# TOPOGRAPHY OF RIGHT VENTRICULAR HYPERTROPHY IN CHILDREN NATIVE TO HIGH ALTITUDE

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A recent study carried out in our laboratory has demonstrated the existence of right ventricular hypertrophy in native children living at high altitude.[1] In the study, the Hermann and Wilson technique,[2] by which the ventricular mass was divided into equal segments from the base to the apex, was followed. On analyzing the data we were of the impression that the right ventricular hypertrophy was not topographically homogeneous. Moreover, electrocardiographic and vectocardiographic studies performed by Peñaloza and associates in children[3] and adults[4] native to high altitudes demonstrated patterns suggesting a predominance of the basal electrical forces in the right ventricle.

In the present study the relation of left to right ventricular weights in several segments was investigated in two groups of children, one from high altitude and the other from sea level.

## MATERIAL AND METHODS

Hearts from 126 children whose ages ranged from stillborn at term to 10 years were investigated. Among these, 66 were from children born at sea level (control group, altitude not over 584 feet) and 60 were from high altitude regions (43 at Cerro de Pasco, 14,300 feet, and 17 at La Oroya, 12,375 feet). Examples of cardiovascular anomaly or chronic pulmonary disease were not included. Death in all cases was attributable to accidents or acute processes.

The heart cavities were packed with cotton soaked in formalin, and the organs were submerged in 10 per cent formaldehyde for 3 to 4 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 atrioventricular 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 (Text-fig. 1).

In each of the blocks the right ventricular portion was dissected from the left, following the method of Lewis[5] and Hermann and Wilson[2] (Text-fig. 2). The total weight of the heart, the weight of the ventricular mass, the separate weights of each ventricle, and lastly, the weight of right and left ventricular tissue were determined for blocks S1, S2 and S4. Block S3 was utilized for dry-weight determinations in a separate study, and S5 only for obtaining the ventricular weights.

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At the time of dissection and weight determination, data relating to the history or derivation of each case was unknown. The method used has been described in greater detail elsewhere.[1]

## Results

Cases were divided according to age into 4 groups: Group 1, stillborn to 7 days; Group 2, 8 days to 3 months; Group 3, 4 to 23 months; and Group 4, 2 to 10 years (Table I).

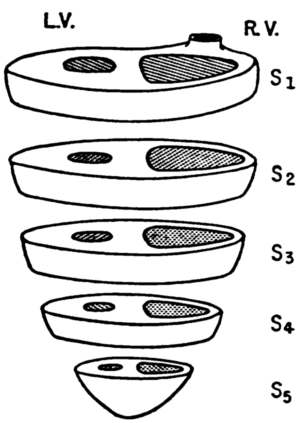
Indexes IS1, IS2 and IS4 (Text-fig. 2) were determined by relating the left ventricular weight to that of the right in the S1, S2 and S4 blocks. Indexes of less than 1 indicated right ventricular predominance; those above 1 reflected left ventricular predominance.

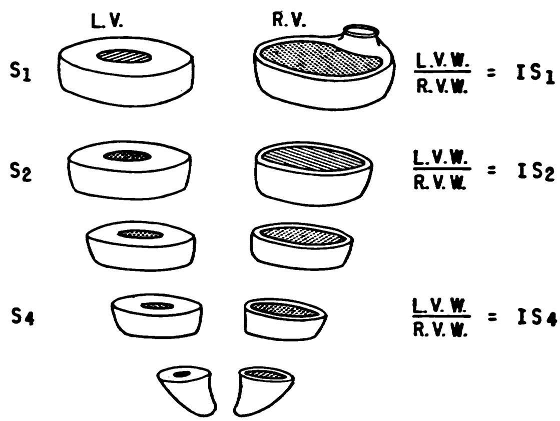
The average values of the indexes IS1, IS2, and IS4 in cases from high altitude, as well as those from sea level, were obtained in each age group. Comparisons between both series were made with these figures (Table I). Indexes in the S3 blocks were like those in the S4.

### *Group 1 (Newborn to 7 Days)*

In this group the indexes at sea level exhibited a predominance of right ventricle weight over that of the left in the blocks S1 and S2, and predominance of the left ventricle in block S4. The corresponding figures were: 0.60 (SD, 0.095), 0.93 (SD, 0.166), and 1.48 (SD, 0.647).

In the high altitude cases, the indexes also exhibited predominance of right ventricle weight over left in blocks S1 and S2, and greater weight of the left ventricle in block S4. The indexes were: 0.53 (SD, 0.113), 0.92 (SD, 0.169), and 1.77 (SD, 0.938). Statistically there were no significant differences between the two groups in any of the 3 blocks.




