injury, epidemiology and control,'' and colleagues, whose landmark 1962 paper described the frequency of specific injuries and variations with age, sex, and skiing experience.[5]

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Persistent Elevation of VEGF and Prostacyclin Following Poor Cardiopulmonary Adaptation to High Altitude

To the Editor:

Hypobaric hypoxemia is a potent stimulus for the release of erythropoietin and for some markers of angiogenesis, such as vascular endothelial growth factor (VEGF).[1] Vascular endothelial growth factor stimulates angiogenesis, and angiopoietin-2 acts with VEGF to stimulate angiogenesis in the myocardium.[2] Similarly, prostacyclin (PGI_2) is a member of the prostaglandin family of lipid mediators, which have potent vasodilator and antithrombotic activities.[3] Some limited data have been reported on the release of selected markers of angiogenesis, including VEGF in climbers exposed to high altitude with or without symptoms of acute mountain sickness (AMS). However, no study has explored the concomitant changes in VEGF, angiopoietin-2, and PGI_2, as well as selected markers of inflammation and oxidation, concomitantly in relationship with good vs poor adaptation to high altitude.

We investigated the changes in selected markers of angiogenesis, prostaglandin, and some markers of subclinical inflammation and oxidative stress 24 hours prior to departure for the Bolivian Altiplano and within 24 hours of return to sea level. The objective of this expedition was to summit Mount Sajama, the highest peak in Bolivia, at an altitude of 6522 m. Participants were exposed to an altitude between 3600 and 6522 m for 19 days.

The study population consisted of 5 participants (4 males/1 female) aged 30 to 64 years living chronically at sea level. The diagnosis of AMS was performed using the Lake Louise[4] and the Hackett[5] scoring systems at the highest point reached during the expedition.

From the 5 climbers, 2 participants developed moderately severe symptoms of AMS. One climber, aged 64 years, experienced mild headache, recurrent difficulty sleeping, profound fatigue, and dyspnea on minimal exertion at an altitude of 4800 m (Hackett score = 4; Lake Louise score = 6). This climber stopped his climb at 5300 m. One participant developed some fatigue and severe intractable headache at 5680 m and returned to base camp at 4800 m (Hackett score = 3; Lake Louise score = 4). Data are presented in the Table.

Table. Changes in plasma markers prior to departure and within 24 hours upon return to sea level*

	No AMS (n = *3)*		*AMS-CP* (n = *1)*		*AMS-CNS* (n = *1)*	
	BSL	*Post*	*BSL*	*Post*	*BSL*	*Post*
VEGF ($pg \cdot mL^{-1}$)	204 ± 38	210 ± 43	222	553	259	244
Ang-2 ($pg \cdot mL^{-1}$)	1605 ± 601	1257 ± 280	1739	1539	1800	1750
6-Keto-$PGF_{1\alpha}$ ($pg \cdot mL^{-1}$)	37.7 ± 36.1	49.5 ± 40.0	118	311	85.4	62.0
IL-6 ($pg \cdot mL^{-1}$)	12.7 ± 15.9	12.2 ± 8.1	11.3	13.7	40.3	51.9
TBars ($pg \cdot mL^{-1}$)	10.8 ± 2.6	9.42 ± 3.70	6.26	13.7	10.0	11.2

*AMS indicates acute mountain sickness; CP, cardiopulmonary; CNS, central nervous system; BSL, baseline; Post, postexpedition; VEGF, vascular endothelial growth factor; Ang-2, angiopoietine-2; 6-Keto-$PGF_{1\alpha}$, 6-keto-prostoglandin F_{α}; IL-6, interleukin 6; and TBars, thiobarbituric acid-reactive substances.

This exploratory study reports for the first time the plasma levels of multiple mediators of angiogenesis and selected markers of inflammation and oxidative stress concomitantly in 5 healthy volunteers prior to departure and within 24 hours of returning from 19 days on the Bolivian Altiplano. We report different plasma levels of VEGF and PGI_2 in 2 climbers who experienced poor adaptation to high altitude. Here, we report a marked increase in VEGF and PGI_2 within 24 hours of returning from an altitude of more than 4000 m for 19 days in the older climber who experienced some delay in the acclimatization process but who also exhibited some cardiopulmonary features of poor adaptation to high altitude. These observations contrast with the findings from the climber who experienced AMS mostly with central nervous system symptoms.

Vascular endothelial growth factor concentrations before the expedition were consistent with levels reported in previous investigations. The change in VEGF in response to high altitude has been a matter of controversy. Reports have shown no increase or a significant increase within 20 hours to 7 days upon exposure to an altitude of 3600 m or higher.[1,6] Vascular endothelial growth factor appears to increase in nearly all climbers in response to hypobaric hypoxemia. Tissot van Patot[1] reported significantly higher levels of plasma VEGF and lower levels of VEGF soluble receptor in participants who had AMS within the first 24 hours upon exposure to 4300 m. In contrast, Dorward et al[6] reported no evidence of an association between AMS and changes in VEGF at either 3650 or 5200 m. However, the clinical characteristics and the mode of presentation of AMS were incompletely reported in that specific study. In addition, none of these reports involved exposure to high altitude for more than a week. Here we also reported a concomitant increase in PGI_2 level in the climber suffering from poor cardiopulmonary adaptation to high altitude, indicating a significant increase in cardiovascular stress.

There are some significant limitations to these observations. Vascular endothelial growth factor levels were not measured at different periods of the acclimatization process nor later during the expedition. In addition, VEGF soluble receptor-fms-related tyrosine kinase 1 was not measured. The participant with poor cardiopulmonary adaptation to high altitude was much older than the other climbers. Also, the small sample size did not allow for adjustment for the age effect, nor did it allow for further analyses about the relationship between clinical characteristics and biomarkers.

In conclusion, our study demonstrates that there were no significant changes in selected markers of angiogenesis, inflammation, and oxidative stress in climbers who did not experience mountain sickness, whereas in the 2 participants who experienced mountain sickness, the plasma concentrations of these biomarkers were perturbed. Vascular endothelial growth factor and PGI_2 may be associated with poor cardiopulmonary maladaptation to high altitude. Whether these vascular biomarkers are truly related to altitude illness or inadequate acclimatization requires study in a larger population.

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