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INFLUENCE OF *TRYPANOSOMA CRUZI* STRAIN ON THE PATHOGENESIS OF CHRONIC MYOCARDIOPATHY IN MICE

SONIA G. ANDRADE

Centro de Pesquisas Gonçalo Moniz – FIOCRUZ/UFBa – Rua Valdemar Falcão, 121, 41930 Salvador, BA, Brasil

The murine model of chronic Chaga's myocardiopathy was developed in 201 inbred and outbred mice. The experimental groups consisted of 1st: 73 inbred AKR and A/J mice inoculated with one of the following Trypanosoma cruzi *strains: Peruvian (Type I), 12 SF (Type II) or Colombian (Type III); 2nd: 128 outbred Swiss mice, chronically infected either with Type II or Type III strains isolated from human patients from different geographical areas. All* T. cruzi *strains were previously characterized by their morphobiological behaviour in mice and by isoenzymatic patterns. For the 1st group the inoculum was* 5×10^4 *for the Peruvian strain and* 1×10^5 *for the 12 SF and Colombian strains. In the 2nd group-Swiss mice the inoculum size varied from* 2×10^4 *to* 2×10^5*. The inbred animals were killed at a 3 time-point scale (90, 180 and 240 days) post-infection. The Swiss mice were killed from 180 to 660 days after infection. The evaluation of parasitemia and serology (xenodiagnosis and indirect immunofluorescent test) was performed. The incidence of macroscopic alterations of the heart and cardiac index were evaluated. Histopathological lesions of the myocardium were graded. The influence of* T. cruzi *strain on the intensity of cardiac lesions was evaluated by the Chi-square test; the incidence of inflammatory lesions and its relationship to the parasite strain was evaluated by the Fisher test. The influence of the duration of infection was evaluated by using the Gamma Coefficient of Kruskal and Goodman and its measure of significance. Slight to severe microscopic alterations occurred in 85% of the chronically infected mice. There were a clear predominance on the incidence and intensity of inflammatory and fibrotic alterations for the mice infected with Type III strains. Statistical analysis has shown significant differences among the infected groups, in the inflammatory and fibrotic lesions. Macroscopic alterations (right cavities dilatation and apex aneurism of left ventricle), differed in incidence according to mice strains; in Swiss and AKR mice, significant differences were seen in mice infected with different* T. cruzi *strains, but the A/J mice failed to show significant differences correlated with different parasite strains. The duration of infection, from 90 to 240 days, could not be correlated with the degree of lesions in the several groups.*

Although not discarding the influence of host strain, statistical analysis of our results indicated parasite strain as the most important factor in determining cardiac lesions in mice, especially when Type III strains are considered.

Key words: *Trypanosoma cruzi* – chronic myocardiopathy – murine model of Chaga's disease – *Trypanosoma cruzi* strains

Among several factors that may influence the course of manifestations during *Trypanosoma cruzi* infection, parasite strains have been considered as an important ones (WHO, 1986). The strains of *T. cruzi* may be classified in three diferent types or "biodemes" according to their morphological and histopathological behaviour in mice (Andrade, 1974, 1985). During chronic infection in mice, different *T. cruzi* strains may determine diverse degrees of cardiac and skeletal muscle lesions, of autonomic neuronal cells involvement and of necrotizing arteriolitis (Andrade & Andrade, 1968). Cardiac lesions seem more prone to develop during chronic infection with Type III strains, as observed with the Colombian strain (Federici et al., 1964; Kumar et al.,

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1969; Andrade & Andrade, 1976) or with other strains possessing similar morphological characteristics (Andrade & Grimaud, 1968).

In this paper a though investigation about the importance of parasite strain on the course of experimental chronic myocardiopathy in mice is undertaken in well representative groups of inbred and outbred mice chronically infected with several *T. cruzi* strains.

MATERIAL AND METHODS

Two hundred and one mice chronically infected with several *T. cruzi* strains belonging to Types I, II and III (Andrade, 1974, 1985) were utilized. When included in the study, the animals had survived to an acute infection and were in apparently good health, 90 to 600 days following inoculation.

The following experimental groups were studied:

Group I – Seventy-three AKR and A/J inbred mice were inoculated with one of the following *T. cruzi* strains: Peruvian (Type I), 12 SF (Type II) and Colombian (Type III). Inocula varied from 5×10^4 (Peruvian strain) to 1×10^5 for 12 SF and Colombian strains. Animals in these groups were killed 90, 180 and 240 days post-infection. The number of mice for each strain of *T. cruzi* is shown in Table III.

Group II – One hundred and twenty eight Swiss outbred mice, being 79 infected with Type II strains of *T. cruzi* isolated from human patients from São Felipe, Mamba!, Firminópolis and Abadia dos Dourados (Brazil), and 49 infected with Type III strains (derived from patients from Montalvania and Morada Nova, Brazil, as well as from Colombia and Bolivia) were used. Inocula varied from $2\ 10^4$ to 2×10^5. Animals were killed 180 to 660 days after infection.

Group III – Consisted of intact control mice, being 15 outbred Swiss, 10 AKR and 10 A/J inbred mice.

