# Sports Nutrition: A Review of Selected Nutritional Supplements For Bodybuilders and Strength Athletes

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## Abstract

Because there is widespread belief among athletes that special nutritional practices will enhance their achievements in competition, the use of supplements has become common. Accompanying the growth in supplementation by athletes has been a corresponding increase in exaggerated claims or misleading information. This article reviews several supplements currently popular among bodybuilders and other strength athletes in order to clarify which products can be expected to produce results. Included in the discussion are creatine monohydrate, beta-hydroxy beta-methylbutyrate, whey protein, phosphatidylserine, and selected amino acids and minerals.
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## Introduction

The increased focus on fitness and subsequent research in the exercise field has expanded the role of nutrition as it relates to sports performance. Because there is widespread belief among athletes that special nutritional practices will enhance their achievements in competition, the use of supplements has become common. Although some of the supplements have proven benefits, historically a great deal of the information on products is either misleading or exaggerated. This is perhaps best witnessed in the products marketed to bodybuilders and other athletes concerned with size, strength, and body composition. This article reviews some of the supplements currently promoted in this market in an effort to determine which contribute to maximizing results. Included in the review are creatine monohydrate, beta-hydroxy beta-methylbutyrate (HMB), whey protein, phosphatidylserine, and selected amino acids and minerals.

## Creatine Monohydrate

Creatine monohydrate has become one of the most popular supplements in the history of bodybuilding. It is used primarily to increase strength and lean body mass and has shown consistent results in promoting these effects in experimental subjects.

In humans, over 95% of the total creatine content is located in skeletal muscle, of which approximately one third is in its free form as creatine, also known as methyl-guanidinoacetic acid, while the remainder is present in a phosphorylated form as creatine phosphate (also called phosphocreatine). Creatine phosphate is utilized within skeletal muscle as a means for storing high energy phosphate bonds.

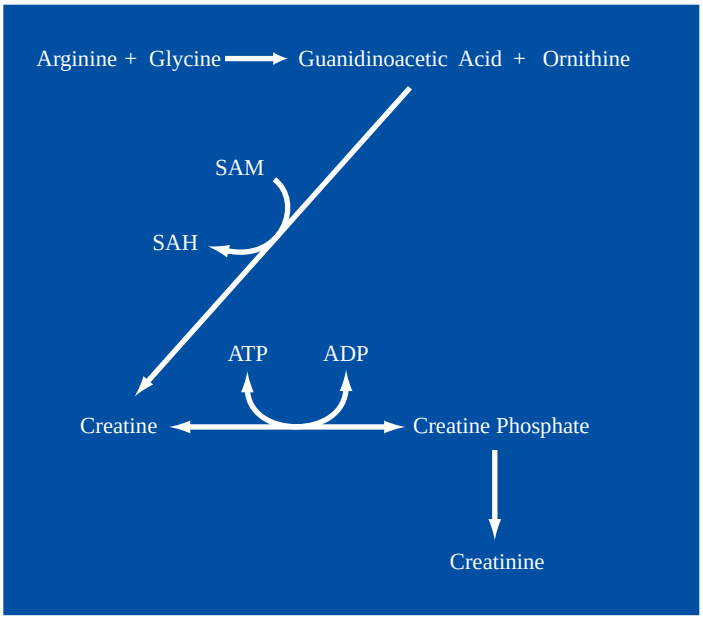
Creatine is formed in the liver, kidney, and pancreas. Initially, arginine and glycine combine to produce guanidinoacetate. A methyl group from S-adenosylmethionine (SAM) is then transferred, resulting in the formation of creatine. The byproduct of this reaction, S-adenosylhomocysteine, is subsequently hydrolyzed into homocysteine and adenosine. In order to optimize endogenous production of creatine, the amino acids arginine, glycine, and methionine must be available as substrates. Additionally, magnesium is required as a cofactor to form SAM from methionine, and B12, folic acid and betaine are required to recycle the homocysteine to methionine for reuse as SAM. See Figure 1.

While creatine can be synthesized endogenously as described above, creatine is also found in a variety of foods in varying concentrations. The richest source is considered to be wild game, but in domesticated meats, beef (lean red meat) is the richest source; 1.1 kg of fresh uncooked steak contains about 5 g of creatine.[1] Fish is also a good source, especially herring, salmon, and tuna. However, it is believed creatine in foods might be destroyed or reduced significantly by cooking.

