

## ORIGINAL ARTICLE

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## Pre-adaptation, adaptation and de-adaptation to high altitude in humans: hormonal and biochemical changes at sea level

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**Abstract** High altitude residence is known to modify body biochemistry and hormone status. However, the effects of such a sojourn on these status observed at sea level both immediately and later after return are not as well established as are the effects of an intermittent acclimation. The aim of this study was therefore to investigate these changes. To achieve our objectives, nine subjects received intermittent acclimation at low pressure in a barometric chamber (8 h daily for 5 days, day 1 at 4500 m, day 5 at 8500 m) before an expedition to the Himalayas. Hormonal and biochemical changes were studied using samples of venous blood taken at sea level before and after acclimation, after return from the expedition and 1 and 2 months after descent. Concentrations of thyroid hormones, adrenaline, noradrenaline (NA), hormones of hydromineral metabolism (aldosterone, renin, arginine vasopressin, atrial natriuretic peptide) as well as prolactin, cortisol, insulin and endothelin 1 were measured. Biochemical measurements made were plasma osmolality, and concentrations of glucose, total cholesterol, total proteins, pre-albumin, transferrin, complement 3C, apolipoproteins A<sub>1</sub> and B and serum iron. *Acclimation* induced no alteration in hormone (except for NA with increases of about 1.5, fold  $P < 0.05$ ) and biochemistry data. *After the expedition*, hormone responses were characterized by a higher total triiodothyronine concentration (+18%,  $P < 0.05$ ) while

other hormones did not vary. A linear relationship was found between thyroid-stimulating-hormone and body mass changes after the expedition ( $r = 0.67$ ,  $P < 0.05$ ). The observed increased concentrations of plasma proteins and total cholesterol ( $P < 0.05$ ) could be related to the restoration of lean body mass. *At 1 and 2 months* after return, no changes in hormones were observed but a significant decrease in transferrin concentration was noticed. The higher serum iron concentration reported after 1 month ( $P < 0.05$ ) could have been the result of a physiological haemolysis. It was concluded that both acclimation and the expedition in the Himalayas affected hormone status and body biochemistry status even though the observed changes were slight and rapidly reversed.

**Key words** Hormones · Biochemical changes  
Pre/de-adaptation · Hypoxia · Thyroid

### Introduction

During high altitude residence changes in body mass and in body fluids have been observed both in acute mountain sickness and in asymptomatic subjects. These alterations could follow changes in status of hormones not only in hydromineral metabolism, corticosteroids, adreno-sympathetic system, thyroid hormones but also to biochemical effects due in part to the hormone changes.

Hormones of hydromineral metabolism during exposure to chronic hypoxia have previously been studied both at rest and during exercise (Slater et al. 1969; Singh et al. 1974; Sutton et al. 1977; Hackett et al. 1978; Milledge et al. 1982, 1983a, b; Milledge and Catley 1987; Maresch 1985; Bärtsch et al. 1991; Rock et al. 1993; Anand et al. 1993; Ponchia et al. 1995). From these studies, it has generally been admitted that hypoxia initially depresses plasma aldosterone concentration which returns to control values after 12–20 days (Milledge et al. 1983b). However, studies concerning plasma

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renin activity (Ward et al. 1989; Anand et al. 1993), atrial natriuretic peptide (Koller et al. 1991; Anand et al. 1993; Ponchia et al. 1995) or antidiuretic hormone (Hackett et al. 1978; Koller et al. 1991; Ramirez et al. 1993) have been conflicting as are the results obtained from corticosteroid hormones (Siri et al. 1969; Maresh et al. 1985; Ward et al. 1989). The adreno-sympathetic system is also affected by high altitude residence as has been shown by Cunningham et al. (1965), Sutton et al. (1986) during operation Everest II, Savard (1993) and Mazzeo (1993). It has been reported that the noradrenaline (NA) response is very different from that observed for adrenaline (A) since resting.

A concentration gradually decreases over time whereas noradrenaline increases (Mazzeo 1993; Antezana et al. 1994) and the response of the heart to adrenergic stimulation becomes blunted.

