

The Ketogenic Diet and Sport: A Possible Marriage?

Antonio Paoli¹, Antonino Bianco², and Keith A. Grimaldi³

¹Department of Biomedical Sciences, University of Padova, Padova; and ²Sport and Exercise Sciences Research Unit, University of Palermo, Palermo, Italy; and ³Biomedical Engineering Laboratory, Institute of Communication and Computer Systems, National Technical University of Athens, Athens, Greece

PAOLI, A., A. BIANCO, and K.A. GRIMALDI. The ketogenic diet and sport: a possible marriage? *Exerc. Sport Sci. Rev.*, Vol. 43, No. 3, pp. 153–162, 2015. *The ketogenic diet (KD) is used widely as a weight loss strategy and, more rarely, as therapy for some diseases. In many sports, weight control is often necessary (boxing, weightlifting, wrestling, etc.), but the KD usually is not considered. Our hypothesis is that KD might be used to achieve fat loss without affecting strength/power performance negatively.* **Key Words:** ketogenic diet, endurance, strength, weight loss, skeletal muscle hypertrophy

Club

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INTRODUCTION

The ketogenic diet (KD) is a nutritional approach consisting of high-fat and adequate protein content but insufficient levels of carbohydrates for metabolic needs (<20 g d⁻¹ or 5% of total daily energy intake (28)), thus forcing the body primarily to use fat as a fuel source. The original KD was designed as a 4:1 lipid:nonlipid ratio, with 80% of daily energy intake from fat, 15% protein, and 5% carbohydrate. Many modifications subsequently have been introduced to the original KD, for example, lowering the lipid:nonlipid ratio or no restrictions in daily energy (in kilojoules) intake with *ad libitum* protein and fat. The main knowledge on the metabolic aspects of KD comes from the pioneering studies on fasting from the Cahill group (17,18); as a matter of fact, fasting (ingesting no or minimal amounts of food and caloric beverages for periods that typically range from 12 h to 3 wk (16)) induces a particular metabolic state called ketosis. Fasting is a practice that is spread widely throughout different religions, even though religious fasts are conceived mainly for spiritual health, they also have the potential to improve physical

health. One example of a positive effect on health by fasting may be found in the Gospel of Matthew, in the episode of the epileptic (demoniac) boy: "And Jesus said unto them, 'Because of your unbelief: for verily I say unto you, If ye have faith as a grain of mustard seed, ye shall say unto this mountain, Remove hence to yonder place; and it shall remove; and nothing shall be impossible unto you. **How be it this kind goeth not out but by prayer and fasting**'" (Matthew 17:14–21). Fasts are indeed present in the three principal fasting periods of Greek Orthodox Christianity (Nativity, Lent, and the Assumption), in the Bible-based Daniel Fast, and in the well-studied Islamic Ramadan. In recent years, many studies have investigated the effects of the daily fasting used during Ramadan that requires a total abstention from food and drink from sunrise to sunset for 1 month. Although such ritual intermittent fasting has only minor effects on the sedentary population, its observance may have important consequences for the training and performance of the athlete. These effects could be of greater importance when the competition is performed in summer when daylight hours are long. In general, studies have found that, in athletes observing Ramadan, the glycemia and tissue hydration decrease progressively from sunrise to sunset. However, overall performance seems to be unaffected if athletes are able to maintain an adequate total energy and macronutrient intake and a correct sleep length and quality and to adjust the timing of the training load, although with many interindividual differences (5,35).

Ramadan fasting is an interesting model for intermittent fasting but is too short to induce ketosis; instead, a good model for prolonged ketosis is the Inuit case, in which the first well-documented fasting was reported by the Schwatka expedition. Lt. Frederick Schwatka was a graduate of West Point and Bellevue Hospital Medical College and he was the leader of an expedition that set out to find the missing Royal

Address for correspondence: Antonio Paoli, MD., Department of Biomedical Sciences, University of Padova, Via Marzolo 3, 35131 Padova, Italy (E-mail: antonio.paoli@unipd.it).
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Navy "Franklin Expedition." On June 1878 when the schooner *Eothen* sailed from New York, Schwatka and the other participants (including Henry Gilder, a scientific reporter from the New York Herald) set up a winter base camp near Daly Bay. The following spring, accompanied by 12 Inuit (indigenous circumpolar people), they began a more than 5000-km sled journey eventually returning to Camp Daly on March 4, 1880, almost 1 yr later (8). Regarding physiological issues, it is worth to underline that, once they finished their initial provisions, the expedition's only source of food was hunting and fishing because there were no other sources of supply along their route. Lt. Schwatka reported in his diary this often-cited sentence: *When first thrown wholly on the diet of reindeer meat, it seems inadequate to properly nourish the system, and there is an apparent weakness and inability to perform severe, exertive, fatiguing journeys. But this soon passes away in the course of 2 to 3 wk (34).* This is the first documented description of the so-called keto-adaptation.

Years later, an anthropologist named Vilhjalmur Stefansson set out to travel throughout the Arctic mainland to study the Inuit language and culture. During his journeys, Stefansson experimented on himself with the typical Inuit's diet, consisting of about 80% to 85% of energy from fat and 15% to 20% from protein, and he reported no observed problems (36). Pressed by the controversy raised from his reports, Stefansson agreed to recreate the Inuit diet under the scientific supervision of Dr. DuBois at the Bellavue Hospital, he confirmed his earlier observations that the adoption of a fat/protein diet was without any impairment or signs of nutrition deficiency. After these earlier reports, however, the study of KD seems to have sunk into oblivion until the 1920s when it experienced a "renaissance" as a therapy for epilepsy. Interest against waned with the introduction of pharmaceutical therapy for epilepsy, but it has been reawakened recently because of the severe side effects of pharmacological treatments (11). It also has been reassessed as having utility in other pathologies such as obesity, polycystic ovary syndrome, cancer, diabetes, neurological diseases, and others (20,21,26). In more recent years, KD mostly have been studied from a weight/fat loss point of view (4). Interestingly, up until now, only a few studies have investigated the relationship between KD and sports performance. There are two main possible applications, in our opinion, of KD in sport: one is the more intuitive weight reduction for sports divided into weight categories (37) and the second is the surprising (based on some studies in the early 1980s) possibility of a positive influence of KD on endurance performance (28).