Parasitology – Animals from all groups were submitted to direct examination of parasitemia in the peripheral blood and to xenodiagnosis with 4 to 5 stage nymphs of *Rhodnius prolixus*. Serological evaluation was by means of indirect immunofluorescence, according to Camargo (1966), using culture forms of *T. cruzi* as antigens and fluoresceinated goat anti-mouse IGg (Cappel Lab., U.S.A.) diluted 1:40. Sera were diluted 1:10 up to 1:640, the titre 1:10 being considered as positive.

Pathology of the heart – Hearts were formalin-fixed *in totum* and weighed. Cardiac index was evaluated for each mouse by correlating body and heart weights. The heart was divided in two equal parts by a middle sagital section and both halves were paraffin embedded and the 5 μm thick sections obtained were stained with hematoxylin and eosin and by the Masson's trichrome method. In 14 cases, serial sections mounted in plastic tapes (Pickett & Sommer, 1960) were used for identification and study of the conduction tissue of the heart.

Histopathological study – Inflammatory and fibrosing lesions were graded on a 3-point scale; + for mild and focal lesions, ++ for moderate diffuse and focal lesions and +++ for severe diffuse lesions. The cytological composition of the cellular infiltration, the topographical distribution of the lesions and the relationship between inflammation and fibrosis within the heart were also evaluated.

Collagen immunotyping – It was performed in 14 Swiss mice infected with Type II or Type III strains, and in sections of the heart cryopreserved with "tissue teck" into liquid Nitrogen. Immunolabelling of the collagen was performed by indirect immunofluorescence in frozen sections, using specific and purified anti-collagen antibodies. Detailled description was published elsewhere (Andrade & Grimaud, 1986).

Statistical analysis – Cardiac index represents the percentual relationship between heart weight and body weight and was obtained utilizing the formula:

$$\text{Cardiac index} = \frac{\text{heart weight} \times 100}{\text{body weight}}$$

It was calculated both for the control, non infected mice of the different strains and for chronically infected mice. According to Snedecor & Cochran Analysis of Variance the Chi-square calculation (Snedecor & Cochran, 1967) was used for evaluating the influence of *T. cruzi* strains on the development and intensity of cardiac lesions observed in Group I inbred

mice (AKR and A/J). The Fisher test (Zar, 1974) was used to evaluate differences in incidence of heart dilatation and apex aneurysm, among the groups of mice infected with different strains of *T. cruzi*. The influence of duration of infection on the inflammatory and fibrotic alterations of the myocardium, as well as on the cardiac indexes and macroscopic alterations (cavities dilatation and apex aneurysm), was evaluated by the Kruskal & Goodman's Gamma Coefficient (Levin, 1978). The statistical analysis was performed only on the data obtained for the Group I (inbred mice), in which duration of infection was stablished in a 3-time point scale (90, 180 and 240 days).

RESULTS

General data – Serological reactions (IIFT) were positive in all chronically infected mice. The titres in the Group I (AKR and A/J inbred mice) varied from 1:10 to 1:80, independently of the parasite strain. In the Group II (Swiss mice) the titres varied from 1:10 to 1:640, both for the infected with Type II and Type III strains of *T. cruzi*.

Patency of the infection was proved for all the experimental animals, either by direct parasitemia or by xenodiagnosis.

Pathology of the heart – The means and standard errors of cardiac indexes obtained in experimental groups of mice were submitted to the analysis of variance, in comparison to non-infected controls. Significant differences were disclosed, for each mouse strain, among the several groups of infected mice and controls at level of 0.05 (Table I). Evaluation of difference among the experimentally infected groups, for each mouse strain, has shown the following results: for the A/J mice, significant variation between the infected with Type II (12 SF) strain and Type III (Colombian) strain ($p < 0.002$) and between Type III and controls ($p < 0.05$). For the AKR mice, significant differences in the cardiac indexes were observed between the infected with Type I (Peruvian) and Type III (Colombian) strains ($p < 0.01$). For the Swiss mice, differences of the cardiac indexes were significant between Type II and Type III strains of *T. cruzi* ($p < 0.02$). Macroscopic alterations of the heart as right atrium and right ventricle dilatation, cavities thrombosis and aneurysm of the apex of left ventricles Figs 1-A, B; 2-A, B, C, D) were described but not measured. They occurred with variable incidence according to mice and *T. cruzi* strains (Table II).

Statistic analysis (Fisher test) confirmed significant differences in the incidence of cavities dilatation among the infected mice of AKR strain, as follows: Peruvian x 21 SF ($p = 0.03$); Peruvian x Colombian ($p = 0.0004$); 12 SF x Colombian ($p = 0.05$). In this same mice strain (AKR) differences were detected in the incidence of apex aneurysm between the Peruvian (Type 1) and Colombian (Type III) ($p = 0.06$), but not among the other strains. In the groups of A/J mice the incidence of heart cavities dilatation and apex aneurym does not differ statisticaly among the groups infected with different *T. cruzi* strains. No significant statistic differences in the incidence of heart cavities dilatation was detected between the Swiss mice infected with Type II and Type III strains. Highly significant statistic difference in the incidence of apex aneurysm was present in the Swiss mice infected with Type II and Type III strains ($p = 0.0009$).

Analysis of Kruskal & Goodman's Gamma Coefficient, did not show any influence of the infection on the cardiac index or on the macroscopic alterations of the heart in respect to Group I, inbred mice.

