Human Heart Weight at High Altitude

By Herbert N. Hultgren, M.D., and Harry Miller, B.A.

SUMMARY
The weight of the right ventricle, left ventricle, and septum determined in 98 hearts of high altitude (12,300 feet) residents in Peru and in 86 hearts from sea level in the continental United States revealed that right ventricular hypertrophy is no greater at high altitude than at sea level in the stillborn-newborn infant heart. Right ventricular weight relative to total heart weight at high altitude exceeds that at sea level beginning about 30 days after birth and reaches a plateau at 56 days. Thereafter the degree of relative right ventricular hypertrophy changes only slightly through the adult years. No evidence was found of postnatal atrophy of the right ventricle either at sea level or high altitude nor of septal hypertrophy accompanying the right ventricular hypertrophy in high altitude. The degree of right ventricular hypertrophy was moderate and variable, and corresponded to the moderate, variable pulmonary hypertension previously demonstrated in high altitude residents. Since total heart weights are similar at high altitude and sea level and since high altitude subjects have a smaller body size, the heart weight/body weight ratio is probably greater in the high altitude subject.

Additional Indexing Words:
Ventricular hypertrophy

Prolonged exposure to high altitude is associated with a moderate degree of pulmonary hypertension. This has been demonstrated by direct pressure measurements in Peru and in continental United States.1-3 Indirect evidence of pulmonary hypertension manifested by hypertrophy of the right ventricle was first demonstrated in Peruvian natives by Rotta4 in 1955. Further studies were carried out by Campos and Iglesias.5 Recently Arias-Stella and Recavarren6,7 reported their observations of ventricular weights in 114 hearts from high altitudes in Peru compared to 127 hearts obtained at sea level. All age groups were represented. Moderate right ventricular hypertrophy was found in all high altitude age groups after approximately 3 months.

This paper reports additional studies of heart weight at high altitude from infancy to adulthood. The technique of dissection employed permits determination of the weight of the free wall of the right and left ventricles after separation from the septum and, therefore, differs from the technique employed by Arias-Stella and Recavarren6,8 in which septal weight was not determined.

Methods
The method of dissection was originally described by Müller.9 Fresh hearts were fixed from 1 to 6 weeks in 10% buffered Formalin. Prior to fixation the atria were opened, blood and clots were washed out, and the heart chambers were loosely packed with cotton. Following fixation and after washing for several hours in tap water, the great vessels, atria, valves, epicardial fat, and coronary vessels were removed by sharp dissection. The right ventricle was first separated from the septum by a sharp scalpel. The plane of the cut was made parallel to the plane of the surface of the septum. The left ventricle was separated from the septum in a similar manner. The free wall of each ventricle and the septum were weighed to the nearest 0.10 g. The relative weight of the right ventricle was expressed as a percentage of the total ventricular mass (RV/T). To determine if septal hypertrophy was present when left ventricular hypertrophy was not present, the weight of the septum was expressed as a

From the Department of Medicine, Cardiology Division, Stanford University School of Medicine, Palo Alto, California.

Supported by Research Contract DA-49-193-MD-2274 from the Surgeon General’s Office and a grant from the San Mateo Heart Association.
percentage of the weight of the left ventricle (S/LV). No systematic study of total heart weight to body weight ratios was made. All dissections were performed by the two authors, and after dissection all segments were compared to be sure that a uniform technique had been employed. It was noted that even easily discernible differences in the line of separation between the septum and free ventricular walls resulted in only slight differences in the RV/T and S/LV ratios or weight of the individual segments.

The hearts of native Peruvians living at high altitudes were obtained from routine autopsies performed at the Chulec General Hospital, La Oroya, Peru. The residents of this area live at an altitude of between 12,000 and 14,000 feet.

The hearts of residents at sea level were obtained from the Pathology Department of the San Mateo Community Hospital and the Stanford Medical School. The residents of this area live essentially at sea level (altitude, 80 feet) and are predominantly Caucasian.

The major cause of death in each group was acute infectious disease, usually bronchopneumonia, which occurred in 52% of the high altitude group and in 38% of the sea level group. Trauma was the second leading cause of death in the sea level group.

Results

The total weight and the relative weight of the right ventricle was greater at high altitude in children and adults (figs. 1 and 2, table 1). When the total weight of the right ventricle was plotted against age, a steady increase in weight was evident in both high altitude and sea level hearts. No evidence of a postnatal decrease in right ventricular weight was found in either group.

