Special problems in COCM: South America

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While this study is closely concerned with the cardiomyopathies, it is also bounded to specific aspects of the problem of social development. In particular, the study concentrates upon a disease which involves some degree of spatial and social adjustment, but it cannot neglect the changes which modify existing geographical distribution of diseases and the eventual relations between different areas.

Compared with Africa and Asia, the South American continent appears to be quite highly 'developed' (per capita income and other welfare indicators). At the same time, it appears far from developed if compared with Europe and North America. Such generalizations, however, hide some important distinctions and ignore the vast differences that exist between the various parts of the continent (Gilbert, 1977).

South America is in several ways heterogeneous. But, if this is so, why continue to imply that it represents a single entity, at least for the purpose of academic discussion? The answer is that while strong differences exist within the continent, the many common social, cultural and economic phenomena justify, within limits, treating it as a single entity. Nevertheless, it would be a gross mistake to ignore regional differences and that particular spatial phenomena are more fully developed or better documented.

During the past two decades the rate of urban growth has been very rapid. By 1980, the share of the population living in urban areas is likely to have increased from 39-1% in 1950 to 60-7% (UN ECLA, 1969). Today foreign immigration is negligible, and everywhere it is rural–urban migration and high-rates of natural increase that are the principal factors behind urban growth. To generalize about the impact of emigration upon an area involves taking into account a whole complex of factors.

The reasons why geographical aspects should be involved in a discussion on cardiomyopathies have already been given by Hutt (1972). He emphasized that by comparing differences in the incidence or prevalence of a disease one may pick up clues to its aetiology. But it is quite clear that emigration from the poor Latin American rural areas alters patterns of health and disease in both urban and rural areas.

The Pan-American Health Organization survey on causes of death showed that cardiovascular diseases hold a position of prominence among the causes of morbidity and mortality of adult population (Puffer and Griffith, 1967). The investigation was designed to present data on mortality for twelve widely separated cities which would not only be accurate but also comparable. In the survey the view of mortality by major groups of causes revealed marked geographical differences, which warrant careful interpretation and further study. Nevertheless, the analysis shows the very great range of mortality from infective and parasitic diseases, certainly one of the leading problems being Chagas' disease.

Chagas' disease is essentially an endemic infection of rural population and has a defined geographical distribution. The disease is known to be widespread in Brazil and cases have also been reported from several countries of Latin America, but reliable epidemiological data are not yet available.

What evidence there is suggests that there are nearly 35 million people exposed to the risk of infection (WHO, 1960). It is difficult to get reliable and comparable figures of the prevalence from different parts, partly because serological studies are not always available. For the sake of illustration, results from rural areas of Brazil (Pedreira de Freitas, 1965) and two rural areas of Venezuela (Puigbó et al., 1966) have shown, respectively, 39-1, 39-7 and 47-3% of their populations being sero-positive. In its chronic phase, cardiac pathology is the most common and serious complication of the disease.

Until quite recently, some authors were complaining that the spatial component had been neglected in planning studies. In particular, it was claimed that the pattern of cardiovascular diseases in large cities had been ignored. New work has appeared which has examined this problem by comparing differences (Laurenti and Fonseca, 1976).

In the city of São Paulo, Brazil, deaths from cardiovascular diseases accounted for 16-1% of all deaths (overall 209-7/100 000 inhabitants) in 1940, while in 1969 that number had increased to 30-2%.
(overall 258.4/100 000 inhabitants). Comparing these figures with those of some other developed countries it will be concluded that in the latter there are higher rates. Considering the different pathologies, ischaemic heart disease (11.5%), cerebrovascular accidents (9.1%), systemic arterial hypertension (2.8%) and rheumatic heart disease (1.3%) accounted for 68.5% of all deaths due to cardiovascular diseases (Laurenti and Fonseca, 1976).

Unfortunately, without casting doubts on these figures, there are certain deficiencies which may have encouraged false conclusions and therefore warrant further studies.

Having suggested that there may be reasons for the pattern, it is pertinent to understand how and why the city social and demographic growing lends itself to modifications. Certainly, there are a large number of migrants who moved from rural areas and therefore their origins should reflect in the pattern of cardiovascular diseases.

This pattern may be compared with the other, reported by the Pan-American Health Organization, related to Ribeirão Preto (Puffer and Griffith, 1967). This city of approximately 250,000 inhabitants is 300 km from the city of São Paulo. In Ribeirão Preto, Chagas’ disease was responsible for 13% of all deaths. Numerically it was more important than any of the following causes: tuberculosis, cerebrovascular accidents, ischaemic heart disease, diseases of the respiratory system, all forms of digestive diseases and all external causes of death. The excessive high death rates from Chagas’ disease in this population were well supported by the recorded diagnostic evidence and must therefore be accepted as real. Chagas’ disease was probably more readily recognized in Ribeirão Preto than elsewhere, remaining questionable whether an equal awareness exists in other cities.

