# Effects of Exercise on Plasma Erythropoietin in Natives Living Permanently at High Altitude

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## Introduction

The effects of inspiratory hypoxia on the erythropoietin (EPO) system decisively depend on the duration of the exposure to the hypoxic environment. Whereas a stay of some hours in a hypobaric chamber leads to markedly increased serum [EPO] (Eckardt et al. 1989), it could be demonstrated by Milledge and Cotes (1985) that members of a Himalaya expedition had, after a rapid increase in EPO values, presented decreasing EPO values during the second half of their altitude exposure. Furthermore, Winslow et al. (1989) showed low EPO concentrations in the blood of high-altitude natives from Nepal and Chile, which are similar to those of subjects living at sea level. The reasons for the adaptation of the EPO response to chronic hypoxia are not completely understood. It may only in part be attributed to other adaptive processes, e.g., increased hemoglobin concentration [Hb] or lower pH values.

As a physiological stimulus, the higher oxygen demand and the suspected systemic hypoxia during heavy exercise are assumed to increase renal EPO production (Galbo 1983). This hypothesis seemed to be proved in the case of long-lasting skiing competitions, when the erythropoietic activity of the plasma was increased (Vedovato et al. 1988). But all these studies used bioassay, which not only include the effects of erythropoietin, but also of other erythropoiesis-stimulating factors. In recent years it has been demonstrated by Berglund et al. (1988) and our group (Schmidt et al. 1990b, 1991), that short-lasting bouts of maximal exercise and long-lasting bouts of submaximal exercise had no direct influence on the plasma EPO level. Moreover, exercise under acute hypoxic conditions corresponding to 3700 m did not exert any additional effect to the isolated hypoxic influence (Schmidt et al. 1991).

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The aim of this study therefore was to investigate the resting EPO levels of natives living at high altitude and to evaluate whether maximal or submaximal types of exercise have any effect on these subjects. If exercise had no stimulating effects on the EPO system under chronic hypoxic conditions, the hypothesis of a systemic (renal) hypoxia during exercise (Galbo 1983) could be rejected.

## Methods

### *Subjects and Protocol*

The experiments were performed with eight subjects in the laboratories of the Bolivian high-altitude institute (IBBA) situated at 3700 m in the city of La Paz.

Seven of the subjects had spent their whole life at the Altiplano between 3700 m and 4100 m. Only one subject was born at 2850 m, but he had lived at 4100 m more than 20 years. All subjects performed a vita maxima test on a cycle ergometer (Monark, Sweden) beginning with 3-min warm-up at 30 w with the work load increased by 15 w every minute until exhaustion. Two weeks after the maximal exercise all subjects performed a 60-min submaximal ergometer test at 60% of their maximal work capacity. Cubital venous blood samples were taken before, during, and up to 48 h after both trials. For determination of the acid base status arterialized samples from an ear lobe were taken before and at the end of both exercise tests.

### *Measurements*

During the tests the expired air was collected in a Douglas bag system. The volume of the bags was determined by a spirometer (Tissaut, France) and the oxygen and $CO_2$ contents were measured by the oxygen analyser Servomex 570 A (UK) and the Capnograph Mark III (Gould Godart, Netherlands).

With exception of erythropoietin all parameters were determined in the laboratories of IBBA at La Paz. The hormone samples were transported in dry ice via airplane within 24 h from La Paz to the laboratories at Hannover, Germany.

[EPO] was determined in serum of the blood samples by a radioimmunoassay as previously described (Eckardt et al. 1988). The assay is based on a rabbit antiserum against pure recombinant human EPO and $^{125}$I-labelled recombinant human EPO (Amersham International, Amersham, UK), used as tracer.

The following parameters were measured in heparinized blood (20 mU Liquemin /10 ml):

- [Hb] by the cyanmethemoglobin method (test kit 3317, Merck, FRG)
- Hematocrit (Hct) value by microhematocrit centrifugation at 20 900 g