Creatine is transported to muscle tissue where it exists in equilibrium with creatine phosphate. Creatine phosphate spontaneously converts to creatinine (estimated to be at a rate of about 2 g per day for a 150 pound male)[2] and is then excreted in the urine. While part of this turnover can be replaced through dietary sources of creatine, especially meat and fish, the remainder must be supplied by endogenous synthesis. Because of this, there is a constant drain on arginine, glycine, methionine, and nutritional cofactors to maintain a supply of creatine and creatine phosphate. In vegetarians, daily needs must be met exclusively by endogenous synthesis. When dietary creatine is high, the synthetic pathway is correspondingly regulated downward.[3]

In addition to its use in skeletal muscle, some creatine is used by cardiac muscle. In fact, chronic heart failure patients might have decreased stores of creatine and have been shown to have improved exercise capacity following administration of creatine.[4] One week of creatine supplementation (20 g/d) to patients with chronic heart failure increased skeletal muscle energy-rich phosphagens and performance as regards both strength and endurance.[4]

**Figure 1.** Formulation of Creatine, Creatine Phosphate, and Creatinine




Creatine phosphate produces energy in the form of ATP in muscle cells for about 10 seconds of activity. After it is depleted, the muscle must shift to anaerobic glycolysis for fuel. It is thought skeletal muscles are capable of storing significantly more creatine than is generally supplied by the diet and by endogenous synthesis. Because of this, increased serum creatine, following an oral dose of creatine monohydrate, will be available for storage in muscle tissue. Over time, this

increased dietary consumption can allow the muscle to become saturated with creatine. When the muscle has this extra creatine, it should theoretically be able to delay fatigue and refuel itself quicker during high intensity, short duration exercise, and so should be capable of greater work.

When muscle absorbs creatine, it is hypothesized it also brings water intracellularly with it, so the muscle becomes more "hydrated." It is estimated muscles are about 70% water, so this results in a larger, fuller muscle. Evidence suggests when a cell is well hydrated it might accelerate its synthesis of new proteins and might also minimize protein degradation.[5]

One gram of creatine monohydrate or less in water produces only a modest rise in plasma creatine concentration; however, a 5 g oral dose has been shown to significantly increase plasma creatine concentration. Repeated dosing with 5 g of creatine monohydrate every two hours then sustains the plasma concentration at around 1000 mmmol/l.[1]

Recent studies have shown feeding large amounts of creatine (typically 20-30 g per day for five days) increases muscle total creatine (and phosphocreatine) content.[1,6] The extent of the increase normally observed is inversely related to the pre-supplementation level.[1,6] Vegetarians, because they have a very low dietary creatine intake and low-normal total creatine content,[1] would be expected to show large increases. Muscle creatine uptake appears to be augmented substantially in individuals adhering to a program of repeated high-intensity exercise during the period of supplementation.[1] Adequate vitamin E status might also be needed to optimize creatine uptake.[7] Resynthesis of phosphocreatine following one minute of recovery from intense muscular contraction is accelerated in individuals consuming creatine.[6]

In eight subjects studied, biopsy samples were taken after five days of ingestion of 20 g creatine/day. In five of the eight subjects, there was substantially increased muscle total creatine concentration and creatine phosphate resynthesis during recovery. In the remaining subjects, creatine supplementation slightly increased total creatine concentration and did not increase creatine phosphate resynthesis.[6] In three subjects measured, uptake into muscle was greatest during the first two days of supplementation, accounting for 32% of the total 30 g of creatine monohydrate given orally per day. In these subjects, renal excretion was 40%, 61% and 68% of the creatine dose over the first three days, respectively. Approximately 20% or more of the creatine taken up was measured as phosphocreatine, while no changes were observed in the muscle ATP content.[1]

Oral creatine monohydrate supplementation has also been shown, in a patient with extra pyramidal movement disorder and extremely low creatinine concentrations in serum and urine, to significantly increase brain creatine levels. Phosphorus magnetic resonance spectroscopy of the brain revealed no detectable creatine-phosphate before oral substitution of creatine and a significant increase afterward. Partial restoration of cerebral creatine concentrations was accompanied by improvement of the patient's neurologic symptoms. Oral substitution of arginine, a substrate for creatine synthesis, was unable to elevate cerebral creatine levels.[8]

Creatine supplementation has been shown to improve performance in situations where the availability of creatine phosphate is important; thus, performance is improved in very high-intensity exercise, especially where repeated bursts of energy are required with short recovery periods.[9-13] Several studies have documented creatine monohydrate's effect on muscle size and strength. Typically, after a 5-7 day loading dose, there is an increase in the amount of work done in repeated bouts of

maximal exercise and a gain in body mass of between 0.5-1.0 kg.[10,12] Earnest et al reported following 28 days of supplementation (20g/day), fat-free mass increased by 1.7 kg.[9]

