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26. Facts that Prove that Adaptation to Life at Extreme Altitude (8848 m) is Possible

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Abstract

With adequate and gradual adaptation, life is possible even at the hypoxic levels of the summit of Mt. Everest. We describe some further examples that provide proof of such a statement: 1) Life at high altitude in the city of La Paz between 3100 and 4100 m where people sustain variable degrees of tissue hypoxia having a very low arterial oxygen tension (PaO2 = 37 mmHg) due to respiratory and/or cardiac disease. 2) It is possible to perform maximal work at extreme altitudes, as evidenced by a soccer match played at 6542 meters, on the summit of Mount Sajama. 3) Severe high altitude pulmonary edema (HAPE) occurred in a rugby player within 72 hours at 3600 m (PaO2 of 27 mmHg and a SaO2 of 45 %) upon arrival from Portugal. 4) In the Triple Hypoxia Syndrome (THS) where Chronic Mountain Sickness (CMS) polyerythrocythemic patients with gradual adaptation to hypoxia, with a high hematocrit can occasionally tolerate a PaO2 of 30 mmHg, for a week or longer, a severe hypoxic condition similar to that on the summit of Mount Everest. 5) Human fetus under normal conditions develop at oxygen tension values equal to the altitude of Mount Everest until delivery (PaO2 = 28 mmHg). They are naturally capable of living in hypoxic enviromental conditions present on our planet.

Consequently, normal subjects with full capacity for adaptation will show that life is possible at any existing altitude on planet Earth, provided that the following conditions are met: adequate environmental temperatures, lodging, food, slow and progressive adaptation. This seems possible in only one generation, as the human organism is provided with the adequate compensation mechanisms thereby acquiring the capacity for reproduction on site.

Keywords: Pulmonary edema, polyerythrocythemia, hematocrit, habitat and acclimatization

Introduction

Based on the observation of man's highest habitats, 5000 m above sea level is considered the highest altitude man can adapt to. Likewise, it is well known that acute exposure of humans to this altitude and above, without any kind of adaptation for tissue oxygenation is not possible.

Short permanence of humans, under acute conditions, with partial and incomplete adaptation with eminent risk of death demonstrate that even at the highest places of the planet Earth, enough mechanisms of tissue oxygenation are still present. The only objective of the ascent is the conquest of

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the summit, even for just a few minutes, demonstrating the extraordinary physical capacity of the human being. This is done even under adverse climatic conditions like extreme cold and storms.

As knowledge and technology improve, man is able to accomplish the most difficult challenges previously considered impossible. The conquest of the summit of Mt. Everest (8848 m) the highest point of the planet, for example, was originally thought to be impossible. Careful preparation of the expeditions, experience, persistence and extraordinary stamina allowed Sir Edmund Hillary and Tensing to stand on top of the mountain. Up to the year 2006, hundreds have reached such extreme altitude, and after Messner and Habeler, some of them without supplementary oxygen. But the question remains: what is the highest possible point of permanent residence?

In the study entitled: "A consideration of the Possibility of Ascending Mt. Everest" Kellas proposes that the "limits of permanent acclimatization to high altitudes", based on his own experience was 6096 m (1). Several decades later most physiologists believed it was much lower but in the north of Chile, the Aucanquilcha mine is at 5950 m.

West, as a distinguished medical historian and scientist who participated actively in high altitude research, is the author of the fascinating book entitled: "High Life" (2). In it, methodic references can be found. He and Houston (3) have also worked on the tolerable limits of hypoxia [West, 1988 #8863]. Roads, transportation facilities, food supplies and improved housing facilities permit life in places never imagined before.

The hypothesis: "man can adapt to the altitude of the summit of Mt. Everest", was born based on experience gained during over 36 years. Ever since its creation, in 1970, the High Altitude Pathology Institute, Clinica IPPA (3510 m), has studied and treated patients (permanent residents and newcomers) in the cities of La Paz and El Alto (3100 to 4100 m) and the surrounding areas in Bolivia (4). It is estimated that in Bolivia more than 5,000,000 people (2/3 of the total population) live above 2000 m. Additionally, the proposed hypothesis is also based on a study of the history of high life and exponentially growing scientific literature on high altitude around the world.

