

Short Communication

Summiting Mount Everest in deuterium depleting nutritional ketosis without supplemental oxygen

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ABSTRACT

During climbing seasons in the Himalaya only a few sportsmen attempt an ascent to and descent from the 8848 m top of the Earth without supplemental oxygen. This short report describes such successful summiting of the Mount Everest that rested with the nutritional, metabolic and exercise ketosis state, i.e., the burning of long chain saturated fat as the source of cellular energy after six failed attempts by the same athlete using carbohydrate-based nutrition. We herein describe the advantage of ketosis from the medical biochemistry angle by characterizing peroxisomal and mitochondrial cross talk as deuterium (heavy hydrogen) depleting principles in natural ketosis. We emphasize the importance of proton (hydrogen) and oxygen recycling via fatty acid deriving hydrogen peroxide produced in peroxisomes, followed by its conversion to metabolic water and O₂ by catalase in mitochondria. Metabolic adaptation to natural ketosis maintains reduced NAD⁺ and ATP pools even in severely oxygen deprived environments. We hypothesize that severely decreased atmospheric oxygen pressure above 7000 m compromises alveolar gas exchange so much that biological oxidation becomes dependent on natural hydrocarbon (fat) based nutritional and consequent metabolic adaptation to natural ketosis. Such substrate level coupling of peroxisomal and mitochondrial metabolism via fatty acid breakdown aids oxygen recycling in muscles and tissues as a lifesaving option for the extreme climber.

Introduction

With at least a dozen unfortunate high-altitude climbers dying and over 20 people missing, or presumed dead on the world's highest peak, 2023 was one of the deadliest mountain climbing seasons on record [1]. Around Hillary Step, which is a nearly vertical rock face located near the summit of Mount Everest about 8,790 m (28,839 ft) above sea-level, high-altitude sickness is to blame for the life threatening metabolic collapse [2]. This brings into focus why some climbers can, while others cannot, return from the top of Mount Everest cleanly, i.e., without supplemental oxygen! High altitude professional mountain climber Adrian Ballinger summited Everest without supplemental oxygen in the metabolic state of ketosis, i.e., burning fat, on May 27, 2017 [3], after six

failed attempts using carbohydrate (glycogenic) diets. This accomplishment makes his case the first one sample cohort (case report) for nutritional, metabolic and exercise ketosis to be considered during high altitude climbs.

To make the long story short, during all unsuccessful climbs Mr. Ballinger was heavily reliant on eating some kind of high-energy bar, gel, or similar product at once-an-hour intervals and his metabolic preference was heavily shifted toward carbohydrate use. The solution was to help Mr. Ballinger become a fat-burner. In practice he had embraced a ketogenic diet, limiting the calories he ate from carbohydrates to just 10 percent of the daily intake, while getting 60 percent from fats and 30 percent from proteins. Accordingly, a successful climbing day included an incredible 4000 kcal of seeds, nuts, meat,

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cheese, and loads of avocado and butter. During preparation prior to unsuccessful climbs, he would eat a whole pizza every day, loved pasta, baked goods, and carbohydrate gels while working out. Removing all of that and replacing them with natural fat based ketogenic food items had induced a major shift in tissue oxygenation and performance. The potential irreversible collapse of sugar burning glycolytic intermediary metabolism rendered Mr. Ballinger able to turn back six times while still able to think, move and orient himself in space and time. Other climbers who continue trap themselves in the deadly spiral of events involving edema of the brain, desiccation, complete exhaustion, and expiration [4]. In nutritional ketosis, or in the ketogenic metabolic state, it seems possible to expand cellular proton and oxygen reserves efficiently to complete the expedition without sustained harm or an imminent life-threatening metabolic collapse.

