Exercise and Cardiac Work Response at High Altitude

By Ernest O. Theilen, M.D., Donald E. Gregg, Ph.D., M.D. and Andrés Rotta, M.D.

The response to treadmill exercise of the left ventricle of natives of the region of Morococha, Peru (elevation 14,900 feet), and of natives of the region of Lima, Peru (elevation 500 feet), was studied at the elevation where they had always lived. In both groups the external work of the left ventricle was effected by a combination of a large increase in cardiac output and a mild increase in systemic blood pressure. Stroke volume and stroke work were only mildly elevated since the heart rate was concurrently greatly increased. As a result, the increase in work of the left ventricle was largely accomplished by an increase in heart rate and to a lesser extent by an increase in stroke work. For comparable amounts of external work, the left ventricle of the native to high altitude and performing at high altitude responded with considerably greater effort than did the left ventricle of the native of low altitude performing at sea level. Some of the data may have approximated the maximum effort of which the normal left ventricle was capable.

This report is concerned primarily with attempts to measure the extent and adequacy of the response of the heart of man to the stress of chronic anoxia at high altitude. Although the native living at a high altitude undergoes considerable acclimatization by changes in his cardiovascular, respiratory, and hematologic systems, the extent of adaptation by the heart in the resting condition and especially in the state of exercise has not been well defined or studied. Measurements of the effect of external work on dynamics of the heart have thus far been limited to determinations at sea level of cardiac output during heavy exercise and of cardiac work during light exercise. In the present study comparisons were made of the response of the left ventricle of the native indigenous to high altitude and living at high altitude, with the response of the heart of the sea level dweller at sea level during exercise on a treadmill at equivalent and at an approximation to maximal levels of muscular work.

Methods and Procedures

Twenty-six male volunteers were studied either at Morococha, Peru (elevation 14,900 feet), or at Lima, Peru (elevation 500 feet). Of the 17 subjects studied at high altitude, 11 were natives of the region of Morococha who had not lived for any length of time at a significantly lower elevation; all were apparently in good health, and were, for the most part, engaged in mining activities. The remaining six subjects studied at the 14,900 foot altitude were normally inhabitants of sea level who had been living at Morococha for only six to eight weeks. Of the nine subjects studied at Lima, Peru, seven were medical students and two were sailors. The ages of the natives at high altitude varied from 19 to 38 years, the medical students from 22 to 28 years, and the sailors from 19 to 23 years.

For control measurements the subjects stood on a motor driven treadmill. The values obtained were not regarded as those from subjects at standing rest, since, without doubt, many were excited and stimulated by the unfamiliar procedures and the presence of strange personnel. Cardiac output was determined by the Evans blue dye-dilution method, using a continuously recording densitometer.

To facilitate sampling of arterial blood, a hyperextended wrist was immobilized in a plaster splint secured to a stationary arm rest. Moderate freedom of movement of the elbow was permitted. A 40 to 50 cm. length of polyethylene tubing was then passed into the basilic vein through a 15 or 17 gage thin-walled needle for dye injection. A 20 gage thinwalled needle was inserted into the radial artery, and after being securely taped to the wrist was connected by a three-way stopcock and a flexible coupling to the densitometer and to a strain gage for measurement of heart rate and mean radial.
blood pressure. The subjects generally were given 2 ml. of heparin sodium (2000 units) intravenously to obviate clotting within the arterial needle. As an additional preventive measure, the needle was flushed with small quantities of saline between determinations of cardiac output. These procedures were effective and no difficulties were encountered with hematomas after removal of the needle. In some subjects a Douglas bag was connected to the mouth-piece for the measurement of expired gases and for the determination of total oxygen consumption. After control determinations were made of the hemoglobin, hematocrit, cardiac output, heart rate, systemic blood pressure, and oxygen consumption (2 to 3 minutes), the treadmill was started and the rate and duration of external work adjusted in an attempt to create a heavy cardiac work load.