While creatine supplementation increased performance in sprint-trained cyclists, it does not appear to improve endurance performance.[14] Balsom et al actually reported a worsening in performance during prolonged continuous exercise following creatine supplementation. This finding remains unexplained, although the authors believe the increase in body mass due to supplementation might be a contributing factor.[15] Results show creatine supplementation has no measurable effect on respiratory gas exchange and blood lactate concentrations during either incremental submaximal exercise or recovery, suggesting creatine phosphate produces energy in the form of ATP in muscle cells for about 10 seconds of activity. After it is depleted, the muscle must shift to anaerobic glycolysis for fuel. Creatine supplementation does not influence substrate utilization during and after this type of exercise.[16]

Results from an unpublished human trial indicate insulin might be a potent upregulator of a muscle's ability to take in creatine. This has resulted in many users supplementing creatine monohydrate with a carbohydrate, such as glucose, dextrose, or maltose, which simultaneously causes a release in insulin. In a four-week trial, a large increase in speed, anaerobic power, and lean body mass, along with a decrease in body fat was reported in individuals receiving doses of 20 g of creatine per day for the first five days followed by 10 g a day for the remainder of the four weeks. An even greater response in these parameters was reported in the athletes using the creatine/carbohydrate mix, which contained creatine monohydrate, dextrose, taurine, disodium phosphate, magnesium phosphate, and potassium phosphate.

Typically, dosing of creatine monohydrate follows a loading and a maintenance cycle. During the loading period, larger doses of creatine monohydrate are ingested for 5-7 days. A typical dose for individuals weighing less than 225 pounds is 5 g q.i.d., while heavier individuals might take up to six doses per day. The maintenance dose would be 0.03 g/kg body weight.[17,18] Larger doses are probably not of any greater benefit since the capability of muscle to take in and store creatine is finite.[1] In fact, this dosing schedule might exceed the ability of most individuals to incorporate creatine into muscle tissue as evidenced by the renal excretion rate of creatine (40-68% of the supplemented dose) reported in individuals given 30 grams per day.[1] A recent study supports the possible use of lower oral doses. Hultman, et al found 3 g/d for 28 days increased muscle creatine and creatine phosphate stores to a level comparable to a loading phase.[17]

Most of the gains in size and strength occur within the first month, after which muscles are generally saturated with creatine. Evidence indicates these gains will remain while supplementation continues, but will gradually disappear over time when the supplement is discontinued. Typically, levels of creatine drop back to pre-supplementation levels about one month after discontinuing supplementation. The size and strength increases resulting from improved muscle cell hydration also disappear over this same time interval; however, actual gains in muscle mass due to increased work capacity while on creatine will remain.

Anecdotal reports suggest 20-30% of individuals who take creatine do not respond with increased muscle mass or strength. Presently, this finding is unexplained; however, individuals with lower initial tissue levels are most likely to benefit.[1] Because of the success of creatine monohydrate, several other forms have become available, including creatine

phosphate and creatine citrate. These are claimed to produce similar results; however, creatine monohydrate is the only form shown to date to increase strength, lean body mass, and tissue creatine phosphate levels.

Reported side effects from creatine supplementation include gastric disturbance, headaches, clenched teeth, and the sound of blood rushing in the ear. Creatine supplementation might cause serum creatinine levels to increase. This is due to the increase in muscle creatine phosphate and its subsequent spontaneous conversion to creatinine. Since most of the studies have only supplemented creatine for short periods of time, and in the single study reporting long term supplementation only 1 g/day was utilized,[19] it is not currently known whether long-term, high-dose supplementation has adverse side-effects.

Some concern exists that caffeine use (0.5 mg/kg per day) can have a negative impact on the effectiveness of creatine. However, in at least one study, participants were instructed to dissolve the creatine monohydrate in tea or coffee before ingestion. Body weight increase was still observed in 7 of 8 subjects and all subjects had increased muscle total creatine and phosphocreatine resynthesis.[6] Although these results suggest caffeine does not negate the results of creatine supplementation, until more is known it might be best to minimize caffeinated substances, or drink them several hours away from supplementation, if seeking optimal results.

Creatine supplementation is widely practiced by athletes in many sports and does not contravene current doping regulations.[3] Since creatine supplementation does not enhance performance in endurance athletes and evidence suggests an actual decline in performance, I recommend endurance athletes avoid creatine supplementation. In athletes concerned with improving strength, body composition, or short-duration repetitive high-intensity exercise, creatine monohydrate can be incorporated into any supplementation protocol. Although quicker results will be seen following a loading dose, the cost-effectiveness of the 3 g/day dose might be a more appealing option for many athletes.

## HMB

HMB (beta-hydroxy beta-methylbutyrate) is a new product only available in limited supply since the end of 1995. The nutritional use of HMB for nitrogen retention has been patented by the Iowa State University Research Foundation and is licensed to Metabolic Technologies.

HMB is a leucine metabolite. It has not yet been established how HMB is synthesized from leucine in humans; however, in animals evidence suggests the majority of circulating HMB is formed following the transamination of leucine to alpha-ketoisocaproate with its subsequent oxidation to HMB.[20] It has not been determined either to what extent HMB is normally produced *in vivo* or which specific cofactors might influence its production.

