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69. Chagas' disease in children

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Introduction

Many studies on the distribution of Chagas' Disease have been made since it was first described by Carlos Chagas in Brazil in 1909. Although the disease has been reported from Central America and naturally infected insect vectors have been found in North America very little attention has been given to it in these places.

Trypanosoma cruzi infections were first recognized in Panama by Miller (1931), De Coursey (1935) and by Johnson and De Rivas (1936).

The difficulties encountered in the diagnosis of this malady, as observed in Panama, have been in large part responsible for our lack of knowledge. In addition to direct microscopic examination of the blood, which is the commonest method of diagnosis, various types of supplementary tests have been used as aids from time to time.

The first case of human American trypanosomiasis or Chagas' Disease, to be recognized in Panama was an eighteen months old baby who was admitted to the Santo Tomas Hospital, in the city of Panama on December 19th 1930; this case and two others, which were discovered about three months later, were reported by Miller (1931). Since that date, cases have been reported in other parts of the western hemisphere. It is likely that the geographical extent of the disease is much greater than has been previously suspected, since it is found usually in children and the period of time that parasites can be demonstrated in peripheral blood films, is relatively short, thus making a diagnosis by this means difficult. Except for the early work of Miller (1931), Clark and Dunn (1932) and Johnson (1932) little attention was given to the problem of Chagas' Disease in Panama until the early 1960s. The staff of Children Hospital and Gorgas Memorial Laboratory have, however, maintained a constant surveillance for acute and chronic cases in communities involved in preventive control programs. Our information suggested the need for more intensive work on this disease to define the ecological, biological and clinical factors characterizing the infection. The objective of this article is to provide this information.

Materials and methods

Surveys of Panamanian children from the age of two months to fifteen years, resident in endemic areas were made by examination of thick smears, stained by the modified Giemsa method, by culture of venous blood on Senekjie's medium.

and by complement fixation reaction (C.F.T.) of sera by the method of Chaffee, Fife and Kent using a strain of *T. cruzi* isolated from a Panamanian child in 1964 and since maintained in culture. These surveys were begun by Johnson and Kelser in 1936 and have been continued until the present time.

Nine of 69 patients diagnosed by thick smear and culture died of acute Chagas myocarditis. The remaining 60 and an additional 84 patients diagnosed serologically, have been studied and followed for one to fourteen years in the outpatient clinic at G.M.L. and Children's Hospital and by repeated visits to their homes by field personnel.

Studies at G.M.L. and the Children's Hospital included determinations of haemoglobin, haematocrit, serum creatine, urinalysis, electrolytes, blood urea nitrogen, blood glucose, serum proteins, serum glutamic acid oxalate transaminase (S.G.O.T.), serum glutamic-acid-pyruvate transaminase (S.G.P.T.), serum cholersterol, serum lactic acid dehydrogenase (L.D.H.), creatine phospho-kinase (C.P.K.), roentgenograms (chest-abdomen-others), electrocardiograms, vectocardiograms, echocardiograms, blood culture for *T. cruzi*, complement fixation test (C.F.T.), xenodiagnosis, Elisa and haemoagglutination. Patients with positive C.F.T. without symptoms were examined every six months. Patients with symptoms were examined every three months or more frequently depending on their clinical cardiovascular condition.

During January 1967 to January 1980 there were 16 deaths among 153 patients under study. Nine patients with demonstrated parasitaemia and seven with positive serology had autopsies.

Results

The highest rate of infection with *T. cruzi* was found in the areas within the provinces of Panama and Colon bordering on Gatun Lake. Trypanosomes were most frequently detected in children; the youngest person with *T. cruzi* was a 2 months old infant from Chorrera. In the trypanosome positive population 75 per cent were less than 15 years old.