When the subject had been exercising at a constant rate of external work for a few minutes and was considered to be in a relatively steady state, determinations of the above parameters (except for the hemoglobin and hematocrit) were repeated. In two subjects in whom the initial rate of doing work was not exhausting, measurements were repeated at the same rate of treadmill exercise. In six other subjects measurements were repeated either at a considerably higher rate of external work on the treadmill and without interruption of it, or, after obtaining values believed to be the response of the heart to the maximum activity on the treadmill of which the subject was capable, the work load was abruptly decreased and observations were made at a lower level of cardiac activity. To attain the various levels of work by the heart, the subjects walked on the treadmill at rates varying from about 4 to 7 miles per hour; the duration of exercise varied from 3 to 10 minutes and the grade approximated either 11 or 20 per cent. The duration of exercise would seem to be adequate for a "steady state", since Donald has shown that the output and arteriovenous oxygen difference become quite constant in one minute.9

Typical patterns of densitometer curves from which the cardiac output values were calculated are illustrated in figure 1. The curves shown were obtained in the same native subject at Morococha at rest and during strenuous treadmill exercise. All calculations of cardiac output were done using calibration curves made with each individual's arterial blood. In the mountains, where the blood was unsaturated, calibration points (dilutions of dye and blood) were made and recorded with the densitometer without exposure to air to avoid changes in saturation.18 Calculations of cardiac output, cardiac work, and stroke work were made as previously described,17,18 except that the cardiac work and stroke work were not corrected for the prevailing left ventricular end-diastolic pressure, which was not measured.

RESULTS

Table 1 contains the original and calculated data from the three groups of subjects. Group 1 (natives at the altitude) and group 2 (medical students at sea level) are considered together. The natives at the altitude had the smaller body surface area and body weight, the latter averaging about 10 Kg. less than the other group. In the natives the hemoglobin varied from 17.7 to 24.3 with an average of 20.2 Gm. per 100 cc. Their hematocrits averaged 59.7 with high and low values of 71.5 and 51. Although in this group most values for hematocrit and hemoglobin were quite high and suggested chronic mountain sickness, all subjects were asymptomatic. At sea level the hematocrit and hemoglobin values were within normal limits. At the altitude of 14,900 feet at Morococha, Peru, all natives were chronically hypoxic. At this altitude (barometric pressure approximately 430 mm. Hg) the partial pressure of inspired oxygen is about 80 mm. Hg and the alveolar oxygen tension approximately 50 mm. Hg with an arterial oxygen saturation ranging from 75 to 86 per cent and a mean of approximately 81.5 per cent.6 Despite this and because of his high hematocrit the mountain native generally has an elevated oxygen content of his blood.

The external work load of the high-altitude native on the treadmill averaged 589 Kg.M. per minute per square meter of body surface area with extremes of 490 and 749. These loads have been arbitrarily divided into two groups in table 1 to more clearly show the effect of varying external work load on cardiac response. In the medical students at sea level the work load considerably exceeded that in the mountain natives, ranging from 704 to 986 Kg.M per
### Table 1. Hemodynamic Studies During Rest and Exercise at Sea Level and at High Altitudes

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age</th>
<th>Wt. Kg.</th>
<th>S.A. M²</th>
<th>Hb. Gm./100 cc.</th>
<th>Hct.</th>
<th>Tm. Work Kg.M/min./M²</th>
<th>Heart Rate Beats/min.</th>
<th>M.B.P. mm. Hg</th>
<th>C.I. L./min. M²</th>
<th>C.W.I. Kg.M/min./M²</th>
<th>S.V.I. cc./min. M²</th>
<th>S.W.I. Gm.M/min./M²</th>
<th>Oxygen Consumption L./min. M²</th>
</tr>
</thead>
<tbody>
<tr>
<td>G. C.</td>
<td>19</td>
<td>56.5</td>
<td>1.57</td>
<td>17.7</td>
<td>54.0</td>
<td>0</td>
<td>72</td>
<td>100</td>
<td>3.73</td>
<td>5.07</td>
<td>52</td>
<td>70</td>
<td>0.138</td>
</tr>
<tr>
<td>G. F.</td>
<td>20</td>
<td>55.5</td>
<td>1.53</td>
<td>17.9</td>
<td>56.0</td>
<td>0</td>
<td>60</td>
<td>90</td>
<td>3.47</td>
<td>4.24</td>
<td>58</td>
<td>71</td>
<td>0.173</td>
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<tr>
<td>T. O.</td>
<td>29</td>
<td>58.0</td>
<td>1.55</td>
<td>23.5</td>
<td>68.0</td>
<td>0</td>
<td>90</td>
<td>116</td>
<td>3.34</td>
<td>5.26</td>
<td>37</td>
<td>59</td>
<td>0.172</td>
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<tr>
<td>R. B.</td>
<td>38</td>
<td>69.5</td>
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<td></td>
<td>67.0</td>
<td>0</td>
<td>96</td>
<td>111</td>
<td>8.14</td>
<td>12.29</td>
<td>85</td>
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<td>1.68</td>
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<td>E. O.</td>
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<td>1.47</td>
<td>24.1</td>
<td>61.3</td>
<td>0</td>
<td>87</td>
<td>85</td>
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<td>4.28</td>
<td>43</td>
<td>50</td>
<td>0.178</td>
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<td>50.5</td>
<td>1.51</td>
<td>18.4</td>
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<td>0</td>
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<tr>
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<td>56.5</td>
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<td>19.8</td>
<td>56.3</td>
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<td>96</td>
<td>96</td>
<td>4.15</td>
<td>5.41</td>
<td>44</td>
<td>56</td>
<td>0.158</td>
</tr>
</tbody>
</table>

