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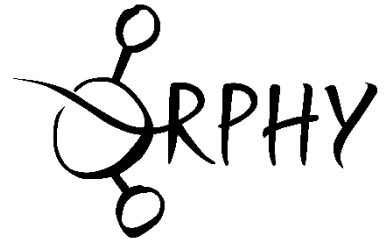
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COMEX (Compagnie Maritime d'Expertises), established in 1962, has positioned itself in the offshore activities sector, where it held a leading international position, becoming the world's foremost company in engineering, technology, and human or robotic underwater interventions. Comex designed a Hyperbaric Testing Center in 1969 and developed its own research programs on various breathing mixtures used in deep-sea diving (helium and later hydrogen). These research efforts led to spectacular advancements in this field, including several world records, both in real conditions and simulations. Comex still holds the world record at -701 meters, achieved in its chambers during Operation HYDRA 10.

The ORPHY laboratory focuses on major physiological functions, their regulation, interactions, and their contribution to the development and prevention of certain pathologies. The primary mechanisms studied involve metabolic aspects (oxygen transport and utilization, energetics, etc.) and electrophysiological aspects (contractility and excitability), mainly related to respiratory, vascular, and/or muscular functions. These mechanisms are studied under various physiological and physiopathological conditions, ranging from the cellular and subcellular levels to the entire organism. In Europe, the ORPHY laboratory is one of the leaders in hyperbaric physiology and diving research.

Being a major player in innovation and expertise in the field of pressure, COMEX maintains a scientific archive from its experimental diving campaigns. The value of this archive is both scientific and historical, as it documents a remarkable chapter in the history of marine exploration and contains results obtained during dives that are very unlikely to be replicated in the future.

Chapter 23

Operation Everest III (COMEX '97)

Effects Of Prolonged And Progressive Hypoxia On Humans During A Simulated Ascent To 8,848 M In A Hypobaric Chamber

Jean-Paul Richalet, Paul Robach, Sébastien Jarrot, Jean-Christophe Schneider, Nicholas P. Mason, Emmanuel Cauchy, Jean-Pierre Herry, Annick Bienvenu, Bernard Gardette and Claude Gortan

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Key words: hypobarica, acclimatization, $\dot{V}O_{2MAX}$, acute mountain sickness

Abstract: Exposure to high altitude induces physiological or pathological modifications that are not always clearly attributable to a specific environmental factor: hypoxia, cold, stress, inadequate food. The principal goal of hypobaric chamber studies is to determine the specific effect of hypoxia. Eight male volunteers ("altinauts"), aged 23 to 37 were selected. They were first pre-acclimatized in the Observatoire Vallot (4,350m) before entering the chamber. The chamber was progressively decompressed down to 253 mmHg barometric pressure, with a recovery period of 3 days at 5,000m in the middle of the decompression period. They spent a total of 31 days in the chamber. Eighteen protocols were organized by 14 European teams, exploring the limiting factors of physical and psychological performance, and the pathophysiology of acute mountain sickness (AMS). All subjects reached 8,000m and 7 of them reached the simulated altitude of 8,848m. Three altinauts complained of transient neurological symptoms which resolved rapidly with reoxygenation. Body weight decreased by 5.4 kg through a negative caloric balance. Only four days after the return to sea-level, subjects had recovered 3.4 kg, i.e. 63% of the total loss. At 8,848m (n=5), PaO₂ was 30.6 ± 1.4 mmHg, PCO₂ 11.9 ± 1.4 mmHg, pH 7.58 ± 0.02 (arterialized capillary blood). Hemoglobin concentration increased from 14.8±1.4 to 18.4±1.5 g/dl at 8,000m and recovered within 4 days at sea-level. AMS score increased rapidly at 6,000m and was maximal at 7,000m, especially for sleep. AMS was related to alteration in color vision and elevation of body temperature. $\dot{V}O_{2MAX}$ decreased by 59% at 7,000m. The

purpose of this paper is to give a general description of the study and the time course of the main clinical and physiological parameters. The altinauts reached the "summit" (for some of them three consecutive times) in better physiological conditions than it would have been possible in the mountains, probably because acclimatization and other environmental factors such as cold and nutrition were controlled.

1. INTRODUCTION

The exposure of humans to the environment of high altitude regions induces various physiological adjustments or pathological manifestations which are not always clearly attributable to one or another stressor associated with this particular milieu. Altitude hypoxia, cold, dryness of air, inadequate food or liquid intake, exhaustion and psychological stress are the main factors that could modify human physiology and behavior at high altitude. The first objective of hypobaric chamber studies is to isolate hypobaric hypoxia from the other stressors. The possibility to use advanced technology and sophisticated equipment as well as ethical and safety considerations give a clear advantage to chamber studies as compared to field studies when the effect of hypoxia is the main question. Paul Bert was the first scientist at the end of the last century to use a hypobaric chamber to study the effect of altitude hypoxia on himself (2) and was able to demonstrate that the well known effects of acute altitude exposure (dyspnea, tachycardia, dizziness) were due to the lack of oxygen and not to hypobaria alone. In 1946, the US Navy promoted a study called "Operation Everest" where four subjects were able to reach the standard altitude equivalent to Mount Everest (235 mmHg) after a 30-day period of confinement in a small chamber (3.3m x 3.3m x 2.3m) (4). In 1985, Operation Everest II was directed by Charles Houston, John Sutton and Allen Cymerman. It was a large scale investigation which produced a lot of new interesting data and allowed the formulation of new concepts in the field of high altitude physiology and medicine (5). Eight male subjects entered the chamber, six of them reached the "summit" (ambient pressure of 240 mmHg) after a 40 day stay in the chamber. In 1989, Operation Everest Turbo demonstrated the positive effects of pre-acclimatization in a hypobaric chamber before an expedition to Mount Everest (8). Six subjects (five male and one female) were intermittently exposed to equivalent altitudes up to 8,848m for 5 days and showed physiological and clinical signs of acclimatization.

The objectives of the present study were to use the advantages of chambers studies (pure hypobaric hypoxia, advanced technology, safety) to address some specific questions remaining unanswered by previous chamber or field studies.

2. SUBJECTS

Selection of subjects. Eighteen male subjects volunteered to take part in the study. We will call them "altinauts", as a combination of altitude and astronauts. Nine were selected from various criterion: experience of mountaineering, maximal oxygen uptake, hypoxic ventilatory and cardiac response to hypoxia at rest and exercise, psychological profile and motivation, interest for science in general and high altitude physiology in particular. Eight subjects and one reserve entered the study for baseline normoxic studies. Finally, eight altinauts underwent the altitude chamber program. Their characteristics were as follows:

1. K.B. 23 yr old, male nurse, high level climber in the Alps, no altitude experience above Mont Blanc (4807m), lives in Chamonix (1035m), smokes 2 cig./day; height 180cm; weight 66.5 kg.
2. E.C. 37 yr old, medical doctor specialized in emergency medicine and mountain rescue, mountain guide, participated in various high altitude expeditions including ARPE scientific expedition to Mount Sajama (6542m) in 1991, reached the altitude of 8,760m without supplementary oxygen on Mount Everest in 1990, lives in Chamonix (1035m), occasional smoker; height 183cm; weight 77.2 kg.
3. G.D. 25 yr old, medical student (last year), has good mountaineering experience, climbed various summits in the Andes and reached the altitude of 6435m, lives in Toulouse (146m), non smoker; height 190cm; weight 80.2 kg.
4. J.F.F. 25 yr old, medical student (last year), has good mountaineering experience, climbed various summits in the Andes and reached the altitude of 6435m, lives in Toulouse (146m), non smoker; height 188cm; weight 82.7 kg.
5. M.G. 26 yr old, medical student (last year), has good mountaineering experience, climbed various summits in the Andes and reached the altitude of 6435m, lives in Toulouse (146m), non smoker; height 176cm; weight 72.2 kg.
7. G.S. 25 yr old, electrician, high level climber in the Alps, no altitude experience above 4100m, lives in Challes les Eaux (310m), smokes 4 to 5 cig. /day; height 177cm; weight 70.3 kg.
8. P.S. 25 yr old, skier, good climber in the Alps, has an experience of trekking in Nepal up to 5200m, lives in Servoz (815m), non smoker; height 172cm; weight 65.4 kg.
9. A. H. 27 yr old, master in law, regular climber, moderately trained as compared with the others, no experience of high altitude above 4300m, lives near Paris (60 m), non smoker; height 176cm; weight 80.3 kg.

3. METHODS

3.1 Location and schedule of experiments

Subjects were studied at the COMEX S.A. facilities in Marseille, France. The hypobaric chamber consisted of three rooms - one spherical study room (diameter 5m, available volume 65 m³) connected to a cylindrical living room with eight sleeping bunks and a table for meals (length 8 m, available volume 32 m³) via an airlock room usable for toilet and shower (available volume 8 m³) (Figure 1). Pressures in the living room and airlock on one side and in the study room on the other side were controlled independently by a computerized system. Food and drinks, urine and blood samples, and any necessary small object could be transferred between outside and inside the chamber via two airlock devices. Altinauts were constantly monitored through five video cameras and audio systems by two technicians who were continuously present to manage the chamber, day and night. During day time, a medical doctor was present in the control room. During night time, a doctor could be called at any time and be present on the site within 15 minutes. Oxygen masks were available at each bed, in the dining room and in the study room. A portable oxygen bottle with a mask was also available within the chamber, as well as an emergency pack usable by one of the subjects, a doctor trained in high-altitude emergencies. In case of severe problems necessitating emergency evacuation, a subject could be taken out of the chamber within 30 minutes from 8,848m equivalent altitude, and more quickly from lower altitudes.

Eighteen protocols were planned and executed by fourteen scientific teams from France, England and the Netherlands to study the effect of prolonged hypobaric hypoxia on various systems:

1. Role of hemoconcentration on aerobic performance, with related hydroelectrolytic hormones.
2. Alpha motoneuron excitability and recruitment of motor units.
3. Sensori-motor control and maximal performance of skeletal muscles.
4. Role of hemoconcentration on aerobic performance, with related hydroelectrolytic hormones.
5. Alpha motoneuron excitability and recruitment of motor units.
6. Sensori-motor control and maximal performance of skeletal muscles.

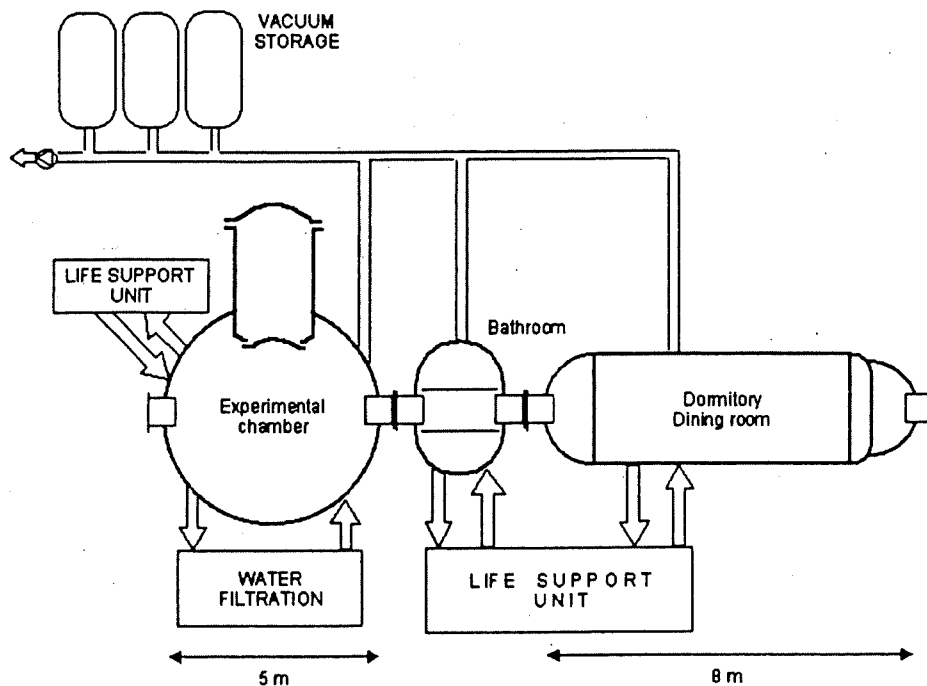


Figure 1. Plan of the hypobaric chambers at COMEX industries.

7. Role of hemoconcentration on aerobic performance, with related hydroelectrolytic hormones.
8. Alpha motoneuron excitability and recruitment of motor units.
9. Sensori-motor control and maximal performance of skeletal muscles.
10. Production of oxygen free radicals at rest and exercise.
11. Coordination during a simulated traverse climb of short duration.
12. Transport of oxygen and oxyhemoglobin dissociation curve.
13. Acclimatization and cardiac and ventilatory response to hypoxia, ventilatory response to CO₂.
14. Role of peripheral chemoreceptors on ventilatory acclimatization.
15. Defense responses of respiratory tract. Variation of cough frequency with altitude.
16. Role of NO, endothelin and eicosanoids in the pathophysiology of pulmonary hypertension. Effects of a supplementation with L-arginine.
17. Cardiac function evaluated by echocardiography. Formation of circulating bubbles.
18. Autoregulation of cerebral blood flow evaluated by transcranial Doppler.
19. Calcium and phosphate metabolism, with related hormones.
20. Measurement of energy expenditure and distribution of total body water by doubly labeled water.
21. Sensitivity of adipose tissue to various lipolytic or antilipolytic agents. Variation in body composition.

22. Psychological adaptation to prolonged hypoxia: cognitive and affective sensorimotor aspects.
23. Psychological adaptation to prolonged hypoxia: individual psychological profile, decision taking and solving group problems.
24. Determinants of food consumption: taste sensitivity, appetite and satiety.

Written informed consent was obtained from all subjects. The protocols were approved, after revision, by the ethical committee of the University Hospital of Marseille. Special recommendations from the committee were to restrict blood gases to arterialized capillary blood sampling, maximal exercise no higher than 7,000 m, dopamine infusion at a maximal dose of 3 $\mu\text{g}/\text{kg}/\text{min}$ for protocol #8, avoid the use of CO breathing to measure plasma volume in protocol #1.

The schedule of experiments was as follows:

3.2 Basal normoxic measurements

Basal measurements were performed on the nine subjects within the chamber with open doors from March 10th to 16th.