In this paper, we also address the issue of the hypothesis: is man able to adapt to life on the summit of Mt Everest in only one generation? The later affirmation pretends to show that man is already genetically prepared to handle life at the highest point of our planet.

Studies and Arguments in Support of the Hypothesis

1) Life at High Altitude

The city of La Paz and El Alto (3100 to 4100 m) with over 1 million inhabitants are two metropolises full of activity in all areas of human behavior. In fact, most people born there don't even realize that they are high altitude dwellers. Through our observation of patients with ventilatory or respiratory impairment developed during many years at high altitude (4), we arrived to the conclusion that even if oxygen supply to the tissues is scarce, life is possible. Polyerythrocythemic patients* are present in around 10% of the population living at high altitude in Bolivia. Depending on the nature of the diseases, from which they were treated leaving sequelae, they are able to live as well as healthy people at high altitude. Hence, adaptation to life even with disease is normal at this altitude.

* new terminology explained further down, under Triple Hypoxia Syndrome.

After the acute phase of exposure to hypoxia where the cardiopulmonary system plays the fundamental role, the increase in oxygen content through the increase in the number of red blood cells is one of the most important progressive mechanisms of adaptation to high altitude along with the cellular and molecular changes as the increase in the number of mitochondria demonstrated by many authors (25).

2) Exercise Studies and Oxygen Consumption of Soccer Players who Carried out a Match at 6542 M.

Aymara residents of La Paz in active duties in the Army (n = 17) were compared to mountain guides and Aymara native porters (n = 7), residents of the Sajama town (4300 m) at IPPA (3510 m). The later group achieved the same exercise through lower oxygen consumption. (5) These subjects then went on to play a soccer match at 6542 m on the summit of Sajama. Bolivian Aymara natives performed this on August 2nd 2001, within 24 hours of arrival including ascent and preparation of the field. They climbed from their town at 4300 to 6542 m. in 9 hours, set up a pitch and played 20 minutes per side and returned in 7 hours. All this was carried out in only 16 hours (6). They interrupted their stay at such altitude only due to stormy weather, which is one of the unfavorable environmental factors that mountain climbers have to face, and that frequently frustrate their goals.

Fig. 1. Bolivian Aymara Porters and guides carrying out soccer match on the summit of Mt. Sajama 6542 m.

This remarkable feat and hypoxic endurance demonstration shows that hypoxia is not necessarily a hindrance to sport. Furthermore, it is possible to perform maximal work at extreme altitudes and under acute conditions of adaptation. There are, naturally, differences in ethnic groups and in individuals, but if sea level residents are previously adapted to an intermediate altitude, they can perform as well as the Aymara players, without the need of generations for adaptation.

3) Severe High Altitude Pulmonary Edema and Tolerance to Extreme Hypoxia.

A Portuguese rugby player arrived on a tour to the city of La Paz (3510 m). He felt slightly short of breath and dyspneic, without evident symptomatology of disease. His mental state was lucid and able to carry out a normal conversation at all times. Upon initial consultation a full-blown high altitude pulmonary edema (HAPE) compromising both lungs was observed. His blood gases reported a PaO2 of 27 mmHg, PaCo2 = 36 mmHg, pH = 7.41 and a SaO2 of 45%. He sustained these hypoxic levels during three days, and fully recovered to later continue to play normally at sea level, upon returning home.

4) The Triple Hypoxia Syndrome in Chronic Mountain Sickness

Chronic Mountain Sickness during many years of studies by different authors has been referred to as Polycythemia, Erythremia, Excessive Erythrocytosis, Increased Polycythemia, terms that etiologically do not adequately relate to the multiple causes of the disease. That is why the most precise term seems to be Polyerythrocythemia (Poly = many, Erythros = red cell, Hemia = blood). Up to now, no one was able to show any deformity or change in the molecular structure of red blood cells that would explain the use of the suffix “osis”, a term more suitable for hematological disease. The only objective sign of this disease is the increase in the number of red blood cells.

