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Physiology in Thin Air

I. Introduction

A. Mt. Everest (8848 m, 29,028 ft) is the highest place on earth.
1. In 1924, two British climbers (Norton & Sommervell) climbed without supplemental O_2 to within 300 m of the summit.
2. In 1953 Edmund Hillary and Tenzing Norgay were the first climbers to reach the summit, but they both used supplemental O_2.
3. Top physiologists predicted that humans could not safely reach the summit without using supplemental oxygen, because the barometric pressure (hence oxygen density) was too low to permit adequate O_2 uptake..
4. In 1978, Reinhold Messner and Peter Habeler reached the summit without supplemental O_2. In 1980, Messner even did a solo climb without O_2!

B. Messner & Habeler were superbly fit athletes, but they moved <u>very</u> slowly at altitude. They took 8 hours to climb the last 850 m in elevation (< 2 meters per minute), and 1 hour to climb the last 60 m in elevation (1 m/min)!

C. Despite low temperatures, both drank huge quantities of water (> 5 liters/day).

D. Why were Messner and Habeler moving so slowly at elevation? Why were they drinking so much water? Why were the physiologists wrong in predicting that humans could not climb Everest without supplemental oxygen?

II. The physical environment at extreme altitude

A. Physiologists are often fond of examining organisms living in "extreme environments," because physiological stresses are often conspicuous there. High altitudes are a paradigmatic example of an "extreme environment." Moreover, the links between physiological systems are also very clear at altitude.

B. Scarcity of oxygen is the key problem -- climbers attempting high summits without supplemental O_2 are exercising near the limit of their aerobic capacities. Why?
1. <u>Oxygen is in very short supply</u>. The air density on the summit is 1/3 that of sea level, such that the pressure <u>gradient</u> from air to alveolar capillary is weak. Thus diffusion will be low; and maximal O_2 uptake will very low. Not surprisingly, arterial saturation (% saturated) drops with altitude, as does maximum oxygen consumption.
2. <u>Oxygen demand is high</u>. Humans and animals traveling at high altitude are exercising, such that their O_2 requirement is elevated above rest.
3. <u>High altitudes are cold, windy places</u>, sometimes placing an additional challenge on limited O_2 supplies. Why is cold a problem in combination with low O_2?

C. Desiccation is also a serious problem at high elevation. Why?
1. From sweating? No, as climbers often aren't sweating that much. [Even so,on a sunny day on an ice field, however, radiant heat loads can be very high.]
2. But thin air at high altitude is very desiccating.
3. Also, recall that cold air (at any given barometric pressure) *holds less water than does warm air*. Each incoming breath of air is cold, so it contains little water. But when heated to lung temperature, that initially dry air will become saturated with H_20 vapor, much of which will then lost upon exhalation!

3. The very high respiratory rates of climbers (hyperventilation, see below) compound this problem. So total respiratory water loss is huge.

D. Not surprisingly, humans don't survive very long at altitudes > 18,000 ft. [Climbers refer such high places as the "death zone."]

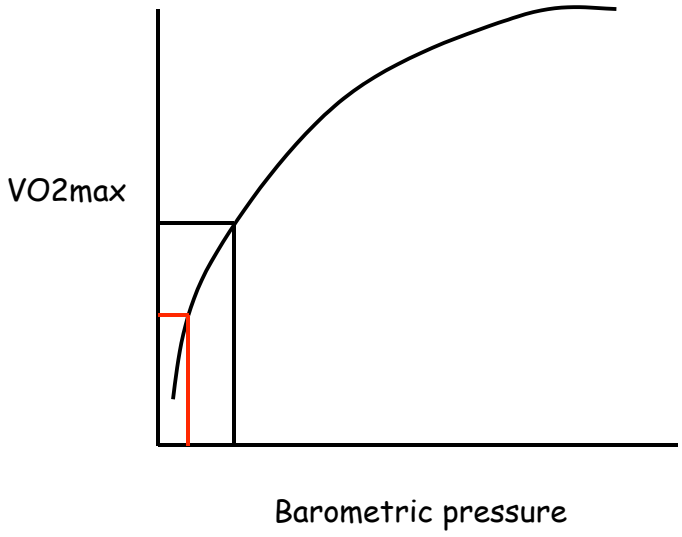
III. Physiological perspectives on high-altitude stresses

A. Physiologists have studied high-altitude physiology either directly on mountains (some even on summit of Everest!) or in "hypobaric" chambers, in which climbs can be readily "simulated" (e.g., "Operation Everest II").

B. For many decades most physiologists thought (prior to 1978) that climbing Everest by "fair means" (i.e., without supplemental O_2) was impossible. Why?

1. Barometric pressure limits maximal O_2 consumption. Barometric pressures on the summit were thought to be so low that a human could barely get enough O_2 to fuel resting metabolic requirements, let alone fuel activity.
2. In other words, the metabolic scope for activity would be close to zero, and climbers could climb very slowly, if at all. In theory then, Everest couldn't be climbed without supplemental oxygen.
3. But Messner & Habeler did climb very slowly (their aerobic scope was extremely low), but *still* they got to the top. So why were physiologists wrong?

C. First, estimates of barometric pressures used in the initial physiological models (235 torr) were low by ~ 5% (actually 250-253 torr at summit). Doesn't seem like much of an underestimate, but arterial saturation and maximum O_2 consumption is very sensitive to barometric pressure in this region (recall O_2 saturation curves). So +5% would increase O_2 availability to climbers and thus increase metabolic scope!