While the mechanism of action of HMB is still equivocal, it is hypothesized HMB decreases muscle-protein turnover and might work primarily by minimizing protein degradation. Suggestive evidence of HMB's effect at blocking catabolism is based on its ability to decrease urinary 3-methylhistidine (a marker of muscle breakdown), and to decrease plasma levels of creatine phosphokinase and lactic dehydrogenase.[21] Anecdotal reports indicate individuals who work out more often and most intensely get the best results with HMB. This is important since typically the more an individual works out, the more muscle catabolism also occurs; so at a certain point, the anabolic gains achieved by stimulating the muscles through training are offset by the catabolic effects of frequent, high intensity workouts. HMB's anti-catabolic effects might move this balance point further in

the direction of anabolic growth, allowing an individual to train more often and still receive positive results in strength and mass gains.

In a human study conducted over a three-week period, 3 g/d of oral HMB supplementation was shown to decrease body fat, increase lean mass and strength, and reduce muscle damage in individuals beginning resistance-training exercises. In this trial, participants also consumed either 117 or 175 g/day of protein. While protein intake did not seem to impact strength, participants with higher protein intakes, independent of HMB supplementation, appeared to have greater increases in lean body mass.[21] Because these results were on individuals who had not previously engaged in weight training, doubt existed as to whether these results would also be reproducible in bodybuilders or other athletes who had already engaged in long-term resistance training. However, in a subsequent study, not yet published as a full paper, researchers indicate HMB feeding resulted in equal increases in strength, body composition, and decreased fat in trained and untrained individuals.[22]

At this point, the primary concern regarding HMB is anecdotal evidence which indicates many individuals have not experienced expected results with this supplement. Since HMB is thought to function primarily as an anti-catabolic substance, it is possible these individuals did not train with enough intensity to optimize its effect. The other possibility is, similar to creatine monohydrate, HMB might be ineffective in some individuals. Since this is such a new supplement, no information is available on its long-term safety.

For athletes wishing to experiment with this product, the recommended dosage for HMB is 3 g/day. Since relatively high protein intake was reported in the study demonstrating HMB's efficacy, and because it is unknown whether the same results will occur while on a low-protein diet, I recommend a similar protein intake of between 120-175 g/day for athletes supplementing with HMB.

## Whey Protein

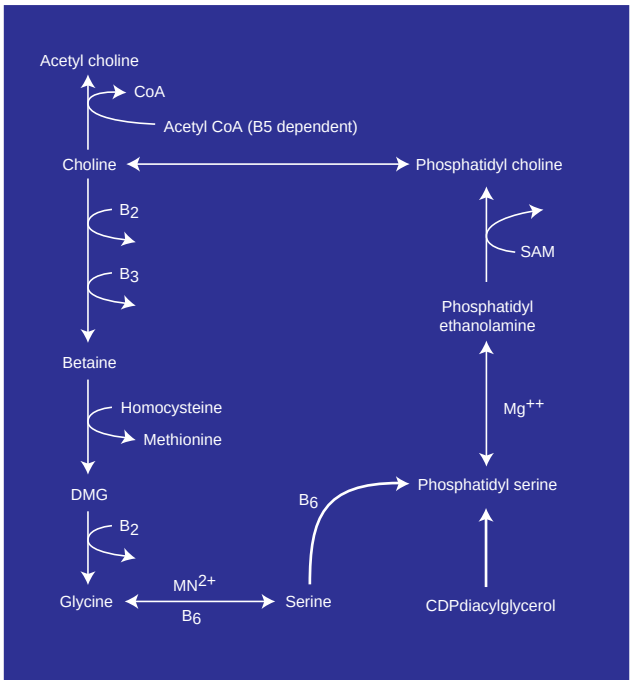
Whey protein, often referred to as lactalbumin, is currently the supplemental protein source of choice for many bodybuilders and strength athletes. Whey proteins represent the major proteins in human breast milk, as opposed to bovine milk which is comprised primarily of casein with lesser amounts of whey. Whey is comprised of alpha-lactoglobulin, beta-lactoglobulin, bovine serum albumin (BSA), and immunoglobulins (IgG1, IgG2, Secretory IgA, and IgM). Other components of the lactalbumin fraction include: enzymes, iron binding proteins, calcium, potassium, sodium, phosphorous, and vitamins A, C, B1, B2, B3, B5, B12, folic acid, and biotin. Whey is a balanced source of essential amino acids and peptides with a high protein efficiency ratio. It is considered to be an excellent source of sulfur amino acids (methionine and cysteine), as well as the branched chain amino acids (leucine, isoleucine and valine), and glutamine. (See sections on branched chain amino acids and glutamine for information on their potential benefits).