The thyroid hormone status is also altered by high altitude residence and an increased concentration of free thyroxine ( $T_4$ ) without change in thyroid stimulating hormone (TSH) has been reported at the beginning of a sojourn (Surks 1966). It has been found that thyroid hormones show concentrations returning towards control values in the 3rd week at altitude (Stock et al. 1978). After return (6–7 days), Rastogi et al. (1977) and Gunga et al. (1994) have not found any thyroid hormone changes whereas Hackney et al. (1995) have reported a “low  $T_3$  syndrome” characterized by a decrease in total and free triiodothyronine  $TT_3$  and  $fT_3$  after 13 days on Denali. Changes in concentrations of other hormones such as insulin, glucagon, prolactin during or after high altitude residence are not well documented. It has been reported however, that resting insulin concentrations were reduced at altitude (Stock et al. 1978) or increased (Young et al. 1992) whereas glucagon (Blume 1984; Young et al. 1992) and prolactin concentrations have been reported to be unchanged (Bangham and Hackett 1978).

Plasma biochemical studies performed during or after high altitude residence have also been rare and often focus on glucide and lipid aspects only. Stock et al. (1978), and Blume (1984) have found a lowered fasting blood glucose concentration and Singh et al. (1974) have reported a persistently raised glucose concentration for 10 months at altitude. During Operation Everest II, Young et al. (1989) have shown that in fasting subjects total cholesterol, high density lipoprotein (HDL) cholesterol concentrations decreased whereas those of triglycerides (TG) increased twofold and free fatty acids were unchanged. These results were not found by Fe-

rezou et al. (1988) who have reported decreases in TG and in total cholesterol without changes in HDL cholesterol concentration.

Consequently, hormone status and body biochemistry are changed during high altitude residence although the results obtained have often been conflicting. However, do these changes persist both immediately and later after return to sea level? Little is known of this de-adaptation process just as the effects of intermittent acclimation are. The aim of this study was therefore to demonstrate some hormone and biochemistry changes in subjects resting at sea-level, firstly, after intermittent exposure to hypoxia in a hypobaric chamber (pre-adaptation) performed before an expedition to the Himalayas (adaptation) and, secondly, 1 and 2 months after return (de-adaptation).

## Methods

### Subjects

Nine healthy male subjects, who had not been at high-altitude for a period of 2 months, were studied during the Everest-Lhotse 93 expedition (Groupe Militaire de Haute Montagne, Chamonix, France directed by C.B. Esteve). Three of them had previously had experience of 8000-m peaks. All the subjects had trained regularly for endurance (running). After the protocol was approved by the Grenoble University Ethics Committee, all the participants signed an informed consent after medical examination. The mean characteristics of the subjects were as follows: age 33.10 (SEM 2.30) years; height 1.75 (SEM 0.02) m. Body mass and percentage body fat changes throughout the experiment are presented in Table 1.

Body mass was measured with an electronic balance (Sauter, France) with an accuracy of  $\pm 20$  g. Body fat content was determined following an equation of Lohman et al. (1975) using skinfold thickness. These were measured with an Holtain caliper (Crymich, UK).

