RIGHT VENTRICULAR HYPERTROPHY IN NATIVE CHILDREN LIVING AT HIGH ALTITUDE

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In past decades the work performed by Peruvian investigators has shown that the hearts of men living at high altitude have radiographic, electrocardiographic and vectocardiographic characteristics which differ from those of individuals living at sea level. Rotta, in 1947,[1] in the course of examining 400 teleradiograms and 100 electrocardiograms, indicated that the cardiac silhouette was increased in its diameter and frontal area and that there existed a predominance of right ventricular electrical forces as compared with those of the left. The studies of Peñaloza, Gamboa, Dyer, Echevarria and Marticorena,[2] Rotta and López,[3] and Pérez Aranibar[4] have served to confirm and clarify these observations and to define some of the characteristics of cardiovascular physiology at high altitude.

In contrast to this interest shown in the clinical and physiologic features, anatomic investigations have received, up to now, little attention. Not until 1955 were the first observations on the anatomic structure of the heart presented. Rotta[5] found hypertrophy of the right ventricle in 4 of 5 adult hearts obtained at necropsy in Morococha (altitude, 14,000 feet). Campos and Iglesias[6] reported right ventricular hypertrophy, at necropsy, in 30 per cent of high altitude adults who were victims of accidents.

There are no anatomic data in children. Physiologically, Peñaloza and co-workers[2] have shown that the characteristic regression of the electrical pattern indicative of right ventricular predominance in newborns at sea level does not occur in children born at high altitudes. Even in those instances with decrease of right ventricular predominance the degree of regression was only slight and in no way comparable to that seen at sea level.

The present report describes anatomic aspects of the heart in children dwelling at sea level and high altitude from birth to 10 years.

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Material and Methods

The hearts of 129 children ranging in age from birth to 10 years of age were examined. In this group, 70 hearts were procured from children at sea level and 59 from children born and living at high altitude. All the sea level cases were individuals living no higher than 584 feet above sea level (Lima), with the exception of 2: case 36, from Chosica (altitude, 2,700 feet); and case 33, from Chaclacayo (altitude, 1,900 feet). Neither of these 2 differed from the others in the group.

The hearts from the high altitude cases were obtained from patients born and living as follows: 29 from La Oroya (altitude, 12,375 feet); 27 from Cerro de Pasco (altitude, 14,300 feet); 1 from Casapalca (altitude, 13,860 feet); 1 from Huancavelica (altitude, 12,144 feet); 1 from Tarma (altitude, 10,190 feet). Specimens obtained from cases at high altitude in individuals born at sea level were not included.

Exact data concerning place of birth, ultimate residence, age, sex and cause of death were carefully obtained. It was not possible to secure information regarding weight and height of the cadaver in every instance. Only cases with no intrinsic cardiovascular alterations were included in the investigation. The cause of death always was in each case an acute illness or an accident.

The hearts, first identified and numbered, were freed of the great vessels at the level of the semilunar valves. Clots were washed from cardiac chambers, after which the cavities were filled with cotton soaked in 10 per cent formalin. This procedure was performed with great care, avoiding pressure upon the heart walls. Specimens were placed in the fixative for periods of 3 to 4 days before further processing.

The heart was then freed of its epicardial fat and coronary vascular system as much as possible by sharp dissection. With a ruler lying at the posterior aspect of the heart, the distance from the auriculoventricular sulcus to the apex was divided into 5 equal parts. At these points of division 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 (Fig. 1). After this procedure the fixation was continued for 24 to 48 hours. The atriums were dissected from the first ventricular section, and the mitral and tricuspid valves were removed from the ventricular walls. The remainder of the nonmuscular tissue (fat, residual attachments of the great vessels and the valves) was now carefully removed.

At this point the technique of Hermann and Wilson [7] was utilized, and segments of the right and left ventricles were separated from each other in each section. Throughout the process of dissection, specimens were kept moist to avoid the loss of weight caused by drying.

At the time the dissection was performed and the weights were obtained, it was not known whether the specimens were from cases of the sea level or high altitude groups.

The total heart weight (THW) represented the individual weights of the atrial segment and the 5 sections of the ventricles. The weight of the ventricular mass (VW) represented that of the 5 ventricular sections alone. The weights of the right (RVW) and left (LVW) ventricles were obtained from the pertinent segments.

