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Arterial Oxygen Saturation During Ascent to 5010 m: Heart Rate and AMS Scores

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Abstract

The hypothesis here is that tissues exposed to the hypoxia of altitude have increased blood flow so that the rate of arrival of oxygen is as rapid as normal. If the ascent is too rapid, the system starts to fail. The study involves an ascent to high altitude (5010 m) during which 59 subjects recorded their resting arterial oxygen saturation (SaO_2), heart rate (HR) and Lake Louise acute mountain sickness (AMS) scores, twice daily. During the major ascent SaO_2 fell progressively. In 42 subjects, HR increased in a highly significant, negative, relationship to SaO_2 . In 10 subjects heart rate (HR) remained unchanged. Three subjects showed extreme HR variability. Data were incomplete in four subjects. For nine of the subjects, showing the progressive HR versus SaO_2 correlation during ascent, the sequence terminated with a lower HR than would be expected from the correlation so far. Individual AMS scores showed no correlation with SaO_2 but averaged values from 19 of the subjects from each 'one night' stopover; showed a strong, negative, correlation. Average stopover HR values correlated negatively with the average SaO_2 values. Cardiac output (CO) is likely to have increased during ascent as HR increased, since there is a progressive relationship between HR and cardiac output (CO). Hence, despite the progressive fall in SaO_2 , tissue oxygen delivery (DO_2) would have remained close to normal in the 42 subjects who showed the significant HR: SaO_2 relationship.

Keywords: high altitude, SaO_2 , heart rate, acute mountain sickness, oxygen delivery

1. Introduction

During ascent to high altitude, the fractional concentration of oxygen in the atmospheric gas is unchanged but overall barometric pressure falls. This means that there are less oxygen molecules per unit volume, so the activity, or oxygen partial pressure, falls. Breathing will only compensate for this, with a closer approach to normal concentration of oxygen in the blood (known as 'content,' CaO_2), if it is increased. Initially, lowered oxygen in the lung and hence in the blood causes blood flow to the brain to increase, washing out carbon dioxide (CO_2) from the brain environment. The increase in blood flow allows the rate of arrival of oxygen at the brain to normalize, the higher flow compensating for the lower CaO_2 . So the rate of arrival of oxygen (oxygen delivery, DO_2) is sustained at or near the normal rate—three times the rate of cerebral oxygen consumption cerebral metabolic rate for oxygen, CMRO_2 [1]. However, the lower CO_2 in the brain, and resulting alkalinity, inhibits breathing via the central chemoreceptor, counteracting the stimulating effect of low oxygen at the peripheral arterial chemoreceptor. There is therefore an initial pause in ventilatory stimulation. Over 2–5 days, for a subject remaining at the same altitude, brain inhibition is removed as acidity is corrected. This restores the central chemoreceptor level of respiratory stimulus (removal of inhibition). So now the ventilatory stimulus from the peripheral arterial chemoreceptor activity stimulates ventilation, with improvement in the arterial oxygen level [1]. Since these effects are operating at the same time as subjects ascend, with environmental oxygen falling progressively, arterial oxygen content (CaO_2) and oxygen saturation (SaO_2) usually fall progressively during ascent.

Since individual breathing responses (known as ventilatory responses) vary between individuals the progressive drop in CaO_2 also varies between individuals. Most of the oxygen in the blood is carried on hemoglobin in the red cells and low CaO_2 is paralleled by lower arterial oxygen saturation of the hemoglobin (SaO_2). With little change in hemoglobin concentration (Hb) during ascent, SaO_2 therefore provides a guide to CaO_2 change. If there was no change in cardiac output (CO) the rate of oxygen delivery to the tissues ($\text{DO}_2 = \text{CO} \times \text{CaO}_2$) would fall in proportion to the fall in SaO_2 . Here we are interested in the possibility that there may be compensatory increases in CO helping to sustain a more normal DO_2 . During ascent, the use of a pulse oximeter provides SaO_2 and also gives the heart rate (HR). Cardiac output is equal to stroke volume (SV) times HR, that is, $\text{CO} = \text{HR} \times \text{SV}$. With only modest changes in SV during ascent HR changes can therefore act as a surrogate for CO changes. Increases in HR as SaO_2 falls during ascent would suggest that CO increases too. Increases in CO as $\text{SaO}_2/\text{CaO}_2$ fall will mean that there is compensatory response helping to maintain DO_2 . It is therefore important to see whether there is a significant HR increase in relation to falling SaO_2 and to see whether this occurs in all or some subjects. Increases in heart rate can therefore be used as an indirect indicator of any cardiac output increase mitigating DO_2 reduction.