Text-figure 1. Division of ventricular mass into horizontal blocks.

Text-figure 2. Separation of right and left ventricular substance (Hermann and Wilson method). Indexes (IS1, IS2, etc.) are derived from the ratios of the weights of the left ventricular mass/right ventricular mass.

TABLE I

WEIGHT INDEX: LEFT/RIGHT VENTRICULAR MASS

| | Block | Group 1 Newborn–7 days | Group 2 8 days–3 mo. | Group 3 4 mo.–23 mo. | Group 4 2 yr.–10 yr. |
|---|---|---|---|---|---|
| S1 | *Sea level* | | | | |
| | Mean ± S.E. | 0.60 ± 0.026 | 1.16 ± 0.066 | 1.33 ± 0.041 | 1.23 ± 0.050 |
| | S.D. | 0.095 | 0.239 | 0.218 | 0.210 |
| | Extreme values | 0.47 — 0.79 | 0.84 — 1.82 | 1.02 — 1.79 | 1.01 — 1.86 |
| | *High altitude* | | | | |
| | Mean ± S.E. | 0.53 ± 0.030 | 0.66 ± 0.036 | 0.66 ± 0.046 | 0.73 ± 0.037 |
| | S.D. | 0.113 | 0.142 | 0.200 | 0.143 |
| | Extreme values | 0.40 — 0.76 | 0.41 — 0.88 | 0.40 — 1.00 | 0.53 — 1.03 |
| | *t* values | 1.7815 | 6.9140 * | 9.7722 * | 7.8984 * |
| S2 | *Sea level* | | | | |
| | Mean ± S.E. | 0.93 ± 0.047 | 1.53 ± 0.064 | 2.04 ± 0.044 | 1.92 ± 0.041 |
| | S.D. | 0.166 | 0.233 | 0.237 | 0.170 |
| | Extreme values | 0.61 — 1.25 | 1.23 — 2.00 | 1.56 — 2.58 | 1.64 — 2.24 |
| | *High altitude* | | | | |
| | Mean ± S.E. | 0.92 ± 0.046 | 1.19 ± 0.078 | 1.22 ± 0.061 | 1.42 ± 0.068 |
| | S.D. | 0.169 | 0.306 | 0.263 | 0.256 |
| | Extreme values | 0.60 — 1.23 | 0.74 — 1.66 | 0.72 — 1.62 | 0.88 — 1.79 |
| | *t* values | 0.1131 | 3.2281 † | 10.5716 * | 2.5039 ‡ |
| S4 | *Sea level* | | | | |
| | Mean ± S.E. | 1.48 ± 0.186 | 2.29 ± 0.209 | 3.24 ± 0.195 | 2.91 ± 0.236 |
| | S.D. | 0.647 | 0.753 | 1.038 | 0.947 |
| | Extreme values | 0.88 — 3.33 | 1.00 — 3.50 | 1.75 — 5.00 | 1.35 — 5.21 |
| | *High altitude* | | | | |
| | Mean ± S.E. | 1.77 ± 0.260 | 2.13 ± 0.253 | 1.71 ± 0.100 | 2.20 ± 0.189 |
| | S.D. | 0.938 | 0.981 | 0.427 | 0.709 |
| | Extreme values | 0.41 — 3.50 | 0.66 — 4.00 | 0.86 — 2.24 | 1.25 — 3.60 |
| | *t* values | 0.8985 | 0.4832 | 6.4895 * | 2.3448 |

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

* p = 0.001
† p = 0.01
‡ p = 0.02

### *Group 2 (8 Days to 3 Months)*

The indexes in this age group exhibited predominance of left ventricle weight in all 3 blocks obtained from sea level cases. In fact, these were all above 1, thus: 1.16 (SD, 0.239), 1.53 (SD, 0.233), and 2.29 (SD, 0.753). In the high altitude cases, the corresponding indexes were 0.66 (SD, 0.142), 1.19 (SD, 0.306), and 2.13 (SD, 0.981). The right ventricle weighed more in the first (basal) block; in the second, the magnitude of the left ventricular predominance was less than that in the sea level group. In the S4 block there was frank predominance of the left ventricle. Statistical analysis established that the difference between the high altitude and sea level cases in block S1 was highly significant, p value, less than 0.001. In the S2 block it was also significant, p value, less than 0.01; in S4 block there was no difference.

