RIGHT VENTRICULAR HYPERTROPHY IN PEOPLE BORN AND LIVING AT HIGH ALTITUDES*

BY

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Radiological studies made two decades ago by Peruvian investigators showed enlargement of the cardiac silhouette of people living at high altitudes (Rotta, 1955a; Pérez Aranibar, 1948). The electrocardiographic investigations of Rotta and López (1959) and Peñaloza *et al.* (1960, 1961) demonstrated a right ventricular preponderance in these people. Recently a mild degree of pulmonary arterial hypertension has been found in natives from high altitudes (Sime *et al.*, 1963; Peñaloza *et al.*, 1963) and anatomical changes in the terminal branches of the pulmonary arterial tree which may explain the origin of the pulmonary hypertension have also been reported (Arias-Stella and Saldaña, 1963).

Studying two series of necropsies of children, one at sea-level and the other at high altitude, we were able to demonstrate the anatomical existence of right ventricular hypertrophy in children born and living at 12,375 to 14,300 feet above sea-level (Arias-Stella and Recavarren, 1962; Recavarren and Arias-Stella, 1962).

Rotta (1955b) found evidence of right ventricular hypertrophy in 4 out of 5 hearts of adults living in Morococha (14,900 feet above sea-level) and in 1957, Campos and Iglesias found evidence of right ventricular hypertrophy in 31.4 per cent of 49 adults who died from accidents in La Oroya, at 12,375 feet above sea-level. This last finding may well raise the question: why do only one-third of the natives from high altitudes show this alteration?

The anatomical characteristics of the hearts of two series of necropsies, one performed at sea-level and the other at high altitude, are investigated in detail in the present study, and it is shown that 93 per cent of the adult natives living from 12,375 to 14,300 feet above sea-level present a certain degree of right ventricular hypertrophy.

MATERIAL AND METHODS

Hearts from 112 people whose ages ranged from 11 to 80 years were investigated. Among these, 57 were from sea-level (control group, altitude not over 584 feet) and 55 from high altitude (42 at Cerro de Pasco at 14,300 feet, and 13 at La Oroya at 12,375 feet). The distribution of control and problem cases in each decade of age was as follows. From 11 to 20 years there were 7 cases from high altitude and 22 from sea-level; from 21–30 years there were 16 cases from high altitude and 13 from sea-level; from 31–40 years there were 16 cases from high altitude and 12 from sea-level; from 41–50 years there were 9 cases from high altitude and 6 from sea-level; from 51–60 years there were 2 cases from high altitude and 1 from sea-level; from 61–70 years there were 4 cases from high altitude and 1 from sea-level; and from 71–80 years there was 1 case

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FIG. 1.—Division of ventricular mass into horizontal blocks. (From the *Amer. J. Path.*, 1962, Vol. 41, No. 4.)

FIG. 2.—Separation of right and left ventricular substance. Indexes (IS1, IS2, etc.) are derived from the ratios of the weights of the left ventricular mass / right ventricular mass. (From the *Amer. J. Path.*, 1962, Vol. 41, No. 4.)

from high altitude and 2 from sea-level. In order to make valid comparative statistical analysis, it was necessary to obtain average values from cases of the same age in the 11–20 years decade at sea-level. This reduced their number from 22 to 11. Thus the total number of individual figures considered at sea-level was 46. Death in all cases was attributable to accidents or acute processes. Examples of cardiovascular anomalies or chronic pulmonary diseases were not included.

The heart cavities were packed with cotton soaked in formalin, the great vessels were sectioned at the level of the sigmoid valves, and then the organ was submerged in 10 per cent formaldehyde for three to four days. After fixation, the atrial mass was dissected from the ventricle, and the heart was freed of its epicardial fat, coronary vasculature, and valves by sharp dissection.