A CLOSER LOOK AT THE KD

What Happens During a Very Low Carbohydrate Diet

After a period of several days, fasting or at least a drastically reduced dietary carbohydrate content (to $<20 \text{ g d}^{-1}$ or 5% of daily energy intake) while maintaining usual energy intake through macronutrient redistribution, glucose reserves become depleted and no longer sufficient for either normal fat oxidation (via oxaloacetate in the Krebs cycle) or to supply energy to the brain and central nervous system (CNS).

At normal body temperature, oxaloacetate is not stable and so cannot be accumulated and stored, but it is required for the continued functioning of the Krebs cycle and is replenished continually by anaplerotic reactions involving the conversion of glucose to pyruvate to oxaloacetate (this process, catalyzed by pyruvate carboxylase, is in fact one of the most important anaplerotic reactions) (Fig. 1). Other anaplerotic reactions involve glucogenic amino acids, for example, the 4-carbon amino acids, which include aspartate and asparagine, are degraded to oxaloacetate and are linked closely to glutamate and alpha-ketoglutarate interconversion by amino transferases. Threonine, another 4-carbon amino acid, can be converted into pyruvate. Also malate, in the mitochondrial matrix, can be converted into pyruvate or oxaloacetate acid, both of which can enter the citric acid cycle.

Regarding the CNS, because free fatty acids (FFA) cannot cross the blood-brain barrier, they are not able to be used as an energy source and therefore glucose is the main energy provider for the brain. During fasting or ketogenic dieting, glucose levels drop and an alternative energy source is required as demonstrated by Owen *et al.* (18). This energy is supplied by the ketone bodies (KB) acetoacetate (AcAc), 3-hydroxybutyrate (3HB), and acetone, which are generated, via a process called ketogenesis, from acetyl-CoA and occurs mainly in liver mitochondrial matrix. Although created in the liver, this organ is not able to use KB because of lack of the succinyl-CoA:3-CoA

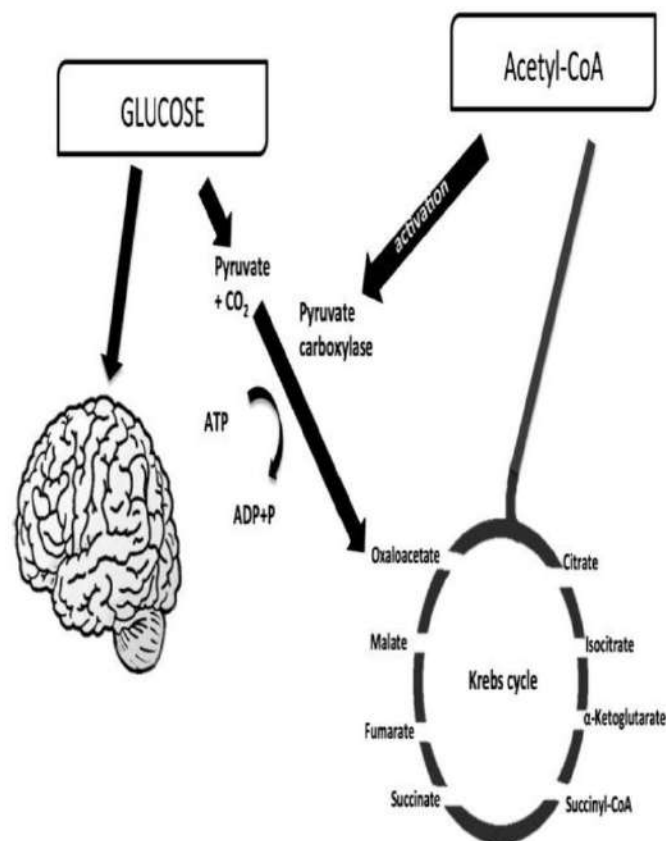


Figure 1. Glucose is essential as an energy supply for the brain and also for the production of oxaloacetate, the levels of which need to be maintained for the functioning of the Krebs cycle. Oxaloacetate is itself unstable and needs to be constantly produced from glucose via pyruvate (which, in mammals, cannot be produced from acetyl-CoA).

transferase enzyme, which is required to convert acetoacetate into acetoacetyl-CoA.

Although acetoacetate is the main KB that the liver produces, it is actually 3-hydroxybutyrate that is the primary form in circulation and in general only negligible amounts of free acetoacetic acid arise, which can be metabolized by striated muscle tissue, including the heart. If there is overproduction of acetoacetic acid, it may accumulate and also be converted partially to the other KB that are eliminated in the urine (ketonemia and ketonuria). Under normal circumstances, the KB concentrations remain very low ($<0.3 \text{ mmol L}^{-1}$), whereas glucose is maintained at $\sim 4 \text{ mmol L}^{-1}$ (22,38). During glucose depletion and as levels of KB rise to approximately 4 mmol L^{-1} , they reach the K_m for the monocarboxylate transporter and can be used as energy sources by the CNS (38). They are used by other tissues as well and the process involves the conversion of 3HB back to acetoacetate and then to acetoacetyl-CoA, which can be processed further into two molecules of acetyl-CoA, which furnish the Krebs cycle (Fig. 2). Utilization of KB creates more energy than glucose because of greater mitochondrial ATP production; for example, the energy liberated by burning 3HB in a bomb calorimeter is 31% higher per C2 unit compared with the combustion of pyruvate (38).

