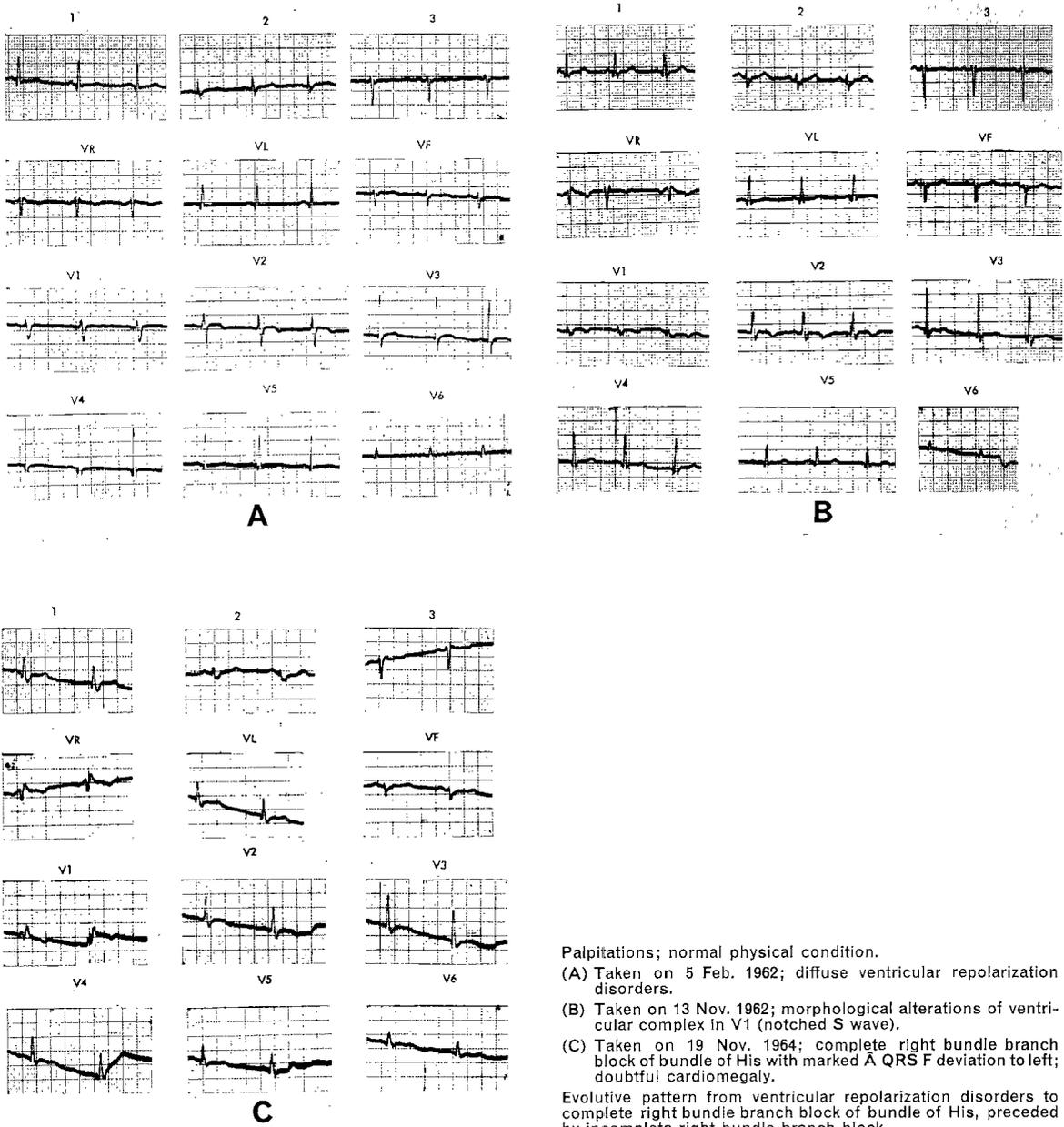
Palpitations; normal physical condition.

(A) Taken on 5 Feb. 1962; diffuse ventricular repolarization disorders.