In a recent high-altitude study [2], undertaken in South America, eight normal subjects acclimatized to moderately high altitude during an initial 5-day sojourn at Cusco (3324 m). This was followed by two brief ascents to around 5000 m over a 4-week period. The preliminary acclimatization and brief ascents meant the subjects were likely to be less stressed by their hypoxic exposure than occurs with progressive ascents from sea level. Total time at high

altitude was 28 days, the largest proportion at Cusco. SaO_2 and HR were recorded twice daily. For seven of the subjects, there was a highly significant relationship between HR and SaO_2 , with the highest HR accompanying the lowest SaO_2 value. The remaining subject sustained near normal SaO_2 and HR. $\text{HR} \times \text{SaO}_2$ (assumed to give a value changing in relation to DO_2) remained near constant throughout the trek in all subjects. Since $\text{HR} \times \text{SaO}_2$ will have a similar trend to $\text{CO} \times \text{CaO}_2$, DO_2 will have been well sustained despite the varying degrees of hypoxia. Despite apparently relatively good DO_2 maintenance, for these subjects, individual mean acute mountain sickness (AMS) scores correlated significantly with mean SaO_2 values both at rest and with mild exercise (30 cm step up over 2 min).

In a second high-altitude study, undertaken by 14 schoolboys and their teacher, an ascent was made to Annapurna base camp (4130 m) [3]. There was no preliminary acclimatization and, due to shortage of stopover sites, the final two ascent stages were large. The subjects each recorded SaO_2 and HR soon after arrival at each new altitude both at rest and with mild exercise. Not all subjects showed individually significant HR versus SaO_2 changes, but the overview across subjects (mean values at each altitude) was highly significant both for rest and exercise. Of interest was the fact that, for exercise, $\text{HR} \times \text{SaO}_2$, otherwise constant, showed a large fall for the last ascent stage and base camp. Anecdotally, most subjects suffered considerable AMS symptoms during the 1 day stop at base camp. A plot of the mean values of HR versus SaO_2 for exercise shows a highly significant trend (**Figure 1**), but the HR value for base camp gives a point lower than expected from the rest of the values trend for HR versus SaO_2 . This may well represent a failure of DO_2 compensation.