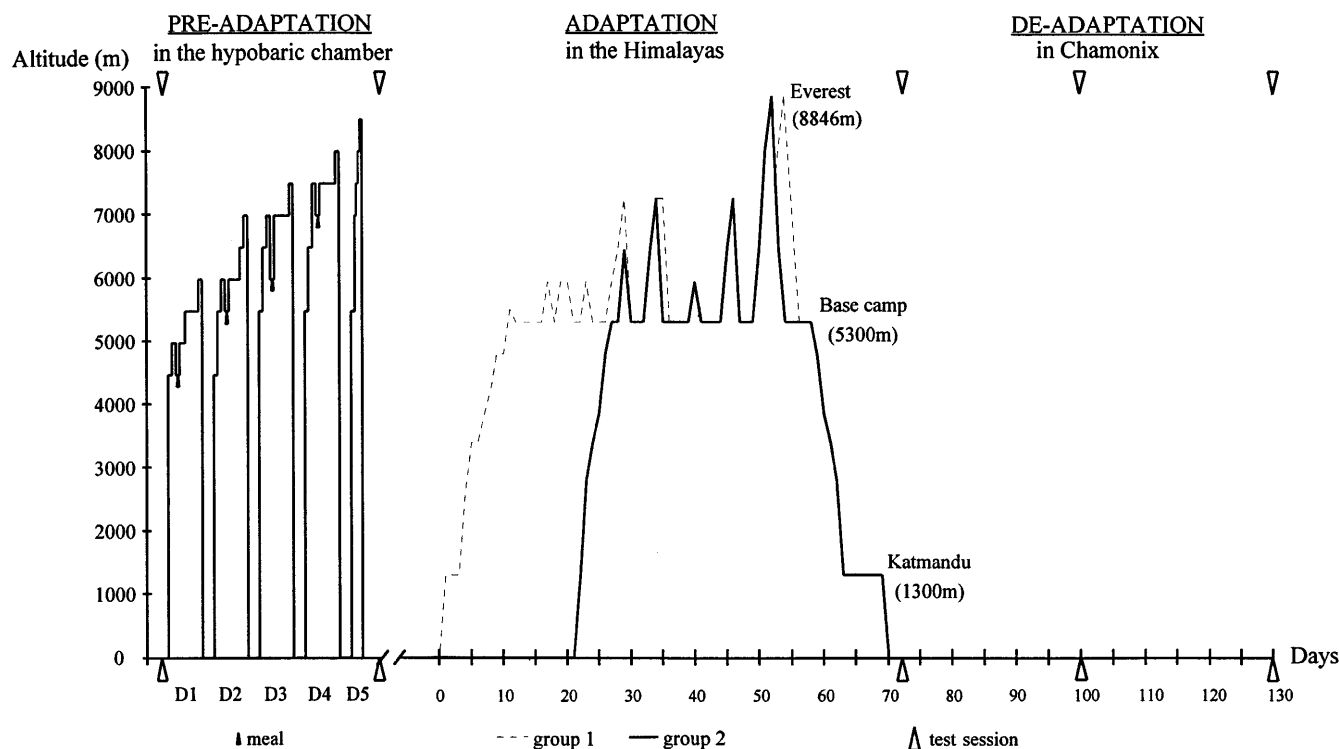
### Pre-adaptation protocol in the hypobaric chamber

This protocol has previously been described (Savourey et al. 1996) and the time course is shown in Fig. 1. Intermittent pre-adaptation to hypoxia was performed at low pressure in a barometric chamber in Grenoble La Tronche (250 m, barometric pressure = 992 hPa) for 5 days (D1–D5). The subjects spent 8 h per day on D1–D4 and 4 h on D5 in this chamber (volume 30 m<sup>3</sup>). They came out of the chamber every evening to have a good meal and slept in town in comfortable conditions. The temperature in the chamber remained constant (20–22°C) except during decompression or recompression. The simulated altitude increased progressively throughout the day and from one day to the next (4500 m–8500 m). During this period drinks and food were available ad libitum. Meals were taken at a reduced altitude (4500–7000 m). The subjects were accompanied by a physician who breathed O<sub>2</sub> through an O<sub>2</sub> diluter demand mask

**Table 1** Biometrical characteristics of the subjects observed throughout the experiment

	Before acclimation		After acclimation		After expedition		1 month after the expedition		2 months after the expedition	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Body mass (kg)	69.38	2.32	68.48	2.47	67.98	2.39*	69.66	2.16	69.51	2.23
Body fat (%)	14.12	0.49	13.52	0.48	13.57	0.38	13.85	0.45	13.60	0.41

\*  $P < 0.05$  Statistical significance between values compared to control values (before acclimation)



(Eros MC 10, Plaisir, France). The chamber was flushed with medical quality gas to maintain the inspired fraction of  $O_2$  at 0.21 and the inspired fraction of  $CO_2$  near 0.0. The subjects listened to music, played games and performed moderate physical exercise on a cycle ergometer. On the day after the protocol was completed, the subjects took a fast train to Paris (60 m) and then flew to Katmandu (1300 m). The first group ( $n = 6$ ) left Paris on Saturday, 14th August, and the second left Paris on Saturday, 4th September. However, the intermittent pre-adaptation protocol was exactly the same for the two groups and was performed between August 9th–13th for the first group and between August 30th–September 3th for the second group. No medical problems were encountered during acclimation except for one subject who presented signs of acute mountain sickness (headaches and nausea) at the end of day 2 only.

