Shear stress and flow-mediated dilation in the normoxic and hypoxic human

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Abstract: The endothelium is a single cell layer that plays a critical role in determining the health and function of blood vessels. Endothelial function is shaped by shear stress, the frictional force exerted by the speed of blood flow, and the thickness (viscosity) of the blood. Exposure to shear stress that reverses direction back-and-forth impairs endothelial function in young men. Whether women are equally susceptible to this perturbation and the isolated impact of a low level of shear stress with and without reversal of shear had not been investigated. Hypoxia, the low levels of oxygen that are experienced at high altitude, has been shown to influence flow reversal and impair endothelial function. However, no previous study had accounted for the changes in blood thickness, and hence shear stress that occur at high altitude. This may be especially important in the context of excessive erythrocytosis, a high-altitude disease characterized by exceptionally thick blood and increased cardiovascular risk. This thesis examined (i) whether there are sex differences in the impact of exposure to low and reversing shear stress on endothelial function; (ii) whether isolated low shear stress impairs endothelial function; (iii) the impact of reversing shear stress on endothelial function in short-term exposure to low levels of oxygen and after trekking to 5050 m in the Himalayas; and (iv) the role of high levels of blood viscosity on endothelial function in high-altitude natives in Cerro de Pasco, Peru (4330 m), with excessive erythrocytosis. We identified that (i) premenopausal women have some protection against reductions in endothelial function after being exposed to reversing shear stress; (ii) isolated low shear stress impaired endothelial function; (iii) short-term exposure to low levels of oxygen and sustained high-altitude exposure reduced endothelial function, while superimposing reversing shear stress had no effect; and (iv) high levels of hemoglobin and blood viscosity contributed to lower endothelial function in Andean high-altitude natives with excessive erythrocytosis. Altogether, this dissertation advances our understanding of how the components of shear stress (the pattern, magnitude, and blood viscosity) impact endothelial function in humans under normoxic (normal levels of oxygen) and hypoxic (low levels of oxygen, such as high-altitude) conditions.

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