**Group 1. Natives at 14,900 feet**

**Averages**

Rest: 4.22 L./min. M². 
Exercise 535 (490-580) Kg.M/min./M²: 7.5 L./min. M². 
Exercise 697 (650-749) Kg.M/min./M²: 13.7 L./min. M².

**Group 2. Medical students at sea level**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age</th>
<th>Wt. Kg.</th>
<th>S.A. M²</th>
<th>Hb. Gm./100 cc.</th>
<th>Hct.</th>
<th>Tm. Work Kg.M/min./M²</th>
<th>Heart Rate Beats/min.</th>
<th>M.B.P. mm. Hg</th>
<th>C.I. L./min. M²</th>
<th>C.W.I. Kg.M/min./M²</th>
<th>S.V.I. cc./min. M²</th>
<th>S.W.I. Gm.M/min./M²</th>
<th>Oxygen Consumption L./min. M²</th>
</tr>
</thead>
<tbody>
<tr>
<td>J. V.</td>
<td>28</td>
<td>77.7</td>
<td>1.86</td>
<td>16.7</td>
<td>49.5</td>
<td>0</td>
<td>100</td>
<td>119</td>
<td>2.44</td>
<td>3.90</td>
<td>24</td>
<td>30</td>
<td>1.06</td>
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<tr>
<td>M. L.</td>
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<td>1.86</td>
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<td>0</td>
<td>67</td>
<td>95</td>
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<td>3.07</td>
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<td>16.3</td>
<td>48.9</td>
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<td>90</td>
<td>96</td>
<td>3.73</td>
<td>4.87</td>
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<td>54</td>
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<td>1.73</td>
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<td>48.8</td>
<td>0</td>
<td>75</td>
<td>89</td>
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<td>1.69</td>
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<td>46.5</td>
<td>0</td>
<td>82</td>
<td>87</td>
<td>2.29</td>
<td>2.71</td>
<td>28</td>
<td>33</td>
<td>0.190</td>
</tr>
<tr>
<td>J. L.</td>
<td>27</td>
<td>64.5</td>
<td>1.70</td>
<td></td>
<td>46.0</td>
<td>0</td>
<td>100</td>
<td>100</td>
<td>3.47</td>
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<td>1.70</td>
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<td>100</td>
<td>9.20</td>
<td>12.51</td>
<td>51</td>
<td>69</td>
<td>1.610</td>
</tr>
</tbody>
</table>

**Averages**

Rest: 2.75 L./min. M². 
Exercise 810 (704-986) Kg.M/min./M²: 8.12 L./min. M².

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385
minute per square meter and averaging 810. This difference is perhaps explained in part by
the fact that these students weighed on an
average approximately 10 Kg. more than the
high-altitude natives.
As might have been expected, considerable
variation in hemodynamic response from indi-
vidual to individual was found. It is doubtful
that the mathematical precision of statistical
analysis would add much to the meaning of this
data. However, fully realizing the limitations of
the measurements, some trends were apparent
which are of interest.

The average control heart rates for the two
groups (altitude natives and sea level medical
students, respectively) were the same at 83 per
minute. In all subjects, except for one native in
the mountains and one medical student at sea
level, the increase of the heart rate was large
during exercise. Increases in rate tended to be
greatest with the greatest treadmill activity;
the average values for the two groups were 161
and 163 per minute.

The average resting values for the mean
systemic blood pressure in the two groups (high
altitude natives and sea level dwellers) were
101 and 96 mm. Hg. In contrast to the large
increase in heart rate the increase in mean
systemic blood pressure was generally mild in
these groups during exercise, the highest
values being 164 in a native at the altitude and
122 in a medical student at sea level. An oc-
casional subject in each group showed no
change or a slight reduction in mean blood
pressure. The averages during exercise for the
high-altitude natives and sea level subjects
were 119 and 109 mm. Hg mean radial pressure,
respectively.