Glycemic Levels During the KD

It is important to note that, although the blood level of glucose drops, it still remains at a physiological level (23), which is maintained through gluconeogenesis involving glucogenic amino acids and also glycerol released from triglycerides. Fasting and very low carbohydrate diets lead to

TABLE. Blood levels during a normal diet, ketogenic diet (e.g., $<20 \text{ g}$ of carbohydrates d^{-1}), and diabetic ketoacidosis (38)

Blood Levels	Normal Diet	Ketogenic Diet	Diabetic Ketoacidosis
Glucose, mmol L^{-1}	4.4–6.7	3.6–4.4	>16.7
Insulin, $\mu\text{U L}^{-1}$	6–23	6.6–9.4	≈ 0
KB, mmol L^{-1}	0.1	7–8	>25
pH	7.4	7.4	<7.3

what is known as “physiological ketosis” where KB levels may rise to 7 to 8 mmol L^{-1} (but without any pH change). In “pathological diabetic ketoacidosis,” on the other hand, ketonemia can exceed 20 mmol L^{-1} and also cause lowering of blood pH (Table). In healthy people, the levels do not rise above 8 mmol L^{-1} because of the efficient use of KB instead of glucose for energy by the CNS.

KD: A Physiological Ketosis

The term “physiological ketosis” was first used by Hans Krebs as he needed to distinguish it from the pathological diabetic ketosis (15). Physiological ketosis is an evolutionary adaptation to counter long periods of undernutrition because of unreliable food supplies. These periods of near starvation are ketogenic, leading to decreases in blood glucose and insulin, along with increases in glucagon as the body attempts to maintain physiological levels of glucose. When the situation of prior food abundance becomes severe food restriction (i.e., fasting) within a few days, there is an increase in KB and,

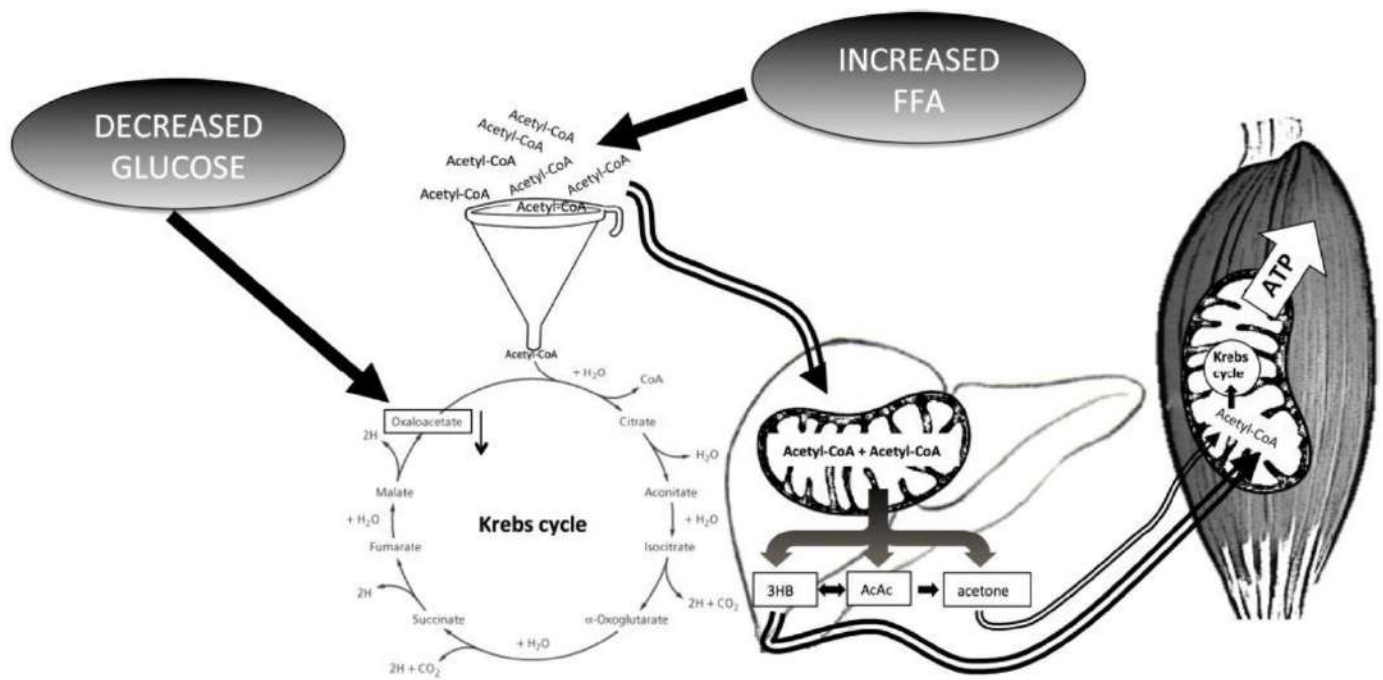


Figure 2. Ketone body (KB) production in the liver increases in response to low carbohydrates and/or high lipids in the diet. The liver produces KB (in the mitochondria) but cannot use them because of the lack of specific enzymes. KB can and are used as an essential energy source by the brain and other tissues like muscles. KB are converted via several steps to acetyl-CoA, which can be used via the ATP-generating Krebs cycle. AcAc, acetoacetate; 3HB, 3-hydroxybutyrate; FFA, free fatty acids.