Histopathological study of the heart – Slight to severe microscopic alterations in the heart were identified in 85% of all the chronically infected mice, with predominance of fibrotic and inflammatory lesions, especially in the right atrium. These lesions showed diffuse or focal distribution, predominantly in the subepicardic and subendocardic areas and in the interatrial septum (Figs 3-A, B, C). Diffuse and focal lesions were also seen in the ventricular walls, predominantly in the higher portion of the interventricular septum, near the basis of the great vessels and in the right ventricular walls (Figs 4-A, B, C). Segments of the conduction system of the heart were identified in serial sections and showed interstitial edema and slight degree of fibrosis and diffuse mononuclear inflammation, vacuolization of myocells and focal necrotic lesions (Fig. 3-D). In several cases, inflammatory infiltration on the interatrial septum extended toward the conduction tissue, with perivascular distribution. The detailled description of conduction tissue lesions and their eletrocardiographic correlations

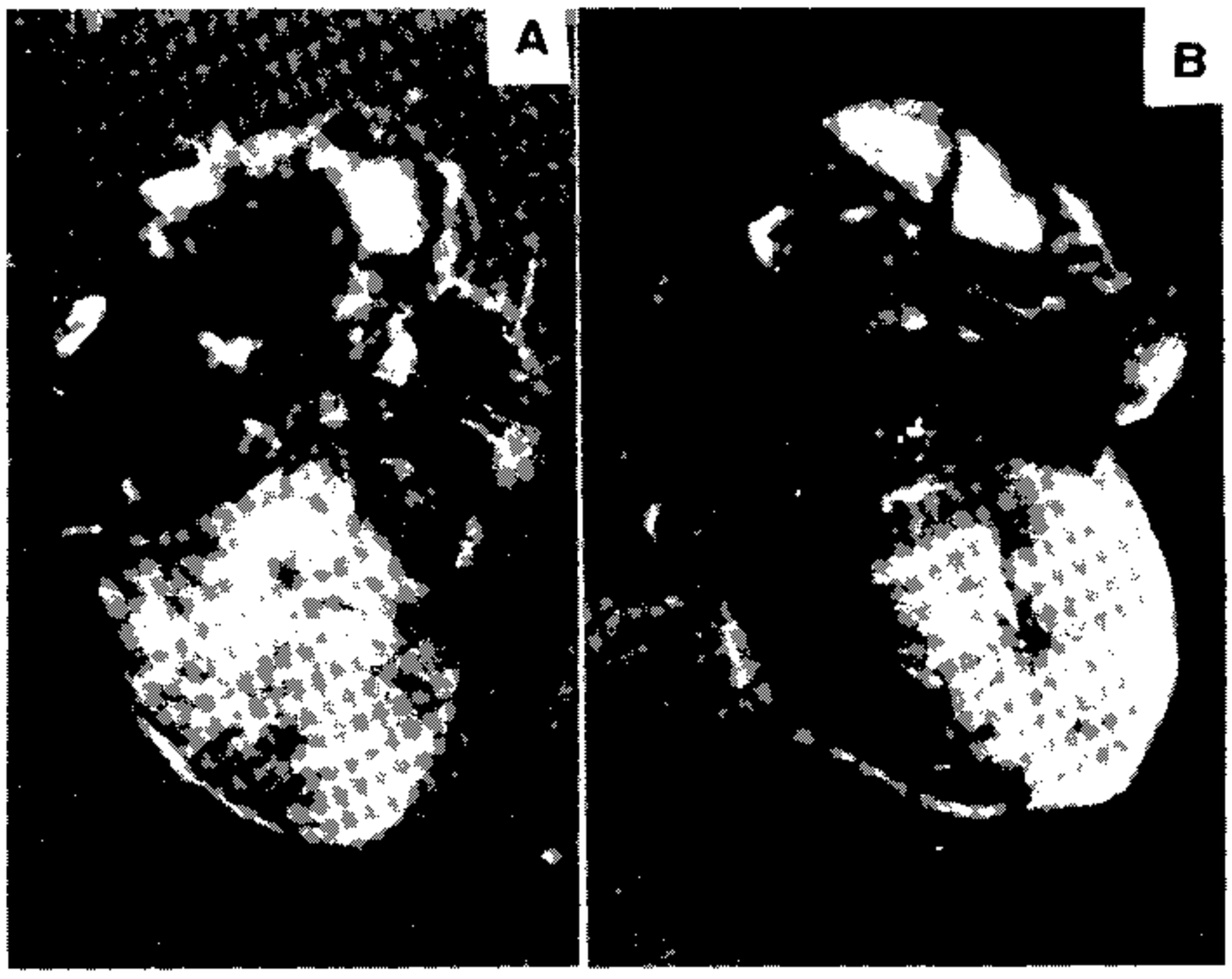

Fig. 1 A, B: cardiomegaly with dilatation of the right atrium and right ventricle and left ventricle hypertrophy in Swiss mouse infected with the *Trypanosoma cruzi'* Colombian strain (Type III).

