# Sleep Apneas in High Altitude Residents (3,800 m)

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**Abstract**

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The question is: to what extent periodic breathing usually observed in translocated subjects at high altitude affects normal and polycythemic residents of high altitude?

Standard sleep parameters, chest wall movements, temperature of ventilated gas and arterial $O_2$ saturation ($SaO_2$) were continuously recorded in 7 normal highlanders (mean hematocrit: 51%) and 14 polycythemic highlanders (mean hematocrit: 68%) during one night in La Paz, 3,850 m, Bolivia. The patterns of breathing instability were analysed by two ways: measuring duration of apneas and counting all the oscillations of $SaO_2$ greater than 1%. Normal and polycythemic highlanders displayed a wide intersubject variability with regard to breathing instability, hence no significant difference in the total number of apneas and oscillations of $SaO_2$ could be evidenced between the 2 groups. However, the longest apneas and the highest number of oscillations of $SaO_2$ were found in the polycythemic highlanders.

**Key words**

Ventilation during sleep, periodic breathing, high altitude natives

## Introduction

Periodic breathing is characterized by repetitive cyclic variations in minute ventilation such that periods of hyperpnea alternate with periods of hypopnea or apnea on a fairly predictable basis (4). This breathing pattern is observed very often during sleep, over long periods of time, in lowlanders translocated at high altitude (1, 6, 9). This periodic breathing induces very regular oscillations in arterial $O_2$ saturation ($SaO_2$). This study was designed to answer the following questions:

Do normal highlanders (HL) display periodic breathing during sleep? What kind of ventilatory instability is observed in subjects with excessive polycythemia who can be considered as overadapted to high altitude?

## Methods:

Six normal HL (41 ± 3 yrs, mean hematocrit (Ht): 50%, range 47–52%) and 14 polycythemic HL were studied during one night in La Paz, Bolivia at 3,800 m. The polycythemic group was divided into two groups according to age so that one group of 9 subjects (39 ± 4 yrs, mean Ht: 67%, range 63–75%) matched the normal group. The other group included polycythemic HL (64 ± 1 yrs, mean Ht: 69%, range 66–77%). Polycythemic HL had normal spirometric data according to age and no clinical signs of right ventricular overload. One polycythemic HL was studied before and 36 hours after bleeding: Ht decreased from 66 to 56%. Sleep studies were conducted at the Instituto Boliviano de Biologia de Altura (IBBA), in a quiet and comfortable room. The protocols were approved by the Scientific Council of the IBBA. Sleep parameters were recorded on a ten-channel polygraph according to standard procedures: 3 EEG leads, electro-oculogram, submental electromyogram. Eye movements were detected by a quartz strain gauge fixed to the eyelid. Chest abdominal wall motions were monitored with circumthoracic and circumabdominal strain gauges and nasal airflow temperature was detected by a thermistance. $SaO_2$ was continuously monitored by an ear oximeter (OHMEDA BIOX 3700) and recorded separately using a potentiometric SEFRAM apparatus with a calibration of 25 cm for 100% $SaO_2$. Sleep recordings were visually scored according to the standard criteria of Rechtschaffen and Kales (7). Instability of breathing was assessed by the number of oscillations of $SaO_2$ greater than 4%. Index of oscillation of $SaO_2$ was calculated as the number of oscillations per hour of total sleep period (TSP). When apneas (respiratory pause exceeding 9 seconds) were present, their number was counted and mean duration measured. $SaO_2$ was averaged every two minutes during TSP and median value of $SaO_2$ during TSP ($SaO_2$ 50% TSP) was calculated. It constitutes a convenient index of nocturnal oxygenation (8). Mean $SaO_2$ was calculated for each sleep stage.

The statistical comparisons were carried out by non-parametric procedures (Chi2, Mann-Whitney test). Correlations were tested using the Spearman rank correlation test.

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**Table 1** Subjects characteristics and nocturnal ventilatory parameters at La Paz, Bolivia (3800 m), in 6 normal and 14 polycythemic permanent residents at high altitude.