The reason why an infective disease should be involved in a discussion on cardiomyopathies, is because in its chronic phase, cardiac involvement is the most frequent and serious complication of the disease. Also to a large extent the clinical concept of chronic Chagas’ heart disease is of a pathology characterized by congestive failure with poor systolic function.

The condition about to be discussed must be briefly defined: Trypanosoma cruzi infection may occur at any age, but usually in the first years of life. Cardiac involvement of greater or lesser intensity probably occurs in almost every acute case, but it seems not to be frequently recognized. Post-mortem examination shows an acute, severe, diffuse myocarditis with T. cruzi in myocardial fibres in all the cases (Laranja et al., 1956).

From a group of patients with a known acute period of infection, 22.7% developed electrocardiographic changes during an average period of 10 years after the acute infection (Laranja et al., 1956). The age distribution of chronic Chagas' cardiopathy shows that nearly 50% of these cases are between 21 and 40 years of age. Focal and diffuse fibrosis of the myocardium is almost invariably present. Inflammatory reactions and foci of parasites are extremely rare in the chronic phase (Köberle, 1963).

The two conditions, acute myocarditis and chronic cardiopathy, have an intimate aetiological relationship. However, it goes without saying that chronic cardiopathy is in direct continuity with a previous myocarditis. It must be emphasized that patients who survive the acute phase remain apparently healthy and asymptomatic for decades before an established clinical diagnosis of heart involvement is made.

The most common recognized clinical signs in chronic Chagas’ heart disease are cardiomegaly, cardiac failure, conduction disturbances and in the repolarization phase of the ECG. The same variety of abnormalities is disclosed by all the reported groups of cases in which the diagnosis was made on a similar basis (e.g. Dias, Laranja and Nobrega, 1945; Rosenbaum and Alvarez, 1955). However, there are discrepancies in relation to the percentage of abnormal tracings and in relation to the frequency of the visible changes. Although the extraordinary high incidence of right bundle branch block (30–55%) and the great frequency of pronounced left-axis deviation in chagasic right bundle branch block (Tranchesi et al., 1971), these electrocardiographic findings are non-specific.

In spite of the overwhelming preponderance of the cardiac pathology, as reported by others and shown here, there were a number of patients with sole involvement of hollow viscera and association of cardiac and digestive disorders (Köberle, 1963).

Over a period of 10 years the author studied a large number of cardiac chagasic patients, the results now presented were obtained from 120 chagasic individuals. A larger number of clinically similar patients seen by the author, but not subjected to cardiac catheterization, are not included. All these individuals had a positive serology.

Results (Tables 1 and 2) reveal that several patients (Group III, n 30) had the haemodynamic features of congestive cardiomyopathy, in accord with those previously reported (Amorim et al., 1968a): decreased cardiac output and stroke volume, and raised systemic and pulmonary venous pressures. However, the data show that a large number of patients with no past or present history of cardiac decompensation (Group II, n 40) had resting haemodynamic data within the range for normal individuals. Normal values were also found in non-cardiac (megalo-oesophagus, megacolon) chagasic...
Table 1. Summary on resting haemodynamics

<table>
<thead>
<tr>
<th></th>
<th>RA</th>
<th>RV</th>
<th>PA</th>
<th>WP</th>
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<th>PVR</th>
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<tr>
<td>GROUP I</td>
<td>Mean (s.d.)</td>
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<td></td>
<td>2-2 (1-87)</td>
<td>21-3/1-7</td>
<td>20-5/7-7</td>
<td>5-5 (2-68)</td>
<td>122-8/68-0</td>
<td>157-8 (48-15)</td>
<td>1,185-3 (276-84)</td>
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<tr>
<td>GROUP II</td>
<td>Mean (s.d.)</td>
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<td></td>
<td>2-7 (1-84)</td>
<td>23-6/2-4</td>
<td>21-2/7-2</td>
<td>6-1 (2-32)</td>
<td>126-5/68-2</td>
<td>158-6 (61-82)</td>
<td>1,258-6 (413-57)</td>
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<tr>
<td>GROUP III</td>
<td>Mean (s.d.)</td>
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<td>10-7 (7-75)</td>
<td>42-8/11-7</td>
<td>43-1/21-2</td>
<td>15-7 (7-89)</td>
<td>117-2/73-0</td>
<td>850-5 (476-87)</td>
<td>2,343-5 (787-52)</td>
</tr>
<tr>
<td>GROUP IV</td>
<td>Mean (s.d.)</td>
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<td></td>
<td>6-0 (4-04)</td>
<td>33-8/6-9</td>
<td>32-5/7-5</td>
<td>11-4 (4-42)</td>
<td>151-5/62-2</td>
<td>330-2 (170-51)</td>
<td>1,945-6 (809-32)</td>
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RA = right atrium; RV = right ventricle; PA = pulmonary artery; WP = 'wedge' pulmonary; SA = systemic artery; S = systolic pressure; D = diastolic pressure; m = mean pressure. Cardiovascular pressure in mmHg; PVR = pulmonary vascular resistance; SVR = systemic vascular resistance. Vascular resistance in dynes sec\(^{-1}\) cm\(^{-2}\). Clinical characteristics of Groups I to IV are described in the text.