Whey transits the stomach quickly and is rapidly absorbed from the human intestine. The beta-lactoglobulin component remains soluble in the stomach and empties rapidly as an intact protein needing further hydrolysis by pancreatic enzymes. Casein, on the other hand, transits the stomach slowly.[23]

Skeletal muscle is the largest repository of metabolically active protein and a major contributor to total body nitrogen balance. Supplying energy alone (i.e., carbohydrate and lipids) cannot prevent negative nitrogen balance (net protein catabolism) in animals or humans; only provision of protein or amino acids allows the attainment of nitrogen balance.

While no studies exist comparing the impact on nitrogen balance, body composition,

Figure 2. Phosphatidylserine Synthesis




or performance of different protein sources in trained athletes, whey has been shown to promote growth and enhance nitrogen balance in experimental animals, low birth-weight infants, and burn victims.[24-26]

Whey protein is rich in substrates for glutathione synthesis,[27] containing substantially more cysteine, which is considered to be a rate-limiting step in glutathione synthesis, than does casein. Whey also contains high amounts of glutamine and glycine.

Glutathione is a powerful antioxidant and is involved in metabolic detoxification pathways. The role free radicals play in the development of exercise-induced tissue damage, or the protective role antioxidants might play, remains to be completely elucidated. Research has indicated free radical production and subsequent lipid peroxidation are normal sequelae to the rise in oxygen consumption with exercise.[28] However, physical training has been shown to result in an augmented antioxidant system and a reduction in lipid peroxidation. Supplementation with antioxidants appears to further reduce lipid peroxidation but has not been shown to enhance exercise performance.[29]

Glutathione levels have been shown to decrease with exercise.[30] Additionally, running a marathon causes a large increase in the tissue content of oxidized glutathione (189%) at the expense of reduced glutathione (-18%).[31] While no information is available on the effects of resistance exercise and glutathione levels, it is hypothesized an increased intake of antioxidants might protect the active person against minor muscle injuries.[32]

Whey protein is more efficient at inducing supernormal glutathione levels than a cysteine-enriched casein diet.[33] A whey-rich diet has been shown to increase heart and liver tissue glutathione content in rats. The whey protein diet appeared to also increase longevity when fed at the onset of senescence.[33] Whey-based formula enhances cysteine retention and results in greater taurine excretion, thought to be a reflection of greater taurine stores.[34] Whey protein fed to three HIV-seropositive individuals over a period of three months, at doses increasing progressively from 8.4 to 39.2 g per day, resulted in progressive weight gain and increased glutathione levels in all three cases.[35]

Experimental studies suggest the whey protein component of milk might exert an inhibitory effect on the development of several types of tumors. It is thought the rich supply of substrates for glutathione synthesis contributes to this inhibitory effect.[36] In experimental animals, a diet consisting of 20 g of whey/100 g diet has been shown to be more protective than similar diets utilizing casein, soybean, or red meat against dimethylhydrazine-induced intestinal cancers.[37] Peptides from whey protein have also been shown to have antithrombotic[38] and immunoenhancing activities.[38, 39]

The primary concerns about supplementing whey protein are the possibility of food allergies, its lactose content, and proposed

links to insulin-dependent diabetes mellitus (IDDM). While the possibility of food allergies from whey has to be considered, it is probable it is no more and possibly less antigenic than soy, casein, or egg-based protein supplements. A significant concern might be the method of processing of the whey protein, since high temperatures during heating or drying can generate browning reaction products by covalent interaction of proteins and lactose. Browned proteins have lowered digestibility and are thought to result in more uptake of intact protein through intestinal mucosa. All whey protein available contains some degree of lactose, although many have very low amounts.

The BSA component of whey has been implicated as a possible trigger for IDDM in children. A similarity exists between the amino acid sequence of the beta cell protein, found on the insulin-secreting beta cells of the pancreas, and BSA. Because elevated levels of anti-BSA antibodies have been found in sera from children developing IDDM, it has been proposed that absorption of BSA, or partially digested fragments of BSA, stimulate the immune system which then incorrectly destroys beta cells.[40] Pardini et al found the prevalence of anti-BSA antibodies was 52% in children with less than one year of IDDM, 47% in children with greater than one year of IDDM, and 28% in the control group. They concluded the prevalence of anti-BSA antibodies is higher in IDDM subjects than in control subjects; however, because of the large overlap of antibody titers observed in patients and control subjects, anti-BSA antibodies were not sensitive nor specific markers of IDDM.[41] Ivarsson et al found IgG antibodies to BSA were not significantly increased at onset of IDDM.[42] Currently, the exact nature of the relationship between BSA and IDDM remains unclear.

The routine use of a post-workout shake might be the most important nutritional supplementation habit for enhancing body composition. It is probably in this manner whey can be best utilized by athletes concerned with maximizing lean body mass and strength.

