Working over 5,000 m: medical check-up


Key words: High altitude, safety risks, occupational medicine, procedure of ascent, work at high altitude
Parole chiave: Alta quota, rischi per la sicurezza, medicina del lavoro, procedure di ascesa, lavori in alta quota

Abstract

Any work activity performed at elevations over 3,000 m above sea level is considered as work at high altitude. The changing environmental conditions result in an adaptation of the human organism, mainly due to a reduced partial pressure of oxygen in the air and a proportional decrease in barometric pressure.

We carried out a systematic review of the scientific literature in this field so as to develop a health and risk protocol as well as a procedure of ascent for researchers and staff expected to work in a science research lab at an altitude of 5,100 m asl.

We wish to highlight the crucial role that occupational medicine plays in the formulation of a medical protocol used to assess the suitability of staff to work in environments posing high risks to human health, as in this case, and of a protocol of ascent minimizing the risk associated with changes in altitude.

Introduction

Any work activity carried out at over 3,000 m above sea level is defined as “high altitude work”.

The environmental changes associated with these conditions (Table 1) pose a serious threat to human health as they determine physiological changes (adaptations) in the organism affecting the cardio-respiratory system, the acid-base homeostasis and the hematopoietic system.

Such variations, if not under control, entail the risk of developing severe pathologies or the aggravation of pre-existing pathologies.

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Table 1 - Environmental modifications related to changes in altitude

<table>
<thead>
<tr>
<th>Decrease</th>
<th>Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air density</td>
<td>UV and Gamma Rays</td>
</tr>
<tr>
<td>Atmospheric pressure</td>
<td></td>
</tr>
<tr>
<td>Partial pressure of oxygen</td>
<td></td>
</tr>
<tr>
<td>Temperatures and humidity</td>
<td></td>
</tr>
</tbody>
</table>

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Physiological modifications related to changes in altitude

Before going into further details, it is important to note that the concentration of oxygen in the atmosphere is 21% and it remains stable at any altitude whereas atmospheric pressure decreases with increasing altitude, thus influencing the exchange of gases within the alveoli (1).

At sea level, the partial pressure of oxygen in the air, equal to the product between atmospheric pressure (760 mm Hg) and oxygen percentage (21%), is 159 mm Hg; the pressure of O2 in the alveoli (PaO2) is 100 mm Hg; hemoglobin saturation is 95-98%.

Atmospheric pressure decreases as elevation increases and partial pressure of oxygen decreases accordingly; indeed at 2,000 m, PaO2 is only 78 mm Hg (Figure 1).

Despite such important modifications, hemoglobin remains 90% saturated and only slightly decreases until 3,000 m, thus posing no particular problems in terms of high-altitude adaptation. Above this altitude hemoglobin saturation starts decreasing and oxygen exchange from the lungs into the blood is progressively reduced (Figure 2).

This is the reason why over 5,000 m asl it is not possible for humans to stay for long periods (2); indeed, at 5,500 m asl, atmospheric pressure decays exponentially as a result of the Earth’s gravitational force of attraction on the atmosphere which makes that pressure drop to approximately half of the value for sea-level, and hence the following physiological changes can be observed:

1) PaO2 <38 mm Hg;
2) O2 saturation < 75%;
3) Hemoglobin dissociation curve rises steeply.

Cardio-respiratory modifications

To compensate for the effects of hypobaric hypoxia during high-altitude stays, hyperventilation occurs as an initial response of the organism to bring the body into balance (3).

At an altitude of 3,000 m, the alveolar O2 partial pressure falls below 60 mm Hg, resulting in the stimulation of the respiratory system that causes tachypnea. At the same

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Figure 1 – How pressure changes with altitude
time, the increased respiratory rate also determines an increased CO₂ partial pressure and the subsequent inhibition of ventilation. This alternation of conditions contributing to and inhibiting ventilation is the cause of the typical Cheyne-Stokes periodic breathing common at high altitude, in which periods of tachypnea and hyperpnea alternate with periods of apnea, especially at rest (4).