With a ruler lying posteriorly, the distance from the atrio-ventricular sulcus to the apex was divided into 5 equal parts. At these points the heart was sectioned at right angles to its greater diameter, from the posterior aspect to the anterior, resulting in 5 blocks, identical in thickness. These were designated S1, S2, S3, S4, and S5 (Fig. 1).

In each of the blocks the right ventricular portion was dissected from the left, following the method of Hermann and Wilson (1921) (Fig. 2). Weights were obtained as follows: total ventricular weight (TVW), right ventricular weight (RVW), and left ventricular weight (LVW). The Hermann and Wilson index was obtained from the ratio LVW/RVW; and the percentage of the right ventricular weight in relation to the total ventricular weight was obtained from the ratio: $RVW \times 100/TVW$.

The weights of right and left ventricular tissues were determined for blocks S1, S2, and S4; the indexes IS1, IS2, and IS4 were obtained by the ratio LVW/RVW in each of these sections (Fig. 2). Block S3 was used for dry weight determination in a separate study, and S5 only for obtaining the ventricular weights.

At the time of dissection and weight determination, data relating to the history or derivation of each case were unknown. The method used has been described in greater detail elsewhere (Arias-Stella and Recavarren, 1962).

RESULTS

The average values of the Hermann and Wilson index, TVW, LVW, RVW, the percentage of the weight of the right ventricle in relation to the total ventricular weight, and the indexes IS1, IS2, and IS4 were obtained in the two series of necropsies.

Hermann and Wilson Index. According to the authors, the normal extreme values of this index are 1.46 and 2.14: figures below 1.46 indicate right ventricular hypertrophy and those above

TABLE I
HERMANN AND WILSON INDEX AT SEA-LEVEL AND HIGH ALTITUDE

						11 to 80 years
Sea-level						46
						Mean $\pm$ S.E.
						S.D.
						Extreme values
High altitude						55
						Mean $\pm$ S.E.
						S.D.
						Extreme values
<i>t</i>						17.2386*

* $p = < 0.001$.

S.E.=Standard error. S.D.=Standard deviation. *t* value=Calculated by Fisher's test.

2.14 indicate left ventricular hypertrophy. The results obtained in the two series were as follows: 1.76 (S.D. 0.15) at sea-level and 1.30 (S.D. 0.13) at high altitude. The statistical comparison gives a highly significant value to the difference ($p < 0.001$) (Table I) (Fig. 3).

Right Ventricular Weight (RVW). The following average figures were obtained: 63.54 g. (S.D. 13.97) for the sea-level series, and 83.85 g. (S.D. 23.07) for the high altitude series. The statistical comparison indicates that the difference is highly significant ($p < 0.001$) (Table II).

Percentage of the Weight of the Right Ventricle in Relation to TVW. The average figures obtained were as follows: 35.54 per cent (S.D. 2.02) for sea-level, and 42.89 per cent (S.D. 2.60) for high altitude. Again the difference is statistically highly significant ($p < 0.001$) (Table III) (Fig. 4).

FIG. 3.—Age distribution and Hermann and Wilson index of cases at sea-level and at high altitude.

TABLE II

RIGHT VENTRICULAR WEIGHT, LEFT VENTRICULAR WEIGHT, AND TOTAL VENTRICULAR WEIGHT AT SEA-LEVEL AND HIGH ALTITUDES

		RVW	LVW	TVW
Sea-level	Number of cases	46	46	46
	Mean $\pm$ S.E.	63.54 $\pm$ 2.0607	112.65 $\pm$ 4.0594	176.20 $\pm$ 6.0348
	S.D.	13.9766	27.5325	40.9303
	Extreme values	29.8-91.4	51.3-159.5	81.1-244.5
High altitude	Number of cases	55	55	55
	Mean $\pm$ S.E.	83.85 $\pm$ 3.1115	109.09 $\pm$ 3.7404	192.82 $\pm$ 6.7413
	S.D.	23.0759	27.7398	49.9949
	Extreme values	35.5-153.4	43.5-177.6	79.0-331.0
<i>t</i>		5.2204*	0.4982	1.8044

* $p = < 0.001$.S.E. = Standard error. S.D. = Standard deviation. *t* value = Calculated by Fisher's test.