Amino acid availability following a workout regulates protein synthesis and degradation. Because of the anabolic effects of insulin on protein synthesis and protein degradation, a rapid synergistic response occurs when both amino acids and insulin increase after a protein-containing meal.[43] It is thought the body is highly insulin sensitive after exercise and preferentially shuttles carbohydrates and protein into muscle cells rather than fat cells. Experts think this sensitivity gradually declines post-workout for about two hours until it again reaches normal sensitivity.

A carbohydrate-whey protein supplement has been shown to be more effective in generating a plasma insulin response than either a carbohydrate or a protein supplement alone during recovery from prolonged exhaustive exercise. The rate of muscle glycogen storage was also significantly faster during the carbohydrate-protein treatment. The participants in this study ingested 112.0 g carbohydrate and 40.7 g protein immediately after each exercise bout.[44]

Whey is an excellent choice as a protein source for the post-workout shake because of its rapid transit into the small intestine and because of its high levels of branched chain amino acids and glutamine. Glucose-polymers or maltodextrins are considered to be the best form of carbohydrates to use because of their ability to stimulate an insulin response. Fat should not be added because it might slow transit and decrease the insulin response.

## Phosphatidylserine

Phosphatidylserine is becoming widely used by individuals engaged in resistance training, primarily due to its presumed ability to prevent muscle tissue degradation. Phosphatidylserine has been shown to have an effect on the body's

production of glucocorticoids. While the mechanism of action of phosphatidylserine is still unknown, it is proposed it exerts an effect on the hypothalamic-pituitary-adrenal axis.[45]

Phosphatidylserine is formed by adding a serine to a phosphatidyl group. This requires pyridoxal 5'-phosphate (active B6), and occurs in the same biochemical loop involved with phosphatidylcholine, choline, betaine, and dimethylglycine metabolism. (See Figure 2.)

Physical exercise induces a clear-cut increase in plasma epinephrine, norepinephrine, adrenocorticotropic hormone (ACTH), cortisol, growth hormone (GH), and prolactin (PRL). It is theorized if the increase in cortisol subsequent to intense exercise is prevented, excess muscle tissue breakdown might be prevented. Pretreatment of eight healthy men with both 50 and 75 mg of intravenous brain cortex-derived phosphatidylserine within 10 minutes of the start of exercise blunted the ACTH and cortisol responses to physical stress.[46] Oral administration of phosphatidylserine derived from brain cortex, 800 mg/d for 10 days, significantly blunted the ACTH and cortisol responses to physical exercise ($P = 0.003$ and $P = 0.03$, respectively), without affecting the rise in plasma GH and PRL. Although participants also experienced reductions in plasma cortisol concentrations at a dose of 400 mg/day of phosphatidylserine, the area under the curve of plasma cortisol was significantly lower after the higher dose of 800 mg/day.[45]

While the results of the work of Monteleone et al appear promising, to date no trials have reported an increase in strength or an improvement in body composition after phosphatidylserine supplementation. Until these results are determined, claims of phosphatidylserine's ability to decrease muscle tissue catabolism should be considered unsubstantiated.

## Arginine

Arginine is an amino acid which is used occasionally by body-builders to stimulate growth hormone secretion. It was very popular in the mid-1980's; however, interest in it has since waned. Several studies have shown its ability to stimulate growth hormone and insulin-like growth factor-1 secretion and improve nitrogen balance after IV administration; however, equivocal results have been obtained following oral supplementation.

Corpas et al found oral arginine/lysine (3 g of each per day) was not a practical means of chronically enhancing GH secretion in older men.[47] Additionally, it is debated whether increasing growth hormone levels in people not already deficient has an anabolic effect.

Arginine is required for creatine synthesis and some believe it will enhance synthesis if supplemented. In rats, arginine and glycine supplementation increased muscle creatine.[48]

Elam et al reported individuals receiving arginine and ornithine, five days a week for five weeks, had higher gains in strength and enhancement of lean body mass when compared with controls. Dosages amounted to 2 g or 1 g each of L-arginine and L-ornithine taken orally, and 600 mg of calcium and 1 g of vitamin C as placebos. Subjects taking the arginine and ornithine also had significantly lower urinary hydroxyproline, a marker of tissue breakdown, than subjects receiving placebo. The authors concluded arginine and ornithine, in conjunction with a high-intensity strength training program, can increase strength and lean body mass, and minimize tissue breakdown.[49]

Based upon the results of Elam et al it appears a combination of arginine and ornithine might exert a positive impact on body composition and strength; however, no additional research has substantiated these findings.