The chief problem is the low atmospheric pressure of oxygen at altitudes over 4000 m. This renders oxygen carrying molecules like hemoglobin less efficient to supply tissues with sufficient molecular oxygen (O_2) from air. This is the oxidant for metabolic hydrogen peroxide and water production in living organisms. Lack of sufficient oxygen decelerates complete substrate oxidation from deuterium loaded carbohydrates to yield CO_2 , mitochondrial matrix water, NADH, ATP and heat energy to life threateningly low levels. This report explains how to maintain sufficient energy production from the medical biochemistry angle via describing peroxisomal and mitochondrial substrate/product exchange reactions in natural deuterium-depleting metabolic and nutritional ketosis.

Hypothesis

High altitude mountaineering exposes climbers to one of the harshest physiological challenges sportsmen can endure under limited oxygen availability. This is combined with strenuous exercise, cold temperatures and declining mental fitness to make critical decisions with little or no help from peers due to very limited resources available. Unpredictable and rapidly changing factors such as windy weather conditions, icy terrains, seismic activities and limited communications, among others, just add to all other hazards including insufficient biological energy production. Nutrient deprivation, disorientation and lack of sufficient ATP due to a life-threatening collapse of mitochondrial metabolism should be among the main concerns to overcome such threats and challenges. Based on the nutritional ketogenic state of metabolism that led to an eventual success in high altitude climbing challenge described above we herein hypothesize that mitochondrial metabolism can readily be enhanced and greatly supported by peroxisomal oxidation of the beta carbon of ketogenic acyl substrates obtained from natural, deuterium depleted animal fat sources. The understanding of peroxisomal and mitochondrial crosstalk through matrix water production to enhance cellular energy production under limited oxygen availability, as the ultimate metabolic constraint, is a potential lifesaving option under extreme sporting conditions.

Mountaineering in thin air

The partial pressure of molecular oxygen (PO_2) in ambient air of the Earth's atmosphere is 20.9 %, which remains unchanged by altitude. Therefore, PO_2 is directly proportional to the atmospheric (barometric) pressure of the air that surrounds climbers [5]. At the summit of Chomolungma (Mount Everest), the barometric pressure is 253 mm Hg (33.73 kPa), which is only about one third of atmospheric pressure (760 mm Hg; 101.3 kPa) at sea level. The normal alveolar-arterial oxygen gradient is 7–10 mm Hg, but at high altitudes this falls to about 5 mm Hg. This is because the extracorporeal pressure is too low for the rapid diffusion of oxygen from lung alveoli to the capillaries. Slow diffusion compromises an equilibrium to be fully developed between alveolar and arterial PO_2 during the transit of blood in lung capillaries. This worsens on climbing due to increased heart rates when blood moves faster in

pulmonary vessels, leaving less time for an oxygen equilibrium to develop.

Indeed, based on previous measurements at 8400 m on Mount Everest, the mean arterial oxygen content at rest is roughly 27 % lower than it is at sea level, i.e., 145.8 ml per liter as compared with 200 ml per liter of blood, respectively. The mean calculated alveolar-arterial oxygen difference or gradient is also only 5.4 mm Hg (0.72 kPa) [6]. From the above, it is easy to see how high-altitude climbers compromise air-derived (external) oxygen delivery to their tissues. On the other hand, it seems that these challenges can be overruled by burning fat primarily as the source of cellular energy in the metabolic state called ketosis. Therefore, it is key to understand how ketogenic substrates and metabolism support cellular energy, heat, ATP and metabolic water production that made Mr. Ballinger's climb possible, without supplementary oxygen, to the top of Mount Everest with safe return.

Peroxisomes and mitochondria at work

The answer lies with peroxisomal metabolism that utilizes molecular oxygen dissolved in plasma to produce short chain fatty acids, ketones, NADH and hydrogen peroxide (H_2O_2), which either decomposes or is rapidly broken down by catalase to metabolic water according to the chemically balanced formula of $2H_2O_2 = 2H_2O + O_2$. In the process, molecular oxygen is distributed in the mitochondrial matrix as well as in other cell compartments. Peroxisomes can also reduce NAD^+ for proton delivery to mitochondria via membrane-based intracellular proton transporters. Peroxisomes operate with molecular oxygen dissolved in blood at concentrations of 3 ml/L or less [7]. As tissues at rest draw 50 to 60 ml of oxygen per liter of blood assuming normal perfusion [8], it is crucial to retain, supplement, and recycle water and oxygen via peroxisomal and mitochondrial metabolic cross talk during high altitude climbs as explained in Fig. 1 and Table 1.

