The following letter is in response to the Point:Counterpoint series "In health and in a normoxic environment, $\dot{V}O_{2max}$ is/is not limited primarily by cardiac output and locomotor muscle blood flow" that appeared in the February issue (vol 100: 744–748, 2006, http://jap.physiology.org/content/vol100/issue2).

To the Editor: Among the factors that potentially limit $\dot{V}O_{2\,max}$, hemorheological factors are often neglected by exercise physiologists. However, $\dot{V}O_{2\,max}$ and blood viscosity factors are strongly correlated (2), but in a complicated way. At high hematocrit, there is increased oxygen binding capacity; however, the simultaneous increase in blood viscosity may limit the transport capacity. These counteracting effects result in an optimal hematocrit value for maximal oxygen availability to tissues (4). Because the viscosity of blood is shear rate dependent, the optimal hematocrit may differ under different circumstances, e.g., rest, exercise, but also in different parts of the circulation. Blood rheological properties are thus able to influence the cascade of oxygen from lungs to exercising muscles.

Impairment in red blood cell (RBC) deformability can alter the diffusing capacity for oxygen from lungs to blood capillaries that may participate to the occurrence of exercise-induced hypoxemia, which may limit $\dot{V}O_{2\,max}$ (3). In the heart, any increase in blood viscosity raises peripheral vascular resistance, which may cause a decrease in maximal stroke volume and, therefore, a decrease in $\dot{V}O_{2\,max}$. In muscular microcirculation, enhanced RBC aggregation causes depressed eNOS activity, resulting in deteriorated NO-mediated relaxation of arterioles (1). This effect of RBC aggregation is explained by the enhanced axial migration of blood cellular elements, reducing the frictional forces affecting on the endothelial cells and downregulating NO synthesis mechanisms.

Although the debate concerning the factors limiting $\dot{V}O_{2\,max}$ is far from being closed (5), central mechanisms seem to play an important role, with hemorheology being among the key factors.

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