### *Group 3 (4 to 23 Months)*

The indexes at sea level showed a predominance of left ventricular weights in the 3 blocks under study; the indexes were 1.33 (SD, 0.218), 2.04 (SD, 0.237), and 3.24 (SD, 1.038), respectively. It is interesting that in this age group the control cases showed the highest indexes. In the cases from high altitude, the S1 block index was less than 1, thus: 0.66 (SD, 0.200), indicating a considerable right ventricular predominance. In the S2 and S4 blocks the indexes exhibited left ventricular predominance: 1.22 (SD, 0.264) and 1.71 (SD, 0.427) respectively. In these blocks the left ventricular predominance was not as marked as in control sea level cases. It is worthy of note that statistical analysis exhibited a most significant difference between the sea level and high altitude cases, with p values of less than 0.001 in the 3 blocks.

### *Group 4 (2 to 10 Years)*

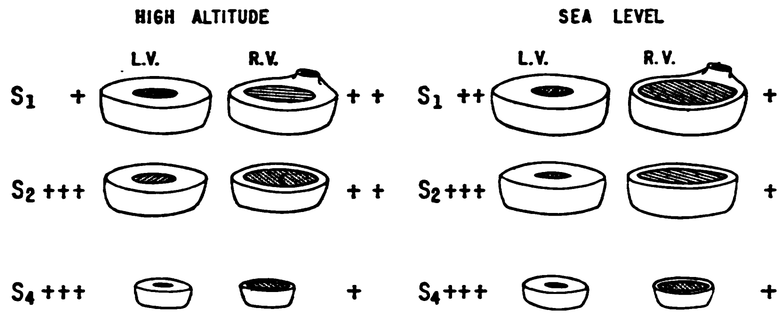
In this group, the indexes in the control cases revealed left ventricular predominance in each of the 3 blocks; the indexes were: 1.23 (SD, 0.210), 1.92 (SD, 0.170) and 2.91 (SD, 0.947). In the high altitude cases the S1 block of the right ventricle weighed more than the left, index, 0.73 (SD, 0.143); in the other 2 blocks, the left ventricle predominated, the index for S2 and S4 being 1.42 (SD, 0.256) and 2.20 (SD, 0.709). Statistically the differences were highly significant in the S1 block, with a p value of less than 0.001; the difference in the S2 block was of lesser degree, p value, less than 0.02, and there was no significant difference in the S4 blocks.

### *Summary of Results*

The results obtained may be summarized as follows:

In Group 1 there were no significant statistical differences between the sea level and high altitude cases. In the other 3 age groups the most significant difference between the high altitude and sea level cases was manifest in block S1. Indeed, at this level in the control series the left ventricle outweighed the right in all 3 age groups; in the high altitude cases the reverse was found—the right ventricle outweighed the left. In the S2 block in both series, the left ventricle outweighed the right, but at high altitude the predominance was of lesser degree. In the S4 block the predominance of left ventricle weight was well defined at both sea level and high altitude.

Text-figure 3 summarizes these results. It is apparent that the phenomenon of right heart hypertrophy occurring at high altitude is fundamentally a feature of the base of the heart. It should be noted, however, that high altitude cases occasionally exhibited marked right ventricular




TEXT-FIGURE 3. Relative bulk of left/right ventricular blocks (Groups 2, 3 and 4; see text). Right ventricular hypertrophy is a feature of blocks S1 and S2. + to +++ = relative weights for comparison of right and left segments.

hypertrophy, with indexes lower than 1 in blocks S1 and S2, and in some instances in S4 as well. This would indicate that the hypertrophy was initiated at the base of the heart and progressed therefrom to the apex.

## Discussion

The most important observation in this study has been the demonstration that the right ventricular hypertrophy in children at high altitude is principally basal in location. Undoubtedly, in order to explain this, some anatomic and physiologic data would be of assistance.

It is known that ventricular myocardial fibers are disposed in two principal layers. One is superficial, thin, and formed by fascicles which, in part, surround both ventricles; the other is more deeply situated and formed by thick muscular bundles originating from the right and left ventricles. The arrangement of the deep bundles is not well determined, but it is accepted that their disposition is partially or completely concentric on a given side, especially near the base of a ventricle.[6,7] The circular disposition of the bundles is complete at the base of the left ventricle and much less so on the right. In the latter region some of the deep muscular fascicles are concentric, others constitute the pulmonary conus, and still others cross the interventricular juncture to terminate in the left ventricle. Experimentally it has been shown that muscles with concentric disposition are responsible for the maintenance of the pulmonary and systemic circulation.[7]

The pulmonary conus is another anatomic element with significance in the interpretation of the results obtained. Its muscular portion provides the basal area of the right ventricle with a mass which does not exist on the left.