An additional source of cellular molecular oxygen and hydrogen is the breaking of water by melanin upon light exposure [9]. Such a mechanism is entertained in connection with improving mitochondrial function and color vision by single exposure to 670 nm red light as an example [10].

Although the partial contribution of all of the above mechanisms is yet to be determined to survive climbing to extreme high altitudes without supplemental oxygen, it is certain that none of the above works well in the glucogenic metabolic state. Intermembrane derived protons due to the high inner membrane gradient also power ATP synthase nanomotors, which are sensitive to deuterium [11] that diminishes their function. The relatively high deuterium (heavy hydrogen) content of carbohydrates and glycolytic amino acids [12], present in most sports related glycolytic nutritional supplements, does not support mitochondrial ATP synthase functions. Such support is critical during climbing for ATP dependent muscle contractions, metabolic water and heat production, as explained in Fig. 1. Energy, in the form of heat, is most efficiently generated, namely, in excess of 280 kJ mol^{-1} , when oxygen and hydrogen form water in mitochondria. On the other hand, there is a strict dependence of peroxisomes on long chain saturated fatty acid substrates with particularly lower deuterium-related chemical mass [12], i.e., the isotopic composition of a molecule, also called molar isotope enrichment. The oxidation of very long chain saturated fatty acid β -carbons, purportedly of animal source, with the help of molecular oxygen, yields the most deuterium depleted hydrogen peroxide by weight (Fig. 1. B). Catalase (EC 1.11.1.6), one of the fastest enzymes in biology with that of isomerases, rapidly and irreversibly produces water from H_2O_2 , while recycling oxygen. Metabolic hydrogen peroxide of fatty acid breakdown with low deuterium consequently provides ATP synthase nanomotor-sparing protons for energy production. Under low external oxygen tension climbers can easily depend on catalase-mediated oxygen recycling. This is because the catalytic process of catalase obeys Michaelis–Menten kinetics, with a Michaelis constant equal to that for the catalytic reaction, i.e., the catalytic reaction of