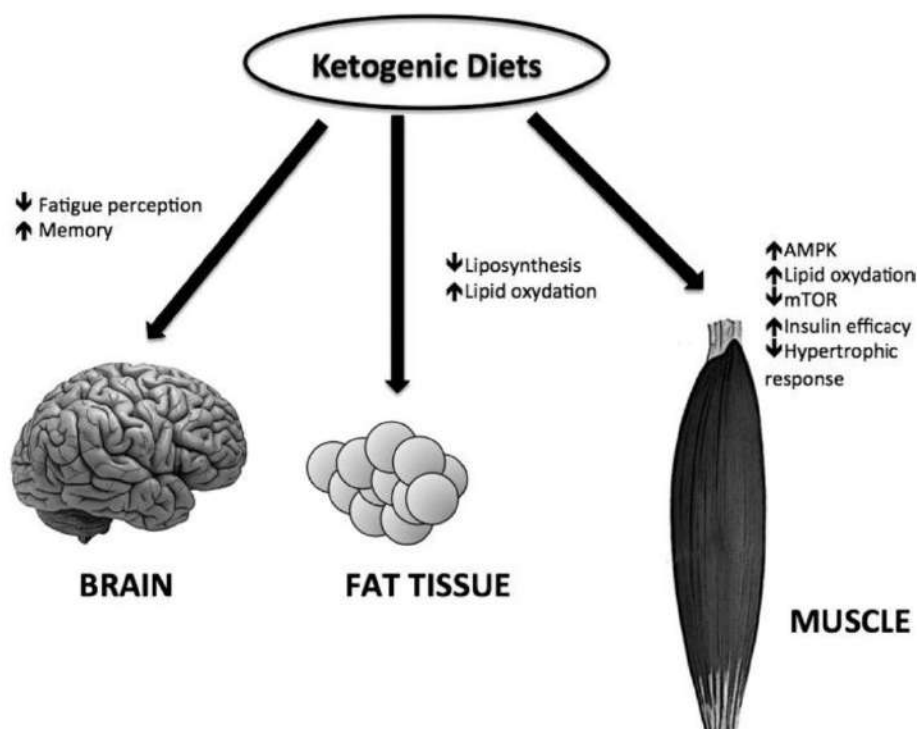


Figure 3. Effects of ketogenic diet on different tissues. AMPK, 5'adenosine monophosphate-activated protein kinase; mTOR, mammalian target of rapamycin.

thus, the energy sufficiency situation of a KD can induce some of the physiological mechanisms that are commensurate with fasting.

EFFECTS OF KD ON BODY FAT AND BODY WEIGHT

The evidence supporting the use of KD in weight loss is undeniably strong (4), but the actual mechanisms by which it is effective remain the source of some debate. Several hypotheses have been proposed — according to one the “physiological ketosis” may be an “expensive” process that leads to a “waste of energy” compared with other types of diets and therefore more effective weight loss.

The biochemical changes occurring during a KD can give some clues to support the “expensive” hypothesis for weight loss. The brain’s metabolism requires about 10 g of glucose d^{-1} ; in the initial phase of KD, about 16% of glucose comes from glycerol (released from triglyceride hydrolysis) and the bulk (60–65 g) from proteins via gluconeogenesis (proteins may be of either dietary or endogenous origin). Gluconeogenesis is energy intense and has been calculated to consume 330 to 360 kJ d^{-1} (39). Even though the use of tissue amino acids as a source of glucose is important in the first days of fasting, its importance gradually decreases; furthermore, the protein supply consumed during a KD “preserves,” as demonstrated, lean body mass (25,42). The importance of glycerol as a glucose source increases progressively during ketosis; in fact, glycerol passes from supplying 16% of total glucose to an average of 60% after many days (>7 d) of complete fasting (from 38% in lean individual to 79% in the obese).

However, there is no direct evidence to support the theory and actually on the contrary, according to a recent study (24),

there actually may not be any changes in resting energy expenditure during or after a KD. Another possibility is that increased weight loss is caused by appetite suppression as a result of the higher satiety effect of proteins, and this also may involve changes in levels of appetite hormones and/or a direct appetite suppression action of the KB themselves (19). Furthermore, in the long-term, the improvement in fat oxidation reflected by a decreased respiratory ratio may go some way to explaining increased fat loss in KD (24) (Fig. 3).

The possible reasons for the effectiveness of KD for weight loss may be listed as follows, in order of evidence, strongest first:

1. Appetite reduction: protein satiety, effects on appetite-related hormones such as ghrelin, and possibly a sort of direct appetite-blocking effect of KB
2. Reduced lipogenesis and increased fat oxidation
3. A reduction in respiratory quotient may indicate a greater metabolic efficiency in fat oxidation
4. A thermic effect of proteins and increased energy usage by gluconeogenesis

KD AND SPORTS

Even though there are still many concerns about the use of KD in sports (10), some encouraging findings on KD and performance (25,42) underline the need for an in-depth understanding of its mechanisms of action for sports purposes. Based on previous research on KD in weight loss, neurological diseases, and, in general, on health-related conditions, we can propose some interesting fields of action of KD in sports. It is a type of diet that appears to have several advantages over other