| | | | Apneas | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Stage 1 | | Stage 2 | | Stage 3+4 | | REM sleep | | I. O. | $SaO_2$ 50% |
| | Age (yr) | Ht (%) | Nb | sec | Nb | sec | Nb | sec | Nb | sec | | |
| Normal Highlanders | | | | | | | | | | | | |
| FUN. | 27 | 52 | 0 | | 0 | | 0 | | 0 | | 9 | 87.9 |
| GAR. | 41 | 50 | 19 | 15 | 6 | 14 | 0 | | 0 | | 23 | 87.9 |
| QUI. | 41 | 52 | 1 | 10 | 3 | 12 | 0 | | 0 | | 25 | 84.9 |
| PAY. | 42 | 49 | 9 | 12 | 1 | 10 | 0 | | 0 | | 7 | 89.5 |
| APA. | 48 | 47 | 0 | | 0 | | 0 | | 0 | | 0 | 89.5 |
| SOT. | 49 | 51 | 19 | 12 | 2 | 19 | 0 | | 0 | | 11 | 89.8 |
| Mean | 41 | 50 | 8 | 12 | 2 | 14 | | | | | 12 | 88.3 |
| SEM | 3 | 1 | 4 | 1 | 1 | 2 | | | | | 4 | 0.8 |
| Young Poilycythemic Highlanders | | | | | | | | | | | | |
| CRE. | 21 | 66 | 2 | 10 | 0 | | 0 | | 0 | | 0 | 89.1 |
| MAR. | 22 | 69 | 9 | 12 | 15 | 13 | 0 | | 1 | 11 | 22 | 78.9 |
| MIG. | 33 | 75 | 81 | 16 | 30 | 16 | 0 | | 0 | | 18 | 73.6 |
| HAL. | 34 | 64 | 11 | 12 | 2 | 13 | 9 | 13 | 12 | 17 | 33 | 84.5 |
| MIR. | 45 | 63 | 0 | | 1 | 10 | 0 | | 0 | | 7 | 85.2 |
| URU. | 46 | 68 | 10 | 14 | 4 | 10 | 8 | 30 | 3 | 12 | 17 | 80.7 |
| GON. | 48 | 72 | 0 | | 0 | | 0 | | 0 | | 5 | 77.8 |
| RIC. | 50 | 62 | 288 | 16 | 57 | 19 | 0 | | 0 | | 68 | 79.5 |
| MEI. | 53 | 63 | 18 | 14 | 13 | 14 | 0 | | 0 | | 23 | 77.5 |
| Mean | 39 | 67°° | 47 | 13 | 14 | 14 | | | | | 21 | 80.8°° |
| SEM | 4 | 1 | 31 | 1 | 6 | 1 | | | | | 7 | 1.6 |
| Elderly Polycythemic Highlanders | | | | | | | | | | | | |
| ARA. | 60 | 77 | 5 | 16 | 3 | 20 | 0 | | 0 | | 32 | 62.0 |
| DAV. | 63 | 70 | 12 | 15 | 11 | 21 | 1 | 11 | 6 | 15 | 57 | 76.9 |
| BOL. | 65 | 66 | 79 | 19 | 121 | 16 | 23 | 16 | 0 | | 38 | 70.2 |
| ROC. | 65 | 68 | 3 | 13 | 0 | | 0 | | 0 | | 28 | 79.2 |
| ESC. | 69 | 66 | 69 | 37 | 44 | 38 | 0 | | | | 33 | 71.0 |
| Mean | 64** | 69 | 34 | 20 | 36 | 24* | | | | | 38* | 71.9* |
| SEM | 1 | 2 | 17 | 4 | 23 | 5 | | | | | 5 | 3.0 |
| ESC. after bleeding | | | | | | | | | | | | |
| | 69 | 56 | 62 | 36 | 28 | 38 | 0 | | 0 | | 37 | 71.5 |

Hematocrit (Ht), Number (Nb) and mean duration in seconds (sec) of apneas during sleep. Index of $SaO_2$ oscillation in number of oscillations per hour (I. O.), median value of $SaO_2$ in % during TSP ($SaO_2$ 50%).
°°: Different from normal HL ($p < 0.01$); *: different from younger polycythemic HL ($p < 0.05$); **: different from younger polycythemic HL ($p < 0.01$).

## Results

### *Sleep organization*

Sleep organization was roughly similar in normal and polycythemic HL of the same age. In polycythemic HL, the amount of stage 3 and 4 sleep decreased in relation to age.

### *Breathing pattern*

Concerning apneas (Table 1): 4 normal HL out of 6 and 13 polycythemic HL out of 14 displayed apneas. In both groups apneas were of central origin, as far as they can be identified with the methods used. In normal HL no apneas were observed during stage 3 and 4 and REM sleep. In polycythemic HL apneas occurred also during light non-REM sleep. Mean number and duration of apneas did not differ between normal and polycythemic HL of the same age. However, mean duration of apneas in stage 2 sleep was longer in elderly than in younger polycythemic HL ($p < 0.05$). Concerning oscillations of $SaO_2$ (Table 1): There was no difference between normal and polycythemic HL of the same age, but the index of oscillation of $SaO_2$ was higher ($p < 0.05$) in elderly than in younger HL.

### *Nocturnal oxygenation*

$SaO_2$ 50% TSP was lower in polycythemic HL than in normal HL of the same age ($p < 0.01$), and lower in elderly than in younger polycythemic HL ($p < 0.05$). The Figure 1 shows that, in each group, $SaO_2$ decreased when sleep deepened. During REM sleep, $SaO_2$ further decreased in normal and younger polycythemic HL but, surprisingly, it increased in elderly polycythemic HL.