Along with these important respiratory changes, even the cardiovascular system reacts to ensure the adequate supply of oxygen to the tissues. In fact, since oxygen is less efficiently carried along the body at high altitudes because of the decreased pressure of respiratory gases, the heart responds with increased cardiac output (CaO), which is the product of stroke volume (SV) and heart rate (HR). In submaximal works performed at 3,000 m asl, CaO increases by 50% while SV remains unchanged (5). The maximal oxygen consumption (VO₂ max) decreases by about 1% per 100 m over 1,500 m (6). A great variation is found during maximal work at high altitude (4,000 m) with a 72% decline observed in VO₂ max along with the inability of maximum ventilation and maximum CaO to provide the organism with the required amount of oxygen (7). Night work brings changes in the cardiovascular system (8) while a prolonged upright posture may result into professional phlebopathies (9).

The up and down fluctuations of the systemic arterial pressure are due to hypoxia through its dual action resulting in:

1) vasodilation mediated by the release of nitric oxide and HIF1 (hypoxia inducible factor 1);

2) vasoconstriction mediated by an increase in plasma catecholamines.

This leads to a pressure variation in healthy subjects in which decreased, unchanged or increased values can occur while in subjects with mild-to-moderate hypertension, pharmacologically untreated, increased values of arterial pressure are observed due to endothelial dysfunction (10-13).

Modifications of the acid - base and hematopoietic systems

Long-term exposure at high altitude has consequences on these two important systems.

Excess CO₂ induced by hyperventilation is regulated through renal reabsorption of bicarbonate ions and an increased production of intraerythrocyclic 2,3-diphosphoglycerate (2,3-DPG) with a rightward shift of the hemoglobin dissociation curve and favorable effects on O₂ delivery to tissues (14).
Bicarbonate reduction has been shown to decrease the buffering capacity of blood, with a paradoxical limitation of lactic acid production (even if the anaerobic glycolytic pathway is functioning) which appears to be due to the reduced ability of the catecholamines to trigger anaerobic glycolysis (15). Changes in plasma volume take place during the early days at high altitude with a passage of water from the blood compartment to the interstitial and intracellular compartment, and this stimulates an increase in hemoglobin concentration, thus raising hematocrit levels (16). Hypoxia stimulates the formation of red blood cells in the bone marrow thanks to an increased production of erythropoietin, within 15 hours after oxygen levels start decreasing (17).

Furthermore, another point worth considering is that the presence of low-dose ionising radiations (gamma rays) at high altitudes may be associated to a reduction of red and white blood cells (18). Secondary polycythemia is observed in the following weeks, with new hematocrit and hemoglobin values becoming stabilized in about a month and remaining stable for the remainder of the stay at altitude, and disappearing within a month after descent to low altitude.

**Acute Pathologies**

Should the organism fail to respond properly to the above mentioned environmental conditions, specific pathological manifestations will be observed. Over 3,000 m asl the following hypobaropathies are likely to occur:

- acute mountain sickness (AMS);
- high-altitude cerebral edema (HACE);
- high altitude pulmonary edema (HAPE).

**Acute mountain sickness (AMS)**

This pathology, whose etiology and pathogenesis is not clearly understood yet (19, 20), is variable in individuals with headache associated with at least one of the following symptoms, usually beginning 6 to 36 hours after arrival at altitude: anorexia, nausea and vomiting, disturbed sleep and a general feeling of malaise (21).

Indeed, headache at altitudes over 4,500 m has been shown to have an incidence of 100% (22), 70% of which (23) with symptoms suggestive of acute mountain sickness.

Acetazolamide can be used as a preventive medication during ascent to prevent respiratory alkalosis caused by high-altitude hypoxia (24-27).

**High-altitude cerebral edema (HACE)**

The etiopathology of high-altitude cerebral edema is not clearly understood and it is presumably due to the low compliance of the cerebrospinal fluid system with increased intracranial pressure (28, 29). It occurs when AMS progresses with neurological signs such as ataxia, hallucinations, decreasing levels of consciousness, analgesics-resistant cephalalgia and vomiting.