CMS is fundamentally caused by pulmonary disease of different ethiopathogenesis (7) although it can disturb different organs and systems (9,10). These patients have lower than normal PaO2 for that altitude. Consequently it is inferred that the tissues of these patients are functioning as if they were normal people at higher altitudes. Figure 1 gives the calculated altitude of residence of these CMS patients that are actually living at around 3500 m.

During the “Triple Hypoxia Syndrome” (THS) in CMS with gradual adaptation to hypoxia, severe hypoxic conditions can be tolerated for a week or longer (12, 13). All these patients have very low arterial oxygen tensions which turn out to be similar to the values (PaO2 = 35 mmHg) calculated from subjects breathing at the altitude of the summit of Mt Everest 8848 m (8), but the later under severe acute conditions (Fig. 2). (14, 15) They evolve over many years and their high hematocrit is regularly controlled at their altitude of residence.

This syndrome, an acute complication in CMS, is actually the superposition of 3 hypoxias. The first hypoxia is that of high altitude, the second hypoxia is that of CMS due to multiple ethiopathogenesis but primarily of pulmonary origin. The third hypoxia is an acute state also due to multiple over imposed causes such as lung disease, influenza, and others. This third stage is reversible with adequate treatment of the underlying cause at the same altitude of residence.

As time passed and we gained more experience, we confirmed that tolerance to chronic hypoxia at extreme altitude is possible, as previously expressed (12). Few days before we wrote this paper, we had a long-standing CMS 84-year-old patient, who came in walking for a consultation. He carried out a