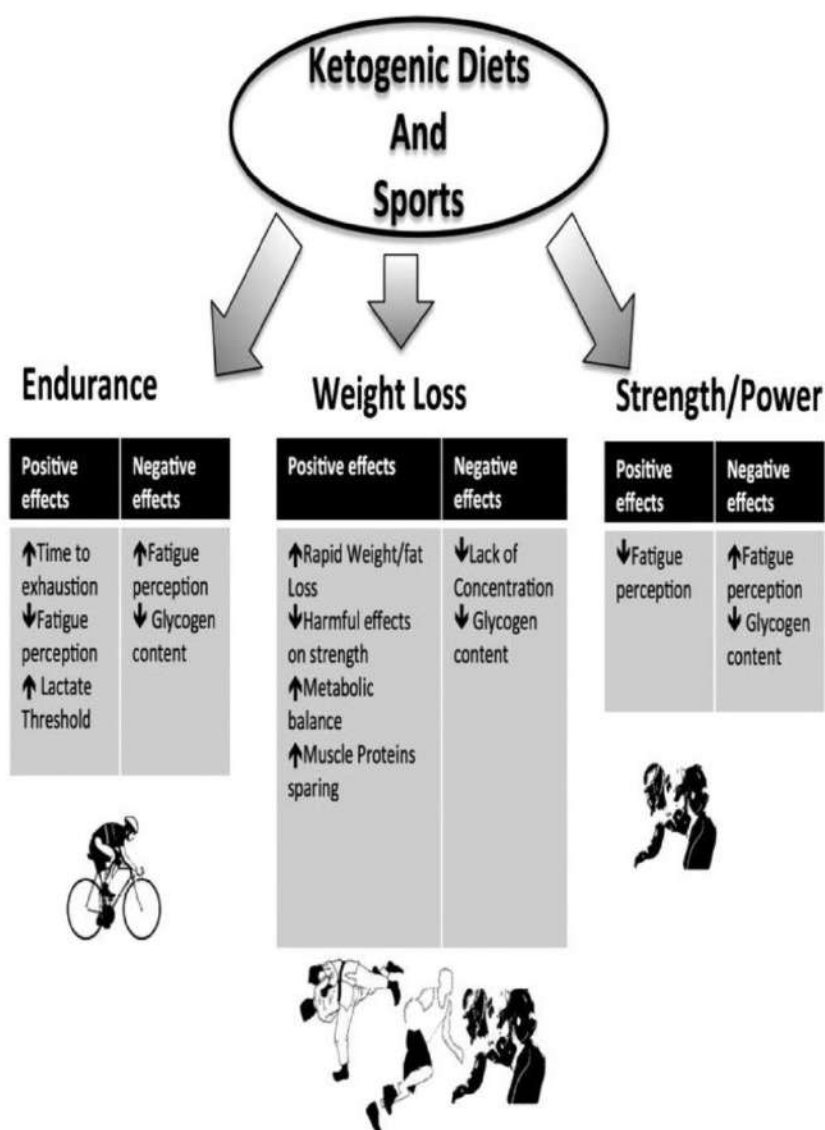


Figure 4. Effects of ketogenic diets in different sports variables and their plausible physiological mechanisms.

types of extreme energy-restricted “crash” diets — the latter, even if used for just a few days, can create situations of undernutrition for essential nutrients (vitamins, minerals, essential fatty acids, and amino acids) as well as depriving the body of other macronutrients that help control oxidative stress and inflammatory processes. An energy-sufficient KD diet with an adequate amount of protein (minimum 1.3–1.5 g kg⁻¹ of body weight) is not an “extreme” diet apart from the very low carbohydrate levels (<20 g carbohydrates d⁻¹) and, as such, it does not lead to metabolic imbalances that can have irreversible effects if nutrient-deficient weight loss diets are repeated on a regular basis.

Sport and Weight Control

There are many motivations that lead athletes to desire weight loss: improving power-to-weight ratio, competing in a more favorable weight category, or, in case of an activity like bodybuilding, to achieve an extreme leanness that is highly desirable for aesthetic reasons. Unfortunately, many common methods that athletes use to reduce weight also may have

some negative side effects that can have a detrimental effect on actual sports performance — this is seen with widely used rapid weight loss methods such as drastic energy reduction, dehydration (e.g., saunas, diuretics, spitting), other medications, and so on. These are of course carried out immediately before competition and with the expected consequences (37) such as the performance reduction, weakness, and so on. These methods are not favorable either for personal health as they upset electrolytes and water balance, glycogen stores, lean body mass (37), and in the case of medications may even be illegal.

Also extremely low energy nutritional approaches are used, and this energy restriction can lead to loss of lean body mass and also can impair performance as seen with dehydration (14). The practice of rapid weight loss (RWL) in weight-dependent sports is not to be underestimated. A recent review by Franchini and coworkers (10) showed that rapid weight loss has a high prevalence in combat sport practitioners such as wrestlers (60%–90%) and in judo (circa 90%). Brito *et al.* (3) reported a similar percentage in judo athletes (62.8%), jujitsu (56.8%), karate (70.8%), and taekwondo (63.3%). Also in weightlifting, RWL appears to be common even though no

precise data are available. There are several generally harmful effects on performance resulting from such a very restricted energy intake (14) as well as harmful effects from specific methods such as dehydration using sauna or diuretics (3). Apart from increasing risks of long-term health problems, there also is an increased risk of weight gain and obesity in middle age (31); furthermore, rapid weight loss can reduce muscle performance and increase muscle damage. Dehydration can impair aerobic performance with a reduced plasma and blood volume (6) even if the actual amount of fluid loss that is necessary to have some significant effects on endurance performance is not so clear. Severe energy restriction often means a reduction of protein intake (as well as other essential nutrients) that, considering the higher needs of athletes, could induce loss of skeletal muscle mass and, in consequence, impairment of strength/power/endurance performance.

KD and Muscle Mass

Unlike severe energy restriction, KD provides adequate amounts of energy and protein to athletes (25), avoiding protein deficiency but, at the same time, the KD, by inducing a “fasting-like” state, leads to alterations in metabolic pathways and processes such as autophagy and stress resistance. KD “mimics” energy restriction effects on 5'adenosine monophosphate-activated protein kinase (AMPK), sirtuin-1 (SIRT-1), and peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC1 α), which become activated by phosphorylation (16). In this state, PGC1 α moves to the nucleus and acts as a transcription factor, increasing the expression of genes that code for proteins involved in fatty acid transport, fat oxidation, and oxidative phosphorylation. The activation by phosphorylation of PGC1 α may occur in several ways involving AMPK, calcium calmodulin-dependent protein kinase, and p38 mitogen-activated protein kinase pathways. SIRT-1-mediated deacetylation also can cause activation. AMPK1 can work in two ways, either by activating PGC1 α by phosphorylation or else directly by promoting the expression of enzymes involved in skeletal muscle oxidative effects and metabolism. This is supported by observations that, in obese subjects, the skeletal muscle is less oxidative and has, during fasting, lower AMPK activation (9). At the same time, AMPK activation also inhibits mammalian target of rapamycin (mTOR) signaling, which is an important factor involved in regulating muscle mass (32).

Macronutrient intake can have an influence on these pathways. It has been shown that reducing carbohydrate intake to very low levels can lead to the activation of AMPK and SIRT-1, increased AMPK1 phosphorylation, and increased skeletal muscle PGC1 α deacetylation but without affecting overall amounts of AMPK, PGC1 α , or SIRT 1. The activations appear to occur in mice within just a few hours (~5 h) of initiation of starvation, currently though similar data are lacking in humans during KD. SIRT-1 and AMPK, when they are activated, can have beneficial effects on glucose homeostasis and insulin action (9).

All these effects are positive in terms of health outcomes, but there is always the other side of the coin: KD, similar to fasting, blunts the insulin-like growth factor 1 (IGF-1)/AKT/mTOR pathway, reducing the possibility of gaining muscle mass despite energy sufficiency (32).