In the stillborn and newborn group, the relative weight of the right ventricle was similar at high altitude and at sea level. An increase in right ventricular hypertrophy at high altitude compared to sea level values was first evident at approximately 30 days; after 56 days, there was only a small increase through the adult years (fig. 3).

Examination of figure 4 reveals a wide dispersion of RV/T values in both high altitude and sea level hearts from all age groups. Dispersion is greater in the high altitude hearts.

There was no difference in the total weight of the myocardium, left ventricle, or septum...
HEART WEIGHT

between the high altitude and sea level groups (figs. 5 and 6, table 1). The relative weight of the septum as estimated by the ratio of septal weight to left ventricular weight was not increased at high altitude (fig. 7).

Although a systematic study of the ratios of heart weight to body weight was not made, a partial evaluation of body weight indicates that sea level patients were heavier than high altitude patients by approximately 67% from birth to 18 months and by 28% in adults. These data clearly indicate that a greater left ventricular and septal weight in relation to body weight was present in the high altitude group in addition to the clear increase in the right ventricular weight to body weight ratio.

Inspection of the RV/T values reveals nine hearts from the high altitude group and one from the sea level group with values greater than 40. The data regarding these cases, including age, total ventricular mass, and cause of death, are summarized in table 2.

---

**Figure 2**
Relative weight of the right ventricle expressed as the ratio RV/T (%) in various age groups at sea level and high altitude (12,300 ft). The brackets represent one standard deviation.

---

**Figure 3**
Graphic analysis of the relative weight of the right ventricle in infancy at sea level and high altitude (12,300 ft).
Two hearts in the series, one from sea level and one from high altitude, exhibited an extreme degree of right ventricular hypertrophy.

**Report of Cases**

The sea level heart with an RV/T ratio of 42.2% was obtained from an 11-month-old Negro child requiring several hospital admissions because of recurrent bronchitis and pneumonia since the age of 4 months. She was below the third percentile in weight at the time of her final hospitalization for pneumonia. She was acutely ill; respiratory rate was 48 and heart rate was 140 per minute. Physical signs of pneumonia and bronchitis were present. Moderate enlargement of the liver was noted. The hemoglobin was 8.0 g% and the leukocyte count was 20,700/mm³. The electrocardiogram revealed a pattern consistent with moderate right ventricular hypertrophy with

Abbreviations: SL = sea level; HA = high altitude; ns = not significant.
*The Herrman index has been calculated for comparison with other studies using this index.
an R/S ratio of 60% in lead aVR. A chest roentgenogram revealed pneumonitis and an aberrant right subclavian artery. The child developed cardiac arrest and died during a lumbar puncture. Autopsy revealed bilateral bronchopneumonia and evidence of moderate right ventricular failure. The right ventricle was hypertrophied. Histological study of the lung revealed bronchitis and bronchopneumonia. Collections of foreign-body giant cells suggested aspiration pneumonitis. In addition, focal areas of scarring and pulmonary fibrosis were present. There were distinct abnormalities of the pulmonary vessels. Thickening of the media was present in numerous small arterioles as well as fibrotic intimal thickening. Pulmonary hypertension was probably the result of pulmonary fibrosis secondary to repeated episodes of pneumonitis.

Less information is available regarding a 1-year-old Peruvian native girl who died of acute bronchopneumonia and congestive failure. The hematocrit was 57%. No cardiac abnormalities were present except for a marked degree of hypertrophy of the right ventricle. Histological study

Circulation, Volume XXXV, January 1967
Graphic analysis of individual RV/T (%) values in various age groups at sea level and high altitude (12,300 ft).

Figure 4

Total myocardial weight (TVM) and weight of the left ventricle in various age groups at sea level and high altitude (12,300 ft).

Figure 5
HEART WEIGHT

Figure 6
Total weight of the septum (S) in various age groups at sea level and high altitude (12,300 ft).