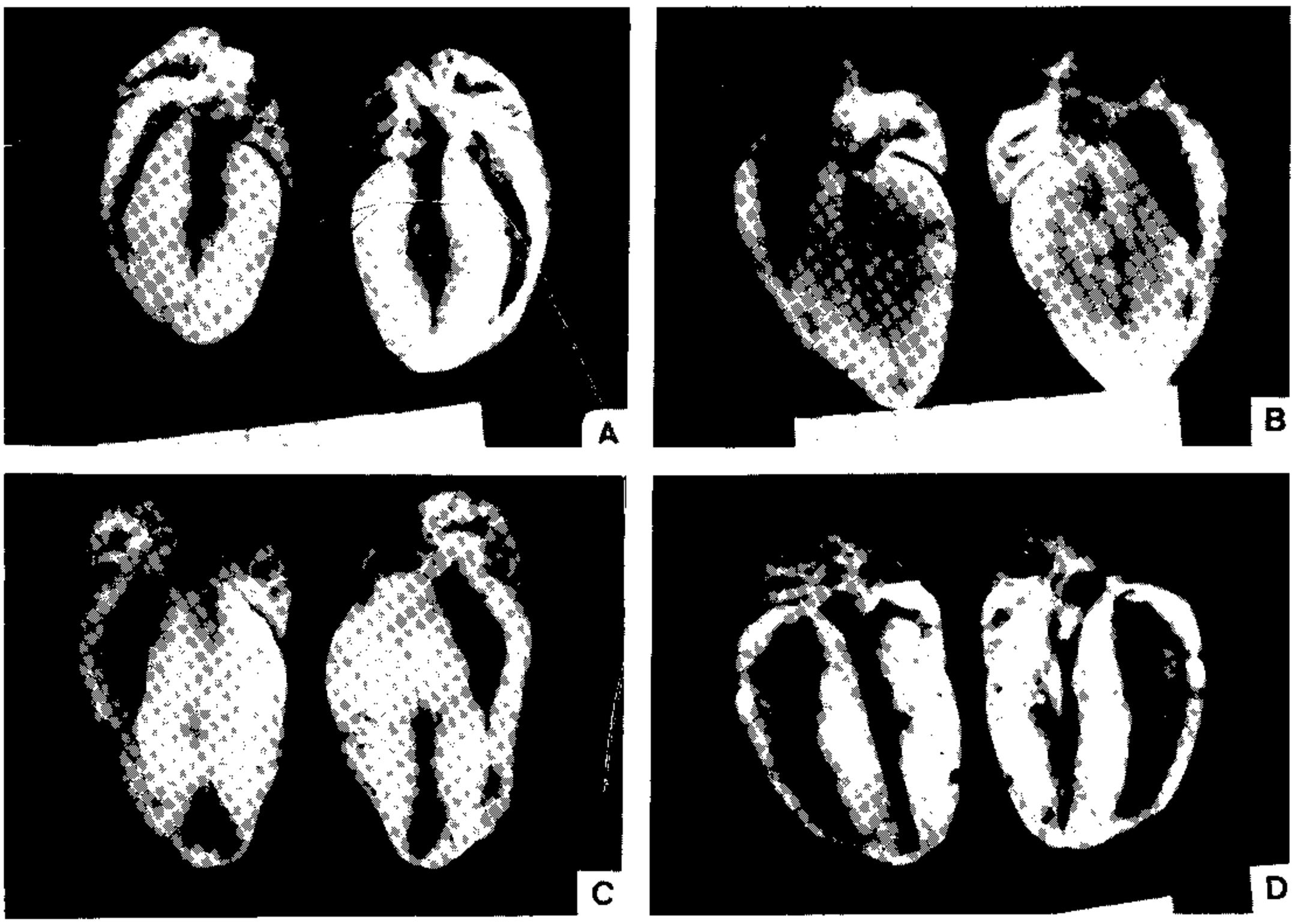

Fig. 2: several aspects of macroscopic alterations of the heart A – cardiac muscle hypertrophy (A/J mouse & 12 SF strain); B – right cavities dilatation (AKR mouse & Peruvian strain); C – right ventricle dilatation, apex aneurysm of the left ventricle, right atrium hipertrophy (Swiss mouse & Colombian strain); D – cardiac dilatation (Swiss mouse & Colombian strain).

TABLE I

Cardiac index in mice chronically infected with *Trypanosoma cruzi* in comparison with control mice

Mice strains	*T. cruzi* strains			No. of mice	Means	Standard error	Variance test
Swiss[a]	Type II	–	São Felipe	14	0.544	0.126	
			Mambaí	24	0.600	0.105	
			Firm. & A. D.	14	0.629	0.135	
	Type III	–	Colombian				
			PMN, Bolivia	17	0.674	0.130	
			Montalvania	16	0.606	0.143	
	Controls		–	15	0.542	0.071	
							$p < 0.55$
AKR	Type I	–	Peruvian	24	0.497	0.093	
	Type II	–	12 SF	5	0.560	0.135	
	Type III	–	Colombian	8	0.618	0.133	
	Controls		–	10	0.476	0.057	
							$p < 0.05$
A/J	Type I	–	Peruvian	5	0.544	0.065	
	Type II	–	12 SF	27	0.486	0.066	
	Type III	–	Colombian	4	0.607	0.125	
	Controls		–	10	0.474	0.066	
							$p < 0.05$

Means and Standard error – Analysis of Variance.
a: Only mice with until 240 days of infection were included.