Our sea level cases, representing normal controls, showed that at the basal level of block S1, the left to right ventricular weight relationship (LV/RV) only slightly favored the left ventricle in age groups 2, 3 and 4. At the levels of blocks S2 and S4, left ventricular predominance was marked. This would indicate that even in the absence of right ventricular hypertrophy, the proportion of muscular mass in the right ventricle is relatively greater at the base.

Since the concentric myocardial fibers play a fundamental role in the forward propulsion of blood, it is logical to expect that these fibers would become hypertrophied earlier and more severely in hypertension of the pulmonary circuit. Many previous observations have made it apparent that right ventricular hypertrophy in the individual living at high altitude is secondary to pulmonary arterial hypertension.[8-10]

From the above data we may conclude that the topography of right ventricular hypertrophy in subjects living at high altitude results from hypertrophy of concentric muscular fibers, which are more numerous at the basal level, and the existence of the pulmonary conus. The degree of hypertrophy in the basal portion of the right ventricle need only be slight for its weight to be above that of the basal segment of the left ventricle. As a result, the left to right ventricular weight ratio in block S1 gives the earliest perceptible evidence of right ventricular hypertrophy.

Occasionally, by relating the total weight of the left ventricle to that of the right, using the method of Hermann and Wilson,[2] or measuring the thickness of the right ventricle wall, normal values may be obtained in spite of the fact that a slight degree of right ventricular hypertrophy indeed exists. In Table II is shown a group of cases which, by the Hermann and Wilson index and by measurement of the right ventricle at its base, fall within normal limits. Nonetheless, the LVW/RVW ratio at the level of block S1 indicates frank right ventricular hypertrophy.

The topography of right ventricular hypertrophy which we have described provides an anatomic basis for a better understanding of the electrical alterations encountered at high altitude.[3,4,11] The electrocardiographic and vectocardiographic studies in man at high altitudes have indicated right ventricular hypertrophy with a marked increase of the final vectors, reflecting activation at the base of the right ventricle.[3,4] It is not our opinion that this pattern is exclusively a feature of individuals living at high altitude. Rather, it represents a natural hypertrophy response to the existence of pulmonary artery hypertension.

The fact that in Group 3 (4 to 23 months of age) there was a more

TABLE II

CASES FROM HIGH ALTITUDE, SHOWING NORMAL HERMANN-WILSON INDEX AND VENTRICULAR THICKNESS IN WHICH THE RELATION LVW/RVW AT S1 CLEARLY DEMONSTRATES THE PRESENCE OF RIGHT VENTRICULAR HYPERTROPHY

| Case | Age | Hermann-Wilson index (Normal 1.46–2.12) | Index S1 | Right ventricular thickness Measurement at the base |
|---|---|---|---|---|
| 186 | 3 mo. | 1.50 | 0.88 (Normal mean value for age group, 1.16) | 2.8 mm. (Normal for age group, 1.7 — 3.3) |
| 107 | 2 yr., 3 mo. | 1.49 | 0.84 (Normal mean value for age group, 1.23) | 2.9 mm. (Normal for age group, 2.0 — 3.8) |
| AK-76 | 7 yr. | 1.51 | 0.71 (Normal mean value for age group, 1.23) | 3.9 mm. (Normal for age group, 2.0 — 3.8) |
| AK-35 | 8 yr. | 1.52 | 0.87 (Normal mean value for age group, 1.23) | 2.6 mm. (Normal for age group, 2.0 — 3.8) |

significant statistical difference between the groups living at sea level and those at high altitude deserves separate comment. This is undoubtedly a reflection of the different rates of growth in the muscular masses occurring in the right and left ventricles at this stage of life. Its peculiarities will be investigated further in a separate communication.

## Conclusions

In 2 groups of children, 1 examined at necropsy at sea level (584 feet) and the other at high altitude (14,300 and 12,335 feet), the relation of left and right ventricle weights in 3 segments (S1, S2 and S4) were investigated. The cases were divided into 4 groups: Group 1, stillborn at term to 7 days; Group 2, 8 days to 3 months; Group 3, 4 to 23 months; and Group 4, 2 to 10 years.

It was shown that right ventricular hypertrophy, characteristic of individuals living at high altitude, was fundamentally a feature of the basal portion of the ventricle.

It was established that the ratio of left to right ventricle weights at the level of the S1 basal section permitted the early detection of right ventricular hypertrophy. In a group of 4 cases standard methods of determining right ventricular hypertrophy failed to demonstrate minimum degrees of right ventricular hypertrophy; this was demonstrable, however, by determining the LVW/RVW ratio in the S1 block at the base of the heart.

The basal localization of right ventricular hypertrophy serves to explain the electrical changes found in subjects living at high altitude.

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