The ratio of LVW to RVW provides the Hermann-Wilson index.[7] According to these authors, the index varies in normal adults between 1.46 and 2.14. Values below 1.46 indicate right ventricular hypertrophy, and those exceeding 2.14, left ventricular hypertrophy.[7]

The volume of the ventricular mass, measurements of ventricular and septal thickness, and the circumference of the valvular insertion rings were also determined. These, however, will be reported elsewhere.

Results

The cases were divided by age into 4 groups: (1) newborn and stillborn; (2) aged 1 day to 3 months; (3) aged 4 to 23 months; and (4) aged 2 to 10 years (Table I, Text-figure 1).

Group 1

The mean Hermann-Wilson index was 0.92 (SD, 0.194) in the sea level cases, and 0.77 (SD, 0.140) in those from high altitude, indicating that in both groups the right ventricle was heavier than the left at this age. The mean and extreme values showed that the high altitude cases apparently had a greater right ventricular predominance. The number of cases in each series did not permit statistical analysis, however; it is uncertain, therefore, whether or not this difference was significant.

Group 2

Here the mean Hermann-Wilson index was 1.32 (SD, 0.387) at sea level, and 1.03 (SD, 0.396) at high altitude. This indicates that at this age, in both groups, the left ventricle tended to outweigh the right. Since the values were below 1.46, however, it may be concluded that right ventricular hypertrophy existed. Again the high altitude cases exhibited a tendency to lower index values, thus indicating a greater right ventricular mass. Comparing the results in the low and high altitude groups, it is apparent that the difference is statistically significant; p value, less than 0.05.

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

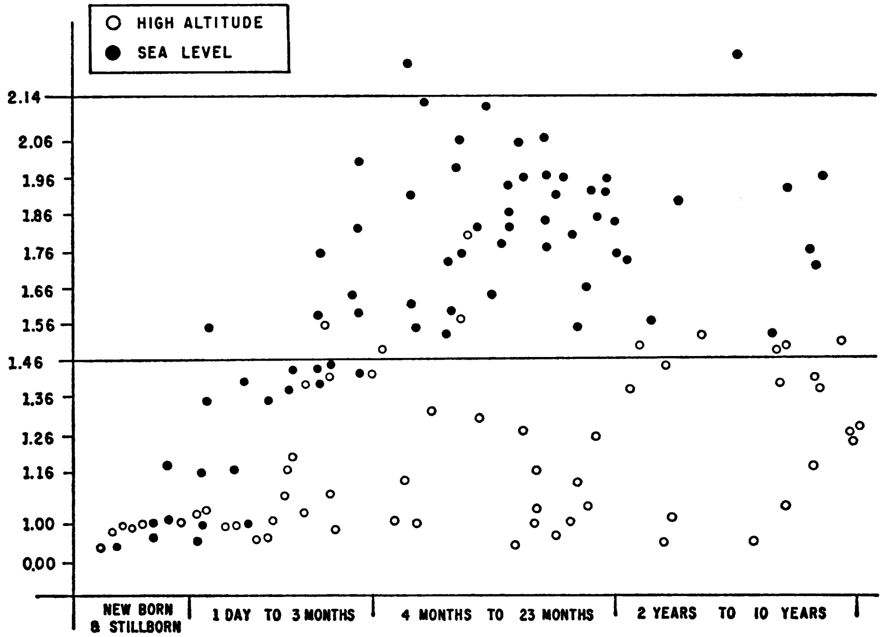
		NEW BORN & STILLBORN	1 DAY – 3 MONTHS	4 – 23 MONTHS	2 – 10 YEARS
SEA LEVEL	NUMBER OF CASES	5	21	33	11
	MEAN ± S.E.	0.92 ± 0.084	1.32 ± 0.084	1.85 ± 0.031	1.83 ± 0.066
	S. D.	0.194	0.387	0.194	0.220
	EXTREME VALUES	0.67 – 1.18	0.81 – 2.00	1.50 – 2.24	1.49 – 2.30
HIGH ALTITUDE	NUMBER OF CASES	6	17	18	18
	MEAN ± S.E.	0.77 ± 0.057	1.03 ± 0.084	1.08 ± 0.093	1.27 ± 0.058
	S. D.	0.140	0.348	0.396	0.250
	EXTREME VALUES	0.50 – 0.90	0.77 – 1.55	0.57 – 1.80	0.67 – 1.52
t			2.3455 *	9.4150 **	6.099 **

* p = < 0.05
** p = < 0.001

t: t values calculated by Fisher's t-test.

