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Circulatory Adaptation to Long-Term High Altitude Exposure in Aymaras and Caucasians

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Abstract About 30 million people live above 2500 m in the Andean Mountains of South America. Among them are 5.5 million Aymaras, an ethnic group with its own language, living on the altiplano of Bolivia, Peru, and northern Chile at altitudes of up to 4400 m. In this high altitude region traces of human population go back for more than 2000 years with constant evolutionary pressure on its residents for genetic adaptation to high altitude. Aymaras as the assumed direct descendents of the ancient cultures living in this region were the focus of much research interest during the last decades and several distinctive adaptation patterns to life at high altitude have been described in this ethnic group. The aim of this article was to review the physiology and pathophysiology of circulatory adaptation and maladaptation to longtime altitude exposure in Aymaras and Caucasians. (Prog Cardiovasc Dis 2010;52:534-539)

Keywords: High altitude; Aymara; Adaptation mechanism; Circulatory adaptation; Pulmonary hypertension

People living at high altitude (HA) are constantly exposed to hypobaric hypoxia due to low ambient partial pressure of oxygen. The resulting alveolar hypoxia affects every step of oxygen transport from the lung to the cellular level, and several adaptation mechanisms are aimed at overcoming this oxygen deficit and maintaining a normal oxygen content in the body.

Some of these adaptation mechanisms are the reason why athletes training for endurance sports prepare for competitions with altitude training and why in general HA dwellers are thought to be capable to perform very strenuous physical activities in hypoxic environments.

The Aymaras of South America are assumed to be direct descendents of ancient cultures who lived more than 2000 years ago in the same vast regions of the altiplano in what is today Bolivia and Peru at altitudes of up to 4400 m. They have developed specific adaptation patterns to HA during the centuries of isolated dwelling in HA regions (Table 1).

Aymaras have been studied for decades, and their raised hemoglobin levels together with increased lung volumes were thought to represent an ideal HA adaptation pattern. Although recent data suggest that Tibetan and Ethiopian HA adaptation patterns may be even more favorable,[1,2] the Andean pattern is still of great interest because, in many respects, it mimics the adaptation pattern seen in disease states associated with chronic hypoxemia in lowland residents of the Western hemisphere.

Adaptation to HA

Healthy HA dwellers and patients with diseases affecting the oxygen uptake develop characteristic anatomical and physiologic changes in their heart and circulation in response to lack of oxygen. The main features are arterial hypoxemia, increased pulmonary artery pressure, and pulmonary vascular remodeling causing right ventricular hypertrophy, stimulation of nitric

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Abbreviations and Acronyms
CMS = chronic mountain sickness
HA = high altitude
NO = nitric oxide

oxide (NO) synthesis, sympathetic activation, increased ventilation, and erythrocytosis.

Pulmonary vasoconstriction

Pulmonary arterial vasoconstriction is a hallmark of the adaptation to hypoxia. It occurs very rapidly after exposure to hypoxia and is intended to reduce blood flow through poorly ventilated alveoli. When self-limited, this vasoconstriction helps to match alveolar perfusion to ventilation. It thereby decreases the shunt effect and attenuates systemic hypoxemia. When exaggerated, however, hypoxic pulmonary vasoconstriction may have detrimental consequences, such as exaggerated pulmonary hypertension, right ventricular hypertrophy, right heart failure, and pulmonary edema—diseases associated with very high morbidity and mortality.[3]

Effects of altitude and hypoxemia on pulmonary artery pressure

There exists a direct linear relationship between altitude and pulmonary artery pressure, whereas there exists an inverse relationship between arterial oxygen saturation and pulmonary artery pressure.[4] Deviations from this linear relationship between altitude and pulmonary artery pressure have led to the concept that some HA population may be better protected from altitude-induced pulmonary hypertension than others.[4,5] HA residents of purely European ancestry who are therefore presumably less protected can be studied in Leadville, Co, at 3100 m. This population has been studied for decades, and already in 1962, Vogel et al[6] reported increased invasively measured mean pulmonary artery pressure at rest and during exercise with mean resting values of 25 mm Hg in 28 adolescent long-term residents from this town. In the Andes, the comparable pulmonary arterial hypertension of HA residents was observed in populations living at much higher altitudes than the people from Leadville. In Morococha, a small town in Peru located at 4540 m, invasively measured mean pulmonary artery pressure at rest was 29 ± 10 mm Hg in longtime residents.[7] In line with this latter observation, we found in a recent study from La Paz, Bolivia, which at 3600 m is 1000 m lower than Morococha but still 500 m above the level of Leadville, that there are no signs of pulmonary hypertension in healthy Aymara residents using echocardiographic estimations of pulmonary artery pressure.[8]

Table 1
Adaptation patterns in Aymara and Caucasians during chronic high altitude exposure

	Aymara	Caucasian
Pulmonary arterial hypertension	+	++
Pulmonary vascular remodelling	+	+
Alveolar to arterial ΔO_2	−	+
Hypoxic ventilatory response	−	+
Arterial hypoxemia	+	+
Erythrocytosis	+	+

Pulmonary artery pressure during exercise

Measurements of pulmonary artery pressure at rest may very imperfectly reflect what is happening during daily activity in HA dwellers. It is known that pulmonary artery pressure increases during exercise even at sea level. The increased oxygen demand during exercise at HA is expected to trigger additional changes in the cardiopulmonary system. In line with this concept, invasive studies in a few subjects reported marked pulmonary hypertension during exercise at HA.[6,7]

In a recent study, we compared pulmonary artery pressure response to light exercise in patients with chronic mountain sickness (CMS), a group characterized by modest pulmonary hypertension at rest, and in control subjects at 3600 m. The modest albeit significant difference of the systolic right ventricular to right atrial pressure gradient between patients with CMS and controls at rest (30.3 ± 8.0 vs 25.4 ± 4.5 mm Hg; $P = .002$) became more than 3 times larger during mild bicycle exercise (56.4 ± 19.0 vs 39.8 ± 8.0 mm Hg; $P < .0001$; Fig. 1).[9] These findings demonstrate how at HA, measurements at rest in patients with mild pulmonary hypertension dramatically underestimate pulmonary artery pressure during daily activity. Most importantly, measurements at

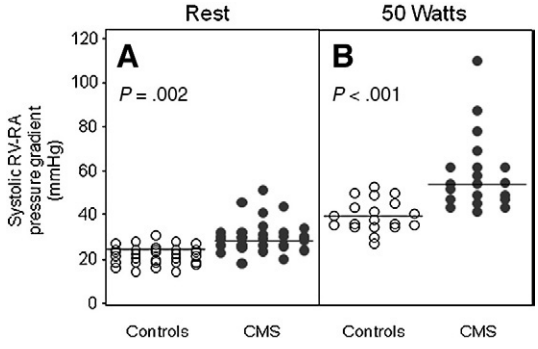

Fig. 1. Systolic right ventricular to right atrial pressure gradient at rest (panel A) and during mild bicycle exercise at 50 W (panel B) in patients with CMS and control subjects at 3600 m. Horizontal bars indicate mean values. Data was derived from Stuber et al.[9]