(B) Taken on 13 Nov. 1962; morphological alterations of ventricular complex in V1 (notched S wave).

(C) Taken on 19 Nov. 1964; complete right bundle branch block of bundle of His with marked Â QRS F deviation to left; doubtful cardiomegaly.

Evolutive pattern from ventricular repolarization disorders to complete right bundle branch block of bundle of His, preceded by incomplete right bundle branch block.

FIG. 6

ELECTROCARDIOGRAM OF 26-YEAR-OLD MALE PATIENT WITH POSITIVE SEROLOGICAL REACTION
SPECIFIC FOR CHAGAS' DISEASE
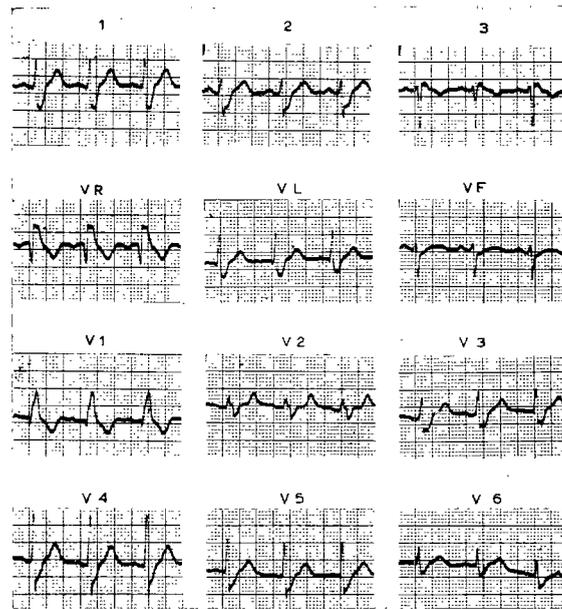
Asymptomatic; abnormal apical impulse; permanent splitting of second sound. ECG shows complete right bundle branch block of bundle of His with Â QRS F deviation towards left; slight cardiomegaly with left-ventricular enlargement; no cardiac pulsation abnormalities.

FIG. 7

ELECTROCARDIOGRAM OF 31-YEAR-OLD MALE PATIENT WITH POSITIVE SEROLOGICAL REACTION
SPECIFIC FOR CHAGAS' DISEASE
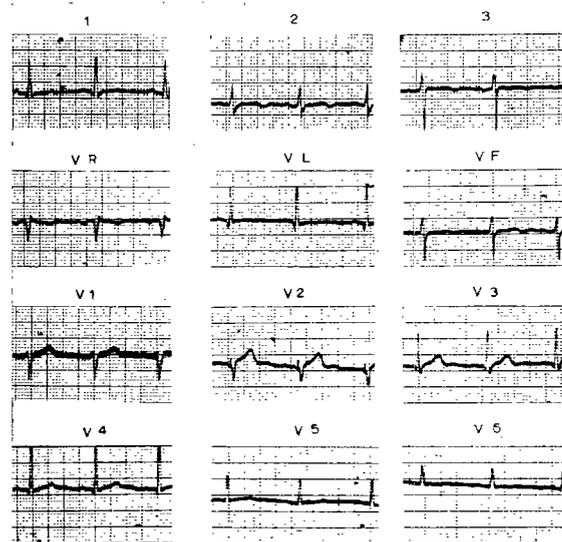
Palpitations; extrasystolic arrhythmia. ECG shows ventricular repolarization disorders associated with Â QRS F deviation towards left; absence of cardiomegaly with diminished apical pulsation.

