Tissue Respiration of Rats Acclimatized to Low Barometric Pressure¹,²

W. C. ULLRICK,³ W. V. WHITEHORN, BETSY B. BRENNAN AND J. G. KRONE. From the Department of Physiology, University of Illinois College of Medicine, Chicago, Illinois

ABSTRACT

Rate of respiration of tissues of male albino rats acclimatized to 18,000 feet simulated altitude for periods averaging 11.2 weeks was determined by Warburg technique under 100% oxygen. Results from 12 experimental animals were compared with 7 controls simultaneously maintained at normal barometric pressure. Acclimatized animals showed no significant changes in growth rate, total metabolic rate or rectal temperature. Hemoglobin values and heart-body weight ratios were elevated. Tissue respiration of brain, small intestine, diaphragm, liver, skeletal muscle, atrium and ventricle was not significantly different from that of controls. Adrenal-body weight ratios were unchanged but increased adrenocortical activity is suggested by a significant increase in adrenal qO₂. Respiration of acclimatized kidney slices was significantly reduced. It is concluded that generalized adaptation of cellular metabolism to hypoxia does not occur in acclimatization but that changes may be demonstrated in tissues specifically involved in the adaptation process.

There are many respiratory and cardiovascular adjustments contributing to altitude acclimatization. These adjustments function to reduce the gradient between the atmospheric partial pressure of oxygen and the partial pressure of oxygen existing at the tissue level, and have been discussed in detail by Stickney and Van Liere (1). In addition to these well recognized factors, it has been postulated, originally by Paul Bert (2), that with acclimatization, body tissues in general may gradually alter their cellular metabolism so as to respiration and function normally at less than normal oxygen tensions, tensions at which the respiration and function of non-acclimatized tissues would be impaired. Since it is generally agreed (see (1) for refs.) that total resting metabolism of acclimatized men and animals is unchanged, investigation at the cellular level seems indicated. Literature in this area is extremely scanty. Sundstroem and Michaels (3) found no change in qO₂ of liver slices from acclimatized rats when determinations were made under 100% oxygen but reported an increased ability of such slices to respire under lower oxygen tensions. Clark et al. (4) found a slight but significant decrease in respiration of acclimatized rat liver slices determined under 100% oxygen. Albaum and Chinn (5) were unable to demonstrate alteration in cellular metabolism of brain in altitude-acclimatized rats.

The present study was designed to gain further information regarding the quantitative respiration of individual tissues of animals acclimatized to a simulated high altitude. The data presented fail to support the concept of generalized metabolic adaptation to chronic hypoxia at the cellular level, but indicate changes in specific tissues associated with the acclimatization process.

METHODS

Male albino Sprague-Dawley rats weighing approximately 180 gm at the start of the experiment were divided into a control group of 7 animals and an experimental group of 16 animals, of which 12 survived the acclimatization procedure. Records of body weight, rectal temperature and basal metabolic rate were taken over a 2-week control period.
were cut to 0.3-0.4 mm thickness with a modified the liver, heart ventricles and hind limb skeletal muscle off with a razor blade and the diaphragm was trimmed without slicing, the adrenals were quartered, the small comprised these tissues. Duplicate determinations both adrenals, due to the small amount of material complete. The entire slicing procedure required about 15 minutes.

Stadie-Riggs microtome. All tissues, sliced or unsliced, were placed in iced Krebs-Ringer solution. The cranium was of this procedure from the time of killing never exceeded a portion of the gastrocnemius muscle were excised and go seconds. The kidney, including both cortex and intestine was split open and the mucosa gently scraped to desired size. The heart, brain, gut and and weighed. Total heart weights were determined from the combined weights of the component parts of each heart. Adrenal weight to body weight and heart weight to body weight ratios were also determined.

RESULTS

The mean values for the rectal temperatures, basal metabolic rates, and body weights are plotted in figure 1. The mean experimental body weight was significantly lower than that of the control, but the ratio of heart weight to body weight in the experimental group was significantly higher than that of the controls, but the slope of the curves of the two groups of animals was not significantly different.

Data on heart weights, adrenal weights, heart-body weight ratio, adrenal-body weight ratio and hemoglobin level are summarized in table 1. Standard errors and levels of significance of group differences are indicated. No significant difference occurred between the mean heart weights of the two groups of animals, but the ratio of heart weight to body weight in the experimental group was significantly higher than that in the control group. The average experimental adrenal weight was significantly lower than that of the control, but since the mean experimental body weight was also reduced, there was no difference.
Table 1. Heart-body weight ratios, adrenal body weight ratios and hemoglobin values

