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Adaptation to life at the altitude of the summit of Everest

История восхождений на Эверест показывает, что даже на такой высоте существуют механизмы тканевой адаптации, способные поддерживать жизнь. Есть данные, свидетельствующие о возможности человека выполнять тяжелую физическую работу на экстремальных высотах. 2 августа 2001 года футбольная команда Боливии успешно покорила самую высокую вершину Боливии пик Сайама (6542 м) и сыграла там футбольный матч. Весь период подъема, игры и спуска занял 17 часов. Далее, пациенты с хронической горной болезнью при ступенчатой адаптации к гипоксии могут переносить в течении недели и более условия, аналогичные высоте Эвереста (8848 м). Есть пример, когда женщина, страдающая хронической горной болезнью с "триадой гипоксического синдрома", повышенным гематокритом до 75% и p_{aO_2} 35 мм рт.ст., обладала физиологическими характеристиками, которые убеждают нас в возможности человека жить на любых земных высотах даже с функциональными нарушениями легочной, сердечной, почечной функций. Индивидуальная адаптация к высотам Эвереста возможна, если обеспечить такие специальные условия, как адекватная температура, ландшафт, пища, вода и медленный ступенчатый подъем.

Since the dawn of history, human population has broad range of terrestrial habitats. Favorite places of residence and foundation of great cities have always been adjacent to water. High altitudes were long feared for their debilitating effects on armies, problems with pregnancies and death from unknown causes. Such problems eventually became attributed to hypoxia, the low oxygen tension due to low barometric pressure.

In his remarkable 1916 study "A consideration of the possibility of ascending Mt. Everest", Alexander Kellas [9] proposed that the limit of permanent acclimatization to high altitudes, based on his own experience, was 6096 m. Several decades later most physiologists would argue that it was much lower. In 1998, John West authored the fascinating book entitled: "High Life" [10], offering detailed references to examples of high-altitude adaptation. Charles Houston has worked on the tolerable limits of hypoxia in Operation Everest II [7]. We used his data to plot altitude versus oxygen tension (see below).

Modern transportation facilities, food supplies and housing today permit to live in places never imagined before. In Bolivia and the North of Chile we find active mines above 5000 m. We can see, then, that people have adapted to live in such high places. But the question remains: what is the highest possible altitude of permanent human residence?

Research has focused upon the negative impacts of high altitude life, more in the context of survival than one of environmental concordance. In this paper we present our hypothesis that humans have the intrinsic potential to adapt to life at the altitude of the summit of Mt. Everest. This hypothesis is based on experience and knowledge built over more than three decades in the heart of the world's greatest high-altitude population

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—La Paz, Bolivia and its hinterlands (3100-4100)[1].

STUDIES AND ARGUMENTS IN SUPPORT OF THE HYPOTHESIS

1) LIFE AT HIGH ALTITUDE

Ever since its founding in 1970, the High Altitude Pathology Institute, Clinica IPPA (3510 m), has studied and treated both permanent residents and visitors from around the world. Through our observation of patients with ventilatory or respiratory impairment developed during many years at high altitude [14], we have arrived at the conclusion that even if oxygen supply to the tissues is scarce, life at high altitude remains completely plausible. Such patients are present in significant numbers—depending on the nature of their underlying diseases, most are able to live as well as healthy people at any altitude. Hence, adaptation to life is normal at this altitude even with disease.

2) EXERCISE STUDIES AT HIGH ALTITUDE

Mt. Chacaltaya (5300 m.), site of one of the world's highest ski slopes (one hour from La Paz by car), is visited frequently by both skiers and tourists. We have performed exercise studies there on permanent La Paz residents using a glass pyramid laboratory constructed for this purpose. Exercise tests were first conducted with the subjects at our clinic breathing ambient air at 3510 m. Immediately thereafter we simulated the altitude of Chacaltaya 5300 m with a P_{IO_2} of 78 mmHg in our laboratory´s high altitude hyperoxic hypoxic chamber [14]. The same subjects (n = 17) in Chacaltaya then performed the same exercise protocol. Results demonstrated that S_{aO_2} levels were similar in the simulated Chacaltaya group and in Chacaltaya. However, V_{O_2} and V_{CO_2} values were significantly lower at Chacaltaya than in the simulated altitude. Work capacity was the same during the three different conditions [15].