[D. Tangent. Barometric pressure varies seasonally at high elevation and is higher in early summer than at other seasons. The seasonal shift is enough to affect maximum O_2 consumption by about 11%! Messner & Habeler climbed in May (near the yearly high), but remarkably a Sherpa later climbed Everest in early-winter, near the yearly low! The physiological height was equivalent to 9 km.]

E. Thus "easier" (or perhaps "less hard") to get O_2 than physiologists had expected.

F. Other factors are involved. The high breathing rates (extreme hyperventilation) of climbers also lowers alveolar CO_2, which drastically increased blood pH (see below), which causes a left shift in the O_2-dissociation curve, which increases O_2 loading on Hb. Some physiologists were skeptical that climbers could tolerate such high pH, but successful high-altitude climbers aren't "most people."

G. Huey & Peter Ward (2005 JAMA) suggest that O2 levels, which varied dramatically over geological time, were high enough only about 30% of the last 570 million years for climbers (had they existed) to reach the summit of Everest.

IV. Hyperventilation -- the key to success (and the curse) at high altitude

A. Hyperventilation (*rapid, deep breathing*) is the key physiological adjustment to high altitude. Climbers have very high breathing rates. [Messner described his feelings near the summit of Everest: "I am nothing more than a single, narrow, gasping lung, floating over the mists and the summits."]

B. Hyperventilation helps maintain favorable O_2 gradients. O_2 in the lungs is constantly diffusing into the pulmonary capillaries, and thus pO_2 obviously drops with time, reducing the pressure gradient. However, by breathing rapidly and replenishing the alveolar air, a climber maintains alveolar pO_2 levels at maximum possible levels. Thus the gradient is as large as possible, so uptake rate is a high as possible.

C. Hyperventilation (i.e., lung flushing) also maintains very low alveolar pCO_2 (7-11 torr), because any incoming CO2 is breathed out quickly. However, there is no such thing as a free lunch, and hyperventilation comes at a real cost in terms of acid-base balance. Recall the dissociation of CO_2 in water

$$CO_2 + H_20 <==> H^+ + HCO_3^-$$

E. During hyperventilation, because the CO_2 is blown off, which favors the reaction moving from right to left (because low CO_2 in the lung increases the gradient from alveolar blood to alveolus, increasing the loss rate of CO_2. Thus H^+ (and also bicarbonate) is depleted, which leads to a marked increase in pH (7.4 to 7.6+) . Why is this bad?

VI. Anaerobic metabolism at elevation

A. If aerobic scope is limited, can't climbers just use anaerobic metabolism for ATP?

B. In fact, lactate levels in blood samples are measurably low above 7500 m. Thus anaerobic metabolism is seemingly reduced near the summit.

C. Why? Tissue buffering capacity is thought to be severely reduced because of the depletion of bicarb (above). If so, then the increase in H^+ concentration (following the production of lactate) will not be buffered and will probably shut off glycolysis, which is strongly inhibited by low pH. (this is speculation!). An alternative idea is that the nervous systems just doesn't enable a climber to do burst activity up high.

D. Anaerobic metabolism would generate extra ATP for only a few minutes, anyway, but would come at a severe cost – a prolonged oxygen debt would follow. Why?

VII. Water balance

A. As mentioned above, rates of water loss are very high at altitude. Athletic performance (useful to a climber!) is severely hurt by desiccation.

B. How to deal with this? Drink as much fluid as possible. But difficult in practice, as one must melt ice and snow. An alternative solution is to make very rapid ascents – thus, to get up and down before desiccation becomes serious. Easier said than done!

VIII. Mountaineering at altitude

A. Given all of the above, it is obvious that climbing at extreme elevation is physiologically debilitating and very dangerous. So is the main cause of death on Everest due to medical problems? No, about 1/3 are from avalanches (or rock fall), 1/3 from climbers falling, and about 1/4 from illness or exposure. Surprisingly, severe weather was a factor in only 11% of all deaths.

B. Given the problems of low O_2 at altitude, does the use of supplemental O_2 promote survival of climbers? What are the death rates of climbers who used (or didn't use) supplemental O_2 on the two highest peaks in the world? Physiological studies at the South Col of Everest have shown that use of supplemental O_2 does enhance arterial saturation and lower heart rate. Let's look at the death rates during descent from the summits of these two peaks. (Huey & Eguskitza JAMA 2000).

C. Everest

Climbers who used supplmental oxygen	3+ % died
Climbers who did not use supplemental oxygen	9% died

C. K2

Climbers who used supplmental oxygen	0 % died
Climbers who did not use supplemental oxygen	19% died

E. Note: these data are correlational, *not experimental*. So assigning cause and effect is risky. Nevertheless, it is likely that the higher death rates of climbers not using supplemental oxygen reflects the stress of severe hypoxia.

F. Age effets. Physical capacity declines from our 20s and 30s, but experience and wisdom increase with age. So does age influence success and death rate? Yes, the probability of success on Everest is maximal for climbers in their early 30s, and declines at older ages. Death rate increases very slightly with age.

IX. Human reproduction at altitutde

A. Because O2 is low, delivery of oxygen to a developing fetus (or to a baby) may be difficult and lead to problems of development.
B. Arterial saturation of infants (esp. at 1 week of age) is very low (~ 80%) at altitude (Leadville, CO, 3100m).
C. Birth weight drops with altitutde, and this is not merely an effect of women being smaller at altitude.
D. A recent study (Beall et al. 2004) shows that the children of Tibetan women with a particular hemoglobin allele (which increases O_2 saturation) have higher infant survival, suggesting a direct effect of O_2 uptake on survival in childhood.