When muscle undergoes mechanical and metabolic stress, an anabolic response is induced and IGF-1 is considered to be the primary mediator. Resistance exercise causes it to be released from local muscle and fat tissue, the version released is an isoform called mechano growth factor ((MGF) a splice variant of IGF-1), which binds to myofibril and satellite cell receptors and initiates translation associated with hypertrophy, which can last for as long as 72 h after exercise. Several pathways are involved in protein synthesis, which are switched on or accelerated by IGF-1; these include the Akt/mTOR and calcineurin pathways. Other hypertrophic processes include the activation of satellite cells that grow, differentiate, and interact with muscle fibers; this also is mediated by IGF-1 and results in formation of new muscle fibers.

Muscle and satellite cells have surface receptors for the MGF isoform of IGF-1 — the IGF-1 receptor (IGF1R), which is a tyrosine kinase and MGF binding initiates intracellular signaling. MGF is a potent activator of the phosphoinositide 3-kinase/AKT/mTOR pathway — phosphoinositide 3-kinase activates AKT, which in turn activates the mTOR, leading to muscle growth. Across recent years that this pathway has been the subject of considerable research on protein synthesis, there is good evidence for AKT's role as the activator of mTOR and also for inducing glucose transport and blocking protein breakdown by repressing the transcription factors of the FoxO family. Also, the AMPK activity is affected, thereby reducing its role in the inhibition of protein synthesis. One of the main targets of mTOR is the serine/threonine kinase enzyme known as p70S6K; when this is upregulated by mTOR, the result is increased phosphorylation by p70S6K of its target substrate, the S6 ribosomal protein, to induce protein synthesis. mTOR also reduces the activity of 4EBP1, which is a translation repressor protein that inhibits protein synthesis (32).

So while KD can be useful in endurance performance, as shown further, it is an oxymoron when the athlete seeks muscle hypertrophy. Hence, it appears somewhat contradictory that there is widespread use of KD in bodybuilders also during “bulk up” periods, while all data regarding biochemical and molecular mechanisms suggest that it is very difficult to increase muscle mass during a KD; use of which really should be limited to the few days immediately before competition in bodybuilding.

KD and Strength

The effects of brief periods of KD on strength and power performance deserve close attention. As previously mentioned, for athletes competing in weight category sports, a safe method of weight loss that does not impair performance can be a legitimate and important tool. Surprisingly, there is only one study, performed by our own group, which has reported on this topic. We have demonstrated recently that, compared with a standard *ad libitum* diet, a 30-d KD did not affect explosive and strength performance negatively in a group of high-level gymnasts (25). It should be underlined that, because of the intense physical activity of competitive athletes, there is an increased demand for protein, and this was reflected in the KD administered in the study, which provided approximately 2.8 g protein kg⁻¹ d⁻¹ (25).

This is a fundamental point: an insufficient protein intake would be likely to negatively affect performance. Even with

this amount of protein though, the athletes showed a decrease in body fat and a maintenance of muscle mass as a result of the well-documented “muscle-sparing effect,” which occurs after a few days of ketosis.

In the early phase of fasting, the CNS is kept supplied with glucose for energy via gluconeogenesis, a process of breaking down muscle tissue to the amino acid precursors. Clearly, this is only a temporary measure, as muscle wasting is compatible with neither optimal performance nor long-term survival. To avoid this, KB are produced at higher levels and provide a fat-based source of energy, an alternative that spares the muscle tissue. As previously mentioned and worth repeating here, the pathways leading to increased body fat utilization have some common features with those that contribute to the lack of muscle mass increase but that normally does not imply muscle loss nor decreased muscle performance. During a ketotic state, the use of KB and FFA for energy slows muscle protein catabolism, but it does not stop it, so the lean body mass generally is conserved. The processes behind this mechanism are not well understood, but the aforementioned “sparing effect” of the use of FFA as an energy source might have a role. Moreover, the relative increase of amino acid uptake in the diet, in particular, leucine, has a well-known protein synthesis effect via mTOR signaling pathway (32), and it has been proposed to be a key factor for the preservation of lean body mass during KD. However, studies in humans are not conclusive regarding this effect whereas another hypothesis is the suppression of some regulatory elements of the ubiquitin-proteasome pathway. Regarding “on-the-field” results, Rhyu and Cho (30) have demonstrated recently that 3 wk of KD improved aerobic capacity and fatigue resistance capacity (exerting also positive effects on inflammatory response) in taekwondo athletes. Furthermore, our data suggest that a 30-d KD does not impair power output in gymnasts; thus, KD could be useful for power athletes to meet weight categories while maintaining power output. Alternatively, a long-term KD can interfere with some muscle hypertrophy mechanisms and this could be counterproductive if the aim of the athlete is to gain muscle mass.

KD and Endurance

The available data on the use of the KD in untrained/sedentary subjects have shown contradictory results, with some reports of improvement (41) and others of reduction (40) in physical performance. For example, in mildly obese untrained individuals, Phinney *et al.* (29) noted that, while undergoing prolonged exercise at a level of 60% VO_{2max} , they can sustain this even with almost no carbohydrate in the diet (<10 g d⁻¹) across a period of 6 wk. Furthermore, after a mean weight loss of 7.1 kg, there was a significant and surprising 155% increase compared with baseline in treadmill duration time (from 168 to 259 min) (29). It has been reported by White and colleagues (40) that a KD (5% of energy provided by carbohydrates) increased perception of fatigue during a 9-min walk; however, it was only the rate of perceived exertion that was significantly higher — there was no actual change in average heart rate or exercise intensity (% HR_{max}), whereas other measures of performance such as VO_{2max} and blood lactate levels were not analyzed. A couple of recent studies demonstrated instead that, in obese subjects, 8 wk of KD enhanced

fat oxidation and had no detrimental effect on maximal or submaximal markers of aerobic exercise performance or muscle strength compared with a high-carbohydrate diet (2). It also was reported that a KD can improve cognitive functioning slightly with respect to speed of processing (12). The authors suggest that a relatively long-term low-carbohydrate diet does not affect the ability to perform endurance or resistance exercises adversely. However, endurance athletes and sedentary subjects are somewhat different, and only very few studies have analyzed the effect of KD in the former. The earliest is the study by Phinney *et al.* (28), which looked at the effect of chronic ketosis on performance in endurance athletes. They reported that 4 wk of ketogenic nutrition did not have any negative effects on the aerobic performance of endurance cyclists. A very recent study by Zajac and coworkers (42) reported a significant increase in VO_{2max} and improvement in the lactate threshold in off-road cyclists after a KD. The authors explained their findings as being caused by reductions in body mass and fat mass and/or a greater oxygen uptake necessary to obtain the same energy yield as on a mixed diet because of increased fat oxidation or by enhanced sympathetic activation even though the maximal workload and the workload at the lactate threshold were both reduced significantly on the KD.