3) OXYGEN CONSUMPTION IN HIGH ALTITUDE SOCCER PLAYERS

La Paz Residents (n = 17) were compared at IPPA´s facilities (3510 m) to Aymara mountain guides and porters (n = 7) from Sajama town (4300 m). The latter achieved the same exercise with lower oxygen consumption [16]. Subjects then went on to play a soccer match on the summit of Mt. Sajama, Bolivia's highest peak. Players ascended from 4300 to 6542 m. during nine hours, set up the pitch and played twenty minutes per side. Following the match they descended in seven hours [14].

This remarkable feat of hypoxic endurance demonstrates that hypoxia is not necessarily a hindrance to sport. Furthermore, it clearly shows that humans are able to perform maximal work at extreme altitudes. There are, of course, ethnic and individual differences, but with prior adaptation to an intermediate altitude, as in the case of the Aymara players, others can perform as well without intervening generations of adaptation.

4) CHRONIC MOUNTAIN SICKNESS

The disease known as chronic mountain sickness (CMS) is found in residents at high altitude with abnormal pulmonary function (increased shunt, impaired diffusion, uneven ventilation and/or hypoventilation), sequelae of pathological disorders of diverse aetiology. Such impairments result in a sustained (and variable) low oxygen saturation and cyanosis, giving rise to pulmonary hypertension and increased polycythemia as compensatory mechanisms of adaptation to the disease under the chronic hypoxic conditions. The symptoms and signs are often reversible by descent to sea level or by increasing the P_{IO_2} [14]. One will note that there is no direct correlation between hemoglobin and P_{aO_2} because of the multiple factors underlying increased polycythemia (Fig. 1). It can although arise from multiple causes and distress different organs and physiological systems [14, 17]. CMS illustrates how these people, who have increased polycythemia

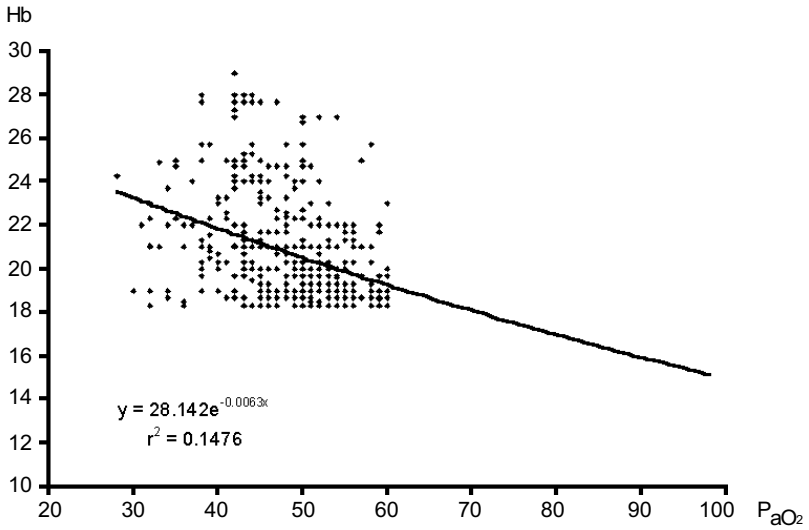

Fig.1. Hemoglobin (Hb) concentration and PaO2 relationship in 480 IPPA patients with increased polycythemia (Hb > 18 gm %). Note that there is no observable correlation and that the logarithmic trend line derived from these points gives an approximate of 16 gm % of Hb for sea level values.

as a prominent secondary manifestation, are able to live at extreme altitude.

