

Adaptive Changes in Cardiac Muscle Activity under Hypoxia of High Altitude

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Abstract

Laboratory rats were housed for 15 days in a barometric chamber programmed to simulate an altitude of 22,500 feet. Control rats were housed under laboratory conditions. Portions of the right ventricles were removed from both groups and bathed in a medium which approximated the ionic composition of rat blood to which glucose had been added. A mixture of 95% oxygen and 5% carbon dioxide was bubbled through the medium. The preparation was stimulated and the developed tension was recorded. After a stable record was obtained, an anaerobic mixture of 95% nitrogen and 5% carbon dioxide was bubbled through the medium.

The time required for the contracting myocardium to reach one half of the preanoxic tension was twice as great in the altitude acclimated rats as it was in the control rats. There was a high correlation between the hemoglobin concentration levels attained and the tissue resistance to anoxia. As the response is blocked by iodoacetate, it is presumed that an alteration in the glycolytic capacity is involved in the high altitude change.

Numerous changes take place in an organism exposed to the hypoxia of altitude for more than several days. These have been well documented and include an increased capacity for breathing, an increase in the oxygen carrying capacity of the blood through increased hemopoietic activity and an increase in the amount of blood pumped by the heart and flowing to the tissues (2, 3).

Less well documented and perhaps of far greater importance, are those changes that take place at the level of tissue or cellular function. In this study the question we have asked is whether or not a tissue isolated from an animal acclimatized to high altitude possesses a greater capacity to function during conditions of oxygen deficiency than similar tissue removed from a control animal. In particular, it is those changes that take place in cardiac tissue that are being studied at the Environmental Medicine Facility at Indiana University.

Methods

Male albino rats were kept in a barometric chamber for 15 days. The chamber was programmed for 20 hours per day at an altitude of 22,500 feet and four hours a day at sea level. The ascent to altitude and the descent to sea level were carried out slowly to maintain pressure equilibration and avoid problems of air embolism.

At the end of the acclimatization period, the hearts were rapidly excised under ether anesthesia and plunged into cold ringers solution which stopped the heart beat. Muscle strips were cut from the right ventricular wall. Several blood samples were taken from the same animal for hematocrit ratio determinations.

The ventricular strips were mounted in a muscle bath which con-

¹Trainee of Public Health Training Program, Grant 1 TIES 75-01.

sisted of 50 ml. of mammalian ringers solutions to which glucose substrate had been added (Figure 1). One end of the muscle was fixed by a clamp to the electrode block. The other was attached to a strain gauge transducer whose signal was directed into an Offner-Dynograph recorder. The muscle was stimulated maximally with square wave pulses at a frequency of 6 per minute. An initial tension was set on the muscle, and the developed tension was then recorded continuously.

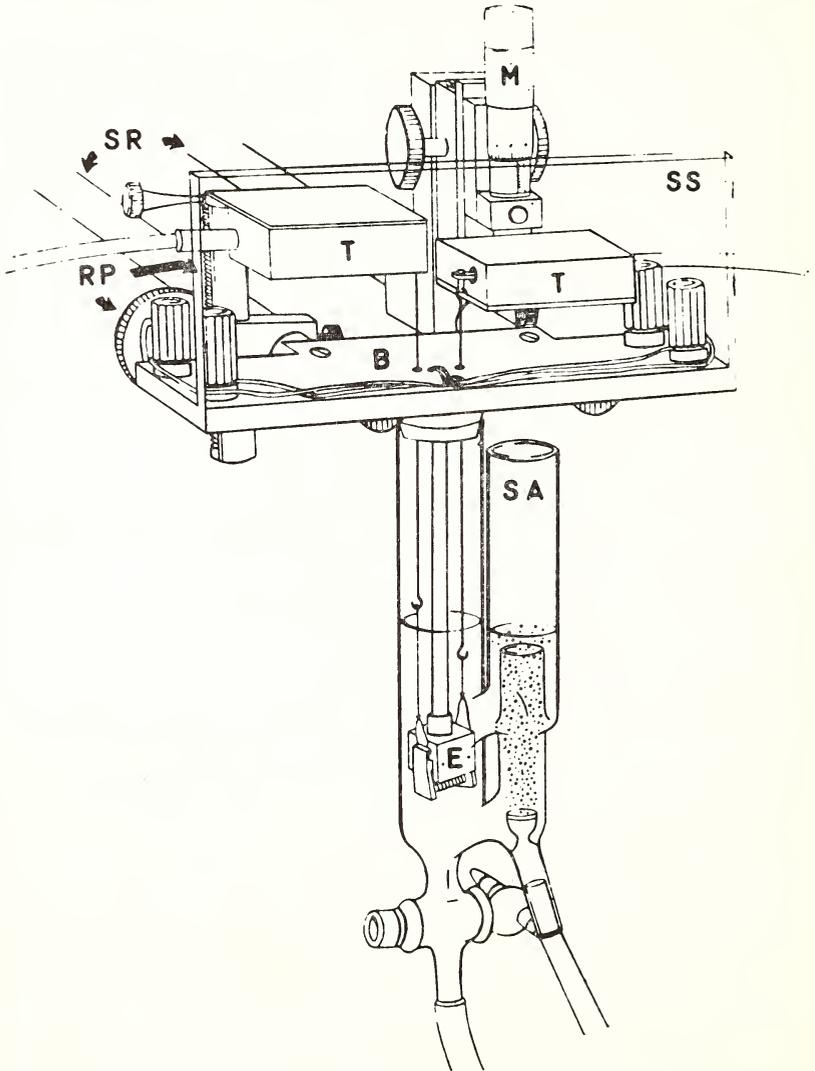


Figure 1. Apparatus for recording the contractions of isolated heart muscle. *E*, electrode block; *T*, transducers; *RP*, rack and pinion; *M*, micrometer. The glass vessel is immersed in a constant-temperature bath during use. From Brinks (1).