#### The expedition in the himalayas

The time course of the expedition is presented in Fig. 1. The first group equipped the base camp, camp 1 (6400 m) and camp 2 (7200 m) and remained above 5300 m until the time of descent. The second group reached the base camp (5300 m) after trekking for 5 days after their arrival in Katmandu. Camp 1 (6400 m) was reached the day after and 2 days after they had started from the base camp they arrived at camp 2 (7200 m). Two subjects reached the summit of Mount Everest without supplementary  $O_2$  and three subjects with supplementary  $O_2$ . The expedition ended after 62 days for the first group and after 41 days for the second group. All the subjects were back in Grenoble for retesting within 10 days after they had left the base camp. No medical problems were encountered during the expedition though an avalanche destroyed camp 2.

#### Biological measurements

Hormone and body biochemistry measurements were obtained from venous blood samples in fasting subjects. An intravenous catheter (Angiocath Deseret Medical 20G 2IN) was inserted in the cubital vein and blood samples were collected at sea-level (992 hPa,

**Fig. 1** Time course of the experiment. The pre-adaptation protocol was performed over 5 days (D1–D5) before the departure to Katmandu (day 0 for the first group and day 21 for the second group). The time course of the expedition in the Himalayas is given for the two groups (dashed line for group 1 and solid line for group 2). Arrows indicate test sessions

220 m) at 8 a.m. after the subjects had been sitting quietly for 30 min at a comfortable ambient temperature (dry bulb temperature  $22^\circ C$ , relative humidity 30%–40%). The subjects then had breakfast. These samples were taken before and after acclimation, after the expedition, and 1 and 2 months later. After collection, the blood samples were immediately placed in ice and then centrifuged at 3200 rpm at  $4^\circ C$  for 15 min. Aliquots of the plasma samples were stored at  $-70^\circ C$  until analysed. All analytical measurements were made in duplicate. Samples for individual subjects were measured in the same assay to avoid run-to-run assay variation.

#### Hormone measurements

Thyroid status was studied from the sterile tubes used to collect the aliquot of blood. Thyroxine ( $TT_4$ ) was measured by an immunological method using fluorescent polarization (FPIA on TDX Abbott Diagnostic) with an assay detection limit of  $8 \text{ nmol} \cdot \text{l}^{-1}$ . The  $TT_3$  concentration was measured by a radioimmunoassay (RIA) method (Gamma-Coat [ $^{125}I$ ]  $T_3$  RIA/clinical assay Incstar) with an assay detection limit of  $0.3 \text{ nmol} \cdot \text{l}^{-1}$ . The  $ft_3$  and  $ft_4$  (free  $T_3$  and free  $T_4$ ) concentrations were measured by RIA (RIA Kits  $ft_3$  and  $ft_4$ , Sclavo, Italy), with an assay detection limit of  $2 \text{ pmol} \cdot \text{l}^{-1}$ . Thyroid stimulating hormone (TSH) concentration was measured by RIA (Kit Gnost h TSH, Behring) with an assay detection limit of  $0.03 \text{ mIU} \cdot \text{l}^{-1}$ .

Among the hormones of hydromineral metabolism aldosterone concentration was measured by an RIA method (CIS bio-international, Gif sur Yvette, France) with an assay detection limit of  $15 \text{ pg} \cdot \text{ml}^{-1}$ . The intra and inter-assay coefficients of variation were

8% and 6%, respectively. Plasma renin concentration was measured using an RIA method (Eria Diagnostic Pasteur, Marne la Coquette, France) with an assay detection limit of  $3.5 \text{ pg} \cdot \text{ml}^{-1}$ . The intra and inter-assay coefficients of variation were 3.6% and 6.9%, respectively.

The RIA of arginine vasopressin (AVP) was performed on extracted plasma (bentonite) and the assay sensitivity was  $0.3 \text{ pg} \cdot \text{ml}^{-1}$ . The intra and inter-assay coefficients of variation were 3% and 11%, respectively. The antibodies were a gift from L. Keil. The atrial natriuretic peptide (ANP) RIA was made after extraction with octadecylsibyl cartbridges (Sep-Pak). The antibodies were a gift from J. Gutkowska. Intra and inter-assay coefficients of variation were 10% and sensitivity was  $1.2 \text{ ng} \cdot \text{ml}^{-1}$ .