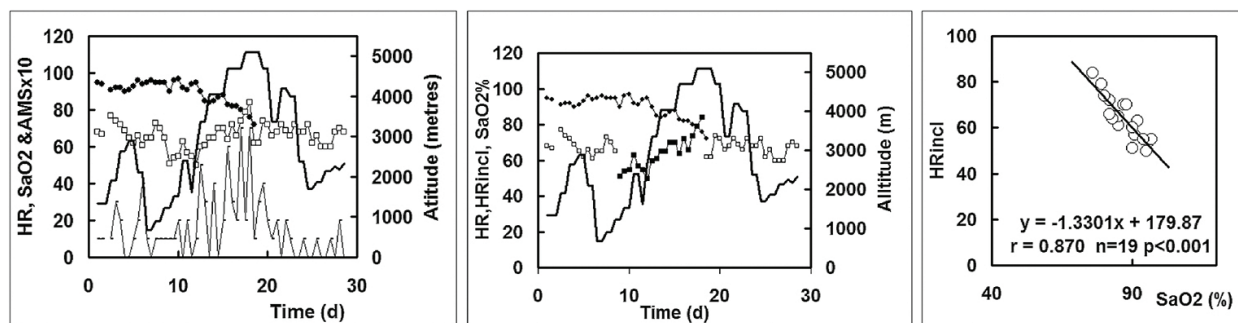


Figure 1. Data from this subject (15) illustrates rising HR during ascent. On the left HR (open squares), SaO_2 (filled circles) and $\text{AMS} \times 10$ scores (mini flags) are shown (left hand axis) with altitude (right hand axis, continuous line). The middle plot shows the ascending values of HR as filled squares and omits the AMS scores. The plot on the right shows the ascending HR values plotted against SaO_2 —slope significant at the $p < 0.001$ level.

1.1. Reasons why DO_2 control is important

Surprisingly, oxygen combines extreme toxicity with capability to provide energy more efficiently than other biochemical means utilized by other species. The ready conversion of oxygen to dangerous free radicals is largely prevented in our cells by the specific energy-generating biochemical sequences, especially featuring the Krebs cycle. There is an optimum

rate at which oxygen flows to a particular tissue and this bears a constant relationship to the rate at which oxygen is utilized (VO_2). Hence, we have values for DO_2/VO_2 which are normally sustained at values specific to the tissue: for the brain 3:1, for heart 1.6:1 and at exercise rates below competitive levels skeletal muscle sustains a ratio 1.5:1 [4]. Maintaining these DO_2 values not only provides sufficient oxygen but also avoids an excess, which would endanger toxicity. Inadequacy of oxygen supply can endanger life following surgery partly from a tendency for an oxygen debt to develop during an operation. This results from reduced arterial pressure since some of the arterial volume escapes into veins relaxed by the anaesthesia. The reduced pressure lowers cardiac output so that DO_2 falls, hence development of an oxygen debt [5].

Cerebral arterial blood flow and metabolic rate obtained by Severinghaus et al. [6] were further examined and showed that cerebral oxygen delivery was sustained after ascent to 3100 m, over the next 5 days. There was an initial fall in SaO_2 and compensatory rise in cerebral blood flow. The acclimatization process allowed the initially lowest SaO_2 to improve over the 5 days at altitude [7, 8].

2. Methods

Fifty-nine normal subjects undertook the trek to Kanchenjunga base camp (altitude 5010 m) from Kathmandu (1345 m). The first leg by plane took them to Tumlingtar (470 m) and then they made an initial partial ascent to 2900 m. There was then a descent to 675 m by the 7th day. From there, the rest of the trek (the main ascent) took around 14 days (a conservative ascent profile of just over 300 m per day). Parties of 7–11 subjects set off from Kathmandu separated by a few days. Each group was accompanied by porters and cooks who went ahead each day to prepare the next stopover site. Porters and yaks carried most of the research equipment for other studies and much of the individual luggage, largely housed in individual 60 L barrels. This meant that each subject carried a low-weight 'day pack.' Each subject measured their arterial saturation (SaO_2) and heart rate (HR) using a (Nonin, model 9500, Nonin Medical Inc. MIN, USA) oximeter. The evening measurement was made after at least 5 min rest, seated in the mess tent prior to supper. Readings were made after around 1 min to allow stability. A second measurement of SaO_2 and HR was made in the morning at each stopover site. Again, each measurement was made after at least 5 min rest in the mess tent prior to breakfast. At both morning and evening sessions, each subject filled in individual 'altitude sickness scores' for each of five symptom complexes (head, guts, tired, dizzy, sleep). Each category belongs to the mode of acute mountain sickness (AMS) assessment known as the Lake Louise consensus AMS scoring system [9]. The numerical system requires scores of 0–3 for each category. The AMS score is the total of the values entered in each category. For each category, zero represents no effect and for three, the symptom in the category is severe. Hence, the total possible range, theoretically, for a given score is from 0 to 15. A subject is deemed to be sick, however, with AMS with scores above 3.