## Branched-Chain Amino Acids

Leucine, isoleucine, and valine are considered branched-chain amino acids (BCAAs) because of their similar chemical structures and interlocking methyl groups. Exercise results in marked alterations in amino acid metabolism within the body. The branched-chain amino acids, especially leucine, are particularly important since they contribute as energy substrates and as nitrogen donors in the formation of alanine, glutamine and aspartate. Calculations indicate the recommended dietary intake of leucine is inadequate, since it is lower than the measured whole-body rates of leucine oxidation. This inadequacy is exacerbated in individuals who are physically active.[50]

Results indicate an increased supply of BCAA might have a sparing effect on muscle glycogen degradation during exercise.[51] Short-term (3-4 hours) infusion of branched-chain amino acids has been shown to suppress muscle protein breakdown.[52] In humans nourished parenterally, provision of balanced amino acid solutions or of only the three BCAA cause similar improvements in nitrogen balance for several days.[43]

Administration of BCAA can greatly increase their concentration in plasma and subsequently their uptake by muscle during exercise.[51] Long-term exercise following BCAA administration results in significantly greater muscle $NH^3$, alanine and glutamine production, as well as lower lactate production, than is observed during exercise without BCAA supplementation.[53]

While evidence indicates BCAA might be significant in enhancing protein synthesis or minimizing protein degradation, supplementation with these amino acids has not produced significant changes in body composition. Because of this I would not recommend additional supplementation if consuming a protein drink. If whey or another top quality protein formula is being used, adequate amounts of BCAA are provided.

## Glutamine

Glutamine is the most abundant amino acid in the blood and in the free amino acid pool of skeletal muscle. Glutamine stimulates the synthesis and inhibits the degradation of proteins, is an important vehicle for the transport of nitrogen and carbon within the tissues, stimulates the synthesis of hepatic glycogen, and is an energy source for cell division.[54] Because glutamine deficiency can occur during periods of metabolic stress, it has led to the reclassification of glutamine as a conditionally essential amino acid.[55] Glutamine is also a precursor for the synthesis of amino acids, proteins, nucleotides, glutathione, and other biologically important molecules.

Glutamine is considered to have an anabolic effect on skeletal muscle. It stimulates the synthesis and inhibits the degradation of proteins. Experiments with various animal models have demonstrated glutamine supplementation can result in better nitrogen homeostasis, with conservation of skeletal muscle.[55] The mechanism by which glutamine affects skeletal muscle protein turnover, and thus muscle protein balance, is unknown. However, glutamine has an anabolic effect of promoting protein synthesis and also might reduce protein breakdown.[56]

Glutamine was shown to increase cell volume, while insulin and glutamine together seem to work synergistically to enhance cellular hydration. The effects of glutamine in skeletal muscle include the stimulation of protein synthesis, which occurs in the absence or presence of insulin, the response being greater with insulin.[57]

During various catabolic states, such as infection, surgery, burns, and trauma, glutamine homeostasis is placed under stress, and glutamine reserves, particularly in the skeletal muscle, are depleted. In these conditions, the body requirements of glutamine appear to exceed the individual's muscle deposits, resulting in a loss of muscle mass.[58] In

critically ill patients, parenteral glutamine reduces nitrogen loss and causes a reduction in mortality.[54]

With regard to glutamine metabolism, exercise stress can be viewed in a similar light to other catabolic stresses. Plasma glutamine concentrations increase during prolonged, high-intensity exercise. However, during the post-exercise recovery period, plasma concentrations decrease significantly. Several hours of recovery are required before plasma levels are restored to pre-exercise levels. If recovery between exercise bouts is inadequate, the acute effects of exercise on plasma glutamine concentrations can be cumulative. It has been observed that overtrained athletes appear to maintain low plasma glutamine levels for months or years.[59] Some experts believe reduced concentration of plasma glutamine can provide a good indication of severe exercise stress.[60]

Results suggest, after exercise, the increased availability of glutamine promotes muscle glycogen accumulation by mechanisms possibly including diversion of glutamine carbon to glycogen.[61]

Following trauma there is a loss of nitrogen, with a concomitant reduction of skeletal muscle protein synthesis. This is accompanied by a decrease in the stores of muscle free glutamine. Nutritional support with either glutamine or its carbon skeleton, alpha-ketoglutarate, has been shown to counteract the postoperative fall of muscle free glutamine and of muscle protein synthesis.[62]

Evidence suggests oral glutamine supplementation results in an increased release of growth hormone. An oral glutamine load (2 g) was administered to nine healthy subjects to determine the effect on plasma glutamine, bicarbonate, and circulating growth hormone concentrations. Eight of nine subjects responded with an increase in plasma glutamine at 30 and 60 minutes before returning to the control value at 90 minutes. Ninety minutes after the glutamine administration load, both plasma bicarbonate concentration and circulating plasma growth hormone concentration were elevated.[63]

Although some advocates recommend as much as 30 g, it is likely only marginal benefits are found at supplementary levels higher than 2-3 g per day.