Table 2. Summary on resting haemodynamics

<table>
<thead>
<tr>
<th></th>
<th>BS (m(^2))</th>
<th>HR (cycles/min)</th>
<th>RR (cycles/min)</th>
<th>Vo(_a) (litres/min/m(^2))</th>
<th>O(_{sa}) (arterial blood oxygen saturation)</th>
<th>O(_{sv}) (mixed venous blood oxygen saturation)</th>
<th>AV (litres/min/m(^2))</th>
<th>O(_{sca}) (blood oxygen capacity)</th>
<th>CI (litres/min/m(^2))</th>
<th>SI (stroke index)</th>
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<tbody>
<tr>
<td>GROUP I</td>
<td>Mean (s.d.)</td>
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<td></td>
<td>1-57 (0-15)</td>
<td>82-7 (13-20)</td>
<td>18-1 (4-04)</td>
<td>232-5 (52-97)</td>
<td>93-9 (2-93)</td>
<td>72-1 (7-36)</td>
<td>4-0 (0-93)</td>
<td>18-0 (2-43)</td>
<td>3-7 (0-60)</td>
<td>46-4 (21-93)</td>
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<td>GROUP II</td>
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<td>1-63 (0-02)</td>
<td>78-0 (13-08)</td>
<td>18-6 (3-45)</td>
<td>222-8 (65-89)</td>
<td>95-5 (2-12)</td>
<td>76-2 (6-96)</td>
<td>3-6 (1-05)</td>
<td>19-0 (2-05)</td>
<td>3-6 (1-02)</td>
<td>47-8 (13-87)</td>
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<td>GROUP III</td>
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<td>1-58 (0-15)</td>
<td>98-0 (19-83)</td>
<td>22-5 (7-40)</td>
<td>233-4 (54-30)</td>
<td>90-4 (6-19)</td>
<td>47-8 (15-49)</td>
<td>7-8 (2-78)</td>
<td>18-2 (1-95)</td>
<td>2-1 (0-80)</td>
<td>22-0 (7-73)</td>
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<td>GROUP IV</td>
<td>Mean (s.d.)</td>
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<td></td>
<td>1-59 (0-14)</td>
<td>39-3 (3-55)</td>
<td>20-6 (3-62)</td>
<td>199-3 (30-19)</td>
<td>95-8 (2-30)</td>
<td>69-2 (11-17)</td>
<td>5-1 (2-25)</td>
<td>18-6 (2-03)</td>
<td>2-6 (0-84)</td>
<td>69-4 (21-27)</td>
</tr>
</tbody>
</table>

BS = body surface (m\(^2\)); HR = heart rate (beats/min); RR = respiration rate (cycles/min); Vo\(_a\) = oxygen consumption (ml/min STPD); O\(_{sa}\) = arterial blood oxygen saturation; O\(_{sv}\) = mixed venous blood oxygen saturation; AV = systemic arteriovenous blood oxygen difference (ml/100ml); O\(_{sca}\) = blood oxygen capacity; CI = cardiac index (litres/min/m\(^2\)); SI = stroke index (ml/beat/m\(^2\)). Clinical characteristics of Groups I to IV are described in the text.

patients (Group I, n 30). The importance of T. cruzi infection as a cause of complete atrioventricular block (Andrade, 1973; Amorim et al., 1975) is such that the author has analysed it as a separate group (Group IV, n 20). The magnitude of changes in resting haemodynamics in the A–V block patients varied in accordance with the clinical situation, i.e. where there was the likelihood of associated marked myocardial involvement.

