

## Response of the Human Red Cell to Muscular Activity<sup>1</sup> (34329)

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(Introduced by D. F. Bohr)

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The human red cell is capable of adaptive response to hypoxia and recent evidence has emphasized the important role of red cell 2,3-diphosphoglycerate (DPG) in this adaptive response (1, 2). The increase in the concentration of DPG in the red cell which occurs in response to hypoxia shifts the oxygen dissociation curve to the right (1, 3, 4) and facilitates the release of oxygen to the tissues (5, 6). Higher concentrations of DPG occur in the red cells of high altitude residents (1, 2), and of patients with hypoxic diseases such as anemia or pulmonary dysfunction (3, 6). In the current study, we have found that a different type of stimulus—extended physical exertion—results in an increase in the concentration of red cell DPG. Further, the rate of increase of red cell DPG during exercise is much more rapid than that previously reported during exposure to altitude (1).

**Materials and Methods.** Red cell DPG and blood lactate concentrations were first measured in 10 adult males (ages 21–45 years) before and immediately after 60 min of moderate exercise (basketball). Analyses for DPG (2) and for lactate (7) were performed by techniques that have been reported previously. In a second study, to obtain a more controlled physiological stress, 10 men pedaled at 50 rpm for 50 min on a bicycle ergometer. The load was adjusted to provide 1200 kg/min of work for 5 trained subjects and 600 kg/min of work for 5 untrained

subjects. These work loads resulted in the attainment of approximately 70% (range 55–90%) of the maximum oxygen uptake of both the trained and untrained subjects. Venous blood samples were drawn at 0, 30, and 50 min, and extracts for DPG and lactate assays were prepared immediately.

**Results.** Following the 60 min of basketball, increases in red cell DPG were observed in all 10 subjects, averaging 18% above the resting values (Table I). Whole blood lactate was elevated 60% over the resting value. The changes in both DPG and lactate were significant at the  $p < 0.01$  level.

In the experiment in which the bicycle ergometer was used, the red cell DPG concentrations after 30 min of exercise did not vary from the resting values. However, after 50 min of exercise increases in red cell DPG had occurred in 7 of 10 subjects (Table I).

TABLE I. Mean DPG and Blood Lactate Changes in Response to Exercise in Two Groups of 10 Adult Males.

Time (min)	DPG ( $\mu$ moles/g of H <sup>b</sup> )	Lactate (mg/100 ml of whole blood)
Basketball		
0	11.14 ( $\pm 1.53$ )	16.9 ( $\pm 1.57$ )
60	13.12 ( $\pm 1.90$ )	27.0 ( $\pm 3.00$ )
$\Delta$	+1.98 ( $t = 3.38$ , $p < 0.01$ )	+10.1 ( $t = 2.99$ , $p < 0.01$ )
Bicycle ergometer		
0	12.84 ( $\pm 2.17$ )	9.3 ( $\pm 4.84$ )
50	13.85 ( $\pm 2.06$ )	24.4 ( $\pm 8.47$ ) <sup>a</sup>
$\Delta$	+1.01 ( $t = 1.26$ , NS)	+15.1 ( $t = 3.29$ , $p < 0.01$ )

<sup>a</sup> Average of the 30- and 50-min lactate concentrations.

<sup>b</sup> Hemoglobin.

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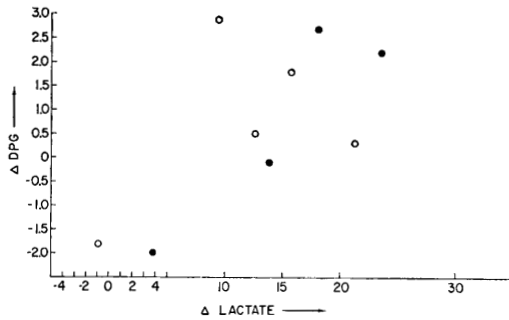


FIG. 1. A scatter diagram showing the correlation between the changes from resting levels in blood lactate and red cell DPG during exercise on a bicycle ergometer; DPG is expressed in micromoles per gram of hemoglobin and lactate in milligrams per 100 ml of whole blood; (●), trained subjects; (○), untrained subjects; correlation coefficient =  $+0.743$ ,  $p < 0.01$ .

Assuming that the increase in blood lactate provides an estimate of the physiological strain induced by the exercise (8), the subjects who evidenced the greatest strain had the largest increases in red cell DPG. The three subjects who did not show increases in red cell DPG<sup>2</sup> displayed slight or negative changes in blood lactate concentrations during exercise. A strong positive correlation existed between the change in blood lactate (the av of the 30- and 50-min concentrations minus the resting lactate concentration) and that in red cell DPG after 50 min ( $r = +0.743$ ,  $p < 0.01$ ) (Fig. 1).

**Discussion.** Although the mechanism by which red cell DPG is elevated during either exercise or hypoxia has not been determined, the greater binding affinity of deoxygenated hemoglobin for DPG (9) might play a regulatory role (10, 11). The increased proportion of deoxygenated hemoglobin during exercise and hypoxia should result in more bound and less free DPG in the red cell. If the amount of free DPG is controlled by the

<sup>2</sup> Since the half response time for blood lactate is approximately 5 min, the resting lactate was subtracted from the average of the 30- and 50-minute lactates as the best index of physiological stress.

enzymes of glycolysis, then a decrease in free DPG would stimulate glycolysis and increase DPG synthesis.

We conclude from the present results that extended physical exertion of adequate intensity will produce increases in the concentration of DPG within the circulating red cell in less than 1 hr. The higher red cell DPG concentrations function to facilitate oxygen transport by shifting the oxygen dissociation curve to the right, thereby increasing tissue oxygen delivery. The enhancement of oxygen delivery through an increase in DPG may be important in adequate homeostatic adjustment to prolonged exertion.

**Summary.** The concentration of 2,3-diphosphoglycerate (DPG) in the human red cell increases significantly during 60 min of vigorous muscle activity. The increase is related to the severity of the exercise. The resultant shift to the right of the oxygen dissociation curve may increase the amount of oxygen delivered to the contracting muscle cells during prolonged physical exertion.

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