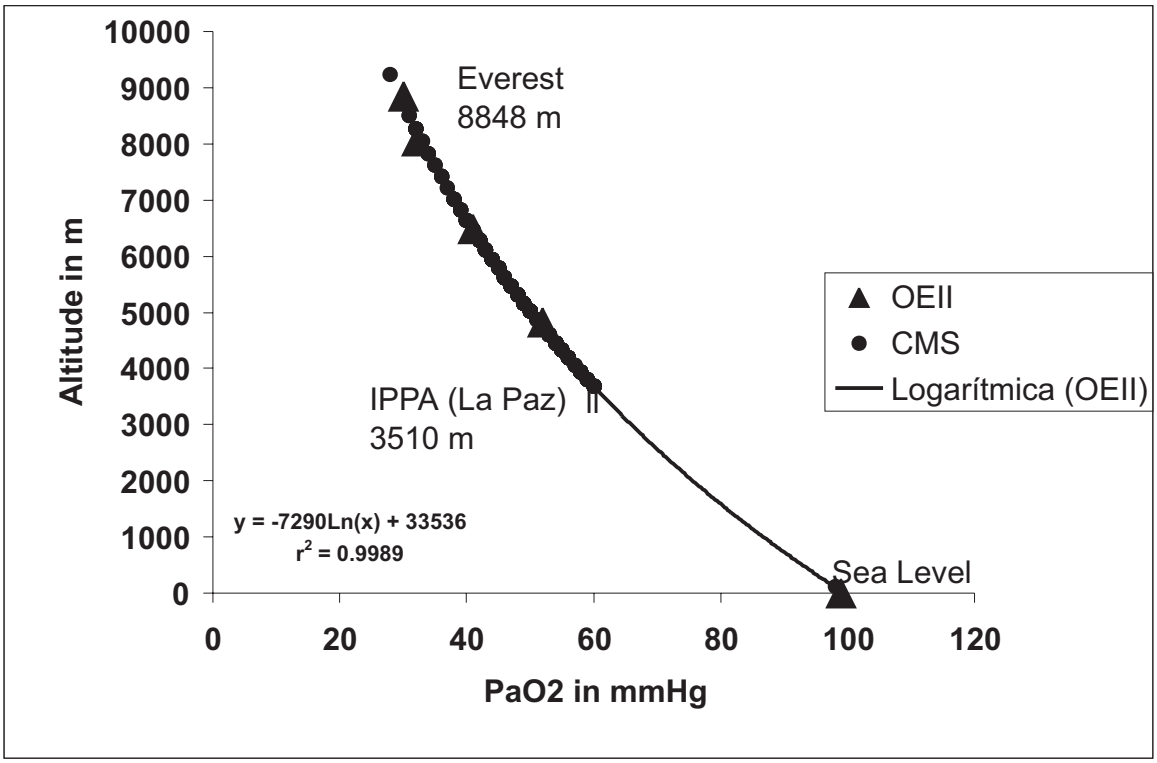

Fig. 2. Curve calculated from data by Houston of Operation Everest II (OEII) and applied to plot the relative altitude of CMS patients living in the city of La Paz and El Alto (3100-4100 m) whose PaO2 were below the normal present at 3500 m.

normal conversation with unquestionable memory. During several weeks his resting blood gases were: PaO2 was 21 mmHg, PaCO2 = 45 mmHg and pH = 7.43, along with a hematocrit of 65%, an extreme case of THS. His FVC was 57% of predicted. Cyanosis and dyspnea were evident along with a very limited exercise capacity. His pulmonary artery hypertension was at 47 mmHg as measured by Doppler Echocardiography. In this patient, the pulse oximeter BCI SensePro was unable to read the SaO2 values. He refused intensive care therapy. Yet he was still attending social activities such as card playing with his friends at home. He had been observed by us 5 years before when his hematocrit was 66%, his PaO2 = 46 mmHg, PaCO2 = 34 mmHg, pH = 7.39 and FVC 66% of predicted. At that time he carried on a "completely normal life".

After a periodical oxygen therapy that lasted several weeks, he died at home, from cardiac insufficiency. This condition showed that his mental capacity was not deteriorated nor impaired at this extreme level of hypoxia. In fact, these values question the current concepts of tolerance to hypoxia. They also contribute an explanation of the existence of oxygen in the lower saturation levels of oxyhemoglobin, that up to now are considered of no use. We are certain that a sea level physician would naturally consider this as impossible.

