High Altitude Pathophysiology

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High altitude triggers a long list of phenomena in the human organism: tachypnea, migraine, tachycardia, arterial hypertension, dyspnea, dry cough, anorexia, sleep apnea, rest dyspnea, insomnia, nausea, gastrointestinal disorders. When the problem becomes severe, incoordination, high altitude psychosis, thorax pain, hemoptysis, slight fever, stertors, changes in behavior (indifference), uncontrollable migraine, central vomiting, laxity and ataxia, failure in keeping a straight line when walking, progressive blurry vision, papilledema, cerebral and pulmonary edema, vein thrombosis, retinal hemorrhage, may lead to death.

The purpose of this presentation is to underscore some aspects of this phenomenon to make its interpretation easier and to have some elements that would enable judicious action.

The environment not only influences the organism or interacts with it, it constitutes it. Water, oxygen, nutrients and atmospheric conditions like humidity, temperature and light affect each organism and/or gradually become part of each individual.

Although there are places with appropriate environmental characteristics for human beings, man can inhabit others, considered extreme, like deserts, swamps, the poles and mountains. Sudden transportation to any of them could bring about serious consequences, even death. Changes should be gradual so as to permit the necessary adaptation that would enable survival and continued living in the new habitat.

Altitude is one of these environmental factors: when somebody from the low lands goes to high levels there are decompensations that are further increased by sports practice.

These phenomena have always been a motive of preoccupation from Icarus to the present era when they began to be dealt with in depth with Bert and his book: “La pression barometrique” (1878) and Viault’s works in the Peruvian Andes (1890). And if we speak of altitude and physical activity, we should remember that Angelo Mosso already worked in a laboratory at 4500 m in Monte Rosa in 1894 (Regina Margherita shelter of the Italian Alpine Club).

In a nutshell, the problem lies in the interaction between environment and organism. The main factor is the atmosphere. Although it is 800 km. thick, about the distance between Tucumán and Rosario, life occurs in a thin 10 km. layer called troposphere. Next comes the stratosphere where life is not possible.

The atmosphere has a weight measured as atmospheric pressure which is the partial pressure of its gases on a surface unit. The reference is taken at sea level where the pressure is equal to 1 atmosphere or 760 mm of mercury. This is optimal pressure to achieve a good blood oxygenation. Oxygen constitutes 20% of the air and it participates in 20% of that atmospheric pressure which is kept in all the atmosphere, regardless of altitude, even when absolute and partial pressures diminish with increasing height.

Normally 500 cc enter the body in each inhalation. Before reaching the alveoli, this amount is filtered, warmed and humidified. Both humidification and the mixture with residual air, (300 cc) stabilize alveolar air composition and O2 partial pressure. In the alveoli there is vapor which also has pressure. The relation partial O2 pressure/oxygenation is not direct because hemoglobin allows a good intake even when there is an important decrease of PO2 (Fig. 1).
As altitude increases

- Atmospheric pressure diminishes not only because there is less atmosphere above, but because air density is lower, a fact mainly due to gravity decrease (in a proportion equal to the square of the distance to the Earth’s center, i.e. 0.003 m/s every 1000 m of ascent). This progressively separates atmospheric molecules [1].
- Air pressure decrease means partial pressure decrease of each air component, among them oxygen, the one we most appreciate.
- Air humidity also goes down.
- Sun radiation increases at a rate of 2 to 4% every 100 m, which is further augmented by snow.
- Temperature decreases, in spite of the Icarus myth, at a rate of 1º C every 150-200 m, because air expansion keeps molecules further apart from each other.

If we analyze these values we will see that at sea level atmospheric pressure is 760 mm Hg, with a partial O2 pressure of 149 (107 in the alveolus). At 3000 m, the values are 526 y 70 respectively, a point where hemoglobin O2 intake begins a sharp decline.