TABLE III

PERCENTAGE OF RIGHT VENTRICULAR WEIGHT IN RELATION TO TOTAL VENTRICULAR WEIGHT AT SEA-LEVEL AND HIGH ALTITUDE

		11 to 80 years
Sea-level	Number of cases	46
	Mean $\pm$ S.E.	35.54 $\pm$ 0.2991
	S.D.	2.0298
	Extreme values	32-39
High altitude	Number of cases	55
	Mean $\pm$ S.E.	42.89 $\pm$ 0.3507
	S.D.	2.6010
	Extreme values	37-49
<i>t</i>		15.5964*

* $p = < 0.001$.S.E. = Standard error. S.D. = Standard deviation. *t* value = Calculated by Fisher's test.

FIG. 4.—Distribution of percentage of right ventricular weight in relation to total ventricular weight by ages.

TABLE IV

WEIGHT INDEX: LEFT/RIGHT VENTRICULAR MASS IN S1, S2, AND S4

		11 to 80 years
S1	<i>Sea-level</i>	
	Mean $\pm$ S.E.	1.05 $\pm$ 0.0264
	S.D.	0.1697
	Extreme values	0.82-1.43
	<i>High altitude</i>	
S2	Mean $\pm$ S.E.	0.66 $\pm$ 0.0141
	S.D.	0.1048
	Extreme values	0.46-0.89
	<i>t</i>	13.6737*
S4	<i>Sea-level</i>	
	Mean $\pm$ S.E.	1.76 $\pm$ 0.0458
	S.D.	0.2986
	Extreme values	1.09-2.52
	<i>High altitude</i>	
	Mean $\pm$ S.E.	1.38 $\pm$ 0.0360
	S.D.	0.2531
	Extreme values	0.89-2.19
	<i>t</i>	6.4922*
	<i>Sea-level</i>	
	Mean $\pm$ S.E.	3.13 $\pm$ 0.1024
	S.D.	0.6586
	Extreme values	2.21-4.54
	<i>High altitude</i>	
	Mean $\pm$ S.E.	2.58 $\pm$ 0.0959
	S.D.	0.6603
	Extreme values	1.52-4.33
	<i>t</i>	3.8955*

* $p < 0.001$.S.E.=Standard error. S.D.=Standard deviation. *t* values=Calculated by Fisher's test.

Total Ventricular Weight (TVW). The average values were as follows: 176.20 g. (S.D. 40.93) for sea-level, and 192.82 g. (S.D. 49.99) for high altitude. The statistical study did not indicate that any significant difference existed between the two series ($p < 0.10$) (Table II).

Left Ventricular Weight (LVW). The average values found for the series under study were 112.65 g. (S.D. 27.53) for sea-level, and 109.09 g. (S.D. 27.73) for high altitude. The difference is not statistically significant ($p < 0.70$) (Table II).

Indexes IS1, IS2, and IS4 (LVW/RVW ratio in S1, S2, and S4). The average values obtained were IS1, 1.05 (S.D. 0.16) at sea-level, and 0.66 (S.D. 0.10) at high altitude; IS2, 1.76 (S.D. 0.29) at sea-level, and 1.38 (S.D. 0.25) at high altitude; IS4, 3.13 (S.D. 0.65) at sea-level and 2.58 (S.D. 0.66) at high altitude. The differences are statistically significant for the three indices ($p < 0.001$) (Table IV).

It is important to note that in the comparative statistical studies the *t* values obtained through Fisher's test were, 13.6737 for IS1, 6.4922 for IS2, and 3.8955 for IS4.