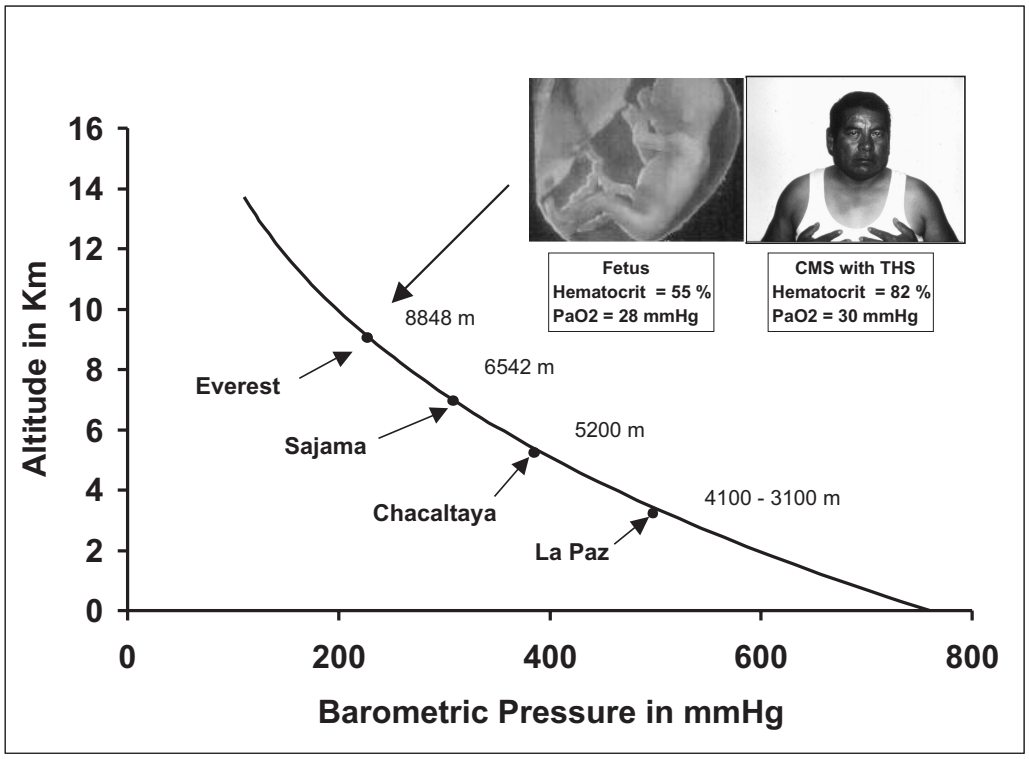

Fig. 3. Active Chronic Mountain Sickness (CMS) with Triple Hypoxia Syndrome (THS) patient living in the city of La Paz between 3100 and 4100 m above sea level, whose tissue hypoxia is comparable to the values calculated for the summit of Mt. Everest showing similar values of PaO2 in a fetus.

5) The Oxygen Levels in the Human Fetus

The fetus lives in optimal conditions in the uterus. He has adequate body temperature, optimal metabolic conditions, and nutrition. His blood gases as reported by as low as 25 mmHg in the ascending aorta (28). In the city of La Paz (3510 m), a normal delivery has been found to give the following umbilical chord values: PaO2 = 28 mmHg, PaCo2 = 29 mmHg and pH = 7.28; PvO2 = 19 mmHg, PvCO2 = 47 mmHg and pH = 7.12.

6) Oxygen Content and Oxygen Affinity

Polyerytrocythemia, that maintains oxygen content, is one of the most important mechanisms of adaptation to chronic hypoxia avoiding a high cost in energy (7).

It is another one of the important mechanisms facilitating the capture of oxygen by hemoglobin. Changes in oxygen affinity are significant mechanisms of adaptation, but are cyclical and constantly fluctuating throughout the circulation. Increased oxygen affinity is not completely defined 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 high altitude animals and man (21, 22, 23). The combination of hemoglobin with oxygen is directly and fundamentally related to the difference in oxygen tension.

The hypothesis is based mainly in the fact that cells at tissue level, can catch oxygen with a very low-pressure difference. It is evident that cells have the same affinity for oxygen as hemoglobin with the difference that it can be used immediately in the metabolic process to produce energy in the ribosome. Hemoglobin captures oxygen in order to gradually release it according to cellular metabolic requirements. Mitochondria are increased in number at high altitude (25).

Conclusions

Short permanence of humans on the highest places of the planet Earth, under acute conditions, without complete adaptation and with eminent risk of death, demonstrates that even at such altitudes, enough mechanisms of tissue oxygenation are still present.

Note, that in severe CMS and in the example of the 84-year-old man with CMS and triple hypoxia syndrome, these walk-in patients can arrive to consultation with a PaO2 of around 21 mmHg. This extreme hypoxic state can be sustained over several weeks if not treated promptly. Such low PaO2 is below that estimated on the summit of Mt. Everest (24). Polyerythrocythemia is not only related to the severity of the respiratory insufficiency, showing that other factors also play a role as many authors point out (7).