**High-altitude pulmonary edema (HAPE)**

High-altitude pulmonary edema is a non-cardiogenic pulmonary edema caused by various factors: vasoconstriction responsive to environmental hypoxia; increase in pulmonary artery pressure; increased pulmonary capillary pressure (30). The increase in pressure results in a non-inflammatory and hemorrhagic failure of alveolar capillaries that unleashes an inflammatory response (31). It usually occurs 24 to 48 hours after arrival at altitude with non-productive cough and dyspnea, initially on exertion and later at rest, followed by cough with pink frothy sputum.

**Purpose**

The purpose of the study is to prepare, through data drawn from the existing
scientific literature, a health and risk protocol as well as a procedure of ascent for researchers working in a high-altitude science research laboratory, above 5,000 meters, in order to protect their health. Occupational Medicine is committed to carrying out such activities, after careful consideration of important environmental risk factors involved at this altitude, such as the decrease in atmospheric pressure, extreme dryness, heat discomfort and solar radiation.

Materials and methods

Our study was conducted through a systematic review of articles analyzing the risk factors associated with the performance of work tasks at high altitude.

The research included papers published from 1966 to 2014.

The papers included were identified through a systematic search on the following online databases:
- MEDLINE/ PubMed
- Scopus
- Cochrane Library

The research was conducted by inserting, in each of these engines and combined together by using Boolean operators, the following keywords: high altitude work, hypobaropathy, acute mountain sickness, high altitude cerebral edema, high altitude pulmonary edema.

Further screening was done by title and abstract focusing on studies reporting the physical examination, medical test and the procedure of ascent.

Papers quoted in the References of each paper were also looked for and examined for wider research.

All abstracts identified from the indexed databases were screened for eligibility and inclusion criteria and exclusion criteria, and the full text of relevant articles was reviewed.

Eligibility and inclusion criteria

Neither language nor publication type restrictions were applied to research. Studies included in this review also described replicable findings on the effects of high altitude on humans, guidelines for use of medical protocols and procedure of ascent to high altitude.

Exclusion criteria

We excluded articles that reported data about health and risk protocol and procedure of ascent at altitudes less than 2,500 meters. We developed specific criteria based on subject matter expertise which excluded secondary reports, editorial opinions, personal communications, and studies published in scientific conferences that were purely descriptive with no quantitative or qualitative inferences.

Results

Using the key search terms, 14,892 records were retrieved from indexed scientific databases [PubMed (6429), Scopus (8399) and Cochrane Library (64)].

Further screening was done by title and abstract focusing on studies reporting the physical examination, medical test and the procedure of ascent. Further 11,784 articles were eliminated with 3,108 remaining articles and 989 of them were also removed because of duplicity.

Of the 2,119 articles based on the general exclusion criteria, a subset of 143 publications remained and was assessed for eligibility by reading the full text. Finally, other 103 articles were also removed based on the subject matter exclusion criteria, limiting the final number of articles included in this review to 40 publications.

The research pointed out areas of interest deserving proper consideration for a correct evaluation of the subjects working in a high-altitude research laboratory and for their safe
ascent to 5,100 m. The conclusion underlines that it is really important to carry out a thorough medical examination, of the kind required by the Italian Legislative Decree (D.Lgs.) 81/2008, including:
1) anamnestic data collection aimed at highlighting pre-existing conditions;
2) physical examination of the worker;
3) 1st and 2nd level medical tests;
4) judgment of suitability for performance of work activities at high altitude.

Following the analysis of the reviewed data, below we describe the sanitary protocol and the procedure of ascent.

**Sanitary Protocol: Anamnestic collection**

It is of the utmost importance that a preliminary anamnestic exam is carried out to establish the presence of any significant pathological condition and to detect possible pathophysiological conditions (Table 2) likely to worsen during the ascent and stay at high altitude (32).

**Sanitary Protocol: Physical Examination and 1st and 2nd level Medical Tests**

They are intended to identify diseases not yet revealed or manifest and pre-existing conditions which might conflict with work in the laboratory; the exam is supplemented by 1st level medical tests, possibly supplemented with 2nd level tests (Table 3).