Plasma A and NA concentrations were measured using the high performance liquid chromatography-ED technique after plasma extraction (Perkin Elmer LC.250, Norwalk, Conn. USA). The reproducibility was 5% and the sensitivity was  $10 \text{ pg} \cdot \text{ml}^{-1}$  and  $35 \text{ pg} \cdot \text{ml}^{-1}$  for A and NA, respectively. The A and NA concentrations were not determined among the data collected 1 and 2 months after the expedition because the plasma aliquots were insufficient at this stage.

Cortisol concentration was measured using the Quanticat TM RIA kits ( $^{125}\text{I}$ -cortisol RIA kit, Kallestad Diagnostic Inc, Chaska, Minn., USA) with a sensitivity of  $0.5 \text{ } \mu\text{g} \cdot \text{dl}^{-1}$ . Insulin concentration was measured using the BI-Insuline RIA Pasteur Kits (Eria Diagnostic Pasteur) with a sensitivity of  $1.5 \text{ } \mu\text{IU} \cdot \text{ml}^{-1}$  and prolactin concentration was measured by immunoradiometric assay (PRL.Irma, Medgenix Diagnostic S.A., Fleurus, Belgium) with a sensitivity of  $0.35 \text{ ng} \cdot \text{ml}^{-1}$ . Endothelin 1 concentration was measured by RIA ( $^{125}\text{I}$  endothelin RIA, Amersham Kit) after the aliquot of plasma was acidified with 6 ml of  $1 \text{ mol} \cdot \text{l}^{-1}$  acetic acid and applied to a C18 SEP-PAK Cartbridge (Waters Associates, Milford, Calif.) prewashed sequentially with 8-ml 100% acetonitrile, and 8-ml 0.2% ammonium acetate, pH 4.0. The sensitivity of the method was  $0.2 \text{ pg} \cdot \text{ml}^{-1}$  and the intra and inter-assay coefficients of variation were less than 10% respectively.

#### Biochemistry measurements

The  $\text{Na}^+$  and  $\text{K}^+$  concentrations were measured using a SMAC-2 Technicon autoanalyser and osmolality using an automated micro-osmometer (13/13 DR, Hessechnick, Berlin, Germany). Blood glucose, total cholesterol, triglycerides, plasma total proteins, albumin, serum iron concentrations were measured using calorimetric methods, with an automated analysis system (BM Hitachi

System 704, Tokyo, Japan). Tranferrin, haptoglobin, complement 3C, pre-albumin, retinol binding protein, apolipoproteins A1 and B concentrations were measured using the immuno turbidimetry method with an automated analysis system (BNA, Rueil Malmaison, France).

#### Statistical analysis

Data were analysed using a one-way analysis of variance (time effect) with repeated measures (Statistica for Windows, Statsoft, Tulsa, Okla., USA). When the overall statistical differences were found without interaction, means were compared using a Tukey post-hoc test. Relationships between variables were studied using linear correlation. The null hypothesis was rejected for  $P < 0.05$ .

## Results

### Biometrical characteristics

As previously reported (Savourey et al. 1996), body mass had decreased after the expedition ( $-1.40 \text{ kg}$ ,  $P < 0.05$ ) but was unchanged after acclimation and 1 and 2 months after return. Body fat percentage did not vary significantly throughout the experiment (Table 1).

### Hormone changes

Hormone concentration changes throughout the experiment are shown in Table 2. Thyroid hormone changes were characterized only by a significantly increased  $\text{TT}_3$  after the expedition ( $+18\%$ ,  $P < 0.05$ ). Concentrations of hormones of hydromineral metabolism (aldosterone, renin, AVP, ANP) were unchanged. The NA concentration increased after acclimation only ( $+52.6\%$ ,  $P < 0.05$ ) whereas those of A, cortisol, prolactin, insulin and endothelin 1 did not vary throughout the experiment.