<table>
<thead>
<tr>
<th>Altitude (m)</th>
<th>Atmospheric pressure</th>
<th>Atmospheric PPO2</th>
<th>Alveolar PPO2</th>
<th>temp</th>
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<tr>
<td>4000</td>
<td>462</td>
<td>87</td>
<td>62</td>
<td>-11</td>
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</tbody>
</table>

Table 1

Temperature decrease is such, that if it is 15º at sea level, it will be -4º at 3000 m.

The blood oxygenation mechanism, the disassociation curve of hemoglobin, and how blood avidly absorbs O2 in the lung to release it in the tissues are interesting processes.

In sports, altitude is considered low up to 1000 meters, medium up to 2000, high until 5500 and very high [2] beyond this figure. Limit altitude is 3.000 m, beyond which, always depending on individual responses, the first symptoms appear.

Hypoxemia
At high altitude, the outstanding phenomenon is low air pressure and density that causes lower O₂ partial pressure in the air and alveoli: oxygenation decreases and HYPOXEMIA appears (Fig. 2)

The consequences of a circulating O₂ decrease are basically 3:

1. The subsequent chemical receptor stimulation
2. Stress
3. Na y K pump performance changes

These 3 responses of the organism should be remembered, since consequences and symptoms may be inferred through them (Fig. 3).

Even though the mechanism of stress is exceedingly well known and accepted, we insist on it because
it is the starting point: hypoxemia affects chemical receptors producing noticeable changes that trigger the secretion of stress catecholamines.

Athletes are very aware of the way their bodies function and immediately notice an increase in their heart and breathing rates which they immediately associate with fatigue. Hence, the importance of psychological preparation to diminish fear of performing at high altitude because this apprehension may have a negative impact by increasing stress and its consequences.

Professor Bernardo Lozada [3] used to say that athletes react as if they had been administered an adrenaline shot. Many of the subsequent symptoms may thus be explained:

- Reflex hyperventilation to compensate
- Heart rate, volume/min and arterial pressure increase through adrenergic effect to better distribute oxygenated blood. Hypertension will be compensated by blood vessel dilatation although individual responses may be different.
- Adrenaline produces energy metabolism changes; many of which are directly related with exercise.
- There is also blood redistribution.
- And pulmonary hypertension, one of the reactions linked to the cardiovascular system (Fig. 4).

Pulmonary hypertension perceived in the ECG resembles that of the acute pulmonary heart: electric axis deviation to the right, V1 and AVR positive, T is inverted from V1 to V5 and a there is a Q wave in D3 similar to that of a diaphragmatic infarction [4].

The thorax X ray shows a normal cardiac outline, but there is a pulmonary artery enlargement and some parahilar cotton-like lung shadows to the right. There may be small pleural effusions.

These symptoms are magnified with physical activity. We should remember that at sea level or at normal altitude, with submaximal effort pulmonary flow increases proportionally to the volume/min rise, but this is compensated by vessel dilatation that diminishes pulmonary resistance. With maximal effort there is a transitory pulmonary hypertension.

When there are high altitud phenomena, to be expected beyond 3000 meters, spontaneous pulmonary hypertension, proportional to effort, appears with individual variations where 15 mm Hg may reach 50, 60 and more than 100.

There is ample bibliography on the subject. Hervé Duplain’s work published in Circulation. 1999;99:1713-1718. 1999 American Heart Association, Inc. is remarkable and it may be read in click here.
Coronary reserve remains normal in healthy persons, even at 4500 m according to Christophe A. Wyss et al. in studies with PET in hypobaric chambers published in *Circulation* 2003;108:1202. The same does not hold true for coronary patients who show a decrease starting at 2500 m. ([http://circ.ahajournals.org/content/vol108/issue10/](http://circ.ahajournals.org/content/vol108/issue10/) may be consulted).

Other symptoms are inferred from chemoreceptor stimulation: reflex hyperventilation increases oxygenation, but it also triggers hypocapnia because of low partial pressure of carbon dioxide which brings about alkalosis and bicarbonates in urine (Fig. 5).

Since altitude also lowers ambient humidity, there is a higher plasma water loss which increases edemas. Hypovolemia with the subsequent cardiac effort favors thrombosis.