3.3 Pre-acclimatization period

In order to shorten the time spent within the chamber, subjects were allowed to pre-acclimatize in the Alps, at Refuge des Cosmiques (3,650m) for one day and Observatoire Vallot (4,350m) for five days. During this period, free climbing activity was allowed and no scientific observation was performed. This period was planned, not only to allow a rapid entrance to the chamber at 5,000 m but also to test the ability of the subjects to withstand high altitude and community life in a hostile environment. During this period, subject #6 suffered from high altitude pulmonary edema (documented by X-ray after evacuation to Chamonix hospital). He was excluded from the study and the alternate subject (#9) was then fully included in the study.

3.4 Hypobaric chamber period

Subjects descended from Observatoire Vallot on April 1st at mid-day and entered the chamber on April 2nd at mid-day. They spend their first night in the chamber at 4500m then went up to 5,000m where they started the experimental procedures. The ascent profile is shown on Figure 2. The pressures were chosen as the real pressures for the latitude of Mount Everest (14), up to 253 mmHg for the altitude of 8,848m. Except in the last period of

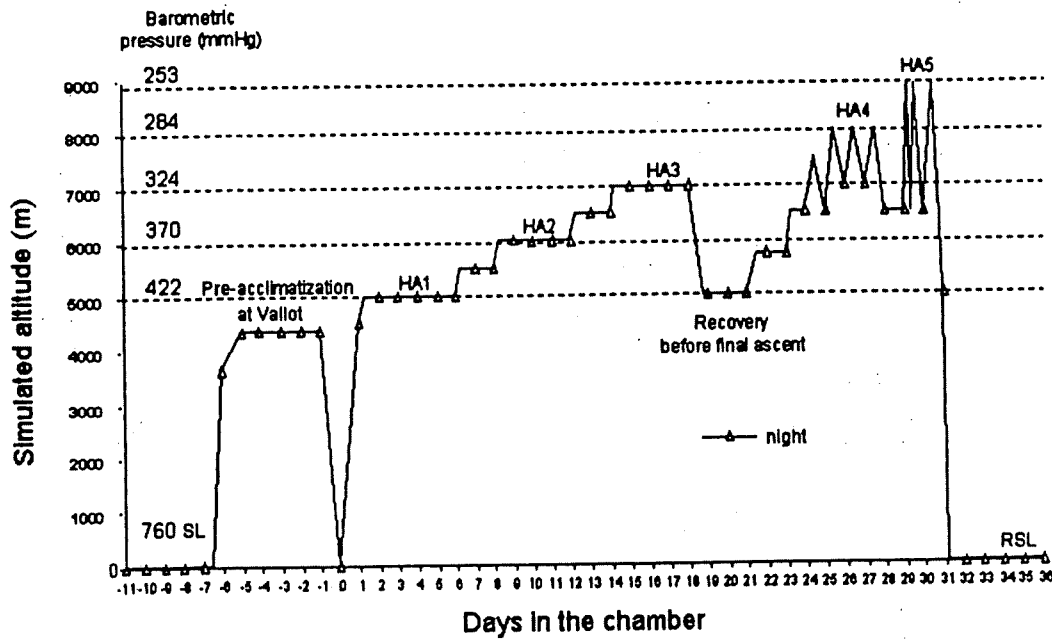


Figure 2. Simulated progression profile. SL, HA1 to HA5, RSL: periods of experimental studies.

ascent to the "summit", the pressure changes were performed early in the morning, before wake up and breakfast, within 15 minutes for an altitude difference of 500 m, 30 minutes for an altitude difference of 1000 m, and 90 minutes for an altitude difference of 1500 or 2348 m. At the lowest barometric pressure of 253 mmHg, the subjects spent 6 hours on day 30 and 4 hours on day 31. Experiments were performed at sea-level (SL), at 5,000m (HA1), 6,000m (HA2), 7,000m (HA3), return to 5,000m (RHA1), 8,000m (HA4), 8,848m (HA5) and after the return to sea-level (RSL). Subjects spent their last night in the chamber at 5,000m, after the last "summit" climb. During the days when no experiments were performed, altinauts were strongly encouraged to do some exercise on the treadmill or on the cycloergometer. Most of them did so (30 to 90 minutes per day), although their motivation decreased considerably with increasing altitude.

3.5 Recovery period

Altinauts left the chamber on May 2nd and underwent the RSL experiments until May 5th. This type of observation is quite unique: very few studies have explored the time course of physiological and psychological parameters after return to normoxic conditions.

Three subjects did not follow the complete schedule. One subject (#1) experienced neurological symptoms at 8,000m (day 25): while performing a cognitive test, he suddenly could hardly speak and write. These symptoms rapidly disappeared when he breathed pure oxygen, but a severe headache of

migraine type could not be relieved by oxygen breathing and was not tolerated by the subject. A decision to evacuate the subject was taken and executed. Subsequent neurological examination, fundoscopy and cerebral magnetic resonance imaging were entirely normal. Subject #8 suffered from neurological symptoms at 8,848m (day 29): he felt dizzy and could not recognize his friends within the chamber and had the sensation of floating in the air. All signs disappeared with oxygen inhalation but the subject and his colleagues were still anxious and for safety reasons, subject #8 was evacuated from the chamber. Neurological examination and magnetic resonance imaging performed after evacuation were entirely normal. Subject #3 suffered from neurological symptoms at his second ascent to 8,848m (day 30): sudden pain in the back, paralysis of the left lower limb, with aphasia and facial paralysis. Symptoms disappeared rapidly with oxygen inhalation. He was brought down to 6,500 m where he felt perfectly well. He was kept under oxygen inhalation while his colleagues underwent their third ascent to 8,848m and stayed with them at 5,000m during the last night in the chamber. Neurological examination and magnetic resonance imaging performed after leaving the chamber were entirely normal. Altogether, 8 out of 8 altinauts reached 8,000m, 7 reached 8,848m among whom 5 reached the "summit" three times, one twice and another one only once. All altinauts, included those who left the chamber before time, underwent the protocols planned during the RSL period, the delay from leaving the chamber being respected. Subjects were not allowed to take medications except paracetamol for severe headache. One subject entered the chamber two days after a dental abscess evacuation and took antibiotics for 5 days within the chamber. Dexamethasone (8 mg IV) was given to subject #1 before evacuation on day 25. Despite strong discouragement against taking any medication for insomnia, sleeping pills (10 to 20 mg zolpidem) were occasionally given to some of the subjects in response to their strong demands and mainly to avoid a severe conflict between altinauts and the staff which could easily have jeopardized the study. As no sleep study was performed and as the plasma half life of zolpidem is 2.4 hours, this drug use was considered as having a potentially minimal influence on protocols performed the day after. However, any effect (mainly beneficial) cannot be excluded either on psychological or physical tests.