3. Results

AMS scores showed no obvious trends during the major ascent for any individual, whereas SaO₂ fell during ascent in all cases (where the data had been recorded—a few subjects omitted variable amounts of data). The heart rate, however, showed an obvious progressively increasing trend in 42 individuals. For 10 subjects, there was no HR change during ascent.

Figure 1 shows a particularly clear example of increasing HR and decreasing SaO₂ for one individual during the major ascent. The AMS score is included in the left-hand panel and omitted in the middle panel, where the square HR symbol during ascent is filled in, to emphasize the progressively increasing HR. In the right-hand panel, HR from the ascent is plotted against SaO₂, showing the highly significant trend in this subject. For the 42 subjects showing increasing HR during ascent and falling SaO₂, individual least squares regression plots (HR versus SaO₂) give significance levels (*p* values). The degree of the HR versus SaO₂ relationship significance is shown for each subject in **Table 1**, according to the subject's identification number. Nineteen subjects (32%) showed significance at the 0.001 level; 17 (29%) at the 0.01 level and for 6 subjects (10%) significance level was only 0.05. The status for each of the remaining subjects is also shown: four subjects with poor data (very few recorded points or none at all), three subjects with apparently random data (labeled 'variability') and the ten subjects in whom HR was effectively unchanged. **Figure 2** shows HR, SaO₂, AMS score and altitude against time for three of the subjects in whom there was an unchanging HR. The first stopped recording prior to reaching base camp, the second stopped recording at base camp and the third continued, at least HR recording, even during descent.

Significance	Subject No.	Total	Percent
<0.001	1,3,6,8,20,25,26,27,30,32,34,36,40,48, 51,54,55,56,57	19	32
<0.01	4,16,17,21,22,23,24,31,33,35,39,43,45,46,47,50,52	17	29
<0.05	14,28,49,53,58,59	6	10
Ns			29
Poor data	2,5,13,29	4	
Variability	12,18,11	3	
Constant HR	7,9,10,15,19,37,38,41,42,44	10	

Table 1. Listing of all subjects according to (a) whether they showed a significant relationship between HR and SaO₂ during ascent in the upper part of the table (*p* < 0.001, *p* < 0.01 and *p* < 0.05) and (b) those without a significant relationship (poor data, variability or a constant HR).

In the face of any clear individual indication of progress of AMS scores during ascent, it was important to see whether the expected general tendency held good. Mean values for AMS scores and for HR and SaO₂ were calculated for 19 subjects (numbers 1–19) at each altitude. Mean AMS increased progressively with increasing altitude and was significantly related to SaO₂ (**Figure 3**, middle panel). This simply confirms the trend expected with ascent to altitude.

Mean arterial oxygen saturation at each one-night stopover fell progressively during ascent (**Figure 3**, left panel, $\text{SaO}_2\% = -0.0043 \times \text{altitude (m)} + 102.24$; $R^2 = 0.972$) though there was considerable variation for the mean values at each stopover site. The error bars show the maximum and minimum individual values.

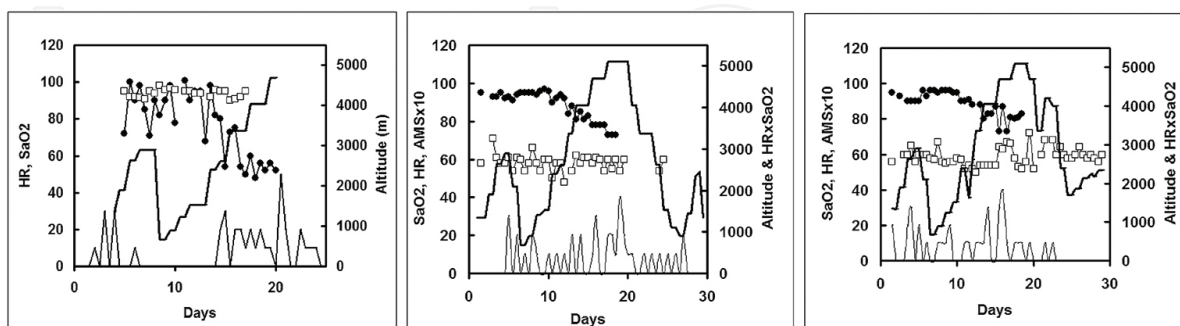


Figure 2. Plots against time of HR (open squares), SaO_2 (filled circles), AMS score (mini-flag) and altitude (continuous line) against time. Each is an example of data from a subject in whom HR remained near constant (subjects, 15, 44 and 38).