Episodes of cardiac failure occurred in 47 of 69 patients with acute Chagas' Disease and in 25 with chronic Chagas' Disease. (Table 69.1) These episodes were associated with roentgenographic evidence of cardiac enlargement and with a variety of electocardiographic abnormalities that are tabulated in Table 69.2. Complete atrioventricular block is relatively infrequent in Panamanian children with chronic Chagas' Disease. The most common abnormalities in the early stages of the disease are first degree atrioventricular block, right bundle branch block (complete and incomplete), ST — T wave changes and arrythmias. But, complete and incomplete left bundle branch block or hemi-blocks are not uncommon. In Panama the appearance of multifocal ventricular extrasystoles were of grave prognostic significance; in our experience, all patients with multifocal PVC's have died in less than two years. All patients with left anterior branch block (hemiblock), after two years of echocardiography follow-up presented significant modification of the septal or left ventricular posterior wall movement. About 10.6 per cent of all cases with chronic Chagas' Disease showed ventricular aneurysms confirmed by fluoroscopy or echoangiocardiography.

Table 69.1 Signs and symptoms in 69 patients with acute Chagas' Disease (A) (47 with cardiac failure) and 76 patients with chronic Chagas' Disease (B) (25 with cardiac failure).

	(A) Acute Chagas'	(B) Chronic Chagas'
Dyspnea	29/69	18/76
Cough	25/69	20/76
Edema	25/69	16/76
Gallop	43/69	21/76
Murmers	16/69	6/76
Cyanosis	21/69	13/76
Arrythmia	48/69	31/76
Pulmonary rales	44/69	32/76
Hepato-splenomegaly	42/69	19/76
Fever	62/69	–/76
Anorexia	57/69	6/76
Convulsion	4/69	–/76
Jaundice	4/69	2/76
Lymphadenopathy	56/69	–/76
Romaña Sign	16/69	–/76
Pallor	50/69	3/76
Headache	51/69	11/76

Necropsy findings

The principal changes encountered in the 16 patients who had an autopsy were: 1. cardiac weights ranging from 230 to 870 grams; 2. dilatation of cardiac chambers with ventricular hypertrophy; 3. apical lesions associated with remodelling of the trabeculae carneae and papillary muscles (thrombi were frequently associated with these lesions); 4. deviation of the interventricular septum to the right; 5. interstitial fibrosis and acute or chronic myocarditis. Dilatation was usually more pronounced in the atria and right ventricle. Dilatation and remodelling of the myocardium in the ventricular apices resulted in a bifid apex in the chronic cases. A characteristic finding in chronic Chagas' cardiomyopathy is the apical lesion which consists of a defect in the myocardium in the ventricular apices and replacement of the muscle by fibrous tissue. It was present in all seven chronic cases who had autopsy.

Studies of the conduction system and of the cardiac ganglia were made in six hearts. Fibrotic and inflammatory changes were seen in the sinus node of one heart, and in the AV nodes of three hearts.

Changes in the bundle of His and its major branches were found in chronic and acute cases. Ganglion counts were not made, but inflammatory and fibrotic changes were seen in a few ganglia.

Discussion

Our experience shows that in Panama a small but appreciable number of children have died with serological and/or anatomic evidence of chronic and acute Chagas' myocardiopathy.

Chronic Chagas' Disease has a slow, insidious, asymptomatic course which may manifest itself only by electrocardiographic or radiologic evidence of

Table 69.2 Electrocardiographic finding in 153 children with Chagas' Disease (Acute and Chronic)