Figure 7
Relative weight of the septum expressed as the ratio S/LV in various age groups at sea level and high altitude (12,300 ft). The brackets represent one standard deviation.
Table 2
Summary of Data on Hearts with RV/T of More Than Forty Per Cent

<table>
<thead>
<tr>
<th>Age</th>
<th>TVM* (g)</th>
<th>RV/T (%)</th>
<th>Cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>High altitude</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stillborn</td>
<td>2.2</td>
<td>42.4</td>
<td>Unknown</td>
</tr>
<tr>
<td>Newborn</td>
<td>12.9</td>
<td>43.0</td>
<td>Unknown</td>
</tr>
<tr>
<td>2 days</td>
<td>5.9</td>
<td>44.0</td>
<td>Bronchopneumonia</td>
</tr>
<tr>
<td>47 days</td>
<td>13.0</td>
<td>44.0</td>
<td>Bronchopneumonia, dehydration</td>
</tr>
<tr>
<td>3 mo</td>
<td>24.8</td>
<td>46.0</td>
<td>Bronchopneumonia</td>
</tr>
<tr>
<td>1 yr</td>
<td>56.5</td>
<td>62.5</td>
<td>Bronchopneumonia</td>
</tr>
<tr>
<td>22 mo</td>
<td>59.2</td>
<td>41.0</td>
<td>Bronchopneumonia</td>
</tr>
<tr>
<td>2 yr</td>
<td>31.0</td>
<td>44.2</td>
<td>Acute bronchitis</td>
</tr>
<tr>
<td>5 yr</td>
<td>80.0</td>
<td>41.0</td>
<td>Typhoid fever</td>
</tr>
<tr>
<td>Sea level</td>
<td>11 mo</td>
<td>58.1</td>
<td>Recurrent bronchopneumonia</td>
</tr>
</tbody>
</table>

*TVM = total ventricular mass.

revealed a moderate diffuse bronchopneumonia. The pulmonary vessels including the arterioles were essentially normal. The liver showed chronic passive congestion compatible with right heart failure. The pulmonary hypertension, in this patient, did not appear to be related to chronic pulmonary infection or congenital cardiac disease.

Discussion

The present study has confirmed the observations of previous workers that right ventricular hypertrophy is present in high altitude residents and that this excess hypertrophy is first evident at approximately 30 days of age. After 56 days, little further relative right ventricular hypertrophy occurs.

These differences between high altitude and sea level hearts are clearly reflected in the electrocardiogram. The pattern of "physiological right ventricular hypertrophy of infancy" is similar in both groups for 30 to 60 days after birth. In the high altitude child, this pattern persists into childhood while in the sea level child, the adult pattern of normal left ventricular predominance begins to appear at this time.10-12

This study has demonstrated that, in the newborn period, the relative weight of the right ventricle is similar at high altitude and sea level. Previous workers at high altitude have not examined enough hearts in this age group to establish this point.8 The data suggest that there is no important additional intra-uterine stimulus to the development of right ventricular hypertrophy at high altitude. It has been previously shown in animals that fetal hypoxia at high altitude is not as severe as one might suppose, since it is diminished by several important physiological mechanisms.13

The present study did not demonstrate any postnatal decrease in right ventricular weight as was observed by Müller,9 Keen,14 and Recavarren and Arias-Stella.8 Our observations are in accord with those of Emery and Mithal.15 Müller's data have been reviewed. While a 17.5% decrease in right ventricular weight was observed at 8 weeks of age, there was during the preceding 4 weeks no increase in septal weight and a 6% decrease in left ventricular weight (fig. 8). This is strongly suggestive of growth failure due to the presence of a systemic infectious disease which was the cause of death in most of Müller's9 cases. It does not suggest selective atrophy of the right ventricle. Keen's14 paper does not contain adequate data for analysis. Recavarren and Arias-Stella8 studied only 17 hearts in the appropriate age group and inspection of his graph reveals that the apparent decrease in right ventricular weight at 10 weeks is due to four heart weights. When the data of Emery and Mithal15 (32 hearts) and Recavarren and Arias-Stella8 (17 hearts) are plotted with the data from the present study (total 155 hearts), no evidence of a
HEART WEIGHT

Figure 8

Mean weights of left ventricle, septum, and right ventricle at various age groups from Müller.9

Figure 9

Graphic analysis of weight of the right ventricle in infants and children at sea level in the present study and from Emery and Mithal15 and Recacarren and Arias-Stella.8 Right ventricular weight in the present paper has been adjusted to be comparable to that obtained in other studies (RV weight = RV + S).
postnatal decrease in right ventricular weight is seen (fig. 9*).