Some patients present with very low arterial oxygen tensions which are similar to the alveolar values (35 mmHg) calculated in subjects breathing at the altitude of the summit of Mt Everest (8848 m) [11], the latter being in severe acute conditions (Fig.2). The stress of such acute exposure to high-altitude hypoxia gives rise to high altitude deterioration because, due to the short time of exposure, there is no opportunity for adaptation [14,17 - 20]. CMS patients develop

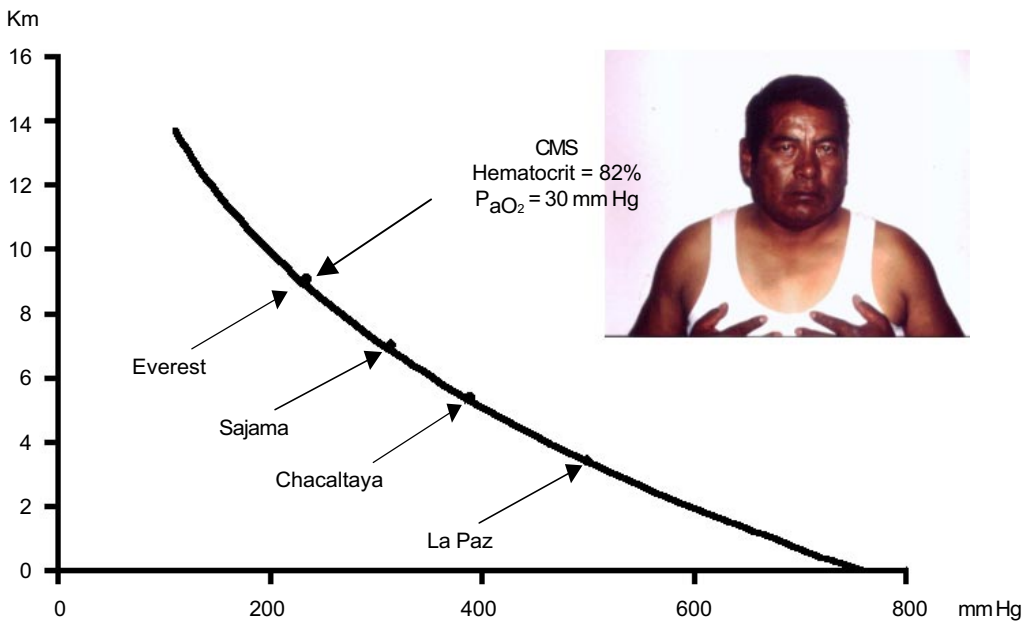

Fig.2. Active CMS patient living in La Paz between 3100 and 4100 m, whose tissue hypoxia is comparable to the values calculated for the summit of Everest.

this physiological adaptation over many years and their increased polycythemia is regularly looked after at IPPA.

5) THE TRIPLE HYPOXIA SYNDROME

We have also described a condition [21,22] which we term "Triple Hypoxia Syndrome" (THS) in which CMS patients, were gradually adapted to hypoxic conditions equivalent to those on the summit of Mount Everest. Such patients often tolerate these attributes for a week or longer. This syndrome, an acute complication in CMS, is actually the superposition of three types of hypoxia: 1) high-altitude; 2) CMS patients with multiple pulmonary aetiology; and, 3) superimposed acute hypoxia, also due to multiple causes such as lung disease and influenza. The third stage of hypoxia is reversible with adequate treatment [22].

An example of triple hypoxia is presented below in Table 1. A CMS female with pulmonary embolism secondary to phlebitis in one of her legs and a hematocrit of 75 % was observed and treated at IPPA [23].

By the seventh day of treatment she had considerably improvement and was able to perform a Bruce protocol exercise test up to the fourth level, a level reached by most CMS patients (normal sedentary residents reach fifth level) In this paper we prefer to use the terms acute tolerance to hypoxia and chronic adaptation [24]. One year later she returned for consultation with a PaO2 of 41 mmHg and a hematocrit of 69 %. She was active doing very well in daily activities, clearly illustrating that hypoxia is not only tolerable by CMS patients with disease at such levels, but that they are adaptable as well.

Treatment data of a 69-year-old female with CMS who presented at IPPA with THS

Parameters	Day 1	Day 7	Normal values for LaPaz3510m
P_{aO_2}, mmHg	35	49	60
P_{aCO_2}, mmHg	34	32	30
PH	7.38	7.38	7.40
Bleod Oxygen saturation, %	68	84	91
Hematocrit, %	75	69	45

Values are shown for day one and following treatment of pulmonary embolism by day seven.