Groups 3 and 4

The mean Hermann-Wilson indexes were 1.85 (SD, 0.194) and 1.83 (SD, 0.220), respectively, at sea level, and 1.08 (SD, 0.396) and 1.27 (SD, 0.250) at high altitude. These results indicate normal values for



TEXT-FIGURE 1. Age distribution and Hermann-Wilson index of cases at sea level and at high altitude.

the sea level cases and definite right ventricular hypertrophy in those at high altitude (Figs. 1 to 4).

There were considerable variations in the magnitude of right ventricular hypertrophy at high altitude. In some cases the hypertrophy was only moderate; in others it was marked. Indeed, there were examples in which the right ventricle outweighed the left. An index lower than 1.0 was found even at the age of 5 years. The few cases from high altitude with indexes within normal limits had values near the minimum limit of the normal scale. The difference between the mean indexes at sea level and high altitude was statistically highly significant, p value, less than 0.001.

In neither group did the atriums, valves or endocardial surfaces exhibit noteworthy variations. The columnae carneae were prominent in those cases with marked hypertrophy.

Discussion and Comment

Müller [8] was the first to point out that the weight of the right ventricle predominated over that of the left at birth and during the first months of life. Using a technique devised by Lewis[9] for the dissection of the heart, Emery and Mithal[10] reported that the weight of the right ventricle was greater at birth than that of the left. Keen,[11] in a detailed investigation using Müller's technique, found that the weight of the right ventricle was equal to and in some instances greater than that of the left at birth. Most authors agree that this situation rapidly changes after birth and that the left ventricle soon predominates. Müller[8] and Lewis[9] considered this change to occur at 3 months of age. Keen[11] considered that the modification occurred during the first month after birth; a minor degree of right ventricular predominance was manifest up to the sixth month, at which time the adult ratio (LVW/RVW) characterizing the remainder of life was established. Our observations in the sea level groups are in agreement with these earlier concepts.

Since the value of the Hermann-Wilson index has not been reported for the ages which we have studied, the data here reported would have significant interest. We have shown that the similarity of weight in both ventricles or the predominance of the right ventricle normally disappears after the third month of life. In our sea level group the left ventricle was always heavier than the right after the third month.

To the contrary, in the high altitude group the right ventricle predominance does not disappear after the third month. Here a significant hypertrophy of the right ventricle was manifest from the fourth month to 10 years of age.

It is of interest that the LVW/RVW index in the high altitude group shows that the magnitude of right ventricular predominance seems to be greater from birth. This observation deserves further investigation since this could have importance in understanding the pathogenetic mechanisms involved. A comparative study of ventricular weights in the hearts of fetuses at high and low altitudes should be made. It would also be desirable to determine whether the right ventricular predominance manifested at or shortly after birth at high altitude is due simply to hypertrophy or to myocardial fiber hyperplasia. An investigation of this nature is now in progress.

Our observations complement those of Peñaloza and co-workers.[2] These investigators showed that at the moment of birth the electrocardiogram was essentially identical in infants born at high altitude and at sea level. After the first week, however, a right ventricular electrical predominance, not noted at sea level, occurred in the high altitude children.

The comparison of the weights determined for the 5 ventricular segments shows that the weight predominance of the right ventricle at high altitude was not the result of a homogeneous ventricular hypertrophy but derived essentially from an increased weight of the basal zone.[12]

At present there is little to be said concerning the pathogenesis of the alterations described. The finding of right ventricular hypertrophy is in agreement with certain experimental observations. Mice subjected to oxygen tensions of 80 to 125 mm. of Hg for 35 to 45 days first developed right ventricular and later left ventricular hypertrophy.[13] After 7 weeks at a simulated altitude of 18,000 feet, right ventricular hypertrophy was observed in the guinea pig.[14] Moreover, right ventricular dilatation and hypertrophy have been described in cattle[15] and sheep[16] at high altitudes.