TABLE II

Macroscopic alterations of the heart. Incidence according to mice and *Trypanosoma cruzi* strains

T. cruzi strains	AKR mice			A/J mice			Swiss mice		
	No. of mice	RA & RV Dil. (%)	AP. AN (%)	No. of mice	RA & RV Dil. (%)	AP. AN (%)	No. of mice	RA & RV Dil. (%)	AP. AN (%)
Type I	24	10 (42)	0 (0)	5	5 (100)	1 (20)	a	a	a
Type II	5	5 (100)	0 (0)	27	22 (80)	1 (3.8)	79	59 (75)	0 (0)
Type III	8	6 (80)	2 (25)	4	4 (100)	1 (25)	49	37 (75)	7 (14)

RA = right atrium; RV = right ventricle; AP. AN = apex aneurysm. Dil. = dilatation.
a: no surviving mice.
Statistic analysis – Fisher test – (See text).

were published elsewhere (Andrade & Sadigursky, 1987). Slight to dense fibrous thickening of the interstitial matrix of the myocardium was present, being usually associated with mononuclear cell infiltration (Figs 4-A, B). Immunotyping of the collagen were performed in 14 of the chronically infected Swiss mice. A predominance of Types III and IV collagen was detected both in the infected with Type II and with Type III strains of *T. cruzi*, as previously described by Andrade & Grimaud (1986). Intracardiac thrombosis occurred in a few cases, into the right atrium and/or into the right ventricle (Fig. 3-C).

Arteriolar lesions, consisting of segmentar necrosis of the vascular walls and infiltration with mononuclear and polymorphonuclear inflammatory cells were present. Aneurysm of the left ventricle apex, described macroscopically, was represented by the thinning of the cardiac muscle, inflammation and fibrosis of the septal myocardium in its upper portion (Fig. 4-D). Intracellular amastigote forms of *T. cruzi* in the miocardium was detected in 15% of the cases, regardless of the parasite or host strain (Fig. 4-C).

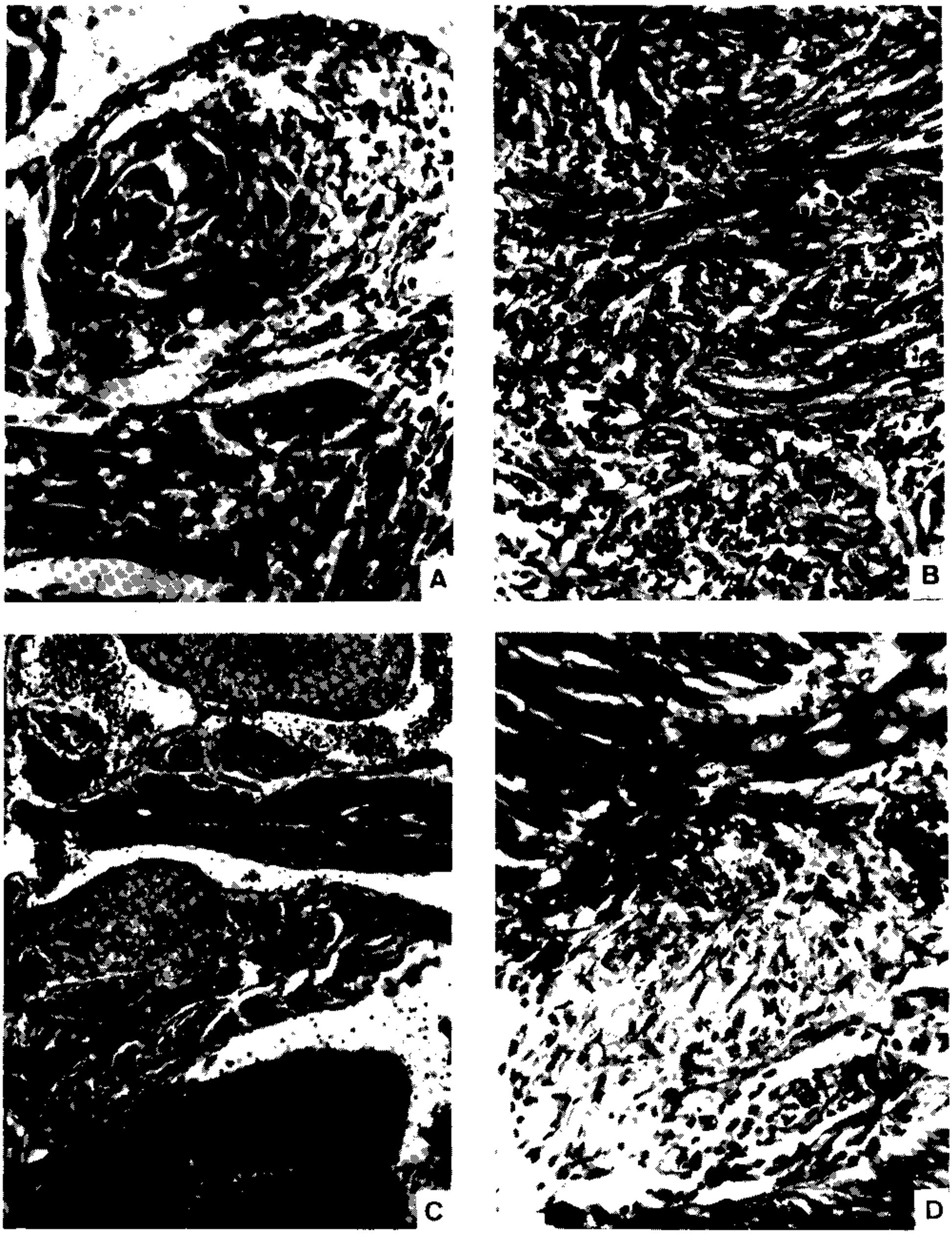

Fig. 3: A – right atrium: subepicardic and interstitial mononuclear inflammatory infiltration (Swiss mouse & Colombian strain), H & E, 250 X; B – right atrium wall: diffuse interstitial mononuclear infiltration (AKR mouse & Colombian strain), H & E, 250 X; C – right atrium: diffuse inflammation, fibrosis and thrombosis (Swiss mouse & 21 SF strain), H & E, 250 X; D – conduction tissue of the heart – His bundle (arrows); myocells vacuolization and inflammatory infiltration (AKR & Colombian strain), Masson's thrichrome, 400 X.