DISCUSSION

The results obtained by the Hermann and Wilson index, the absolute weight of the right ventricle and the percentage of the weight of the right ventricle in relation to the total ventricular weight

FIG. 5.—Sections S1 at sea-level and at high altitude. There is conspicuous right ventricular thickening in the case from high altitude. High altitude case is a 21-year old man. Sea-level case is an 11-year-old boy.

indicate that at high altitudes there exists an increase in the muscular mass of the right ventricle. No abnormality has been found in the muscular mass of the left ventricle. Though the total ventricular weights of the hearts of dwellers at high altitude are greater than those of dwellers at sea-level, the differences are not statistically significant.

The anatomical findings described have a close relation with the hæmodynamic characteristics of the individual at high altitudes (Sime *et al.*, 1963; Peñaloza *et al.*, 1963). The degree of right ventricular hypertrophy can be related to the calculated greater right ventricular work performed at high altitude and to the moderate pulmonary arterial hypertension described in these subjects (Peñaloza *et al.*, 1963). The lack of difference in the weights of the left ventricles agrees with the fact that there are no differences in mean and diastolic blood pressures, nor in the calculated left ventricular work, at high altitude and sea-level (Peñaloza *et al.*, 1963).

The study of the relation LVW/RVW at S1, S2, and S4 has demonstrated that in the adult, as previously shown in children (Recavarren and Arias-Stella, 1962), the hypertrophy of the right ventricle is a phenomenon mainly localized at its base (Fig. 5). In fact, it is interesting to notice that the *t* values obtained through Fisher's test for IS1, IS2, and IS4 indexes decrease progressively, indicating that the magnitude of the hypertrophy at high altitudes diminishes from the base to the apex. This finding can be explained on the basis of the anatomical structure of the myocardial fibres. It is accepted that those fibres having a concentric disposition are the ones responsible for the maintenance of the output of the blood, and these fibres are localized mainly at the base of the ventricle (MacCallum, 1900; Robb and Robb, 1942). Therefore if the myocardium does more work, the fibres at the base are the ones that would become more severely hypertrophied. We have already indicated that the existence of the pulmonary cone supplies the basal section of the right ventricle with a portion of muscular mass that does not exist in the left side, and this adds to the influence in weight at basal level on the right side (Recavarren and Arias-Stella, 1962).

Contrary to the finding in children, the hypertrophic phenomenon in the right ventricle in the adult does not only involve sections S1 and S2, but also S4. This finding enables us to confirm our earlier observation that the hypertrophic phenomenon is of a basal localization at the onset, and from this area it progressively involves the region of the apex with a rapidity and magnitude that are determined first by the degree of pulmonary hypertension, and secondly by the length of time during which the hypertensive factor is present.

Considering the index of the basal section (IS1) as the most acceptable indicator of the presence or absence of right ventricular hypertrophy (Recavarren and Arias-Stella, 1962), it is found that of the 55 cases at high altitudes 93 per cent had right ventricular hypertrophy.

The cardiac electrical activity of the heart in these subjects indicates predominance of the right ventricular forces, which is in accordance with our anatomical findings; on the other hand the delay

in the registration of the last electrical vectors described at high altitudes (Peñaloza *et al.*, 1961) corresponds well with the topographical distribution of the right ventricular hypertrophy which is greater at the base.

CONCLUSIONS

The ventricular weights are studied in two necropsy series, one from people born and living at altitudes from 12,375 to 14,300 feet above sea-level, and the other from natives and residents of sea-level. Ages ranged between the second and eighth decade of life. Deaths were due to accident and acute illness, and patients with cardiac and pulmonary disease were excluded.

The study of the absolute weight of the right ventricle, the relation RVW/LVW, and the percentage of weight of the right ventricle in relation to the total ventricular weight demonstrated the existence of right ventricular hypertrophy in those living at a high altitude.

The morbid anatomical study of the right ventricular hypertrophy established that though the anatomical alteration involved all the muscular mass of the right ventricle the localization of hypertrophy was mainly at the base of the ventricle.

Interpretation of the results in relation to current hæmodynamic and electro-vectorcardiographic studies at high altitudes is attempted.

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