6) OXYGEN CONTENT AND OXYGEN AFFINITY

Increased polycythemia as a compensation of reduced arterial or atmospheric oxygen content is one of the most important mechanisms of adaptation to chronic hypoxia. During acute exposure to high altitude hypoxia, most of the body's energy expenditure is allocated to the pneumodynamic (lungs) and hemodynamic (heart) pumps (We introduced the term hemodynamic pump in order to associate it adequately to the well-known term pneumodynamic. A slide of the presentation on CMS in our web page [4] explains this clearly) [14]. In other words, faster breathing and increasing heart rate and cardiac output have a higher energy cost than that expended in increasing blood hemoglobin. Hyperventilation and increased heart rate and cardiac output are radical responses to acute conditions which enable a person to survive temporarily at extreme altitudes. In normal people, polycythemic adaptation averts such severe energy expenditure by gradually increasing the number of red blood cells to a level where oxygen transport is most beneficial, up to the level when the increased viscosity can occur. (Another important adaptation is an increase in capillary bed density). Hematocrit counts are quite different in healthy high altitude residents and unhealthy people. The latter develop severe polycythemia as the primary mechanism of oxygen transport.

Phlebotomy (apparently beneficial in some patients), is frequently used by physicians to decrease physically and acutely the number of red blood cells in CMS patients at high altitude, is believed to improve the cardio-respiratory system by stimulating ventilation and cardiac output and hence oxygen saturation [2,3]. However, from our point of view, such procedures are ques-

tionable, particularly when there is a proven pulmonary shunt. Phlebotomy results in compensation loss in the patient's organism. As noted above, this is at a great expense of energy resulting once again in system imbalance.

What about increased oxygen affinity? According to some authors [1,8,12], this is another important mechanisms facilitating the capture of oxygen by hemoglobin. Changes in oxygen affinity are the significant mechanism of adaptation, but it is cyclical and constantly fluctuating throughout the circulatory system. However, increased oxygen affinity is not completely understood if it pertains only to change in the molecular aspects of hemoglobin or other factors, which participate in this supposedly beneficial change as described in humans and animals living at high altitude [4 - 6]. More important is the combination of hemoglobin with oxygen that is directly and fundamentally related to the difference in oxygen tension which is the relevant factor to be considered.

Our hypothesis regarding adaptation to extreme altitudes is based primarily on the observation that tissues can continue to capture oxygen at a very low pressure gradient. It is evident that tissue cells have the same affinity to oxygen as hemoglobin, with the difference that tissue oxygen can be used immediately in the metabolic chain.

Cells and other microorganisms are able to utilize oxygen as long as there exists a tension gradient between the environment and the cell structure. Yeast, as a comparative example, will consume oxygen until the level of oxygen tension is 0 mmHg. Only 1 mmHg of pressure gradient is sufficient to sustain life at the tissue level at 37 degrees C. Under these conditions life is possible at such extreme high altitudes as Mt. Everest.

CONCLUSIONS

Centuries have shown us that as far as knowledge and technologies improve, humans are able to surmount challenges previously considered impossible. Less than forty years ago, some scientists believed that prolonged human occupation of altitudes over 3000 meters was impossible. (In fact, this remains a belief among those for whom comfort is the main objective in life). However, such perspectives fail to consider the growing evidence that humans (and animals) have an extraordinary adaptive capacity to survive in the