Age groups		Months					Years					
ECG finding		0–3	4–6	7–9	10–11	T	1–3	4–6	7–9	10–12	13–15	T
Atrial Arrythmia	1. Fibrillation	–	–	1				1			1	
	2. Flutter	1							2	3		
	3. AV Dissociation					4	1			1		11
	4. Wandering											
	5. Pacemaker	1			1			1			1	
Atrial Enlargement	1. Right	1					1	3	2	3	2	
	2. Left					5		1	2	1	3	20
	3. Both		2		2			1		1		
Ventricular arrythmia	1. Isolated unifocal extrasystole	1		2	4		3	4	7	11	16	
	2. Multifocal extrasystole		1	2	2			2	1	1	3	58
	3. Idioventricular pacemaker				1		2	1				
	4. Ventricular paroxysmal tachycardia				1				1	3	2	
Right ventricular enlargement		2	2	3	1	8	*	4	3	4	5	23
Left ventricular enlargement		1			4	5	2	3	2	2	3	13
Right bundle branch block	Incomplete			5	3	18	3	4	4	8		30
	Complete		2	3	2		2	2	3	2	6	
Left bundle branch block	hemiblock			1	2				2	4	4	
	left anterior hemiblock					8				1		15
	left posterior complete			1					2	1	2	
	Total block (probable)				1				1	1		7
Atrioventricular block	First degree	4	3	3	8		2	3	4	5	3	
	Second degree				1	16				1		18
	Complete AV	–	–	–	–		–	–	–	–	–	
Ischaemia	Sub-epicardial	2	3	5	5		2	4	3	5	4	
	Sub-endocardial					15						18
Injury	Sub-epicardial			2	3	5	1	2	2	0	1	9
	Sub-endocardial											
Necrosis or suspected aneurysm					1	1		3	2	2	4	11
Normal		2	1		1	4	3	2	2	4	0	11

cardiac damage or serological evidence of infection. Attempts to demonstrate *T. cruzi* in chronic Chagas' Disease by xenodiagnosis, culture and histopathologic examination have failed. The evidence that the patients we have examined have chronic Chagas' Disease consists of one or more positive complement-fixation tests and/or the demonstration of characteristic cardiac disease by cardiological methods or characteristic cardiac lesions at necropsy.

Apical lesions, chronic myocarditis, and the incorporation of the ventricular

wall into trabeculae have been described by Laranja et al (1956) and Koerberle (1957) in Brazil; Moia in Argentina; Morales and Mijares in Venezuela and by Edgecomb (personal communication 1973). In all three countries, parasites were encountered in chagasic hearts, and culture and xenodiagnosis were positive for *T. cruzi*. This is not the case in Panama. Absence of megacolon, mega-esophagus, and other mega disease is noteworthy. Mega disease has not been described in Colombia orVenezuela. All our studies suggest that it does not occur in Panama. Why it does not occur is not known, but a difference in strains of *T. cruzi* seems a likely hypothesis.

In Panama Chagas' infection is relatively common, and most patients come from well-known endemic areas of Central Panama. The disease is maintained as a zoonosis in wild animals (rats, oppossums) in sylvatic and paradomestic species of bugs.

Cardiac failure and multifocal ventricular extrasystoles were grave prognostic signs. In patients with pulmonary edema, the edema may be considered the cause of death. But many patients in failure die suddenly, probably of arrythmias, idiopathic in origin or associated with toxicity to cardiotonic and other drugs.

Koeberle has ascribed chronic myocardiopathy and 'mega' disease to destruction of the parasympathetic ganglion cell. He has reported greatly reduced numbers of ganglia cells in the viscera, and affected hearts — 20 per cent in hearts and 80 per cent in the gastrointestinal tract. In Panama, where 'megas' do not occur, we have been more impressed by the degree of myocarditis, fibrosis and myocardial hypertrophy in Chagas hearts and the gross changes associated with its hydrodynamic pumping function. It is our impression that a positive complement fixation test indicates the persistence of *T. cruzi* antigen in the body, probably in the heart. Therefore, some small numbers of parasites undetectable by present parasitological methods, must persist. The relative importance of incomplete parasympathetic denervation, inflammation produced by autoantibody reactions, and of alterations in catecholamines and other metabolites is unknown.

If this view of chronic Chagas' Disease is correct, porevenatative treatment of patients with positive serology, and/or radiologic and electrocardiographic changes or parasitemia to destroy all parasites and convert the C.F. test to negative is indicated. But the scarcity of hospital beds and the residence of most patients in rural areas, their need to work for a living, and their reluctance to take drugs for long periods of time when they feel well, require that the drug be relatively effective in a short time and sufficiently free of toxicity to be taken.

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