The wide dispersion of the degree of right ventricular hypertrophy in both high altitude and sea level hearts has been noted in previous human and animal studies. Individual variations in dissection technique cannot account for the observed differences since even gross differences in technique cannot result in the dispersion of values noted. The dispersion is probably due to variations in pulmonary artery pressure. Hemodynamic studies of high altitude residents have demonstrated moderate variations in resting pulmonary artery pressure and wider variations during exercise. The degree of variation in such values at sea level is less than at high altitude.

Dispersion of RV/T values and pulmonary artery pressures at high altitude are paralleled by a similar degree of variability in the electrocardiogram. In 20% of high altitude residents, the electrocardiogram may be normal but in the remainder, abnormal patterns compatible with mild-to-severe hypertrophy are present. Pryor and his workers suggested that the high altitude electrocardiogram was best correlated with the pulmonary artery pressure during exercise, but their data demonstrate only an approximate relationship.

The amount of anatomic right ventricular hypertrophy observed at high altitude is usually moderate and corresponds to an increase of 51% in the total weight of the right ventricle. This is comparable to the observed moderate degree of pulmonary hypertension present at high altitude. Similar pressures, right ventricular weights, and electrocardiographic features are present in sea level cases of pulmonary emphysema. In cardiac disease with severe pulmonary hypertension at sea level RV/T ratios of as high as 62% have been observed in our laboratory.

In both cattle and lambs the weight of the right ventricle is proportional to the pulmonary artery pressure. Hence the relative weight of the right ventricle may be used as a rough indication of the height of the pulmonary artery pressure. Comparison of the response of man and different animal species to high altitude can therefore be assessed.

The same dissection technique has been employed in six animal species living at similar altitudes in Peru. The degree of relative right ventricular hypertrophy observed in these animals is compared to the human studies reported in this paper (fig. 10). The human responds to high altitude with a similar degree of right ventricular hypertrophy to that seen in lambs and pigs, but with less hypertrophy than occurs in rabbits and guinea pigs.

Two hearts with an extreme degree of right ventricular hypertrophy have been described in detail. In one instance, there was evidence of recurrent infectious pulmonary disease and abnormalities in the pulmonary vessels. Such a factor cannot be completely excluded as being responsible for severe degrees of right ventricular hypertrophy which are out of the usual range. The use of hearts from patients free of any present or past history of pulmonary disease would eliminate this problem.

Septal hypertrophy does not accompany right ventricular hypertrophy at high altitude. This is consistent with observations of right ventricular hypertrophy in disease at sea level where septal hypertrophy only occurred when right ventricular hypertrophy was severe. Arias-Stella and Recavarren have demonstrated that at high altitude the outflow portion of the right ventricle tended to be more hypertrophied than the inflow portion. Absence of septal hypertrophy therefore indicates that only the free wall of the right ventricle is hypertrophied and not the adjacent septal portion.

An increase in the ratio of heart weight to body weight appears to be present at high altitude which is not due to right ventricular hypertrophy alone but involves to a lesser extent the septum and free wall of the left ventricle. Several factors may be responsible for a higher ratio of heart weight to body weight.
at high altitude. Increased blood volume, greater physical activity, and a smaller amount of adipose tissue should be considered.

Acknowledgment

The authors wish to thank the following, whose cooperation made this study possible: Arthur Lack, M.D., San Mateo Community Hospital, California; Alvin Cox, M.D., Stanford Medical Center, California; and Emilio Marticorena, M.D., Chulec General Hospital, Peru.

References

10. Penaloza, D., Gamboa, R., Dyer, J., Echevarria, M., and Marticorena, E.: Influence of high altitudes on the electrical activity of the heart: I. Electrocardiographic and vectorcardiographic observations in the newborn, in-

Ancient Fatalism

An old legend tells of a merchant in Bagdad who one day sent his servant to the market.

Before very long the servant came back, white and trembling, and in great agitation said to his master:

"Down in the market place I was jostled by a woman in the crowd, and when I turned around I saw it was Death that jostled me. She looked at me and made a threatening gesture. Master, please lend me your horse, for I must hasten away to avoid her. I will ride to Samarra and there I will hide, and Death will not find me."

The merchant lent him his horse and the servant galloped away in great haste.

Later the merchant went down to the market place and saw Death standing in the crowd.

He went over to her and asked,

"Why did you frighten my servant this morning? Why did you make a threatening gesture?"

"That was not a threatening gesture," Death said.

"It was only a start of surprise. I was astonished to see him in Bagdad, for I have an appointment with him tonight in Samarra."