In Fig. 6, hypoxia and its effect on the Na and K pump is briefly described with such consequences of high altitude as edemas, particularly cerebral edema, which may provoke death.
Incoordination, behavior changes (indifference), failure in keeping a straight line when walking, uncontrollable migraine, should be a serious warning since they precede laxity, ataxia and progressive blurry vision. Immediate descent is prescribed before the onset of central vomiting and papilledema.

It should be kept in mind that people who occasionally and brusquely travel to high altitudes may, or may not, have symptoms depending on their personal responses. This happens to tourists who visit La Quiaca (3400 m) or Socompa (6100 m) or those who travel in the Train to the Clouds (4200 m).

The chances that they may have symptoms are increased with physical exertion. Up to 3000 m a sportsman with no pathologies will have bearable signs and symptoms or no problems at all. At higher altitudes precaution is called for. As a reference, it should be remembered that Bogotá is at 2600 m, Quito at 2800 m and La Paz at 4100 m.

Habitual responses to mountain sickness or puna or apunamiento may result in complications like acute pulmonary edema, cerebral edema and thromboses when the responses are exaggerated. The mere suspicion that the clinical picture may be rotating towards these complications is enough to prescribe immediate descent to prevent a fatal outcome (Fig. 7).
It should be remarked that not all responses to hypoxemia are similar. There may be different clinical pictures with predominance of any of these symptoms.

**Chronology**

The clinical picture requires between 4 and 36 hours to be totally established during which symptoms may become more serious or new ones may appear. The picture starts to be stable at day 3 and they diminish gradually while the organism achieves new adaptations to what it now considers to be a new habitat.

Since symptoms reach a peak on the second or third day of staying at high altitude, many athletes prefer to compete immediately rather than wait to become used to the new environment.

To interpret specific response to sports practice at high altitude, it is necessary to consider:

- Length of stay in the place
- Stimuli or competition length
- Type of event and elements employed

**Length of stay:** the clinical picture is not fully established when competing before 4 hours have elapsed. Between 4 and 36 hours: the picture reaches a peak which gradually decreases between the 3rd and 9th day, after which adaptation begins and is completed 21 days later.

**Competition length:** high altitude effects will be more noticeable in aerobic sports. Weight lifting or throwing use energy previously accumulated in the muscle and there is no oxygen requirement. A prolonged activity, on the other hand, will be influenced by altitude. Hence, tactical changes should be considered in team sports.

**Type of event:** throwing, lifting or jumping will be favored by less gravity and air resistance since air is thinner.

**Adaptations:**

- After 3 to 6 days cardiac output decreases, both at rest and submaximal exercise due to a fall in systolic volume and cardiac frequency. This is partially due to adrenergic receptor adaptation and psychological acceptance of the new situation.
- 2,3-DPG remains high during the high altitude stay with the corresponding deviation to the right of the hemoglobin dissociation curve, O2 thus being freely released to the tissues.
- RBC (red blood cell) production increases since the 4th day of exposition. This is due to a
higher production of erythrocytes in the bone marrow which is stimulated by EPO (erythropoietin) (renal hypoxias). A minimum altitude of 1500 m is necessary for this response to take place. It becomes evident at approximately day 20.

- Oxygen transport in blood improves, mitochondrial number and size and oxidative enzymes increase in the tissue myoglobin. There are changes in muscle fibers too: most authors state that their thinning would improve oxygen intake.
- Pulmonary resistance decreases.

The purpose of this account is to understand the high altitude responses of athletes and non athletes through the analysis of environmental conditions and the subsequent hypoxia so that it may be useful for those who are not familiar with the subject. Cardiovascular responses were particularly kept in mind in order to have an ampler treatment of some aspects.

Notas:
1. This is important to interpret some facts observed in sports practice
4. El corazón y la altura: Dr. Gustavo R. Zubieta-Calleja, IPPA, Instituto de Patología en la Altura, La Paz, Bolivia http://www.altitudeclinic.com

Bibliography
- Zubieta-Calleja, G., El corazón y la altura, del Instituto de Patología en la Altura, La Paz, Bolivia, en: http://www.altitudeclinic.com

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