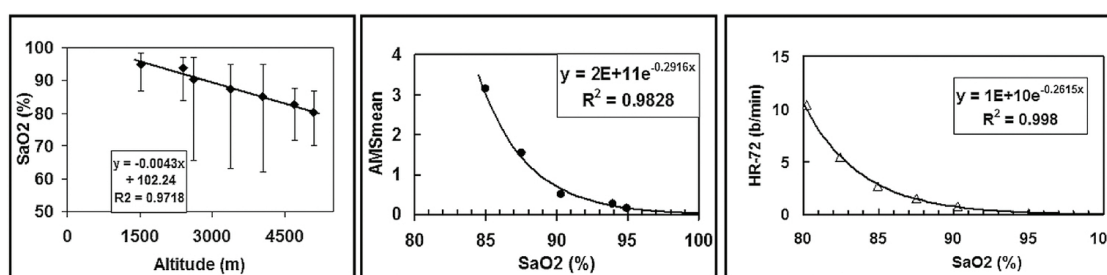


Figure 3. Mean values at each altitude of, $\text{SaO}_2\%$, AMS score and HR. The left panel shows SaO_2 against altitude with maximum and minimum values as 'error bars.' The middle panel shows mean AMS score against SaO_2 for one-night stopovers during the major ascent. The right-hand panel shows mean (HR - 72) plotted against $\text{SaO}_2\%$ above the first two stopovers of the major ascent. The points are from the lowest altitudes were probably from subjects who were not fully rested).

For mean HR (minus 72 as an assumed normal at sea level), values at each stopover site show a smooth relationship to SaO_2 for altitudes above 2400 m (**Figure 3**, right-hand panel). The higher mean HR at lower SaO_2 is consistent with the tendency for an increasing heart rate during ascent, found for most individuals.

Most subjects in the present study ($n = 42$, 71%) showed the significant HR: SaO_2 relationship. The trend relative to SaO_2 was sustained in 33 subjects; however, for nine subjects (numbered: 20, 25, 48, 50, 52, 53, 55, 56 and 57), the trend ended at the lowest SaO_2 with a lower HR than predicted by the trend to date. **Figure 4** shows an example (subject 25). HR (open rectangles) changes in the figure during base camp to larger open circles, where the points are obviously lower than expected from the trend during ascent. Although anecdotal, it may be no coincidence that the AMS scores are at their maximum at the same time.

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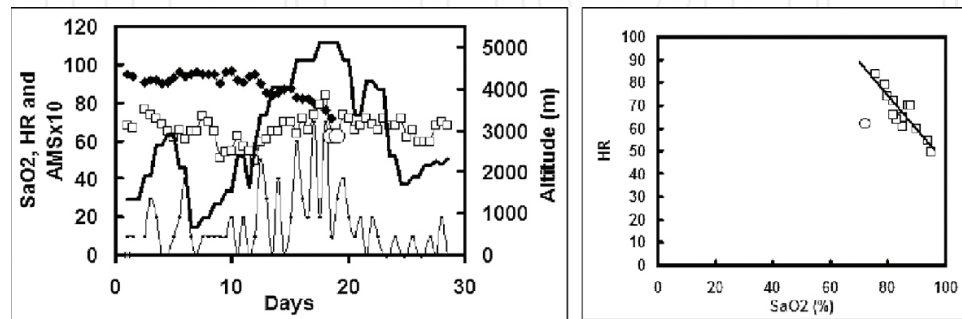


Figure 4. Example of late fall in HR. For subject 25, there was a steady rise in HR (left figure, open squares) during ascent (the period 9–18 days—from 1235 m to base camp at 5100 m). The next two values of HR after reaching base camp (large open circles) were significantly reduced. SaO₂ (filled diamonds) had fallen as usual during ascent. On the left, altitude is shown as a continuous line and AMS score ($\times 10$) shows as a thin jagged line. The plot on the right shows HR during the ascent plotted against SaO₂. The open circle represents the one of the two lower HR values for which SaO₂ was recorded. The lowered HR is thought to reflect impaired compensation for hypoxia.