**Table 2** Hormone changes observed during the experiment.  $\text{TT}_3$ ,  $\text{fT}_3$  Total and free triiodothyronine,  $\text{TT}_4$ ,  $\text{fT}_4$  total and free thyroxine,  $\text{TSH}$  thyroid stimulating hormone  $\text{AVP}$  arginine vasopressin,  $\text{ANP}$  atrial natriuretic peptide

Quantity	Before acclimation		After acclimation		After expedition		1 month after the expedition		2 months after the expedition	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
$\text{TT}_4$ ( $\text{nmol} \cdot \text{l}^{-1}$ )	78.3	6.3	87.6	6.3	86.8	5.7	79.6	4.9	79.3	5.3
$\text{fT}_4$ ( $\text{pmol} \cdot \text{l}^{-1}$ )	12.0	0.45	12.7	0.59	12.7	0.54	12.0	0.35	12.9	0.40
$\text{TT}_3$ ( $\text{nmol} \cdot \text{l}^{-1}$ )	2.28	0.10	2.32	0.09	2.69	0.13*	2.33	0.13	2.14	0.08
$\text{fT}_3$ ( $\text{pmol} \cdot \text{l}^{-1}$ )	5.80	0.17	6.09	0.21	6.42	0.15	6.03	0.20		
$\text{TSH}$ ( $\mu\text{IU} \cdot \text{ml}^{-1}$ )	1.68	0.23	1.60	0.28	2.22	0.46	1.56	0.28		
Aldosterone ( $\text{pg} \cdot \text{ml}^{-1}$ )	237.2	24.2	290.3	43.8	304.1	66.8	209.9	25.9		
Renin ( $\text{pg} \cdot \text{ml}^{-1}$ )	12.36	1.89	19.70	4.65	14.34	4.00	10.68	1.58	8.12	2.22
AVP ( $\text{pg} \cdot \text{ml}^{-1}$ )	2.18	0.80	1.75	0.36	1.42	0.23	1.31	0.19	0.94	0.12
ANP ( $\text{pg} \cdot \text{ml}^{-1}$ )	33.6	3.2	31.0	2.5	42.3	4.7	41.9	5.5	36.6	2.9
Noradrenaline ( $\text{pg} \cdot \text{ml}^{-1}$ )	365.7	33.5	558.2	78.1*	380.6	35.2				
Adrenaline ( $\text{pg} \cdot \text{ml}^{-1}$ )	632.4	266.8	604.1	106.0	373.8	141.7				
Cortisol ( $\mu\text{g} \cdot \text{dl}^{-1}$ )	19.07	1.31	17.07	1.56	16.03	1.42	14.96	1.17	16.49	1.62
Prolactin ( $\text{ng} \cdot \text{ml}^{-1}$ )	4.21	0.49	4.61	0.47	5.02	0.36	4.79	0.36	4.70	0.29
Insulin ( $\mu\text{IU} \cdot \text{ml}^{-1}$ )	25.11	5.31	38.32	5.06	34.54	7.71	29.30	6.85		
Endothelin 1 ( $\text{pg} \cdot \text{ml}^{-1}$ )	21.2	2.9	14.5	2.4	14.9	2.0	14.3	1.3	16.2	1.3