These are the facts that gave rise to the hypothesis that animals and human beings can adapt to the altitude and hypoxic conditions similar to that of Mt. Everest (26). If and only if, they avoid the adverse factors such as cold, inadequate housing, inadequate nutrition, associated with altitude and facing exclusively the hypoxia but gradually and after long periods of adaptation to incremental altitudes. Cells and other microorganisms utilize oxygen while there is a small tension gradient between the environment and the cell structure. Yeast cells, for example, consume oxygen until the level of oxygen tension is 0 mmHg. Only 1 mmHg of pressure gradient is enough to sustain life at the tissue level at 37 degrees centigrade. Under these conditions life is possible at such extreme high altitude. Fetal circulation is a physiological remarkable adaptation in order to tolerate low levels of oxygen. A PaO2 of 25 mmHg has been found tolerable in a low cardiac output due to its relatively high fetal hemoglobin concentration (27).

If we accept that sick people with advanced pathological lesions are able to adapt to such hypoxic conditions as shown above, normal people should be able to do that more easily, accepting that there are different capabilities, in different races and groups of people. Furthermore, when a patient with CMS has a low PaO2, it is as if he would actually be living at a higher altitude. In order to show this, a graph plotting the PaO2 at different altitudes was adapted to depict at what relative altitude CMS patients seem to be living (fig. 1).

We are not pretending or suggesting to send people to live on the summit of Mt Everest, of course. But the biological conditions of man and animals allow for the possibility of adaptation to extreme hypoxia. So life is possible anywhere on this planet, provided that adequate nutrition and housing are available, and enough time is allowed for slow adaptation. This knowledge permits us to understand the mechanisms of adaptation to tissue hypoxia. Maybe some day human beings will confront such adverse environmental conditions where this knowledge will be beneficial.

In this paper we explain the foundations of the hypothesis: man is able to adapt to life on the summit of Mt Everest in one generation. Reproduction will be feasible once adaptation is acquired. The first generation will continue increasing the population. The later affirmation pretends to show that man is

already genetically prepared for life on the highest point of planet Earth. But not every single human being, as some will be genetically incompatible or incapable. For example those suffering pulmonary fibrosis or Down's Syndrome or thousands of genetic variations that can be present in people living at sea level and that are incompatible with hypoxic environments

References

1. West, J.B., *Alexander M. Kellas and the physiological challenge of Mt. Everest.* J Appl Physiol, 1987. 63 (1): 3-11.
2. West, J.B., *High Life: A History of High-Altitude Physiology and Medicine*. 1998: American Physiological Society Oxford University Press.
3. Houston, C.S. and A. Cymerman, *Hypoxia: the tolerable limits: Operation Everest II*, in *Hypoxia. The Tolerable Limits*, J.R. Sutton, C.S. Houston, and G. Coates, Editors. 1988, Benchmark Press: Indianapolis, IN. 3-8.
4. Zubieta-Castillo, G. and G.R. Zubieta-Calleja, *www.altitudeclinic.com.* 1996.
5. Zubieta-Calleja, G.R., Zubieta-Castillo, G., Zubieta-Calleja, L., Zubieta, N., *Exercise performance of Bolivian Aymara in 3 conditions: at La Paz 3510 m, breathing a hypoxic mixture simulating Chacaltaya and at Chacaltaya 5200 m. (Abstract).* HAMB, 2002. 3 (1): 114.
6. Zubieta-Castillo, G.R., Zubieta-Calleja, G.R., Zubieta-Calleja L., Zubieta, N., *Bolivian Aymara that played soccer at 6542 m maintain higher oxygen saturation and lower oxygen uptake during maximal exercise (Abstract).* HAMB, 2002. 3 (1): 114.
7. Zubieta-Castillo, G. and G. Zubieta-Calleja, *New Concepts on chronic mountain sickness.* Acta Andina, 1996. 5 : 3-8.
8. West, J.B. and P.D. Wagner, *Predicted gas exchange on the summit of Mt Everest.* Respir Physiol, 1980. 42 : 1-16.
9. Zubieta-Castillo, G. and G.R. Zubieta-Calleja, *Chronic mountain sickness and miners (Spanish).* Revista de la Academia Nacional de Ciencias de Bolivia, 1985. 4 : 109-116.
10. Zubieta-Castillo, G. and G. Zubieta-Calleja, *Pulmonary diseases and chronic mountain sickness (Spanish).* Revista de la Academia Nacional de Ciencias de Bolivia, 1986. 5 : 47-54.
11. Zubieta-Calleja, G.R., Zubieta-Castillo, G., Zubieta-Calleja, L., Zubieta, N., *Exercise performance in chronic mountain sickness (CMS) patients at 3510 m. (Abstract).* HAMB, 2002. 3 (1): 115.
12. Zubieta-Castillo, G. and G. Zubieta-Calleja, *Triple hypoxia syndrome.* Acta Andina, 1996. 5 (1): 15-18.
13. Zubieta-Castillo, G., Zubieta-Calleja, G., *The triple hypoxia syndrome at altitude (Abstract).* Amer Rev Respir Dis, 1988. 137 (4): 509.
14. Zubieta-Castillo, G., Zubieta-Calleja G.R. , Zubieta-Calleja, L., *Exercise performance in a woman with CMS, following triple hypoxia syndrome treatment (Abstract).* HAMB, 2002. 3 (1): 114.
15. Zubieta-Calleja G.R., Z.-C., G., *CMS exercise (Abstract).* 1992.
16. Cruz, J.C., *et al.*, *Phlebotomy improves pulmonary gas exchange in chronic mountain polycythemia.* Respiration, 1979. 38 : 305-313.
17. Dayton, L.M., *et al. Symptomatic and pulmonary response to acute phlebotomy in secondary polycythemia.* Chest, 1975. 68 (6): 785-790.
18. Winslow, R.M., C.C. Monge, and N.J. Statham, *In vivo blood oxygen affinity in high altitude natives (Abstract)*, in *Hypoxia: Man at Altitude*, J.R. Sutton, N.L. Jones, and C.S. Houston, Editors. 1982, Thieme-Stratton: New York, NY. 202.
19. Aste-Salazar, H. and A. Hurtado, *The affinity of hemoglobin for oxygen at sea level and at high altitudes.* Am J Physiol, 1944. 142 : 733-743.