Experimental Protocol

Initially an aerobic mixture was bubbled through the medium and the contractions were recorded. After the contractions had stabilized, a five minute record was taken which was designated as the control period. This was used in subsequent calculations. At the end of the control period, an anaerobic mixture was bubbled through the medium for a 20 minute period. At the end of the anaerobic period the aerobic mixture was reintroduced into the bathing fluid.

Results

It can be seen in Figure 2, a recording from a control ventricular strip, that developed tension decreases under anoxia. This decrease in developed tension was seen to occur along a time course that differed in the altitude and control groups. Table 1 shows that the time required for the strength of contraction to become half of its pre-anoxic value was 5.7 minutes for the sea level animals and 13.4 minutes for the experimental group. Statistical analysis reveals the difference between these two values to be significant at the .001 level.

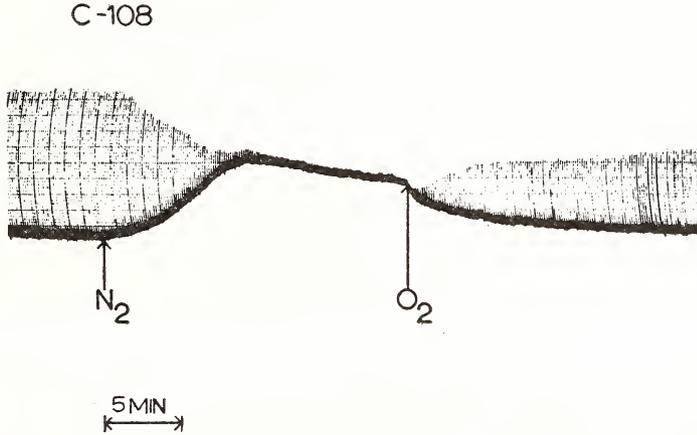


Figure 2. Record from a control ventricular strip. At N₂ an anoxic mixture of 95% N₂ and 5% CO₂ was bubbled through the bath. At O₂ a mixture of 95% O₂ and 5% CO₂ was bubbled into the bath.

TABLE 1

Group	Sea Level	Altitude
n	9	9
mean time to ½ strength in minutes	5.7	13.4
standard deviation	±1.3	±3.9

TABLE 2

Group	Sea Level	Altitude
n	9	9
mean hematocrit ratio (%)	46.8	76.1
standard deviation	± 4.3	± 6.3

We then wondered if this change which we had noted could be related to another manifestation of altitude stress. Hematocrit ratios were determined in both groups. Table 2 reveals the great increase in the hematocrit ratio with altitude as had been well documented. A comparison of the hematocrit ratios and the time required for a preparation to reach its half strength of contraction were found to be correlated. Statistical evaluation revealed a parametric correlation coefficient of 0.8.

Finally, it was observed that the increase in resistance to anoxia was particularly sensitive to treatment with iodoacetate. This can be seen in Figure 3 which is a record taken from an altitude animal. When nitrogen was administered the first time, the normal time course in the decline in developed tension for an altitude animal was seen. However, after the preparation was brought back to a steady value with oxygen, and iodoacetate was administered, a marked change was seen in the time course of the decline in developed tension.

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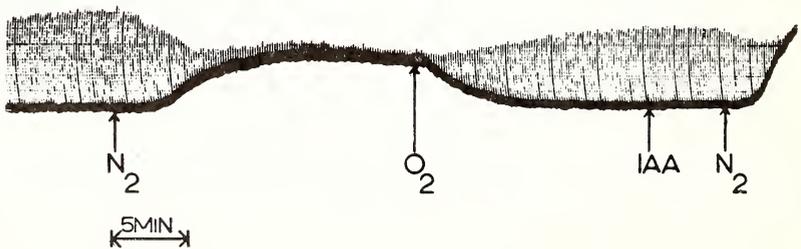


Figure 3. Record from an altitude ventricular strip. At N₂ an anoxic mixture was bubbled through the bath. Twenty minutes later, at O₂ the anoxic mixture was replaced with an aerobic mixture. At IAA iodoacetate was administered, followed 2 minutes later by the anoxic gas mixture.

The experimental animals, after iodoacetate treatment, closely resembled the control groups in decline in developed tension with anoxia. It should also be observed that in the 2 minutes between the time the iodoacetate was administered and the preparation was made anoxic, there was no decline in developed tension. Since iodoacetate is known to block glycolysis, it is suspected that the increased resistance of the

tissue from the altitude acclimated animals is due, in part, to a higher capacity for anaerobic glycolysis.

Conclusion

In conclusion we feel that this study indicates that an adaptive response to high altitude exposure does occur at the level of tissue function. This response can be seen as a greater capacity for the myocardium to continue to contract under conditions of oxygen lack. Further, this response appears, at least in part, to be dependent on anaerobic glycolysis because it is apparently blocked by iodoacetate. Finally, that the response can be correlated with other adaptive responses, such as the hematocrit ratio, provides that tissue level adaptation is another manifestation of exposure to the hypoxia of high altitude.

Literature Cited

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