\*  $P < 0.05$  Statistically significant compared to values before acclimation

**Table 3** Biochemical changes observed throughout the experiment

Quantity	Before acclimation		After acclimation		After expedition		1 month after the expedition		2 months after the expedition	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Na <sup>+</sup> (mmol·l <sup>-1</sup> )	140.6	0.53	141.3	0.88	141.7	0.50	142.4	1.45	141.6	0.65
K <sup>+</sup> (mmol·l <sup>-1</sup> )	4.10	0.07	4.08	0.07	4.01	0.07	4.04	0.09	4.00	0.12
Osmolality (mosmol·kg <sup>-1</sup> H <sub>2</sub> O)	292.7	1.27	292.9	1.41	294.7	0.88	295.8	1.68	293.3	0.71
Glucose (mmol·l <sup>-1</sup> )	5.24	0.17	4.95	0.41	4.11	0.29	4.73	0.24	4.65	0.32
Total cholesterol (mmol·l <sup>-1</sup> )	5.13	0.37	4.76	0.23	5.89	0.33*	5.13	0.27	4.57	0.16
Triglycerides (mmol·l <sup>-1</sup> )	1.11	0.20	0.97	0.07	1.54	0.21	1.02	0.14	0.93	0.22
Serum iron (μmol·l <sup>-1</sup> )	17.3	1.1	14.1	2.2	25.3	1.7*	21.4	1.3*	18.2	1.3
Proteins (g·l <sup>-1</sup> )	75.7	1.7	75.0	1.4	81.4	1.4*	75.2	2.0	73.4	1.7
Albumin (g·l <sup>-1</sup> )	54.0	1.3	53.0	1.1	56.2	1.1*	52.6	1.0	52.0	0.8
Complement 3C (g·l <sup>-1</sup> )	0.79	0.04	0.72	0.02	0.80	0.04	0.64	0.03**	0.64	0.03**
Transferrin (g·l <sup>-1</sup> )	2.81	0.09	2.64	0.09	2.98	0.08	2.43	0.10**	2.46	0.10**
Haptoglobin (g·l <sup>-1</sup> )	0.98	0.01	1.15	0.09	1.56	0.30	1.09	0.21	0.94	0.15
Prealbumin (g·l <sup>-1</sup> )	0.34	0.01	0.33	0.01	0.39	0.01**	0.32	0.01	0.31	0.02
Retinol binding protein (g·l <sup>-1</sup> )	0.05	0.003	0.05	0.002	0.06	0.003**	0.05	0.002	0.05	0.003
Apolipoproteins A1 (g·l <sup>-1</sup> )	1.69	0.08	1.53	0.05	1.70	0.07	1.58	0.08	1.53	0.07
Apolipoproteins B (g·l <sup>-1</sup> )	0.81	0.07	0.72	0.04	0.99	0.06*	0.84	0.04	0.76	0.04

Statistical significance compared to values before acclimation \*  $P < 0.05$ , \*\*  $P < 0.01$

### Biochemical changes

Plasma Na<sup>+</sup> K<sup>+</sup> and concentrations and osmolality were unchanged throughout the experiment as well as the concentrations of plasma glucose and triglycerides (Table 3). However, concentrations of total cholesterol, total proteins, pre-albumin, retinol binding proteins and apolipoproteins B varied only after the expedition (+14.8%, +7.5%, +14.7%, +20% and +22.2%, respectively,  $P < 0.05$ ). The serum iron concentration increased both after the expedition (+46.2%,  $P < 0.01$ ) and 1 month after return (+23.7%,  $P < 0.01$ ). Complement 3C and transferrin decreased only 1 and 2 months after descent ( $P < 0.05$ ).

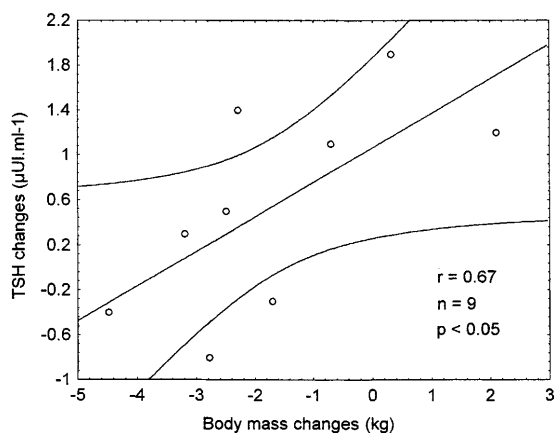
### Discussion

This experiment illustrates both the effects of intermittent acclimation in a hypobaric chamber performed before acclimatization in the Himalayas and the physiological de-adaptation from high altitude observed 1 and 2 months after descent from the point of view of hormone and body biochemistry changes studied at sea level.

As has previously been reported by Savourey et al. (1996), the acclimation protocol is efficient in inducing pre-adaptation to high altitude, which is characterized by ventilatory and haematological changes. However, these physiological mechanisms of pre-adaptation to hypoxia were not accompanied by significant body biochemistry or hormone changes except for NA concentration, which was 52.6% higher than control values, whereas A did not vary. This discrepancy has already been reported by Young et al. (1992) during operation Everest II, Antezana et al. (1994) and Anand et al. (1993). The absence of changes in concentration in the

hormones of hydromineral metabolism is not surprising since, firstly, plasma Na<sup>+</sup>, K<sup>+</sup> and osmolality were unchanged by acclimation as shown in this study and secondly, because heart rate and arterial blood pressure were also unaffected by acclimation as has previously been reported by Savourey et al. (1996). These results are in line with those of Koller et al. (1991) who have demonstrated that ANP and AVP concentrations were unchanged in acclimatized subjects except for acute subjects with mountain sickness. In the same way, it appeared that thyroid status was unaffected by intermittent hypoxia as has been observed after several weeks at high altitude by Stock et al. (1978), and Gunga et al. (1994). Consequently, it would seem that the hormone and (or) body biochemistry changes often reported during acute hypoxia exposure are quickly reversed since intermittent exposure to acute hypoxia did not disturb hormone status and body biochemistry studied at sea level.