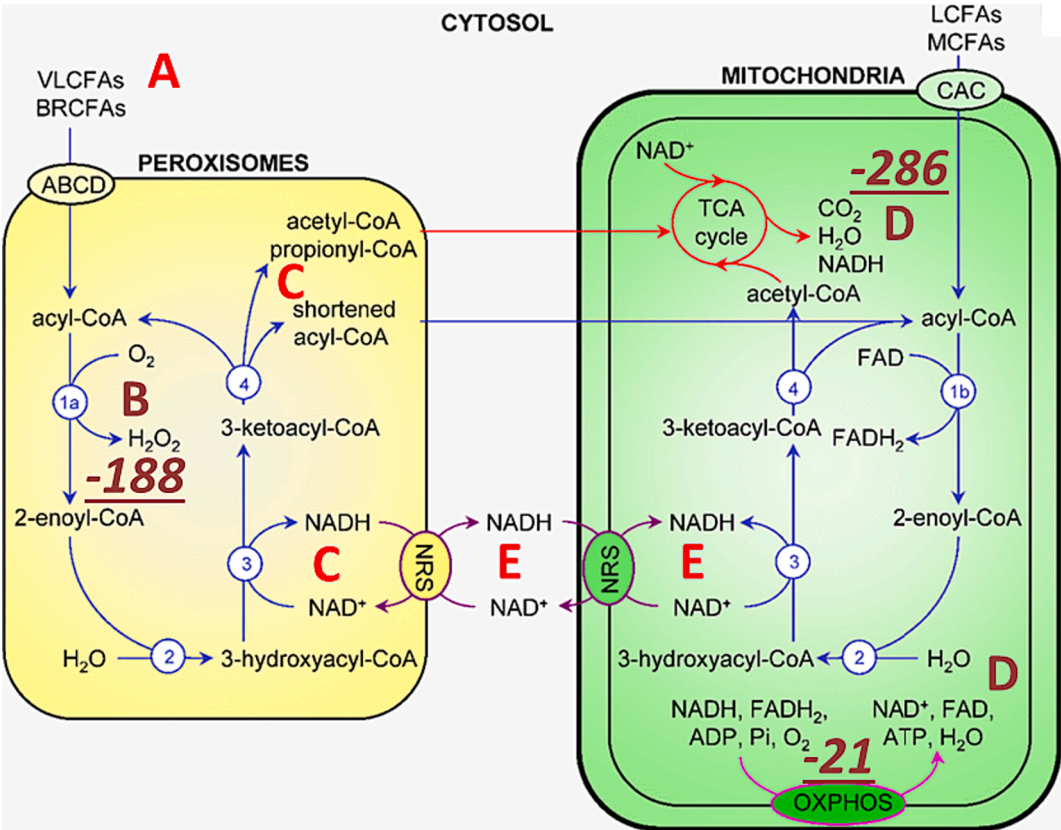


Fig. 1. Metabolic cross talk and energy yield balance between peroxisomes and mitochondria. Peroxisomal metabolism utilizes very long and branched chain fatty acids (A) as well as dissolved molecular oxygen (B) carried in plasma. Peroxisomes produce short chain fatty acids via beta-carbon oxidation, ketones, NADH (C) and hydrogen peroxide (B). H₂O₂ is rapidly converted to metabolic water by catalase that also yields molecular oxygen for the mitochondrial matrix (D) as well as for other cell compartments. Peroxisomes can also reduce NAD⁺ for proton delivery to mitochondria via membrane-based intracellular proton transporters. Energy yield (enthalpy) of exothermic metabolic reactions in kJ/mol values during peroxide, water and ATP formation are also shown with dark brown numbers [16]. Standard enthalpy of formation (on chemically balanced sheets) from H₂, O₂ and adenosine diphosphate (ADP): $\Delta H_{\text{reaction}}^{\circ} = \sum H_{\text{products}}^{\circ} - \sum H_{\text{reactants}}^{\circ}$ are shown during H₂O (D; mitochondrial water), H₂O₂ (B; hydrogen peroxide in peroxisome) and ATP (OXPHOS; C₁₀H₁₆N₅O₁₃P₃ adenosine triphosphate) from ADP. Note: Joule (J): the energy dissipated as heat when an electric current of one ampere passes through a resistance of one ohm for one second. (Image: Share and Cite [40])

Table 1
Oxygen-constrained metabolic reactions in absolute kJ^a mol⁻¹ values during energy yielding metabolic water formation reactions in cells [16].

Chemical Formula	State of Matter	H ^o : Enthalpy ^b
H ₂ O (mitochondrial water)	liquid	[285.83]
H ₂ O ₂ (hydrogen peroxide in peroxisome)	liquid	[187.78]
C ₁₀ H ₁₆ N ₅ O ₁₃ P ₃ adenosine triphosphate ATP	solid in solution	[20.5]

^a Joule (J): the energy dissipated as heat when an electric current of one ampere passes through a resistance of one ohm for one second.
^b standard enthalpy of formation (on chemically balanced sheets) from H₂, O₂ and adenosine diphosphate (ADP): $\Delta H_{\text{reaction}}^{\circ} = \sum H_{\text{products}}^{\circ} - \sum H_{\text{reactants}}^{\circ}$.

catalase, in the limit of zero reaction time. It has also been confirmed that catalatic activity is substantially independent of pH in the range 4.7–10.5 that makes catalase a safeguard to operate in the generally low pH environment, characteristic of metabolic ketosis [13]. Lifesaving ketosis during extreme high altitude climbs can be achieved only by adaptation to reliable proton and oxygen recycling mechanisms, as described herein, even under extremely challenging physical conditions and mental stress.