The average control cardiac work index was
higher in the group of mountain natives, in
whom the value was 6 compared to 3.6 Kg.M.
per minute per square meter in the other group.
In two mountain natives in whom measure-
ments were repeated at the same rate of tread-
mill exercise the values for cardiac work index
(also cardiac index, stroke volume index, and
stroke work index) were fairly constant indi-
cating that in the period of two to four minutes
a reasonably steady state for these parameters
was obtained. With one exception values for
cardiac index and cardiac work index increased
as the level of treadmill activity was increased.
This was also true of stroke volume index and stroke work index in sea level subjects and in the majority of the natives at high altitude.

Keeping in mind the individual variations in the response of the cardiac index to exercise, for a lesser treadmill work load, the average value for cardiac index in the high-altitude native was somewhat greater than that of the sea level subject (9.5 versus 8.1 liters per minute per square meter, respectively). It is of interest also that when the work levels of the high altitude natives are broken down into groups, at work levels ranging from 490 to 580 Kg.M. per minute per square meter (average 535), the cardiac index averaged 7.5 L per minute per square meter, while at 650 to 749 Kg.M. per minute per square meter (average 697), the cardiac index averaged 13.7 L per minute per square meter. This contrasts with the average value of 8.1 L per minute per square meter for sea level subjects working at rates varying from 704 to 986 Kg.M. per minute per square meter (average 810).

As a result of the large increase in cardiac output in all subjects and the mild increase of mean systemic blood pressure, the cardiac work index rose greatly with exercise. This was especially evident in the group of natives in whom the average value was 16 as compared to 12.1 Kg.M. per minute per square meter in the medical students, despite the fact that the natives were doing considerably less work on the treadmill. In the natives who were working at only 490 to 580 Kg.M. per minute per square meter the average cardiac work index was 12.3 Kg.M. per minute per square meter but in the natives exercising at 650 to 749 Kg.M. per minute per square meter (still less than in the medical students) the cardiac work index was 23.4 Kg.M. per minute per square meter. The possible influence of such factors as the difference in body type and weight in these two groups must be kept in mind; their importance in attempting to compare cardiac response to equivalent work loads is unknown.

At rest the stroke volume index of the natives in Morococha was higher with an average value of 51 compared to 33 cc. per minute per square meter in the group of medical students at sea level. From a combination of the competing mechanisms of a large increase of heart rate and cardiac output, the stroke volume index was only moderately increased with exercise. In that portion of the group of natives who were performing at an external work level (650 to 749 Kg.M. per minute per square meter) only moderately below that of the medical students, the average stroke volume index was 80 cc. per minute per square meter; in the natives who worked at a considerably lower rate (490 to 580 Kg.M. per minute per square meter) the stroke volume index of 49 cc. per minute per square meter approximated that of the sea level exercising student.

At rest the natives of Morococha had a considerably greater stroke work index than the sea level medical students. During exercise, as the result of a mild augmentation of stroke volume and systemic blood pressure, these values were increased, average figures being 97.5 and 75 Gm.M. per minute per square meter with the greater value being in the native at the altitude. Again in the mountain native whose external work level more nearly approximated that of the medical student, the stroke work index averaged 135 Gm.M. per minute per square meter, while at the lesser work level this averaged 79 Gm.M. per minute per square meter or about the same as that of the medical student doing much more work.

Calculation of the arteriovenous oxygen difference at rest and during exercise has been made in those instances in which both cardiac output and oxygen consumption were measured. Such values are obviously only an approximation since data for cardiac output and oxygen consumption are based on quite different time intervals. However, they should represent trends. The control data in the mountain native for the calculated arteriovenous oxygen difference averaged 5.72 cc. per 100 cc.; during exercise this increased to 13.86 cc. per 100 cc. At sea level in the medical students for a somewhat greater level of treadmill work the average calculated arteriovenous oxygen difference was 16.86 per 100 cc. The values reported here during exercise are in the same range as those calculated by Asmussen and Nielsen using the dye-dilution technic, and as those reported by Donald and co-workers (9),
in which the arteriovenous oxygen difference was determined directly with the Fick procedure.