<table>
<thead>
<tr>
<th></th>
<th>Control (7 animals)</th>
<th>Experimental (12 animals)</th>
<th>Level of Significance*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean heart wt.†</td>
<td>180.8±7.5†</td>
<td>186.3±6.9</td>
<td>.50</td>
</tr>
<tr>
<td>Mean adrenal wt.†</td>
<td>13.6±1.39</td>
<td>10.3±0.65</td>
<td>.02</td>
</tr>
<tr>
<td>Mean body wt. (grams)</td>
<td>333.9±7.2</td>
<td>278.8±12.8</td>
<td>.01</td>
</tr>
<tr>
<td>Ratio heart wt. to body wt.</td>
<td>0.54±0.018</td>
<td>0.69±0.020</td>
<td>.01</td>
</tr>
<tr>
<td>Ratio adrenal wt. to body wt.</td>
<td>0.04±0.004</td>
<td>0.04±0.002</td>
<td>.50</td>
</tr>
<tr>
<td>Hemoglobin (grams %)</td>
<td>17.0±2.0</td>
<td>24.4±1.17</td>
<td>.02</td>
</tr>
</tbody>
</table>

* t = x \sqrt{\frac{n_1 s_1^2 + n_2 s_2^2 - 2}{(n_1 + n_2) Sx^2}}
† Milligrams dry weight of tissue.
‡ Standard error.

Discussion

The lack of change in the metabolic rate and rectal temperature confirms previous observations indicating that changes in overall metabolism play no part in acclimatization. Significant increase in heart-body weight ratio supports the view that cardiac hypertrophy develops in association with the well known cardiorespiratory adaptations.

The lower mean body weight of the experimental animals upon reaching simulated altitude seems related to the stress of acute hypoxia. Recent work suggests (7) that water loss may contribute significantly to the deficit. Since the slope of the experimental weight curve essentially paralleled that of the control during subsequent exposure to the reduced barometric pressure it is felt that the experimental conditions satisfied the requirements for 'true acclimatization' as defined by Campbell (8).

With regard to the respiratory rate of the brain, small intestine, diaphragm, liver and heart, one must conclude that under 100% oxygen these tissues from acclimatized animal respire no differently than do those of controls. The data give no evidence of cellular adjustment to chronic hypoxia in these tissues and are in agreement with the similarly negative observations of Sundstroem and Michaels (3) and Albaum and Chinn (5). They do not confirm the slight reduction in liver slice \( qO_2 \) reported by Clark et al. (4), nor do they eliminate the possibility of modifications of metabolism apparent only under conditions of reduced oxygen tensions.

In contrast to the lack of change in respiration of the tissues listed above, the results indicate significant elevation of adrenal respiration and reduction of kidney \( qO_2 \). The significance of these findings deserves comment.

Many workers (9-12) have reported hypertrophy of the adrenal glands during hypoxia, but these experiments have not involved acclimatization of the animal, but rather from the control. However, the experimental kidney respiration was significantly reduced and the oxygen consumption of the adrenals of the experimental group was found to be significantly greater than that of the controls.
acute exposures, often repetitive, to low oxygen pressure. Sundstroem and Michaels (3) found that in rats acclimatized for 3 weeks at 14,000 or 20,000 feet, the wet weight of the adrenal glands did not vary from the normal. However, the adrenal weight was somewhat increased over normal in rats acclimatized to 25,000 feet, and nearly trebled in value in rats acclimatized at 29,000 feet. As they admit, however, some of the increased weight may be due to hemorrhages, hyperemia and edema in the adrenals. Darrow and Sarason (13) reported no significant change in adrenal weight in rats exposed to simulated altitude of 20,000 feet for periods up to 7 days. These observers found a normal adrenal lipid content in such animals but noted changes in skeletal muscle compatible with increased adrenocortical activity. Dalton et al. (14) found a normal adrenocortical lipid pattern in histologic studies of rats exposed discontinuously to low pressure for 6 weeks or more. Shorter exposures induced changes characteristic of stimulation with ACTH. Such observations lend support to the conclusion of Stickney and Van Liere (1) that increased adrenocortical activity is primarily a feature of early phases of acclimatization or of incomplete acclimatization to severe degrees of hypoxia.

Our data provide additional information in this connection. Lack of adrenal hypertrophy is in keeping with reports cited above, but the significant increase in adrenal respiration reported here suggests increased adrenal activity in the acclimatized animal on the basis of increased activity per unit of adrenal tissue rather than by actual increase in the size of the gland.

The significance of reduced kidney respiration in acclimatized rats is not apparent. Studies on renal function in acclimatization are scanty and provide no basis for rational speculation. The relation of renal hypertrophy and hyperemia (15, 16) to changes in tissue metabolism is not clear. Moreover as Van Slyke et al. (17) have noted, the oxygen consumption of the kidney seems largely related to its nonexcretory functions. The nature and relation of such functions in acclimatization remain to be defined.

The authors wish to express gratitude to Dr. J. P. Marbarger and the staff of the Aeromedical and Physical Environment Laboratory of the University of Illinois for the use of equipment necessary for these experiments.

REFERENCES