3.6 Environmental conditions

Pressure variations were continuously monitored in the chamber. Mean values for the altitudes where experiments were performed are shown in Figure 2. Variations in the chamber temperature are shown in Figure 3 (top). During experiments, temperature was, most of the time, kept between 18°C

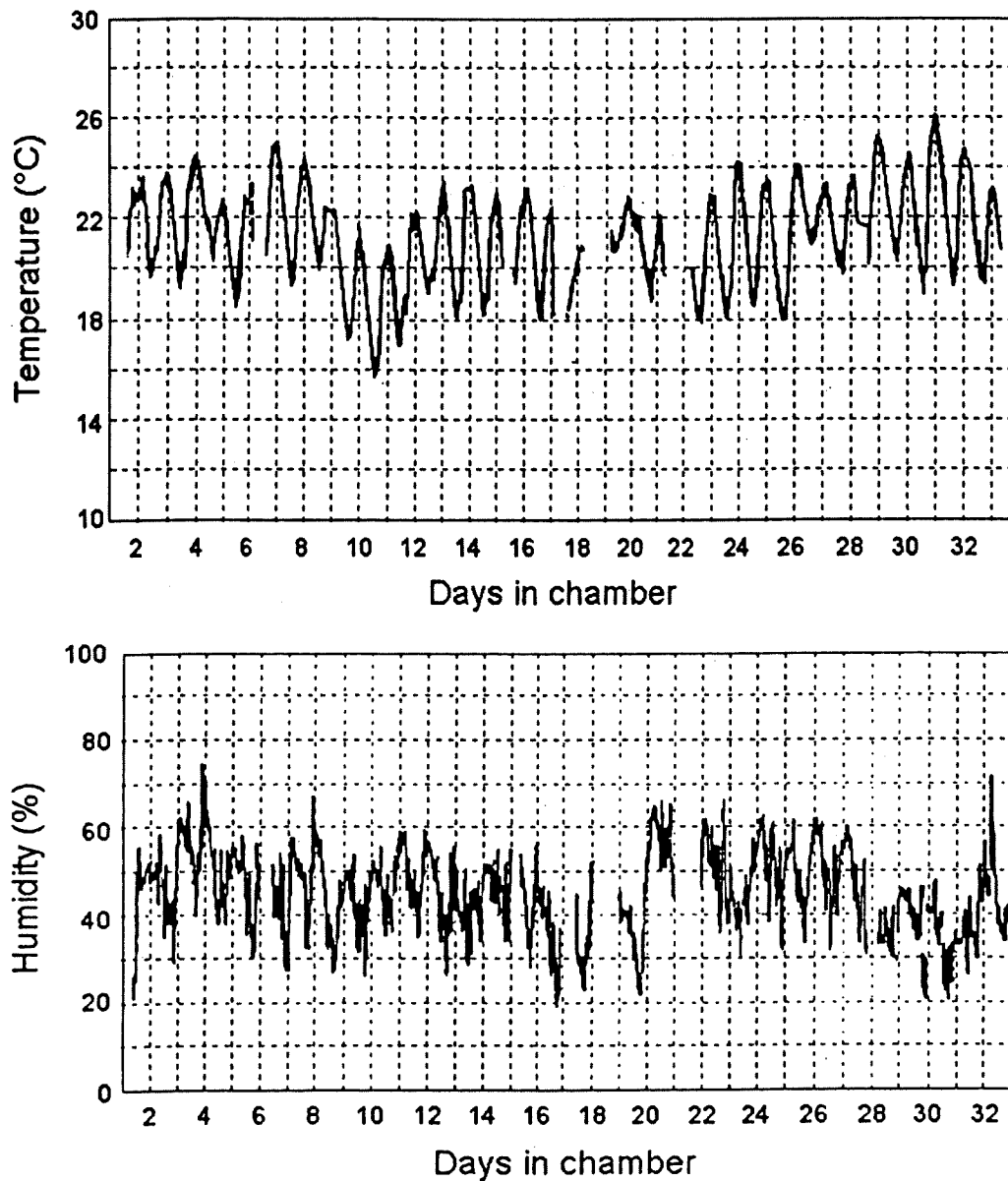


Figure 3. Variations of ambient temperature (top) and humidity (bottom) in the main experimental chamber.

and 24°C. Percentage of humidity in the chamber is shown in Figure 3 (bottom). It varied with outside ambient humidity and was mostly between 30 and 60 %. Day/night rhythm was maintained: altinauts woke up at 07:00 - 07:30 and went to bed between 22:00 and midnight. Ambient (dry) PiO_2 and $PiCO_2$ were monitored continuously and are shown on Figures 4.

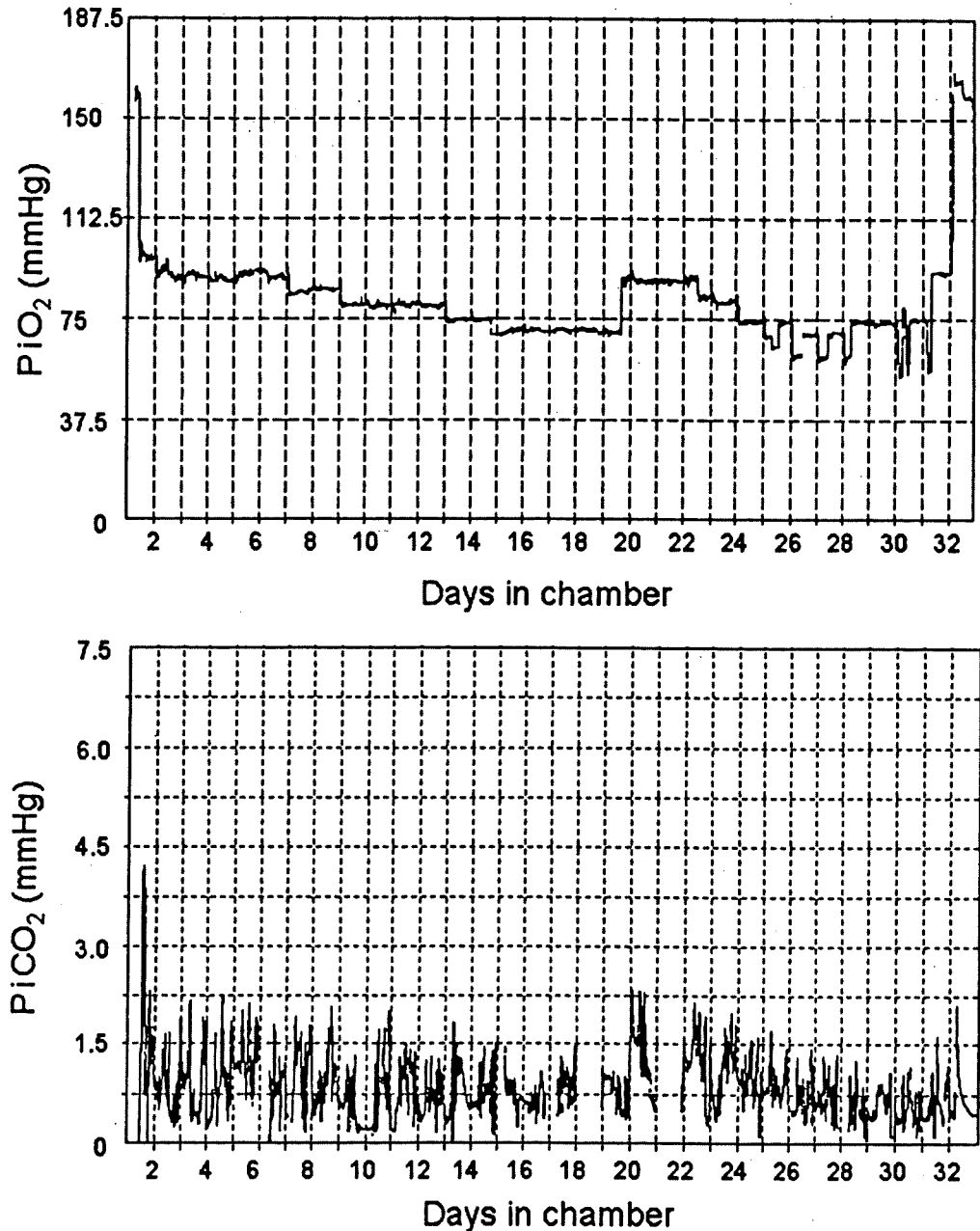


Figure 4. Variations of PO_2 (top) and PCO_2 (bottom) in ambient air (dry) of the main experimental chamber.