$SaO_2$ 50% TSP was correlated with the total number of apneas ($p < 0.01$), the index of oscillation of $SaO_2$ ($p < 0.001$) and the mean duration of apnea ($p < 0.001$).

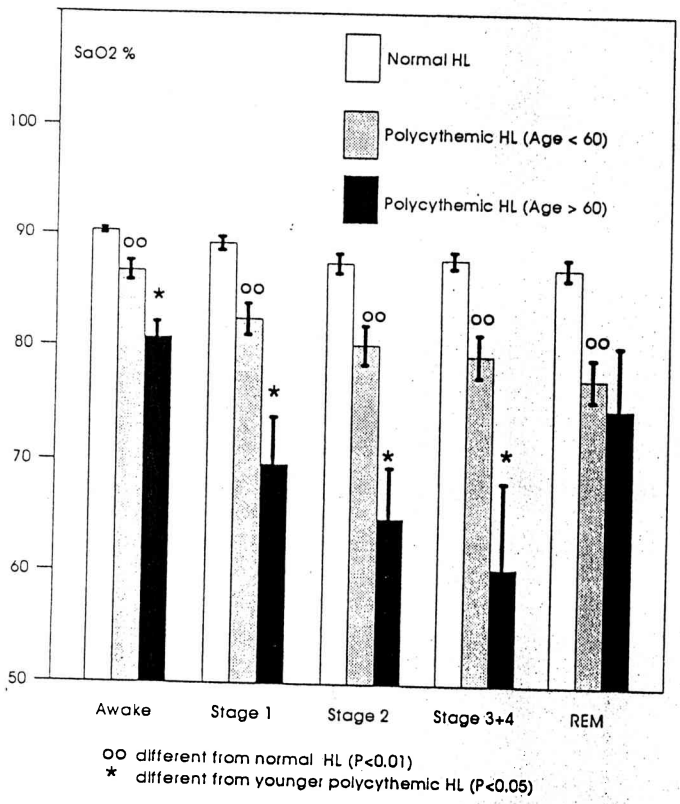


Fig. 1 $SaO_2$ during sleep stages in 3 groups of native highlanders.

### *Effect of bleeding*

In subject ESC. 36 hours after bleeding, Ht decreased from 66 to 56%. The number of apneas, their mean duration, the index of oscillation of $SaO_2$ and $SaO_2$ 50% TSP remained unchanged.

## Discussion

The main result of this study is that the three groups of HL are characterized by a wide inter-subject variability. Instability is however higher in elderly than in younger polycythemic HL as shown by their higher value of oscillation index and mean duration of apnea. This study shows also that nocturnal $SaO_2$ is lower in polycythemic HL than in normal HL of the same age and much lower in elderly polycythemic HL. $SaO_2$ 50% TSP is not improved by bleeding in subject ESC. despite a decrease of Ht from 66% to 56%. Hence, the lower values of $SaO_2$ in polycythemic subjects are likely the consequence of hypoventilation and not of maldistribution of intrapulmonary Ht (2). Figure 1 demonstrates that hypoventilation increases when the subjects (mainly polycythemic) pass from stage 1 to stage 4 sleep. In addition, $SaO_2$ 50% TSP is inversely correlated to the index of oscillation, the number of apneas and the mean duration of apneas. These correlations suggest that the phases of hypopnea during instable ventilation might participate to the nocturnal desaturation.

Which mechanisms can be evoked to explain these observations? The absence of hypoxic ventilatory response explains the hypoventilation in polycythemic subjects. The decrease in $CO_2$ sensitivity with age reported by others at sea level (5) might explain the worsening of hypoventilation as a function of age. Concerning ventilatory patterns, decrease in chemosensitivity should lead, according to the Khoo's model (3), to a higher stability in breathing. Hence, a decrease in the number of apneas and in the index of oscillation should be expected in polycythemic HL and especially in the elderly. That is not the case. Khoo (4) suggests that, when chemosensitivities to $O_2$ and $CO_2$ are low, as in patients with primary alveolar hypoventilation syndrome, the respiratory system is very sensitive to external influences and therefore instability in breathing might occur, depending on other organ systems. In these patients, the cessation of apnea is achieved when blood gases are deteriorated, by restoring the wakefulness respiratory drive to some extent. Then, after some deep breaths, deepening of sleep occurs leading to a further deterioration of blood gases. The reiterated occurrence of such cycles leads to a periodic breathing. Khoo (4) shows that this periodic breathing is characterized by long cycle length and longer apneas. The elderly subjects in this study look like such patients, on account to their decrease in chemosensitivity. Their longer apneas would explain that their instability in breathing increases nocturnal desaturation as shown by the correlations we reported between $SaO_2$ 50% TSP and instability in breathing. In conclusion, lower chemosensitivity in polycythemic HL leads to lower nocturnal $SaO_2$, but the mechanism of instability is more likely related to nervous central factors than to peripheral chemosensitivity.

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