What to eat - that is the question

A closer look coming from the above reveals that adaptation to high altitude climbs should adhere to the following measures as essential contributions from medicinal and extreme sport biochemistry:

1. Only sufficient naturally produced long chain saturated animal fat diets from pasture fed herds [14] should be consumed for at least six months before the climb as the most efficient deuterium depleted proton and water source among all ketogenic, glucogenic and protein-based substrates via complete biological oxidation.
2. Plant based shorter chain unsaturated “oily” fat sources may not be desired due to compromised proton to carbon ratios, along with potential plant toxins, industrial organic solvent treatments and agricultural pesticide contaminations [15].
3. Deuterium depleted water intake as the only source of liquids should be added upon thirst. Raw melted snow close to peaks may serve just perfectly due to high altitude deuterium fractionation [17]. Such drinking water serves to protect mitochondrial ATP synthase nanomotors, especially via quantum proton tunneling, as well as that of other moving proteins involved in proton transfer reactions [18].

Metabolic cross talk via several levels of proton carrying substrate-to-product exchange processes introduced herein is only possible under fat mobilizing and hydrocarbon burning conditions, not that of burning carbohydrates. Those fats serve as efficient energy and water production/recycling systems shared among mitochondria and peroxisomes strictly from dietary and endogenous liver-deriving triglyceride fat. This is important because the long-time notion that mitochondrial energy is supplied almost entirely via ATP synthesis and breakdown may not hold. This should be credited to matrix water formation instead as shown in Fig. 1. The chemistry of water dominates metabolism and

energy production whilst it also drives biological synthesis and degradation [19]. Therefore, the limiting of deuterium related kinetic isotope effects in thin air via deuterium depleting natural ketosis seems critical to reconcile glycogenolysis-first versus ketosis-first theories for nutrition under extreme sporting challenges. We have herein identified sufficient proton and oxygen sources via recycling peroxide and breaking water by light and melanin, additionally, to attack high altitude peaks with more success. Of course, turning around is still the safest when it comes to risking high altitude sickness or death, as Adrian Ballinger did six times in glucose burning conditions [3].

Implications

Database searches reveal randomized studies that address oxygen metabolism during moderate altitude climbs (2320 m) using, for example, antioxidant-rich food. In order to further explore the benefits of ketogenic nutrients/food in medicine, especially in the form of antioxidants, one study employed mixed models for measuring antioxidant capacity [uric acid-free (ferric reducing ability of plasma (FRAP)), oxidative stress (8-epi-PGF2 α), inflammatory biomarkers, VO₂ max ramp test and a 100 m swimming challenge. It was established that increased intake of antioxidant-rich foods, enhanced with oily nuts and carbohydrate free dark chocolate, elevated the antioxidant capacity and attenuated some of the altitude-induced systemic inflammatory markers in elite athletes [20]. Additional reports demonstrated that hemoglobin concentration increases in the antioxidant group [21], antioxidants protect cells from damage caused by free radicals and reduce oxidative stress associated with high altitude climbs [22,23]. There is also improved oxygen utilization [24,25] and cardiovascular support [26] imposed by antioxidants. An important discussion about peroxisomes in a close context with our present work describes crucial antioxidant enzymes to mitigate oxidative stress considerably. These effects occur when peroxisomal and mitochondrial catalases break down cellular hydrogen peroxide to produce water and oxygen by using either iron or manganese as a cofactor [27]. Deutenomics related biochemical principles of the peroxisome-mitochondria connection should be considered by high altitude climbers to reduce deaths under such harsh conditions [28].

Conclusions

Well positioned medical biochemistry with deutenomics reasoning dictates that dissolved molecular oxygen from both external and recycled (internal) sources can run the peroxisomal and mitochondrial fatty acid oxidation system in deuterium depleted (depleted) natural ketosis most efficiently at extreme high altitudes. As carbohydrates and amino acids are not oxidized by peroxisomes, glycogenic metabolism and glycolysis may not be entertained, experimented with or even desired during high altitude climbs. Spatial compartmentalized substrate-product related electron, proton tunneling and oxygen exchange reactions between peroxisomes and mitochondria, as described herein, increase metabolic water's molar deuterium enrichment from intermediary glucogenic metabolites [29,30]. This fundamental biochemical paradigm is readily retained herein to explain additional factors in deutenomics including disproportional deuterium accumulation in biomolecules and nutritional supplements of industry source to compromise energy production upon extreme environmental challenges [31].