3.7 Investigators

They were no more than two investigators at the same time in the chamber. At very low barometric pressures (284 and 253 mmHg), they breathed pure oxygen for 30 minutes before entering the chamber in order to avoid decompression sickness. They were using supplemental oxygen at all altitudes. Oxygen supply was through a kind of space suit with a hood (not a mask). Exhaled gas was pumped directly from the hood. The possibility for leakage of oxygen to the chamber was thus minimal and the comfort of the investigator maximal. However, at the lowest barometric pressure of 253

mmHg, some leakage occurred for a short period, leading to discard values of blood gases taken in two subjects during this specific period.

4. METHODS

Each protocol will be described in detail in other articles. The main purpose of the present paper is to give a general description of the study and the time course of the main clinical and physiological parameters. Daily questionnaire, body weighing and basal physiological parameters were recorded in the morning just after waking up, before breakfast, except at HA4 and HA5 where they were recorded after two to three hours of exposure to the corresponding altitude. Body weight was measured by a whole body scale ± 0.01 kg (Mettler-Toledo, type Sider 1-150, Switzerland). Body mass index was calculated as body weight / height² as an overall indication of fat proportion in body composition. Liquid and food intake were carefully measured daily by weighing all food and drinks entering and leaving the chamber, for each subject. Day time food intake, outside principal meals (breakfast, lunch, dinner) was noted by the subject himself by careful weighing using a table food scale within the chamber (Kern, model 440-53, Prolabo, France). Twenty four hour urine was collected and weighed daily, outside the chamber. Acute mountain sickness (AMS) score (Lake Louise Consensus, (12)) was self recorded (headache: 0 to 3; gastrointestinal symptoms: 0 to 3; fatigue/weakness: 0 to 3; dizziness/lightheadedness: 0 to 3), as well as an evaluation of insomnia, ataxia and dyspnea (each coded from 0 to 3). Rectal temperature was taken every morning before getting up. Heart rate, systemic arterial pressure and transcutaneous arterial saturation were measured daily in the morning before breakfast (Hewlett Packard, model Viridia M3). Color vision was evaluated at the same time by an anomaloscope, as an objective measurement of AMS (9). The color vision index presented here for each individual is the variation from the sea-level basal value. Blood hemoglobin concentration was obtained through peripheral venous blood sampling and measured by a CO-oximeter (Chiron Diagnostics, model 270). The CO-oximeter was kept inside the chamber and was calibrated for each chamber pressure. Blood gases were measured from arterialized capillary blood obtained from an ear lobe previously heated with capsaicin cream. The blood gas analyzer (Chiron Diagnostics, model 348) was outside the chamber and capillary blood samples were passed through an air lock and analyzed within 2 minutes after sampling. Maximal oxygen uptake was measured using a step by step progressive exercise regime on a cycloergometer (Monark) until exhaustion. Ventilation, oxygen and CO₂ concentrations were analyzed using a Medical Graphics system (CPX/D

Cardiopulmonary exercise system, Minneapolis, MN), modified for low partial pressures of O₂ and with a more powerful gas pumping system for high altitudes. The apparatus was kept within the chamber and functioned perfectly up to 7,000 m.

4.1 Statistics

Values presented are mean±standard deviation. Analysis of variance with repeated measures was used to assess the significance of variations with time and altitude.

5. RESULTS

Variations of each symptom forming part of the AMS score as well as the total AMS score, insomnia, ataxia and dyspnea scores are shown in Figure 5.

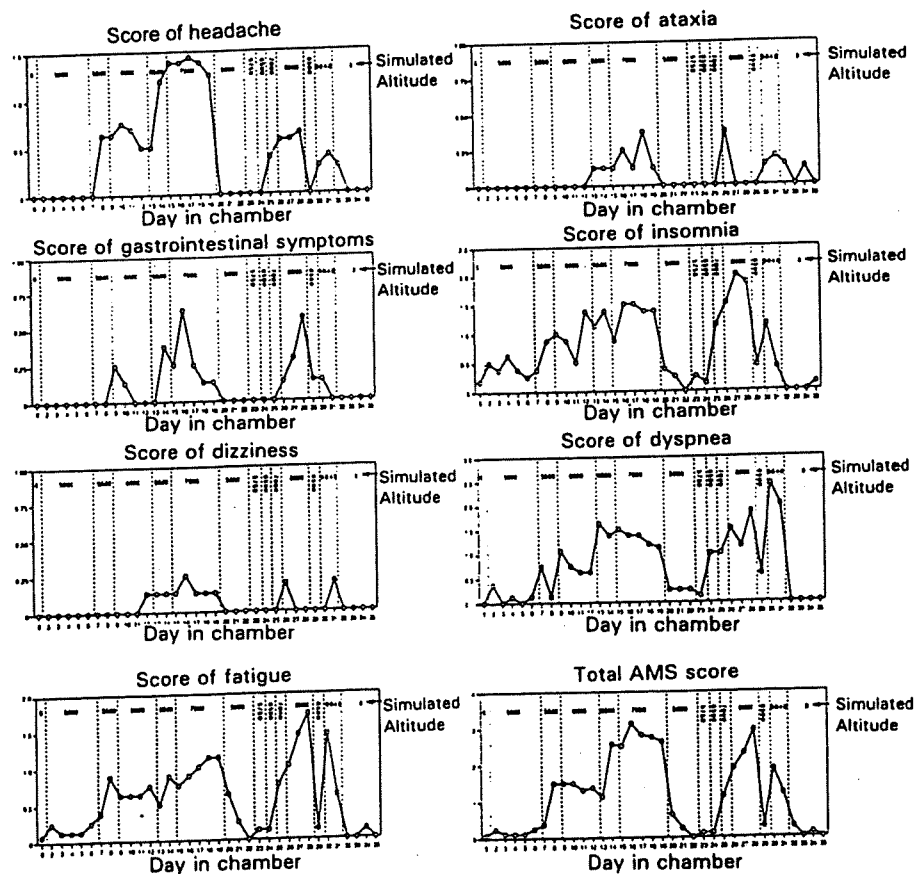


Figure 5. AMS score. Total score, and scores for headache, gastrointestinal, dizziness, fatigue, insomnia, ataxia and dyspnea. Mean values for the group. Standard deviations are not shown. $n=8$ except from day 27 to 32 where $n=7$. Note: the insomnia score at 8000m is for sleep at 7000m and the insomnia score at 8848m is for sleep at 6500m (see profile in Figure 2).