In order to assess the suitability to the specific task of laboratory researchers working at high altitude, our research team is also developing an index called “DMindex” to predict the reduction of the maximum oxygen consumption at high

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**Table 2 - Controversindications to suitability**

<table>
<thead>
<tr>
<th>Condition</th>
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<tbody>
<tr>
<td>Pregnancy and breast-feeding up to three months after delivery</td>
</tr>
<tr>
<td>Type I and type II uncontrolled diabetes mellitus</td>
</tr>
<tr>
<td>Uncontrolled arterial hypertension</td>
</tr>
<tr>
<td>Ischemic heart disease with recent onset (&lt;12 months)</td>
</tr>
<tr>
<td>Repetitive ventricular arrhythmias</td>
</tr>
<tr>
<td>Mild and severe degree of valvular heart disease</td>
</tr>
<tr>
<td>Mild or severe degree of obstructive and restrictive lung disease</td>
</tr>
<tr>
<td>Respiratory failure</td>
</tr>
<tr>
<td>Obstructive Sleep Apnea Syndrome (OSAS)</td>
</tr>
<tr>
<td>Severe obesity (BMI &gt; 35 Kg/m 2)</td>
</tr>
<tr>
<td>Chronic kidney disease, even in a mild stage (creatinine clearance &lt; 90 ml/m)</td>
</tr>
<tr>
<td>Glaucoma and retinopathy</td>
</tr>
<tr>
<td>Recent-onset and/or treated neoplastic diseases</td>
</tr>
<tr>
<td>Untreated coagulopathy</td>
</tr>
<tr>
<td>Cerebrovascular disease (TIA, ischemic or hemorrhagic stroke) with recent onset (&lt;12 months) or with disabling outcomes</td>
</tr>
<tr>
<td>Migraine not fully responsive to the specific drug treatment</td>
</tr>
<tr>
<td>Neurologic diseases (multiple sclerosis, epilepsy, Parkinson’s disease, neuropathies, myopathies, etc.)</td>
</tr>
<tr>
<td>Uncompensated psychiatric disorders</td>
</tr>
<tr>
<td>Hemoglobinopathies (sickle cell anemia) and severe untreated anemia</td>
</tr>
<tr>
<td>Acute or chronic hepatitis with organ failure</td>
</tr>
<tr>
<td>Untreated ulcerative colitis in the gastrointestinal tract (UG, UD, RCU)</td>
</tr>
<tr>
<td>Previous episode of acute cerebral edema and acute pulmonary edema</td>
</tr>
<tr>
<td>Ongoing anticoagulant therapy</td>
</tr>
</tbody>
</table>
The DMindex is calculated by dividing the VO2 max of the individual (Table 4) by the METs (Metabolic Equivalent) value of the work performed in the laboratory (Table 5) through the following formula:

$$\text{DMindex} = \frac{\text{VO}_2 \text{max}}{\text{METs}}.$$ 

\(\text{DMINDEX} > 0: \text{VO}_2 \text{max} \text{ is sufficient to perform the specific task.}\)

\(\text{DMINDEX} < 0: \text{VO}_2 \text{max} \text{ is not sufficient to perform the specific task.}\)

When all tests have been carried out, the occupational physician formulates a judgment of suitability for work at high altitude which could possibly include a number of prescriptions, limitations or even be negative.

The procedure of ascent

As far as the procedure of ascent to the research laboratory is concerned, our study has examined the Wilderness Medical Society Practice Guidelines in view of preparing an ad hoc protocol of ascent effectively preventing the onset of acute high-altitude illnesses (37). The guidelines provide, in addition to pharmacological prophylaxis with acetazolamide, where necessary, a seven-day pre-acclimatization period at an altitude between 2,200 and 3,000 m, before ascending to higher altitudes, emphasizing the importance of giving proper consideration to the altitudes where to sleep.
during the days of ascent (see Tables 6 and 7) and the procedures of ascent. 

Above an altitude of 3,000 m, individuals should not increase the altitudes where to sleep by more than 500 m per day.

Our group had to examine the sites (refuges) (Table 6) already existing on the route to the laboratory and to evaluate the possibility of stops, to facilitate acclimatization and reduce the risk of hypobaropathies (38-40). Thanks to the visits we carried out in situ it was possible to establish a procedure of ascent to reach the laboratory at 5,100 m with stops in refuges over a seven day period (Table 7).