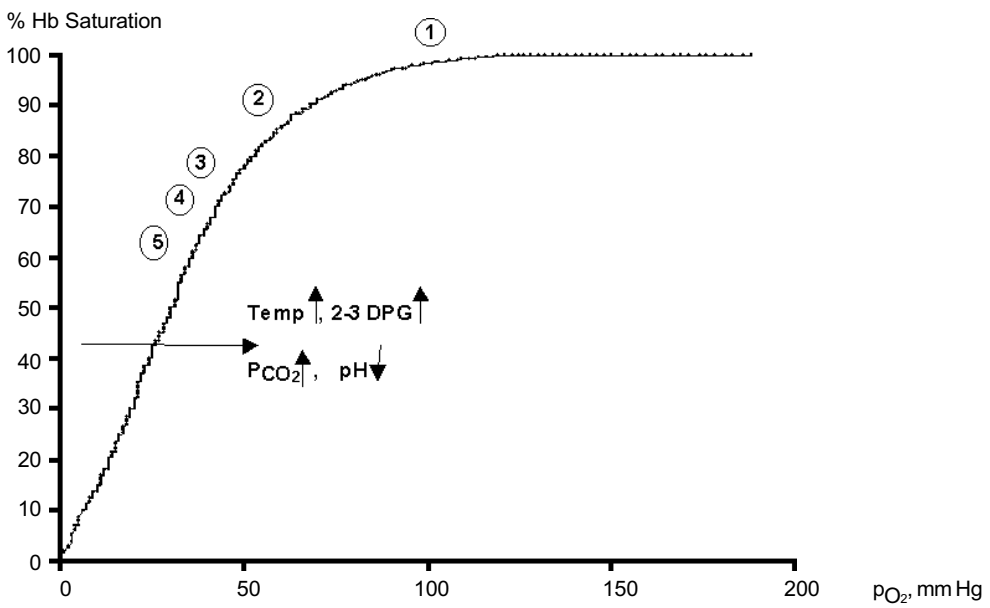

Fig. 3. The oxygen dissociation curve depicting oxygen saturation levels at different altitudes. Sea Level. 2) The city of La Paz 3510 m. 3) Chacaltaya 5200 m. 4) Mt. Sajama 6542 m and 5) Mt. Everest 8848 m. This figure suggested the current hypothesis.

most difficult environments presented on the planet.

From the 19th century it was claimed that Mt. Everest was impossible to climb, through Mallory´s inconclusive effort to the ultimate oxygen-assisted success of Norgay and Hillary (and later Messner and Habeler´s oxygen-less ascent), demonstrated hundreds of times that humans have the physiological capacity to ascend the highest point of the Farth. Careful preparation of the expeditions, experience, persistence and extraordinary stamina allowed Sir Edmund Hillary and Tensing Norgay to stand on the top of the mountain—and such is the approach of those who have followed. But the remarkable conclusion to be drawn from the history of such feats, combined with our current knowledge of the potentialities of human physiology, is that not only humans can ascend to such altitudes, but that they can dwell there, as well.

Human excursions to the highest realms of the planet, under acute conditions without complete adaptation and with imminent risk of death, demonstrate that sufficient mechanisms of tissue oxygenation are present to warrant such radical conclusions as prolonged habitation at these same extreme altitudes.

We have noted that in severe CMS and in the example of the woman with CMS and triple hypoxia syndrome, patients continue to arrive *ambulatory* at IPPA for consultation with a p_{aO_2} of around 35 mmHg. Such extreme hypoxic states can be sustained over several weeks, if not treated promptly. These low p_{aO_2} values are comparable to those estimated for humans at the summit of Mt. Everest [13]. Increased polycythemia is related not only to the severity of respiratory insufficiency— other factors play a role, as many researchers pointed out at the 4th World Congress on Mountain Medicine and Physiology Arica, Chile 2000 [14].

If we acknowledge that individuals with advanced pathological lesions are able to adapt to such hypoxic conditions as shown above, normal people should be able to do so even more easily (with the qualification that there are different individual and ethnic capacities). Furthermore, when a patient with CMS has a low p_{aO_2}, it is as if he or she were actually living at a higher altitude. In order to better illustrate this, we present an adapted graph plotting p_{aO} at different altitudes to depict at what relative altitude CMS patients are living (Fig. 4).