We further emphasize that most cellular energy is provided as heat by the exothermic reduction of air's oxygen to hydrogen peroxide and water by food derived hydrogens (protons) in mitochondria. The most efficient and robust source of the reducing proton pool is saturated natural long-chain fatty acids to induce metabolic ketosis from deuterium depleting grass fed animals. Those substrates power and spare ATPase nanomotors when high altitude survival is at stake. The sparse deuterium composition of fat in ketosis, which is the source of metabolic

water upon oxidation, determines the ability of climbers to use this water also as the constitutional reaction solvent [19]. As a last energy resort, quantum destabilization of structured water protons in hydrophobic mitochondrial membrane nanoconfinements [32] in the atomic nuclear quantum events (NQEs) space may also become important for the electromagnetic energy balance generated in the matrix, where deuterium is also undesired [33,34].

Natural ketosis that involves peroxisomes to yield energy using dissolved O₂ gas in blood serum and the recycling of it in tissues as metabolic water with the help of catalase have broad applications in biology. One example is the bombardier beetle that liberates oxygen from hydrogen peroxide to oxidize hydroquinones with an exothermic energy yield of $\Delta H^{\circ} = -202.8$ kJ/mol. This is a strategy to rapidly heat hydroquinone oxidation mixtures to boiling point as a repellent [35]. The rapid decomposition of H₂O₂ yields molecular oxygen in a 2:1 stoichiometry, consistent with a catalytic mechanism with a rate constant of 0.0346/second [36]. The increased temperature of mitochondria in mammalian cells by about 10 °C to that of the cytosol is consistent with direct heat production in mitochondria via water formation along with ATP production [37]. The advantage of such a strategy during high altitude climbs is that the rate of H₂O₂ decomposition is not influenced by respiratory glycogenic substrates, e.g., succinate, glutamate or malate, suggesting that cytochrome c oxidase and the glutathione-glutathione peroxidase system are not significantly involved in the regulation of the catalytic process. Instead, rapid H₂O₂ decomposition is compatible with the presence of endogenous heme-containing catalase, which also contributes to mitochondrial protection against endogenous or exogenous H₂O₂ [38]. Mitochondrial catalase in liver and muscles represents regulatory control of bioenergetic metabolism as a lifesaving biochemical reserve during extreme sports with adaptation to nutritional, metabolic and exercise ketoses, most efficiently.

It is not only extreme sportsmanship but clinical and translational medicine targeting chronic metabolic disease conditions such as diabetes, obesity and cancer that could include and benefit from a more thorough understanding and utilization of deuterium depleted metabolic water chemistry in their therapeutic arsenals. Such conditions and treatment efforts are often hampered by insufficient tissue oxygenation with consequent limited ATP energy production. Deuterium depleting natural ketogenic dietary interventions, using natural ketogenic substrate oxidation as the prime source of cellular energy, offer novel and efficient approaches to clinically assist in integrative medicine and human well-being.

Testing of the hypothesis set forth in this article could involve hypobaric oxygen chambers or moderate altitude mountaineering under various nutritional guidelines to compare ketosis versus glucosis, i.e., when metabolizing glucus (old name for glucose), sweet or grape sugar, extremely rich in deuterium loaded carbohydrates [41].

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CRedit authorship contribution statement

László G. Boros: Conceptualization, Formal analysis, Funding acquisition, Project administration, Resources, Supervision, Validation. **Stephanie Seneff:** Conceptualization, Data curation, Formal analysis, Methodology, Supervision, Writing – original draft, Writing – review & editing. **James C. Lech:** Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Validation. **Marianna Túri:** Data curation, Resources, Software, Validation, Writing – original draft, Writing – review & editing. **Zoltán Répás:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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