4. Discussion

This HR, SaO₂ and AMS data, collected during a high-altitude trek to Kanchenjunga base camp in 1998, has shown important variations in individual responses. These differences raise questions concerning physiological mechanisms, such as the reason why a significant proportion of subjects (10 out of a total of 59 or 52 if we exclude 3 with inadequate data and variability—see **Table 1**) maintained a constant resting HR, despite falling SaO₂ during ascent. In contrast, in most subjects (42), HR increased in relation to falling SaO₂. Despite inspection of the individual time-based plots of AMS scores, there seemed no help there with its prediction, though there was, of course, the overall upward trend in the average AMS scores during ascent, accompanying lowered SaO₂ (**Figure 3**, middle panel).

A highly significant difference in vulnerability to acute mountain sickness (AMS) has been shown to be related to differences in the type of ACE gene (angiotensin-converting enzyme) carried by the subject. It is part of the renin-angiotensin system, which regulates blood pressure and the balance of fluids and salts in the body. Those with so-called ‘double insertion’ of the ACE gene experience far less trouble with high-altitude ascent than do those with ‘double deletion.’ Subjects with the mixed ‘insertion/deletion’ properties are intermediate [10]. It seems likely that good compensation with maintained DO₂ will be the background reason for the

altitude advantage of those with double insertion ACE gene but this, of course, would need detailed examination in a major study. It is also possible that the subjects who sustained a constant heart rate with progressive lowering of SaO_2 belong to the double deletion group. Specific measurement would be required in the study to answer this question. There seems no known difference in responses to hypoxic exposure between men and women.

The significant inverse correlation between HR and SaO_2 in 42 subjects is consistent with the DO_2 priority of body tissues, illustrated for skeletal muscle [11], the brain [7, 8] and heart [4] and demonstrated for the whole body [12] in subjects breathing 12% oxygen—resting DO_2 for each individual was the same on 12% oxygen as on air, despite variations in SaO_2 in each individual on 12% oxygen.

It has been pointed out that HR usually increases as CO increases, but there may not have been complete DO_2 compensation in those who increased their HR during ascent. It is possible that the CO increase falls short of sustaining normal DO_2 . Again, it would be useful to know whether the compensation indicated by the HR increase with falling SaO_2 is actually complete.

The depression of HR below that expected from the trend, usually found when it occurs, close to or actually at base camp was most likely to reflect inadequate DO_2 . If this did represent a significant fall in DO_2 such subjects could be more vulnerable to AMS. For the subject, illustrated AMS scores were already increasing. It would be helpful in confirmation or refutation of assertions about HR if CO (in preference to HR) could be measured during ascent. Suitable portable equipment is awaited though none is at present on the horizon.

4.1. The value of the study

It is hoped that the illustration here of a variety of different features of the responses of individuals to the hypoxic environment of altitude will help guide future investigation and throw light on mechanisms responsible for AMS.

The study reported here is consistent with the ability of the body to sustain normal and adequate rates of oxygen delivery to the tissues. This has been shown to be limited by the severity of the hypoxic exposure with variation between subjects as to whether the limit is reached, the level of SaO_2 at which it happens, and the fact that a significant proportion of subjects do not make the compensatory adjustments seen in the majority.

The novelty of this study is the new insight that the heart rate increase is a reflection of increased cardiac output sustaining a compensatory rate of oxygen delivery to the tissues. When the heart rate fails to increase as expected from results to date it may be a clue that compensation is failing.

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