FIG. 8

ELECTROCARDIOGRAM OF 40-YEAR-OLD MALE PATIENT WITH POSITIVE SEROLOGICAL REACTION
SPECIFIC FOR CHAGAS' DISEASE
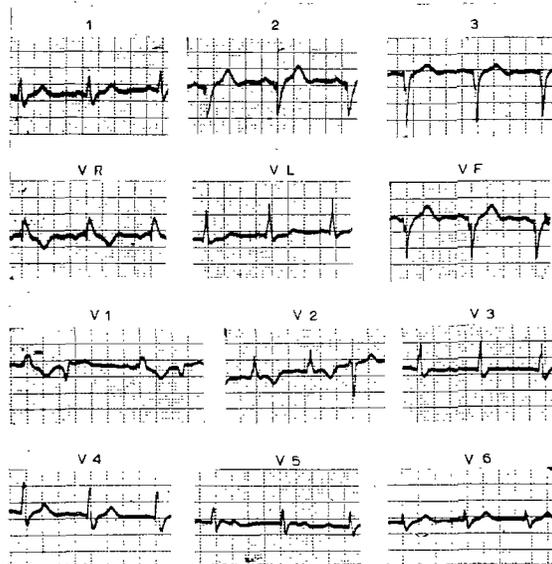
Palpitations; permanent splitting of second sound. ECG shows complete right bundle branch block and marked Â QRS F deviation towards left; flat T wave in lead V3; slight cardiomegaly with left-ventricular enlargement; normal cardiac pulsations.

FIG. 9

ELECTROCARDIOGRAM OF 41-YEAR-OLD MALE PATIENT WITH POSITIVE SEROLOGICAL REACTION
SPECIFIC FOR CHAGAS' DISEASE
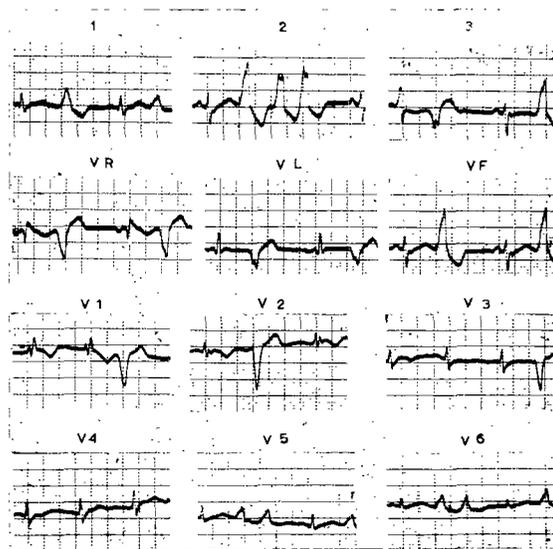
Palpitations accompanied by leipothymia and syncope; presystolic gallop rhythm; permanent splitting of second sound; frequent extrasystoles. ECG shows complete right bundle branch block of bundle of His. Ventricular extrasystoles; ventricular repolarization disorders; neither cardiomegaly nor cardiac pulsation disorders.

In the present series, the incidence of electrically inactive zones and A-V conduction disorders was low, which contrasts with the findings of other workers (Rosenbaum & Alvarez, 1955; Hernández, 1961). This discrepancy may be due to differences in the nature of the material studied.

Study of electrocardiographic alterations permitted the 88 abnormal electrocardiograms referred to earlier (p. 660) to be classified into two principal groups (Fig. 7-9, Table 13): (a) patients with intraventricular conduction disorders (52.3 %) and (b) patients without intraventricular conduction disorders (47.7 %).

In the latter group, the predominant electrical pathological phenomenon was an alteration of the ventricular repolarization. Occasionally, a combination of intraventricular block and modification of the ventricular repolarization was found. The other associations more frequently found for the two groups were cardiac rhythm disorders and Â QRS F deviation towards the left. The associated enlargement that predominated was that of the left ventricle.

The results of the photofluorographic and fluoroscopic examinations showed a cardiomegaly frequency of approximately 10%, when figures for pathological and doubtful cases were combined.

The abnormalities of the cardiac pulsations (diminished amplitude of the cardiac pulsations of the left contour and paradoxical pulsation) were highly significant when they appeared early in cases with slight cardiomegaly; its segmentary nature was determined. This radiological finding was fully confirmed in subsequent radiokymographic studies and has been related to the existence of the apical lesion (Gil Yépez et al., 1962, 1964) or to areas of fibrotic replacement which decrease the contractility of the heart and cause parietal weakness.

In the more advanced cases, this paradoxical pulsation may have its clinical manifestation in a rocking movement that is evident at the precordial area.