The incidence of inflammatory lesions in the ventricles and atria and their relationship to the parasite strain appear in Table III. The percentual data disclose a clear predominance of a diffuse inflammatory process for the mice infected with Type III strains. Statistical analysis of the influence of *T. cruzi* strains in the intensity of inflammatory and fibrotic alterations of the myocardium, in the AKR and A/J mice (Group I), are shown in Tables IV and V respectively. Significant differences was seen among the mice infected with different strains of *T. cruzi* when compared by the Chi-square test (Table IV). The inter-*T. cruzi*

TABLE III

Incidence of inflammatory alterations of the myocardium in mice chronically infected with different strains of *Trypanosoma cruzi*

Groups		*T. cruzi* strains			Incidence of diffuse and focal lesions of the myocardium[a]					
					Ventricles			Atria		
Mice strains	No. of mice	Types[b] No. of mice			Type I	Type II	Type III	Type I	Type II	Type III
Group I		I	II	III						
AKR	37	24	5	8	20.8%	20.0%	87.5%	87.5%	40.0%	100%
A/J	36	5	27	4	40.0%	11.1%	50.0%	60.0%	77.7%	100%
Group II										
Swiss	128	c	79	49	c	36.7%	53.0%	c	73.4%	85.7%

a: only concomitant diffuse and focal lesions are considered.
b: type I (Peruvian); Type II 12 SF (AKR, A/J) and several strains (Swiss mice); Type III Colombian (AKR, A/J) and several strains (Swiss mice).
c: no surviving mice.

TABLE IV

Influence of *Trypanosoma cruzi* strain on the inflammatory alterations of the myocardium in the chronic phase of the infectiwn

Mouse strain	No. of mice	*T. cruzi* strain	Localization and grade of lesions															
			Atria								Ventricles							
			Focal lesions				Diffuse lesions				Focal lesions				Diffuse lesions			
			0	+	++	+++	0	+	++	+++	0	+	++	+++	0	+	++	+++
AKR	24	Peruvian	3	17	4	–	1	14	8	1	9	14	1	–	18	6	–	–
	05	12 SF	1	2	2	–	2	1	1	1	–	5	–	–	4	–	1	–
	08	Colombian	–	2	4	2	–	2	5	1	–	5	3	–	1	2	4	1
No. of mice	37		4	21	10	2	3	17	14	3	9	24	4	–	23	8	5	1
A/J	05	Peruvian	–	3	1	1	2	–	2	1	2	2	1	–	3	2	–	–
	27	12 SF	4	21	2	–	2	18	7	–	16	10	1	–	22	5	–	–
	04	Colombian	–	1	3	–	–	1	3	–	–	2	2	–	2	2	–	–
No. of mice	36		4	25	6	1	4	19	12	1	18	14	4	–	27	9	–	–
Statistic Analysis: Chi-square test																		
AKR			X^2 = 13.902 p = 0.0307				X^2 = 13.036 p = 0.0425				X^2 = 9.964 p = 0.041				X^2 = 20.221 p = 0.0025			
A/J			X^2 = 18.592 p = 0.0049				X^2 = 17.538 p = 0.0075				X^2 = 9.849 p = 0.043				X^2 = 1.970 p = 0.373-NS			

TABLE V

Influence of the strain of *Trypanosoma cruzi* on the grade of fibrosis in chronically infected AKR and A/J mice

Mouse strain	No. of mice	*T. cruzi* strain	Atria				Ventricles			
			0	+	++	+++	0	+	++	+++
AKR	24	Peruvian	18	6	–	–	20	4	–	–
	05	12 SF	3	1	1	–	4	1	–	–
	08	Colombian	1	6	1	–	1	3	4	–
No. of mice	37		22	13	2	0	25	8	4	0
A/J	05	Peruvian	2	2	1	–	4	1	–	–
	27	12 SF	17	10	–	–	23	4	–	–
	04	Colombian	1	2	1	–	2	–	2	–
No. of mice	36		20	14	2	0	29	5	2	0
Statistic Analysis: Chi-square test										
AKR			X^2 = 12.601 p = 0.0134				X^2 = 20.299 p = 0.0004			
A/J			X^2 = 7.409 p = 0.11				X^2 = 17.242 p = 0.0017			