Cuba[16] thought that primary anoxia led to "basophilic degeneration" in myocardial fibers and that this was an explanation for heart failure in lambs with polycythemia and cardiac decompensation. It seems unlikely that myocardial anoxemia could be a basis for the right ventricular hypertrophy found in human subjects at high altitudes. We have not seen histologic evidence in support of such a mechanism in the material we have examined. There has been hypertrophy of muscle fibers, but evidence of "basophilic" or other forms of myocardial degeneration have been lacking.

It has been our belief that right ventricular hypertrophy in these cases has been one indication favoring the existence of pulmonary hypertension.[17–19] It appeared that after the third month of life there was a well defined right ventricular hypertrophy in children dwelling at high altitudes. The lower LVW/RVW values in high altitude cases in groups 1 and 2 suggest the possibility that pulmonary hypertension may have been an early feature.

Conclusions

The ratio of left and right ventricular weights (LVW/RVW, Hermann-Wilson index) was investigated in 70 infants and children born and living at sea level and in 59 like subjects from high altitudes (12,225 to 14,300 feet). In both, the cases were divided into 4 groups according to age: newborn or stillborn; 1 day to 3 months; 4 to 23 months; and 2 to 10 years.

It was shown that at sea level the Hermann-Wilson index attained values corresponding to those characteristic of adults, beginning at the fourth month of life. In the high altitude group the ratio indicated a persistent right ventricular predominance; normally present at birth, this ordinarily gives way in due course at sea level to left ventricular dominance. The apparent right ventricular hypertrophy persisted from the fourth month of life up to the maximum age investigated (10 years).

It was also observed that the degree of right ventricular predominance at birth and up to age 3 months was greater in the infants born at high altitudes.

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LEGENDS FOR FIGURES

The left ventricle is shown on the left of each block illustrated, and the right ventricle on the right.

FIG. 1. Case 154, high altitude, age 5 months; Hermann-Wilson index, 1.33. The serial division of the ventricles into 5 blocks is shown. Relative thickening of the right ventricle is manifest.

FIG. 2. Case AK 29 (left), high altitude, age 2½ years; Hermann-Wilson index, 1.37; and case 1035 (right), sea level, age 1–9/12 years; Hermann-Wilson index, 1.83. A moderate degree of right ventricular thickening in case AK 29 as compared to case 1035 (sea level) is readily apparent.

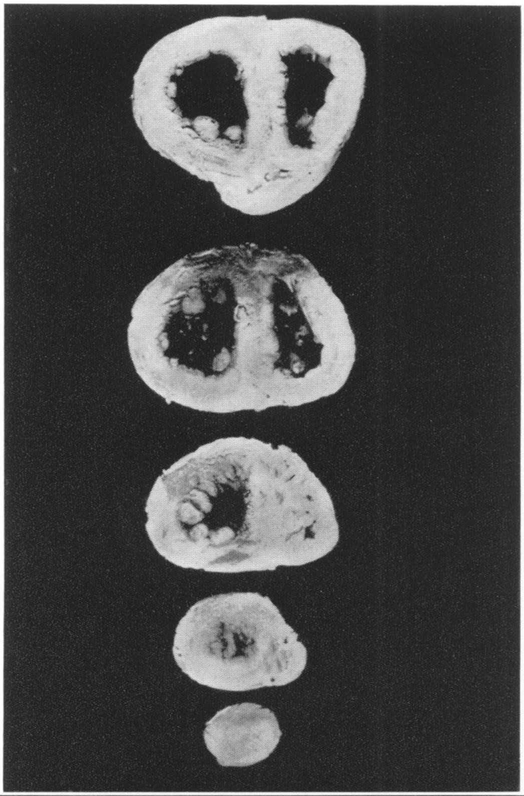

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FIG. 3. Case 161 (left), high altitude, age 1–7/12 years; Hermann-Wilson index, 1.14; and case 1032 (right), sea level, age 2 years; Hermann-Wilson index, 1.72. There is a disproportionate degree of right ventricular hypertrophy in case 161.

FIG. 4. Case 175, high altitude, age 5 years; Hermann-Wilson index, 0.77. A severe degree of right ventricular hypertrophy is shown; the right ventricle is heavier than the left.