Total AMS score was almost zero at 5,000m thanks to the pre-acclimatization period on Mont Blanc. Symptoms appeared at 5,500m and 6,000m, were increased at 6,500m and maximal at 7,000m. During the recovery at 5,000m, AMS score went back to zero after 3 days, stayed very low upon re-ascent until 7,000m was reached again, peaked on the third ascent at 8,000m, but was lower during ascent to 8,848m. One subject still felt some symptoms one day after leaving the chamber (day 32). Among the four items included in the AMS score, the trend for each symptom was different. The headache score was zero at 5,000m, peaked at 7,000m and was relatively low at 8,000m and 8,848m. At 6,000m and 7,000m, there was a progressive decline with time due to clinical acclimatization. Gastrointestinal symptoms were zero up to 5,500m, increased on the first days at 6,000m, 7,000m then declined rapidly with time at a given altitude. However, it increased with the successive intermittent exposures to 8,000m. Fatigue increased with time and altitude up to 7,000m, progressively returned to zero after 3 days of recovery at 5,000m, then rose again with altitude and reached its maximum on the third exposure to 8,000m, whereas the exposure to 8,848m was better tolerated, probably because it was shorter. Dizziness score was very low during the whole period, peaked at 7,000m and showed only a small rise at 8,000 and 8,848m. Dyspnea score always showed a peak on the first day at a new altitude, progressively increasing with altitude with a peak at 6,500m, did not completely returned to zero on recovery at 5,000m, increased again with re-ascent and reached its maximum at 8,848m. Ataxia score was very low during the whole period except at 7,000m, on the first exposure to 8,000m and at both exposures to 8,848m. Some alpinists still complained of one of these symptoms one to three days after return to sea-level. Quality of sleep was already not perfect at 5,000m, progressively deteriorated with altitude up to 7,000m, took three days to restore on recovery at 5,000m, increased again and was lowest during the nights spent at 7,000m between days at 8,000m. Recovery after descent to sea-level was immediate.

Mean variations in body weight are shown in Figure 6. Body weight loss was maximal on day 29: 5.4 kg (7.3% of initial body weight, $n=7$). During the preacclimatization period on Mont-Blanc, 1.4 kg were already lost. Then, the loss was progressive up to 7,000m. As soon as the first day of recovery at 5,000m, 0.7 kg were recovered and 0.15 kg more within two more days. Re-ascent to 8,848m led to a further loss of 1.7 kg in 7 days. The individual maximal weight loss varied from 2.9 to 10.0 kg and was related to initial body mass index ($r=0.877$, $p < 0.005$). The rate of weight gain after return to sea-level was dramatically high: after 4 days of recovery, mean body weight increased by 3.4 kg, i.e. 63% of the total weight loss.

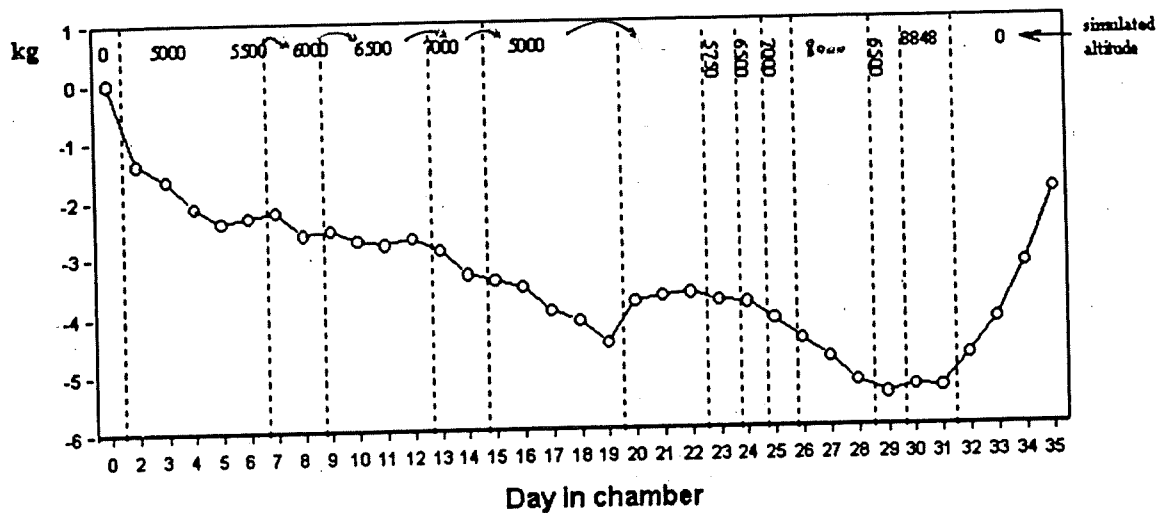


Figure 6. Mean variations in body weight. Standard deviations are not shown. $n=8$ except from day 27 to 32 where $n=7$.

Mean caloric input decreased by 11% at 5,000m, by 22% at 6,000m, by 44% at 7,000m, and by 55% at 8,000m (Westerterp et al., submitted).

Resting heart rate and transcutaneous arterial saturation are shown in Figure 7. SaO_2 decreased with altitude and increased with re-exposure to the same altitude, due to ventilatory acclimatization. The lowest mean resting SaO_2 was reached at 8,000m : 67.9 %. Heart rate increased with altitude, up to 7,000m and mirrored variations in SaO_2 . No further increase was observed at 8,000m and 8,848m. During return to sea-level, some individuals showed values of heart rate lower than before entering the chamber.

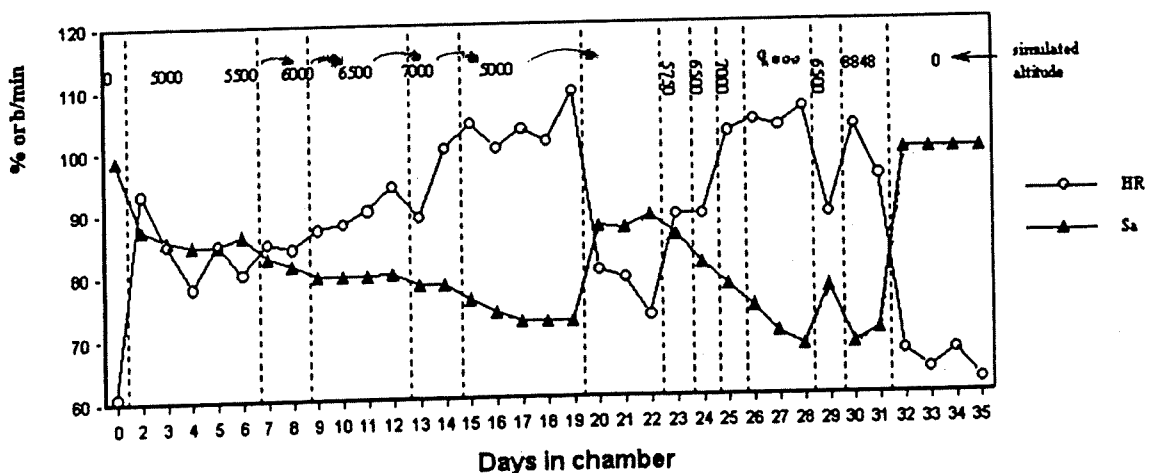


Figure 7. Mean resting heart rate and transcutaneous arterial saturation. Standard deviations are not shown. $n=8$ except from day 27 to 32 where $n=7$.