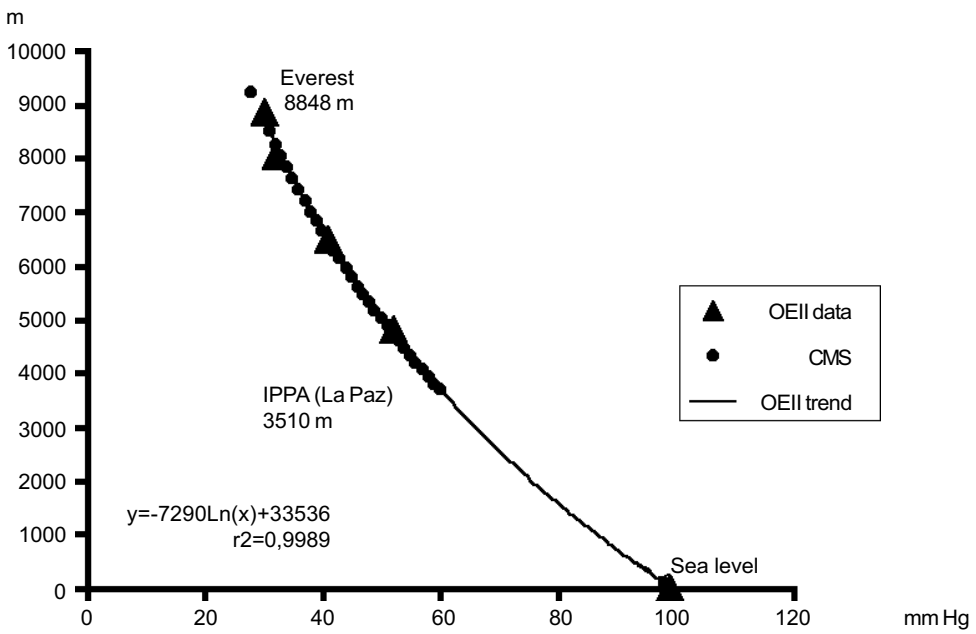

Fig.4. Curve calculated from data by Houston of Operation Everest II (OEII) and applied to plot the relative altitude of CMS patients living in the city of La Paz and El Alto (3100-4100 m) whose p_{aO_2} were below the normal present at 3500 m.

Thus, the forgoing observations have led to the formulation of our hypothesis that human beings can adapt to the altitude and hypoxic conditions found at the summit of Mt. Everest. Such adaptation, of course, is predicated upon adequate protection from the cold, appropriate shelter and proper nutrition for such an environment. Furthermore, our hypothesis stipulates gradual exposure to increased hypoxia over extended periods at intermediate altitudes, though within an individual's lifetime. We can summerize that, prolonged human occupation is possible at such extreme altitudes as Mt. Everest. If history is any guide, it may be inevitable, as well.

Hematological adaptation to high altitude conserves energy expenditure of the pneumodynamic and hemodynamic pumps which work harder at the beginning of acute exposure to hypoxia (such as happens during exercise and after phlebotomy), in the interim of adaptation at the tissue level. The first, then, is an acute phase and the other is a chronic phase.

Of course, we are not suggesting that colonies could be established on the summit of Mt Everest. But we are convinced that the physiological attributes of humans allow for such possibility of adaptation to extreme hypoxia. Life is possible anywhere on this planet, providing adequate nutrition and housing, and enough time is allowed for gradual adaptation. This knowledge permits us to understand the mechanisms of adaptation to tissue hypoxia in such a manner that may someday be applicable and beneficial to habitation of such adverse environments.

In this paper we have tried to explain the foundations of our hypothesis that humans have the capacity to adapt to life on the summit of Mt Everest in one generation. If there is no first generation in a new environment we cannot expect that other generations will follow. The latter affirmation suggests that humans are already genetically prepared for life in the highest point of the planet—although not every single human being. Some will be genetically incompatible or incapable, as for example those suffering pulmonary fibrosis or Down's syndrome or thousands of other genetic variations in people living at sea level which are not conducive to high altitude adaptation.

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Please see our PowerPoint presentation on the IPPA website: http://www.high-altitude.org and [14].

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[1] It is estimated that more than five million Bolivians (two-thirds of the total population) live above 2000 m.
[2] Please see our PowerPoint presentation on the IPPA website: http://www.high-altitude.org and [4].