Left-ventricle enlargement was predominant in the initial stages of the disease and biventricular and global involvement during the evolutive and final stages.

The pathological results obtained so far confirm the existence of an inflammatory myocardial heart disease of unspecified nature in the area studied which occurs with hypertrophy and dilatation of the cardiac chambers in varying degrees, left-ventricular apical lesion at different evolutive stages, and frequent intracavitary thrombosis.

TABLE 13. ANALYSIS OF 88 ABNORMAL ELECTROCARDIOGRAMS

Type of block	No. without associated change	No. of cases with block	Number and type of associated changes											
			Ventricular repolarization disorders	Rhythm disorders	Voltage		Â QRS F deviation towards left	Ventricular enlargement			Inactive electrical zone	P-wave alterations	AV block (first degree)
					Low	High		Left ventricle	Right ventricle	Both			
Incomplete right bundle branch block	2	10	3	4	1	2	5	0	0	0	1	1	2
Complete right bundle branch block	4	20	10	7	2	3	17	5	0	0	2	5	1
Incomplete left bundle branch block	3	3	3	0	0	1	1	1	0	0	1	1	0
Unclassified intraventricular block	0	4	4	3	3	0	4	2	0	0	1	1	1
Total	9	37	20	14	6	6	29	8	0	0	5	8	4
Without block	42		35	16	8	3	7	2	1	1	4	3	1

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RÉSUMÉ

Les auteurs ont choisi deux zones rurales du Venezuela et ont effectué dans l'une (Eneal) une étude transversale et dans l'autre (Belén) une étude longitudinale de la population dans le but de déterminer la prévalence des cardiopathies dues à la maladie de Chagas. Au préalable, le pourcentage des maisons infestées par *Rhodnius prolixus* avait été déterminé: il était de 75,5% à Belén et de 52,6% à Eneal. Quant à l'indice d'infection du vecteur par *Trypanosoma cruzi*, il atteignait 25,8% à Belén et 9,1% à Eneal. L'étude a révélé un taux élevé d'infection humaine par *T. cruzi* dans cet échantillon de population considéré du point de vue épidémiologique comme représentatif. Le pourcentage des cardiopathies était de 12,9% (Eneal) et de 17,3% (Belén). Les cas de myocardiopathies chroniques, avec diagnostic sérologique de maladie de Chagas, étaient de loin les plus nombreux (84,8-88,5%). Le pourcentage des autres cardiopathies (ischémiques, hypertensives, syphilitiques et secondaires à l'anémie chronique) a été peu élevé. On n'a observé aucun cas de cardiopathie rhumatismale.

La plupart des cas de myocardiopathies chroniques à sérologie positive présentaient une bonne capacité fonctionnelle (classes I et II). Le travail analyse les symptômes cliniques observés chez des sujets de moins de 50 ans appartenant à ces catégories. Les altérations du choc de la pointe se sont manifestées précocement et avec une intensité variable. Dans les phases avancées de la maladie, les auteurs ont noté un mouvement de bascule dans la zone précordiale correspondant à l'apex, lié à la débilité pariétale du myocarde. Sur 1210 tracés électrocardiographiques, 16,4% présentaient des altérations. Les différentes anomalies électrocardiographiques et les modes d'évolution observés au cours de cette étude sont analysés et illustrés. Les résultats de l'interprétation d'électrocardiogrammes successifs, qui constituait un des objectifs de cette étude, seront rapportés ultérieurement. Les anomalies segmentaires de la cinétique cardiaque ont été fréquentes et précoces dans les cas de cardiomégalie peu prononcés; les perturbations de la cinétique au niveau du contour gauche de l'ombre cardiaque allaient de la diminution localisée de l'amplitude des battements aux pulsations paradoxales. Ces altérations étaient dues à une lésion de la région apicale du cœur et/ou de la paroi ventriculaire.

L'étude anatomopathologique de sept des cas a confirmé l'existence de myocardiopathie inflammatoire chronique non spécifique. Les lésions apicales du ventricule gauche atteignaient plusieurs degrés de gravité et ont pu être observées dans tous les cas.

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