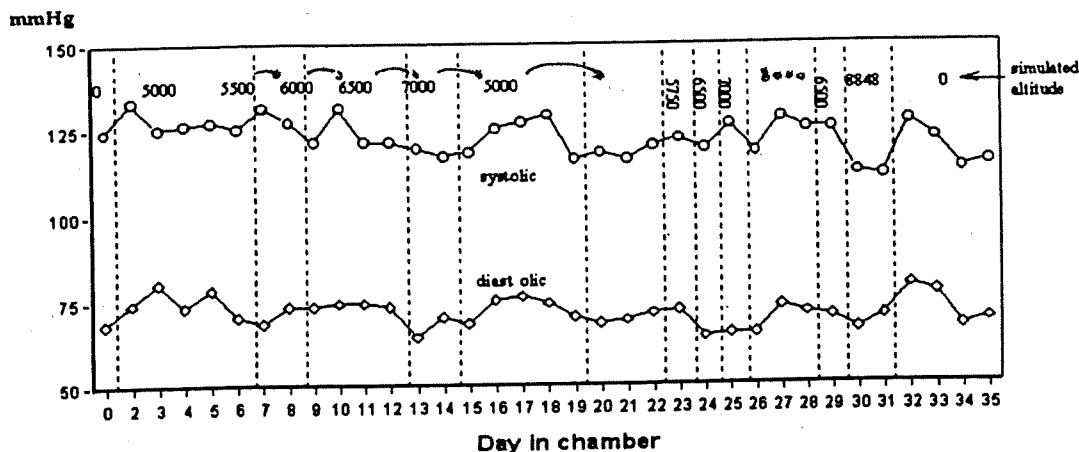


Figure 8. Variations of mean systolic and diastolic arterial pressures. Standard deviations are not shown. $n=8$ except from day 27 to 32 where $n=7$.

Systolic and diastolic arterial pressures are given on Figure 8. No significant variations were observed, neither in systolic nor in diastolic arterial pressures.

There was a progressive slight increase of rectal temperature with altitude, but the most striking observation was that temperature peaked at 7,000m in some subjects, with a concomitant rise in the clinical AMS score (Figure 9). The high values of rectal temperature were only seen when the AMS score was high (Figure 10).

Variation of color vision index in the red/green axis with altitude is shown on Figure 9. Color vision index decreased with altitude at and above 6,000 m, showing a slight relation with AMS: color vision index was lower when AMS was different from zero (significant when score equals 2 or 3).

As expected, maximal oxygen consumption decreased with altitude (Table 1): -44% at 5,000m, -58% at 6,000m and -59% at 7,000m. One subject refused to perform a maximal exercise test at 7,000m ($n=7$). Maximal performance recovered almost completely with return to sea-level (n.s. between SL and RSL). Resting values of PO_2 , PCO_2 and pH in arterialized capillary blood at different altitudes are shown in table 1. At the lowest barometric pressure (253 mmHg), some oxygen enrichment occurred within the chamber during a short period and values of blood gases sampled in two subjects during this period were discarded. Hemoglobin concentration increased with altitude exposure. Four days after leaving the chamber it was not different from basal SL values (Table 1).

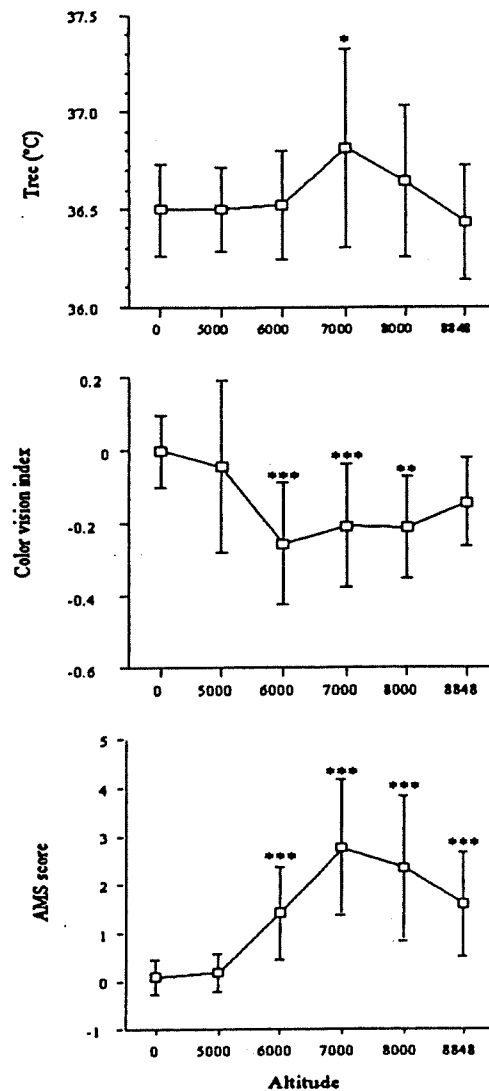


Figure 9. Variations of rectal temperature (Trec), Color vision index and AMS score with increasing altitude. Mean \pm SD. Altitude vs sea-level: **, $p < 0.01$; ***, $p < 0.001$. $n = 8$ except for 8848m where $n = 7$.

From other protocols, we can select some observations already published. Nocturnal cough frequency and cough receptor sensitivity to citric acid challenge increased with altitude. This observation refutes the common hypothesis that altitude cough is due to cold, dry air and suggest that other mechanisms such as pulmonary interstitial edema might be involved (7).

Cognitive performance, evaluated by visual reaction time, Pegboard psychomotor test and number ordination test was not significantly altered below 8,000m, suggesting efficient compensatory mechanisms to hypoxic stress, at least below a certain threshold (1).

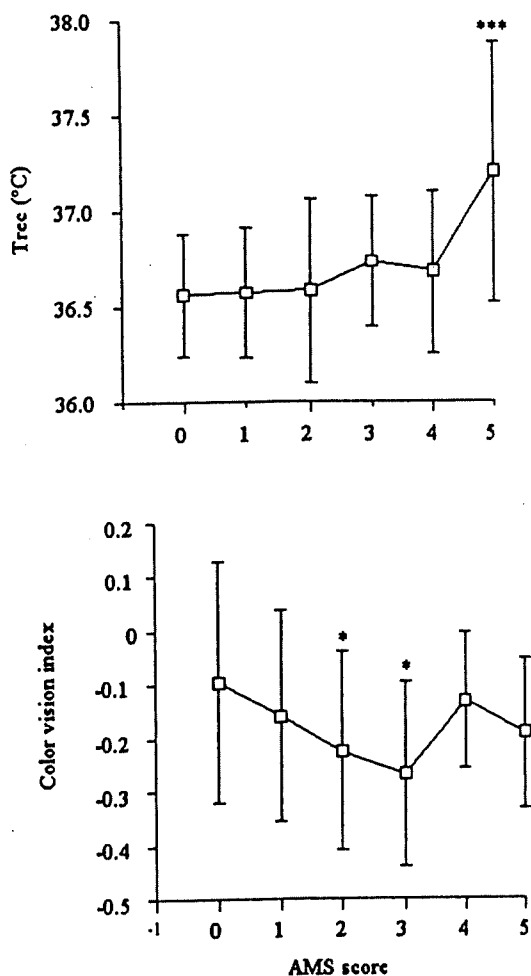


Figure 10. Variations of rectal temperature (Trec) and color vision index as a function of each individual level of AMS score. Mean \pm SD. AMS score different from 0 vs AMS score = 0 : *, $p < 0.05$; ***, $p < 0.001$.

6. COMMENTS

Detailed results of each protocol will be presented and discussed elsewhere. However, general observations and comments can be made. This operation was a great success, both from a scientific and from a human point of view. Approximately 80% of the expected studies have been completed. Seven out of eight altinauts reached the maximal equivalent altitude of Mount Everest. No major accident occurred. The only comparable study previously organized along similar lines was Operation Everest II (OEII) in 1985 (5). No major difference in the main clinical and physiological measured parameters was found between the two studies. However, some interesting variations resulted from the different profile of ascent.