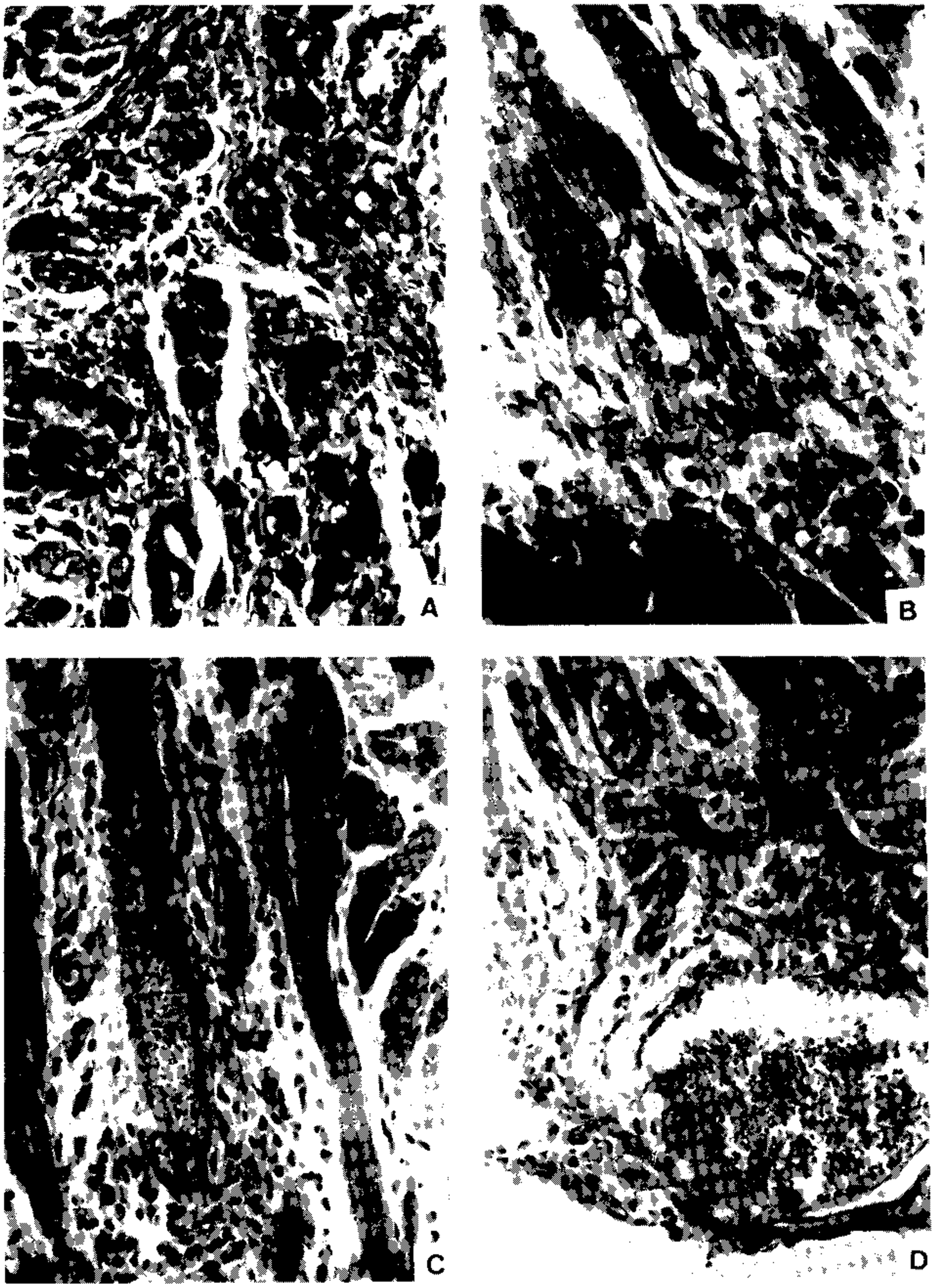

Fig. 4: A – right ventricle wall: diffuse mononuclear infiltration and interstitial fibrosis (Swiss mouse & Colombian strain), H & E, 250 X; B – left ventricle wall with focal area of substitution of cardiac fibers by fibroblasts, collagen deposit and mild inflammatory infiltration (Swiss mouse & Montalvania strain), H & E, 250 X; C – right ventricle – amastigote forms of *Trypanosoma cruzi* into myocardial cell, inflammatory infiltration and fibrosis (A/J mouse Colombian strain), H & E, 250 X; D – left ventricle: apex aneurysm, fibrosis and mononuclear infiltration in the interventricular septum (AKR and Peruvian strain), H & E, 250 X.

strains comparison, has shown significant differences as follow: *AKR mice* – Peruvian x Colombian strains (focal atrium lesions) $p = 0.0081$; Peruvian x 12 SF strains (diffuse atrium lesions) $p = 0.0449$; Peruvian x Colombian (focal ventricular lesions) $p = 0.0471$; Peruvian x 12 SF (0.0482) and Peruvian x Colombian (0.00028), in relation to diffuse ventricular lesions. *A/J mice:* 12 SF x Colombiana (focal atrial lesions) $p = 0.0027$; Peruvian

x 12 SF (diffuse atrial lesions) $p = 0.0055$; 12 SF x Colombian (focal ventricular lesions) $p = 0.0059$.

There were significant differences in the degree of fibrosis between the mice of both strains (AKR and A/J) infected with different *T. cruzi* strains (Table V). Inter-*T. cruzi* strains comparison has shown significant differences as follow: *AKR-mice* - significant differences in the grade of atrial fibrosis between Peruvian x Colombian strains ($p = 0.0042$); of ventricular fibrosis between Peruvian x Colombian ($p = 0.0001$) and of 12 SF x Colombian ($p = 0.0397$) was present. *A/J mice* significant differences were detected between Peruvian x 12 SF strains ($p = 0.20$); in the atrial fibrosis and between 12 SF x Colombian ($p = 0.00006$) in the ventricle fibrosis.