Although these studies report disparate results, there are several factors that could explain the contradictory findings:

- a) the fact that approximately 7 d are required for full adaptation to physiological ketosis. Studies showing a detrimental effect of a KD on performance were performed for less than 2 wk (40) that, according to Phinney (27), is not sufficient for the effects of full keto-adaptation to be seen. It takes 7 d to adapt, leaving just a few days in which any effects may be seen — thus, a 2-wk protocol would be marginal at best. Thus, athletes should program a KD for weight loss at least 2 wk before competition, even though a recent article by Sawyer and colleagues (33) reported that power output was not affected negatively in 31 trained individuals after only 7 d of a KD (5.4% carbohydrate, 35.1% protein, and 53.6% fat);
- b) whether or not electrolyte supplements were given — during a KD, sodium and potassium need to be supplied to maintain tissue function and nitrogen balance (27);
- c) the amount of protein given — during a KD, the need for protein is higher because of gluconeogenesis; thus, a low intake of protein may affect negatively the athlete’s muscle mass.

KD and Psychological Issues

Studies investigating common rapid weight loss systems indicate that RWL may cause decreased concentration, short-term memory loss, and lower self-esteem, as well as increasing confusion, fatigue, and depression traits (10). All these modifications can contribute to impaired performance in athletes. A lack of concentration could affect the ability of the athlete to focus on technique that would result in loss of performance. Short-term memory is fundamental for an athlete to retain essential precompetition information, and impairment can cause a technical/tactical disadvantage. A reduction of self-esteem can affect many aspects: confidence, the approach to a competition, the extent of risk taking

within a competition — negative attitudes can contribute to an overall subdued performance. Regarding fatigue and depressive traits, it is axiomatic to affirm that an increase in either condition can affect negatively a performance in any type of sport.

Considering the KD as a type of modified fasting (as discussed earlier), these negative observations associated with common rapid weight loss diets may not apply. The reasoning is that physiological ketosis is a specific metabolic state that is quite different from the mechanisms induced by simple but extreme energy restriction. The few studies available about the effects of a KD on mood and cognition suggest that (mostly) a short-term consumption of a moderately energy-reduced low-carbohydrate diet has similar effects on the psychological well-being of overweight and obese persons compared with an isoenergetic conventional diet (2,12). The same group though also reported a more favorable effect on mood variables of low-fat diets compared with a low-carbohydrate diet after 1 yr in overweight and obese individuals (1). It is noteworthy that the KD (<20 g of carbohydrates d⁻¹) was maintained only for 8 wk at which point there were no psychological differences between the two diets. After 8 wk, carbohydrate intake was increased to a non-KD (<40 g of carbohydrates d⁻¹) and this might help explain these results. Regarding others psychological issues, it has been noted that, in rodents, fasting can improve brain function as measured by behavioral and motor performance tests, learning, and memory (16). The improvement in behavioral test scores during fasting has been associated with an increased synaptic plasticity (16). The KD mimics a limited food availability condition that triggers an adaptive response involving several different factors such as the brain-derived neurotrophic factor, which is a regulator of energy intake and expenditure in mammals and of synaptic plasticity, neurogenesis, and neuronal resistance to stress. Furthermore, KD can act through various other pathways affecting psychological aspects as shown by mood improvement, which has been confirmed, beyond experimental studies, by a bulk of clinical evidence that supports strongly an involvement of KD in mood improvement in humans (19).

In summary, KD appear, at least in the short-term such as that might be used by athletes, to be able to alleviate depressive symptoms and also diminish perceptions of fatigue, although this has not been investigated in athletes adherent to a KD.

FUTURE DIRECTIONS, PRACTICAL APPLICATIONS, AND CAVEATS

An increasing amount of research has been carried out on KD during recent years, but only a few studies are available on KD and sport performance, whereas anecdotal reports about athletes' use of KD are very common on the social media and news media. One of the main concepts to underline is that, to define a nutritional approach as a KD, some specific end points are essential:

1. a KD shall contain less than 5% of total daily energy from carbohydrates or less than 20 g of carbohydrate daily
2. In athletes, to preserve lean body mass, the daily requirement for protein should be in the range of 1.2 to 1.7 g kg⁻¹

body weight (27–29) (up to 2.5 g kg⁻¹ body weight) (25). This amount is needed to ensure the minimum quantity for body protein replacement and for gluconeogenesis. A lower quantity of protein may impair performance as demonstrated by Davis and Phinney (7) who showed that subjects consuming 1.1 g of protein kg⁻¹ of body weight experienced a significant reduction in VO_{2max} during a 3-month period during a KD compared with subjects given 1.5 g kg⁻¹ body weight. On the other hand, an excessive protein intake (>2.5 g kg⁻¹ body weight or more than 25%–30% of daily energy expenditure) might suppress ketogenesis. Another issue is the so-called rabbit starvation; in 1956, in the book *The Fat of the Land*, an extended version of *Not by Bread Alone*, Stefansson stated: “Rabbit eaters, if they have no fat from another source — beaver, moose, fish — will develop diarrhea in about a week, with headache, lassitude, a vague discomfort. If there are enough rabbits, the people eat till their stomachs are distended; but no matter how much they eat, they feel unsatisfied. Some think a man will die sooner if he eats continually of fat-free meat than if he eats nothing, but this is a belief on which sufficient evidence for a decision has not been gathered in the North. Deaths from rabbit starvation, or from eating of other skinny meat, are rare — for everyone understands the principle, and any possible preventive steps are naturally taken” (36). He described the “consumption” caused by an excess of lean meat without enough fat to provide the required daily energy.