Conclusions

High-altitude work involves a very limited group of workers, especially researchers who exercise their profession in an environment offering a place, unique in the world, for the detection of Earth and space geophysical conditions.

At an altitude of 5,100 m the organism is exposed to environmental stressors that cannot be compensated with acclimatization thus making it necessary to avoid an extended stay for researchers in the lab, always carefully monitoring them in order to better protect their mental and physical health. The proposed procedure of long-lasting ascent allows researchers to start from the first day the positioning of equipment required to carry out all measurements and on the seventh day to be able to work at the altitude required. The authors are convinced that (1) the proposed procedure of ascent will make the stay in the laboratory safe for researchers; and (2) the occupational physician is the right professional to preparing a health and risk protocol as well as a procedure of ascent in order to safeguard the health of researchers working at extreme altitude.

Table 5 - Workload MET values

<table>
<thead>
<tr>
<th>Workload</th>
<th>METs</th>
<th>Type of work activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>very light</td>
<td>&lt;3</td>
<td>Sitting (clerical activities); Standing (a store clerk); truck driving; crane manoeuvring</td>
</tr>
<tr>
<td>mild</td>
<td>3-5</td>
<td>Filling up shelves (with light objects); light work of welding and carpentry; assembling machines; repairing cars; sticking wallpaper</td>
</tr>
<tr>
<td>moderate</td>
<td>5-7</td>
<td>Performing masonry work; shoveling the earth; mounting tires</td>
</tr>
<tr>
<td>heavy</td>
<td>7-9</td>
<td>Working as a stoker; digging a ditch; digging and shoveling</td>
</tr>
<tr>
<td>very heavy</td>
<td>&gt;9</td>
<td>Working as a lumberjack and manual labourer</td>
</tr>
</tbody>
</table>

Table 6 - Sequential numbering of refuges and associated altitude

<table>
<thead>
<tr>
<th>Refuge</th>
<th>Altitude</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2,600 m</td>
</tr>
<tr>
<td>2</td>
<td>3,200 m</td>
</tr>
<tr>
<td>3</td>
<td>3,800 m</td>
</tr>
<tr>
<td>4</td>
<td>4,000 m</td>
</tr>
<tr>
<td>5</td>
<td>4,400 m</td>
</tr>
</tbody>
</table>

Table 7 - Procedure of ascent to the laboratory (lab) at 5,100 m

| Day I-II | Ascent from 1,000 m to lab (5,100 m) and descent to 2,600 m and sleep there 2 days |
| Day III  | Ascent to lab (5,100 m) and descent to 3,200 m and sleep there                     |
| Day IV   | Ascent to lab (5,100 m) and descent to 3,800 m and sleep there                     |
| Day V    | Ascent to lab (5,100 m) and descent to 4,000 m and sleep there                     |
| Day VI   | Ascent to lab (5,100 m) and descent to 4,400 m and sleep there                     |
| Day VII  | Ascent to lab (5,100 m) and stay and sleep there for the following days            |
High altitude work and health

Author Disclosure Statement
No conflicting financial interests exist

Riassunto
Lavoro a più di 5000 metri: il controllo medico

Qualsiasi attività lavorativa ad altitudini superiori a 3.000 m dal livello del mare è considerata lavoro in alta quota. Il cambiamento delle condizioni ambientali porta ad un adattamento dell’organismo umano principalmente per la riduzione della pressione parziale di ossigeno nell’aria e la riduzione proporzionale di pressione barometrica. La nostra ricerca ha effettuato una revisione sistematica della letteratura scientifica al fine di elaborare un protocollo sanitario e di rischio e una procedura di salita per ricercatori-lavoratori che prestano servizio in un laboratorio di ricerca scientifica, che si trova ad un’altitudine di 5.100 m. Si evidenzia il ruolo fondamentale della Medicina del lavoro per la predisposizione di un protocollo medico atto a valutare l'idoneità del personale, relativo alla permanenza dei lavoratori in ambienti che presentano elevati rischi per la salute come in questo caso, ed un protocollo di salita che riduca il rischio legato alle variazioni di altitudine.

References


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