The influence of duration of infection evaluated by the Gamma Coefficient, did not reach statistical significance.

DISCUSSION

The evolution of Chagas' disease in man is characterized by a spectrum of cardiac alterations, from the acute phase to the chronic form of the disease. The influence of different *T. cruzi* strains in the evolution of this cardiopathy may be investigated by the use of well developped experimental models.

In the search for a suitable model for the chronic cardiopathy of Chagas' disease, the mouse has been utilized by several investigators (Laguens et al., 1980; Bolomo et al., 1982; Bijovsky et al., 1983). However, the influence of parasite strain is rarely considered (Gonzalez Cappa et al., 1980; Schlemper Jr. et al., 1983; Postan et al., 1987). The Colombian strain of *T. cruzi* has shown a peculiar capacity to produce chronic myocardiopathy in mice (Federici et al., 1964; Kumar et al., 1969). This same strain was characterized as Type III according to Andrade's classification (1974). The histopathological lesions produced in mice during the acute phase of infection with this strain, clearly differed from the lesions produced by the Y strain (Type I) (Andrade & Andrade, 1966) and by the 12 SF strain (Type II) (Andrade et al., 1970; Andrade, 1974). The possibility of including several *T. cruzi* strains into three limited types or patterns has contributed to a better evaluation of the importance of the parasite strain on the development of cardiac lesions in chronic infection. Several parameters are considered, such as the patterns of parasitemic curves, morphological characteristics, virulence and pathogenicity, tissue tropism and histopathological lesions (Andrade, 1985; WHO, 1986). A positive correlation between *T. cruzi* biological classification of strain types and their respective isoenzymic patterns has been disclosed (Andrade et al., 1983).

In the stablishment of a chronic infection in mice, some factors are involved, such as parasite strain and host response. There are an individual variability of pathological lesions in the chronically infected mice, even in the inbred ones, the lesions being absent in a percentage of animals or varying from slight to marked within a same group. However, by utilizing isogenic mice and controlling several factors such as duration of infection and inoculum size, it was possible to stablish some correlations between the type of strain of *T. cruzi* and the incidence and intensity of the histopatological lesions. Isolated items such as virulence, have been taken into account in comparative studies (Schlemper Jr et al., 1983) considering the virulence of the strain in the acute phase as the main factor in determining the severity of the lesions during the chronic phase. In our present study, the inbred (AKR and A/J) mice were inoculated with the Peruvian (Type I) and the 12 SF (Type II) strains, both showing high virulence, and so the inter-types comparison was not precluded by virulence as the isolated factor. The Colombian (Type III) less virulent, was the most pathogenic and determined the highest degree of lesion during the chronic phase.

Detailled statistical analysis have shown that duration of infection, from 90 to 280 days, does not influence the degree and incidence of inflammatory and fibrotic lesions. Even the inoculum size seems no influence on these regards (data not shown). However, it was shown a significant influence of the parasite strain on the development of cardiac lesions as heart dilatation and apex aneurysm and on the inflammatory and fibrotic process in the myocardium.

The influence of the mouse strain on the development of the heart lesions was also present and the statistic analysis have shown

different inter-*T. cruzi* strains correlations, depending upon the mouse strain. In the AKR mice, significant differences in the incidence of heart dilatation and apex aneurysm were observed in the mice infected with different strains of *T. cruzi*. On the contrary, in the A/J mice, no significant differences were detected among the three groups.

Electrocardiographic alterations in chronically infected mice were also influenced by parasite and mouse strain as well (Sadigursky & Andrade, 1986). This latter study showed that in the AKR mice, the electrocardiographic alterations occurred in 80 to 87% of the animals infected with either one of the three types of strains; in the A/J mice, there was a clear difference between those infected with Type I and Type III (100% of alterations) and those infected with Type II (26%). In the Swiss mice, the electrocardiographic alterations occurred in 53.4% of those infected with Type II and in 71.4% of ones infected with Type II strains. Although the mice strain appeared as highly important as far as the determination of ECG alterations was concerned, *T. cruzi* strain was important not only for the frequency but also for the type of electrocardiographic alterations, as observed in the A/J and Swiss mice. Similar observations were performed by Postan et al. (1987) in the chronic infection of C57 and C3H mice with clones of the strains Sylvio and Miranda of *T. cruzi*.

Therefore, the use of isogenic mice rises the problem of the influence of this factor on the development of chronic lesions. It is known from previous studies (Andrade, V. et al., 1985a) that the patterns of resistance of the inbred mice to the infection with *T. cruzi* are determined by the parasite strain. This means that each strain maintained its basic features in different mouse strains (Andrade, V. et al., 1985b). Thus the parasite strain seems more important than the mice strain for the determination of tissue lesions. Our results have shown that there are differences in the incidence of the cardiac lesions when AKR, A/J and Swiss mice are compared, which represents, perhaps, an indication that the genetical background of the host is also important for the differences in the clinical manifestations of the Chagas' disease in patients of the same endemic area. The murine model has shown that when statistically significant differences were present among mice infected with different strains of *T. cruzi*, whatever the mouse strain, there is always a predominance of lesions determined by the Type III strains.

The Swiss mice represent a most heterogeneous group, but perhaps, the most representative for what happens to the human populations in endemic areas.

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