3. Fats are fundamental to reach the total daily energy requirement (as stated); thus, for athletes, fat could/should be provided *ad libitum*.
4. Another important factor is an adequate mineral intake. The Inuit people during the periods spent on the coast usually consume soups made with meat in a broth made with brackish (a mild saline) water. During hunting journeys in the backcountry, they traditionally added caribou blood (a rich source of sodium) to their soup. These traditional techniques suggest that sodium and potassium could play a central role during KD. Phinney and colleagues demonstrated that supplementation with 3 to 5 g d⁻¹ of sodium and 2 to 3 g d⁻¹ total potassium enabled their subjects to maintain their circulatory reserve (thus, allowing vasodilatation during submaximal exercise) and neutral nitrogen balance.
5. Subjects should be compliant, and the diet plan should be checked by an expert nutritionist or registered dietitian to avoid KD-like protocols and to confirm the KD's adherence.
6. Blood analysis should be performed to confirm that subjects are in ketosis; blood examinations using a device that uses capillary blood are preferable to urine examinations because often a lack of KB in urine does not mean necessarily a nonketotic state.

When planning a KD, a few things should be kept in mind:
a) During the first days of KD, the main contributor to weight loss is muscle glycogen and, thus, water — it is well known that there are about 3 g of water stored with each gram of glycogen. The contribution of fat gradually increases across

the days; it should be expected that a significant fat oxidation increase could be observed after 5 to 7 d;

- b) In athletes, it seems reasonable to suppose considering available data, a weight loss of about 1.2 to 1.6 kg in lean subjects of about 70 to 73 kg of body weight (25,27) during 3 to 4 wk of KD.
- c) If the period of keto-adaptation is respected and energy balance is maintained, no decrease in power output should be observed (25).

However, more information is still needed from well-controlled, randomized, controlled trials to confirm the effects of KD on strength/power athletes and to help dietitians provide adequate nutritional plans for athletes.

Another issue is the use of KD in young athletes. It should be underlined that young athletes are under pressure from influences of parents and coaches, and this could lead to maladaptive perfectionist tendencies. Even though there are convincing data about its efficacy and tolerability in children with difficult-to-control seizures in epilepsy (11), a precautionary approach should be observed with young athletes.

CONCLUSIONS

The use of KD in sports is still a twilight zone... “the middle ground between light and shadow, between science and superstition.”

There are some encouraging data that are suggestive of a useful role of KD in certain sports, and these include those with weight categories and aesthetic and endurance sports, but it is necessary that trainers, sports physicians, and dietitians are aware of strengths and limitations of this nutritional strategy.

Many sports require weight control, and specific sports have very strict weight categories. All athletes are by definition competitive but also are in general very young and often under great pressure to perform. As we have discussed, necessity for rapid weight loss is a very common situation that occurs regularly in an athlete's life, and the temptations are to try any means possible to lose a few kilograms in the weeks before a competition. It is an advantage to be just at the top of the weight range of the lower category rather than be at the lower end of a higher category. So to compete in a particular weight category brings advantages but, if incorrect rapid weight loss is used to get there, many of the advantages will be lost. Even worse, in the long-term, repeated inappropriate weight loss efforts can lead to long-term difficulties in maintaining the correct body weight (10,31). Many of the techniques used have been shown to be inappropriate for many reasons. These include “crash” diets with extreme energy restriction, dehydration attempts, and use of pharmaceuticals. The KD is fundamentally different from many other types of weight loss diets — it induces distinct physiological changes and exploits natural mechanisms that have evolved to cope with the historically normal situations of frequent short-term food shortages. The KD also is different from the more studied Ramadan fasting mainly because, during Ramadan, fasting subjects do not become ketotic (5,35). It should be emphasized again that the induced ketosis actually is defined

as “physiological ketosis,” it is not a pathological situation such as observed in “diabetic ketosis.” It is a form of dietary pattern that has been subject to intense scrutiny especially across the decades since the popularization of the Atkins diet and, apart from its positive effects on weight loss, the short-term use of energy-sufficient KD has not been associated with any long-term health issues; the few symptoms such as fatigue and headaches disappear after a few days (22). Biochemical, physiological, and observational studies also provide good evidence that an actual KD (*i.e.*, where adherence is checked) can lead to fat loss with little or no loss of muscle mass (13,25). Indeed, it is a common misconception that the KD intuitively is unsafe because it is a “high-protein, high-saturated fat” diet. This is not the case. The key feature is an energy sufficiency while with a very low carbohydrate intake, but this is compatible entirely with normal protein consumption and a rich nutrition providing full complements of micronutrients and essential macronutrients. Overall, the KD may well be one of the most intensely studied and characterized nutritional systems that exist for weight loss. It also is being used more frequently as a long-term therapy for several pathologies, including epilepsy, and others (20) and, moreover, is a traditional dietary pattern of Circumpolar populations. In view of these considerations and the fact that there will always be athletes who will want to do, or be pressured into doing, almost anything required that may give even a small advantage, at the very least protocols that are *known* to be damaging should be avoided in favor of methods that may be effective and unlikely to be harmful. The evidence reviewed here and elsewhere suggests that properly designed KD could be such a candidate.

Regarding weight category sports, it should be remembered that:

- rapid weight loss should, in principle, be avoided
- long-term planning and gradual body weight reduction is recommended
- if necessary, a KD may be a viable route but at least 2 wk is necessary to avoid any negative effects on performance

Regarding aesthetic sports such as bodybuilding:

- as noted previously, rapid weight loss should be avoided
- it is very difficult, maybe impossible, to gain muscle mass during a KD
- a KD may be used during the final days before a competition, bearing in mind that it causes a glycogen depletion (*i.e.*, reducing muscle volume and vascularization)

Regarding endurance sports, there are some interesting preliminary findings suggesting that the KD may be an instrument to improve fat metabolism and oxidation with improvements performance (Fig. 4).

Finally, the various studies reviewed here demonstrate, in our opinion, that the use of KD in sports both deserves and requires more research, and we would invite researchers to explore the effects of KD in sports.

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