The de-adaptation process concerning changes in hormone status and body biochemistry must be discussed taking into account the changes induced by the expedition. As has been reported by Kayser (1992, 1994) an important point is the decreased body mass (-1.40 kg,  $P < 0.05$ ) commonly observed after a high altitude expedition. This loss of body mass only concerns lean body mass since body fat content is unchanged. Conversely, 1 month later body mass had returned to control values attesting a restoration of lean body mass. In those conditions, disturbances in hormone and (or) body biochemistry data would be expected, especially, in the components involved in muscle synthesis. Indeed, after the expedition, thyroid status was modified though the observed values remained within the physiological range. The significant increase in concentrations of TT<sub>3</sub> ( $P < 0.05$ ) with an increase in TSH (+32%,  $P = 0.08$ ) demonstrated that the thyroid gland was stimulated.



**Fig. 2** Relationship between body mass changes and thyroid-stimulating hormone (TSH) changes observed after the expedition, showing the calculated line of regression and 95% confidence limits

These results differ from those reported by other authors. For instance, Gunga et al. (1994) have shown that thyroid status was unchanged at sea level after 5 days at 2315 m and Hackney et al. (1994) have reported a "low  $T_3$  syndrome" after 13 days on Denali. However, that the last result could be better explained by cold exposure, as mentioned by the authors themselves and by Savourey et al. (1994). Moreover, it seems that thyroid status could be disturbed after a high altitude expedition following the loss in body mass as suggested in this study because we found a linear relationship between changes in body mass and TSH concentration changes (Fig. 2,  $r = 0.67$ ,  $P < 0.05$ ); whereas body mass was unrelated to other thyroid hormones. This relationship indicated that body mass loss and (or) body mass recovery is affected by (or affect) thyroid status. Those results are difficult to interpret and need further study since the relationships between body mass recovery and thyroid hormones after a high altitude sojourn are not well documented in the literature. In the future, it will however be necessary to take into account body mass changes to interpret thyroid hormone changes, especially after high altitude residence.

It is also well known that thyroid hormones activate protein synthesis. This fact is suggested in this study since concentration of total plasma proteins, pre-albumin, apolipoproteins B and retinol binding proteins significantly increased after the expedition and remained unchanged 1 and 2 months later. The origin of this increased protein synthesis was probably the liver since all these proteins come from this organ. Total cholesterol concentration was higher after the expedition ( $P < 0.05$ ) and remained unchanged later. These results are not in line with those reported by Young et al. (1989) during operation Everest II and by Ferezou et al. (1988) who have shown a decrease in total cholesterol concentration. However, blood samples in both studies were performed at altitude whereas our measurements were made at sea level. In these circumstances, comparisons between results are difficult.

At 1 and 2 months after descent, all the hormone and body biochemistry changes returned towards control values, as described above, except for transferrin and complement 3C concentration which decreased ( $P < 0.05$ ). Serum iron concentration increased both after the expedition and 1 month later. These results could have been related to a physiological haemolysis as suggested by Savourey et al. (1996) who have reported that the polycythaemia of high altitude persisted 1 month and disappeared 2 months after return. An alternative explanation could be an overshoot increase in the absorption of iron, stimulated by the increased utilisation. The reduction in serum iron concentration found after acclimation (but not significant) could provide evidence of this stimulus. However, additional biochemistry measurement would be necessary to confirm this possibility.

In conclusion, this study showed that intermittent acclimation in a hypobaric chamber did not alter hormones and body biochemistry at sea level except for NA concentration. After the expedition in the Himalayas, changes in hormones and body biochemistry at sea level were only characterized by increased concentrations of  $TT_3$  and plasma proteins. Moreover, thyroid hormones concentration changes (attested by TSH changes) were related to changes in body mass suggesting a contribution of thyroid hormones to the restoration of body mass after high altitude residence. All these observed changes had disappeared 1 month later.

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