Although attempts were made to stress the left ventricle to maximum external effort, whether this was accomplished either in the mountains or at sea level is not known. The data for the last five natives in table 1, group I are suggestive of maximum cardiac effort. Each of these subjects stated at the end of exercise that he was "very tired" or "completely exhausted." In these five individuals at the higher levels of treadmill work (650 to 749 Kg.M. per minute per square meter) the cardiac work index was quite high ranging from 18.06 to 46.43 Kg.M. per minute per square meter and averaging 26.19 Kg.M. per minute per square meter. In those medical students at sea level, who were working at a considerably higher level of treadmill exercise (725 to 986 Kg.M. per minute per square meter) and who were quite tired, cardiac work index ranged from 11.37 to 15.14 Kg.M. per minute per square meter and averaged 12.93 Kg.M. per minute per square meter.

The data obtained on the cardiac response of the partially acclimated subjects at the altitude is presented for completeness. In these the treadmill work load approximated the lower level of work performed by the natives in the altitude and was considerably less than that of the sea level medical students. The values varied from 545 to 602 Kg.M. per minute per square meter (average 572). Compared to the other two groups, the hemoglobin and hematocrit values were intermediate, with the hemoglobin varying from 15.9 to 18.4 Gm. per 100 cc. (average 17.7), and the hematocrit averaging 54.2 with extremes of 50 and 55.9. The heart rate and systemic blood pressure before and during exercise were of the same order of magnitude in all three groups. During exercise the average cardiac index (5.46 L. per minute per square meter), cardiac work index (8.66 Kg.M. per minute per square meter), stroke volume index (34 cc. per minute per square meter), and stroke work index (55 Gm.M. per minute per square meter) were less than the corresponding parameters at sea level and in the fully acclimated high altitude native. However, because of the small number in the group and the presence of upper respiratory infections with fever in some subjects, these results are regarded as equivocal and no interpretation can be made.

**Comments**

The data suggest that the subject who is native to an altitude of 15,000 feet has a greater cardiac output, cardiac index, cardiac work index, stroke volume, and stroke work index in the standing position than does the sea-level medical student studied at sea level. During treadmill exercise, the external work obtained by the left ventricle was effected by a combination of a large increase in cardiac output and a mild increase in systemic blood pressure. Stroke volume and stroke work index were only mildly elevated since the heart rate was concurrently greatly increased to approximately 180. As a result, the increase in minute work of the left ventricle was largely accomplished by an increase in heart rate and to a lesser extent by an increase in work response with each systole.

The average level reached during exercise for heart rate and blood pressure was approximately the same, but the average values for cardiac index, cardiac work index, stroke volume index, stroke volume, and stroke work index were all higher in the natives at high altitudes than in the medical students at sea level. Since in the students at sea level the rate of performance of external work was considerably greater than in the other group (810 versus 589 Kg.M. per minute per square meter) and since the oxygen consumption during treadmill work was not greatly different in the two groups, the data suggest that for comparable amounts of external work the heart of the native at the altitude responds with a greater effort than the heart of the native sea level dweller at sea level.

An effort was made to elicit the maximum response of cardiac work by the left ventricle. Although it is believed that some of the figures reported here may approximate the maximum effort of which the normal left ventricle is
capable, it is not known whether this was accomplished because of inability to assess properly the degree of exhaustion of the subjects.

**SUMMARIO IN INTERLINGUA**

Le responsa que exercitos in le ambulometro provoca in le ventriculo sinistre esseva studiato in nativos del region de Morococha in Peru (altitude 4540 m) e in nativos del region de Lima in Peru (altitude 150 m). Omne le subjectos esseva studiato al altitude al qual illes habeva vivite omne lor vita. In ambe grupplos—illo de Morococha e illo de Lima—le labor externe del ventriculo sinistre esseva effectuate per un combination de un grande augmento del rendimento cardiac e un leve augmento del pression sanguinee in le circulation major. Le volumine per pulso e le labor per pulso esseva solo levemente elevate pro que le rapiditate del corde esseva simultaneamente molto augmentata. Per consequente le augmento del labor del ventriculo sinistre esseva effectuate in grande mesura per le acceleracion del corde e in minor mesura per le augmento del labor per pulso. Con comparabile quantitates del labor externe, le ventriculo sinistre de nativos de grande altitudes, examine in grande altitudes, respondeva per un considerabilemente plus grande effortio que le ventriculo sinistre de nativos de basse altitudes, examine al nivello del mar. In alin casos le valores obtenite se aproximava possibilemente al maximo del capacitace del ventriculo sinistre.

**ACKNOWLEDGMENT**

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