A patient with cardiomyopathy often presents with evidence of heart failure in the absence of apparent underlying cause, as a likely result from disease of the heart muscle itself. It was generally thought that Chagas’ disease was a chronic myocarditis. However, a chronic inflammatory infiltrate is out of proportion with the degenerative changes and, therefore, the resulting clinical picture. Routine examination of the heart often fails to disclose any reason for its frequent severe dilatation and hypertrophy.

The exact mechanism of the pathogenesis of Chagas’ disease remains unknown. The various theories proposed to explain the pathogenetic action of T. cruzi in the human organism (e.g. Chagas and Villela, 1922; Torres, 1941; Britto and Vasconcelos, 1954; Köberle, 1957; Muniz et al., 1970) include vascular, toxic, inflammatory, neurogenic and immunological pathways.

The author’s investigations of cardiac cases have concentrated particularly on autonomic impairment. The physiological consequences of a possible loss or impairment of autonomic control (Amorim et al., 1968b; Manço et al., 1969; Gallo et al., 1975; Marin Neto et al., 1975) and the correlation between neuronal degeneration and autonomic impairment (Amorim et al., 1973) have been presented elsewhere.

It appears that an abnormal heart rate response by chronic cardiac chagasic patients is an indication
of patients, the immune response is the result of neuronal destruction from the acute phase of the disease; but that a chronic infection and/or a continuous liberation of auto-antigens from injured tissue may stimulate a continuing autoimmune response.

This latter suggestion would render the development of an abnormal heart involvement more plausible. In fact, those patients with a positive serum only and those with signs of hollow viscera (i.e., megaloe-oesophagus) only, could develop or have a 'sub-clinical' type of cardiac disease, i.e. one without heart symptoms and even with a normal ECG.

In several respects chronic Chagas' heart disease may be of interest to the studies related to congestive cardiomypathy. The most commonly recognized clinical syndrome is of congestive failure with poor systolic function, therefore comparable to the obscure types of cardiomypathies (Goodwin, 1970; Amorim et al., 1970; Oakley, 1972; Olsen, 1972). But in view of the high incidence of positive serology in people in areas endemic for Chagas' disease, it is possible that this disease is over-diagnosed on account of congestive cardiomypathy.

The differential diagnosis between chronic Chagas' heart disease and congestive cardiomypathy may be difficult in the living patient, but at post-mortem the apical aneurysm of Chagas' disease is frequent and distinctive (Andrade, 1956; Koberle, 1968). These apical aneurysms of the left ventricular cavity can be seen clearly during contrast visualization of the heart chambers. Although it is not clear how far the antibodies against myocardial structures are involved with the aetiology and pathogenesis of Chagas' disease, Cossio et al.'s (1974) results are of great interest because in certain cases, chronic Chagas' heart disease can be considered as unlikely when the serum γ-globulin factor which reacts with endocardium and vascular structures is absent. Also the fact that patients with cardiomypathies of obscure aetiology respond differently from those with Chagas' disease strengthens the evidence for the specific loss of autonomic control in the latter (Amorim et al., 1970).

But a large number of patients are asymptomatic or have minor symptoms and the diagnosis is eventually confirmed by ECG. At rest they have normal cardiovascular dynamics. This may be considered as one 'experimental model' for the better understanding of congestive cardiomypathy. It should be emphasized that the chronic stage and its clinical manifestations are established some decades after the acute phase. The cause of death in chronic Chagas' heart disease is attributed to myocardial failure, arrhythmias, and the thrombo-embolic complications as in congestive cardiomypathy.
It is recognized that the screening of an asymptomatic population of chronic cardiac chagasic patients is feasible and therefore endomyocardial biopsy should be seriously considered (Olsen, 1975; Olsen and Florio, 1976). What cellular and subcellular evidence is there of changes developing from an ‘early’ stage (minor or no symptoms) to an ‘established’ (congestive) stage? Also what are the prognostic implications of high incidence of bundle branch block and of the immunological processes as in congestive cardiomyopathy? (Loogen and Kuhn, 1976; Bolte and Crothey, 1976).

Reports from different geographical areas suggest that hypertrophic obstructive cardiomyopathy and endomyocardial fibrosis are not confined to any particular locality, and it is quite obvious that nowadays in South America this is a matter of pure scientific interest.

In order to clarify the subject and hoping that a clinical presentation would lead to its increased recognition, Guimarães et al., (1971) reported a few cases of endomyocardial fibrosis, eight of which were confirmed at post-mortem. These authors also stressed the difficulty of making a differential diagnosis between endomyocardial fibrosis, Chagas’ heart disease, rheumatic heart disease, and pulmonary schistosomiasis, especially when the first is associated with arterial pulmonary hypertension.

Acknowledgment

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