Table 1. General characteristics of the subjects. Maximal oxygen uptake, resting blood gases and hemoglobin concentrations. Mean \pm SD. BMI: body mass index. n=8, except + where n=7 and \$ where n=5. γ : p<0.001, **: p<0.01, *: p<0.05 vs SL

Day in chamber	-10	2	10	17	26	30	35
Condition	SL	5,000	6,000	7,000	8,000	8,848	RSL
Age (yr)	26.6 ± 4.3						
Height (cm)	180 ± 6						
BMI (kg.m ⁻²)	22.9 ± 1.5						
Body weight (kg)	74.3 ± 6.6	72.9 $\pm 6.2^*$	71.6 $\pm 6.0\gamma$	70.4 $\pm 5.8\gamma$	69.8 $\pm 5.8\gamma$	70.2 $\pm 5.4\gamma$	72.2 $\pm 6.4\gamma$
VO _{2max} (ml/min/kg)	56.8 ± 5.0	32.0 $\pm 2.4\gamma$	23.6 $\pm 2.8\gamma$	22.9 $\pm 2.4\gamma$	/	/	50.8 ± 6.8
PO ₂ (mmHg)	101.8 ± 3.9	51.1 $\pm 3.4\gamma$	49.3 $\pm 3.3\gamma$	40.2 $\pm 5.0\gamma$	37.0 $\pm 4.6\gamma$	30.6 $\pm 1.4^s\gamma$	102.3 ± 6.0
PCO ₂ (mmHg)	40.3 ± 3.1	27.5 $\pm 1.4\gamma$	19.8 $\pm 2.0\gamma$	18.0 $\pm 2.6\gamma$	14.3 $\pm 2.1\gamma$	11.9 $\pm 1.4^s\gamma$	31.6 $\pm 2.1\gamma$
pH	7.41 ± 0.03	7.47 $\pm 0.02\gamma$	7.51 $\pm 0.02\gamma$	7.49 $\pm 0.02\gamma$	7.57 $\pm 0.02\gamma$	7.58 $\pm 0.02^s\gamma$	7.43 ± 0.01

Pre-acclimatization at Observatoire Vallot allowed a much better clinical status at 5,000 m during OEIII than during OEII: symptoms of AMS appeared at 6,000 m only. However, with exposure above 7,000 m, headache, dyspnea and lethargy were similarly present in both Operation Everest II and III. Body weight loss, mainly due to dramatic decrease in food intake, was similar, although slightly less in OEIII: 7.3% vs 8.9% of initial body weight (10). A great care was given to the choice of palatable food that was every day adapted to the mood and cravings of the altinauts. This may explain part of the difference. The decrement in $\dot{V}O_{2MAX}$ was greater in OEIII than in OEII, at 5,000m and 6,000m. However, basal SL $\dot{V}O_{2MAX}$ was higher in the present study (56.8 ml/min/kg) than in OEII (51.2 ml/min/kg) and it has been suggested that subjects with higher $\dot{V}O_{2MAX}$ at SL may show a larger decrease at high altitude (3). The further decrease in $\dot{V}O_{2MAX}$ between 6,000 and 7,000m was insignificant, probably because the 7-day period of acclimatization between the two altitudes was efficient to minimize the effect of increasing altitude. After 1 to 3 days of recovery in normoxia, $\dot{V}O_{2MAX}$ was not different from baseline values when expressed in ml/kg/min (Table 1), but significantly different (p<0.05) when expressed in l/min (results not shown), resulting from an incomplete recovery of body weight.

Blood gases were very similar in both OEII and the present study, including at extreme altitude (11). These values obtained in chamber (n=6 for OEII, n=5 for OEIII) were slightly higher than the value (n=1) obtained during the AMREE expedition in 1981 (13).

The speed of recovery from hypoxia when leaving the chamber was quite surprising, especially the gain of body weight (63% of total loss was regained in 4 days). Hemoglobin concentration also went back to sea-level values within four days. This rapid hemodilution effect of reoxygenation (or recompression) is concomitant with a great increase in plasma volume (Robach et al, submitted).

No clear variation of systemic blood pressure was observed along the stay in the chamber, suggesting that despite probable increased blood viscosity and adrenergic activity, there is no sensible increase in peripheral resistance.

The relation between severe AMS and raised body temperature was recently suggested (6) and confirmed in the present study. It may indicate that an inflammatory process is concomitant with the development of AMS. Color vision is slightly altered at high altitude, especially in subjects suffering from AMS. This observation confirms previous findings (9) and may help in providing an objective measurement in the evaluation of AMS. However no clear correlation was found between the variation in color vision index and the intensity of AMS evaluated by the subjective Lake Louise scoring system.

7. HOW DOES A CHAMBER STUDY DIFFER FROM FIELD CONDITIONS ?

The easy availability of palatable food, the absence of cold stress, the relatively low energy expenditure and absence of prolonged physical exercise, the absence of the dangers of climbing mountains and the confinement within a closed space, are factors which differ from field studies. The relative good clinical status of our altinauts throughout the study, their ability to withstand for a few hours extreme hypoxic conditions lead us to think that, in comparison with OEII experiment, the pre-acclimatization period in real mountain conditions and the recovery period at 5,000m before the final ascent may have had a beneficial physiological and psychological impact.

Brain function, as a whole, appeared to be maintained below 8,000m whereas physical performance is known to decline even at moderate altitudes. Hopefully, we can say that the brain is better than the muscle in compensating the lack of oxygen. However, at extreme altitudes, both are compromised, exposing the mountaineer to considerable dangers (Figure 11).

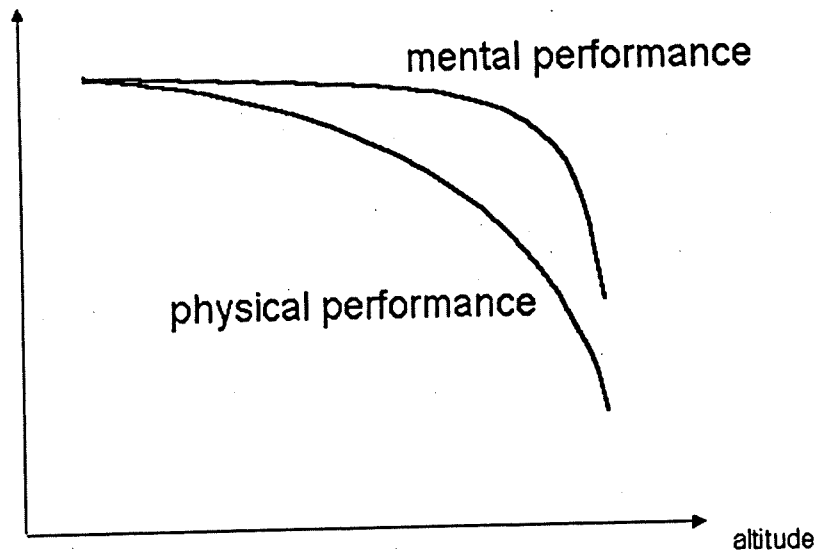


Figure 11. Schematic representation of the variations of mental and physical performance with altitude.

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