20. Samaja, M., A. Veicsteinas, and P. Cerretelli, *Oxygen affinity of blood in altitude Sherpas.* J Appl Physiol, 1979. 47 : 337-341.
21. Hebbel, R.P., *et al.*, *Hemoglobin oxygen affinity and adaptation to altitude: Evidence for pre-adaptation to altitude in humans with left-shifted oxyhemoglobin dissociation curves.* J Clin Invest, 1977. 60 : 213-228.
22. Eaton, J.W., T.D. Skelton, and E.M. Berger, *Survival at extreme altitude: Protective effect of increased hemoglobin-oxygen affinity.* Science, 1974. 183 : 43-44.
23. Hebbel, R.P., *et al.*, *Human llamas: Adaptation to altitude in subjects with high hemoglobin oxygen affinity.* J Clin Invest, 1978. 62 : 593-600.
24. West, J.B., *Man on the summit of Mount Everest*, in *High Altitude and Man*, J.B. West and S. Lahiri, Editors. 1984, American Physiological Society: Bethesda, MD. 5-18.
25. Lukianova LD. Molecular Mechanisms of tissue hypoxia and organism adaptation. J Fiziol 2003 49: 3; 17-35.
26. Zubieta-Castillo G, Zubieta-Calleja GR, Zubieta-Calleja L, Zubieta-Calleja, N. Adaptation to life at the altitude of the summit of Everest. Fiziol Zh. 2003; 49(3): 110-7.
27. Huikeshoven FJ, Hope ID, Power GG, Gilbert RD, Longo LD. A comparison of sheep and human fetal oxygen delivery systems with use of a mathematical model. Am J Obstet Gynecol. 1985 Feb 5; 151(4): 449-55.
28. Huikeshoven FJ, Hope ID, Power GG, Gilbert RD, Longo LD. Mathematical model of fetal circulation and oxygen delivery. Am J Physiol. 1985 Aug; 249(2 Pt 2): 192-202.