## Ornithine Alpha Keto-Glutarate (OKG)

Ornithine alpha-ketoglutarate (OKG) is a salt formed of two molecules of ornithine and one molecule of alpha-ketoglutarate. OKG has been successfully used by the enteral and parenteral route in burn, traumatized, and surgical patients, and in chronically malnourished subjects. According to the metabolic situation, OKG treatment decreases muscle protein catabolism and/or increases synthesis. In addition, OKG promotes wound healing. The mechanism of action of OKG is not fully understood, but the secretion of anabolic hormones (insulin, human growth hormone), and the synthesis of metabolites (glutamine, polyamines, arginine, ketoacids) might be involved.[64]

This supplement has been available for several years. It has been used successfully in hospitalized burn victims to slow protein loss. In one study on physical performance, OKG (10 g/day with 75 g of carbohydrates) was given for six weeks. The OKG group experienced a significant increase in bench press strength and biceps circumference. Body weight and percent fat were not different between groups. No differences in growth hormone levels were seen between groups. Body composition changes were seen among several individuals in the OKG group but no significance was found either within or between experimental groups.[64]

Anecdotal reports from some individuals supplementing with OKG indicate increased appetite and better disposition to train.

Some anecdotal reports claim great results while others experience no results. If OKG is utilized as a supplement, the dosage recommended is 10 g along with a 75 g carbohydrate drink.

## Vitamin C

There have been several investigations during the past four decades of the potential effect of high-dose vitamin C supplementation on physical performance. However, the results have been equivocal. Most studies could not demonstrate an effect. On the other hand, a suboptimal vitamin C status results in an impaired working capacity which can be normalized by restoring vitamin C body pools.[65]

A potent antioxidant required for collagen synthesis, ascorbic acid might help protect muscles from excessive damage due to training or trauma. Data suggests prior vitamin C supplementation might exert a protective effect against exercise-induced muscle damage.[66]

Ascorbic acid might decrease cortisol production.[67] It has also been suggested ascorbic acid might have a role in facilitating an adequate response to stress.[68]

Because of ascorbic acid's potential for minimizing muscle damage and cortisol-induced muscle catabolism, it is recommended that 1-3 grams be supplemented daily.

## Minerals

There are at least 60 trace minerals having some impact on health in animal models. Many of these have not been adequately studied in humans, and even fewer have been looked at for their effect on athletic performance. While it is possible deficiency in any of these trace minerals would detrimentally impact performance, this review will selectively focus on boron, chromium, selenium, vanadium, and zinc.

## Boron

Recently, a proliferation of athletic supplements has been marketed touting boron as an ergogenic aid capable of increasing testosterone. While this might to be true in some populations under specific conditions, boron's impact on testosterone is still equivocal.

Boron appears to increase testosterone levels in rats in a time- and dose-dependent manner.[69] In postmenopausal women, increasing dietary intake of boron from 0.25 to 3.25 mg/d has been reported to more than double plasma testosterone.[70] In a subsequent study of healthy men, boron supplementation resulted in an increase in the concentrations of both plasma estrogen and testosterone.[71] However, Beattie and Peace reported changing boron intake had no impact on testosterone levels in postmenopausal women.[72]

The effect of boron supplementation was investigated in 19 male bodybuilders ages 20-27 years. Ten were given a 2.5-mg boron supplement, while nine were given a placebo every day for seven weeks. Both groups demonstrated significant increases in total testosterone, lean body mass, and one-repetition maximum squat and bench press; however, analysis of variance indicated no significant effect of boron supplementation on any of the dependent variables. The authors concluded the gains were a result of seven weeks of bodybuilding, not of boron supplementation.[73]

It is prudent to supplement the diet with 3 mg of boron per day to ensure against deficiency; however, an expectation of increased strength and improved body composition is unrealistic.

## Chromium

Chromium is highly promoted in bodybuilding circles as a fat-burning supplement and as an aid in increasing lean mass. Available research does not support either of these claims.

Changes in body weight, a sum of three body circumferences, a sum of three skinfolds, and the one-repetition maximum for the squat and bench press were examined in 59 college-age students over a 12-week weightlifting program. Half of the students were given 200 mcg/day elemental chromium as chromium picolinate, while the other half received a placebo. No treatment effects were seen for the strength measurements. The only significant treatment effect found was an increase in body weight observed in the females supplementing with chromium.[74]

The effects of nine weeks of daily chromium supplementation (200 mcg chromium as picolinate) were investigated in a double-blind design in football players during spring training. Chromium picolinate supplementation was ineffective in bringing about changes in body composition or strength.[75]

Hallmark et al found 200 mcg of chromium supplemented to untrained males (23 +/- 4 yr), in conjunction with a progressive, resistive exercise training program, did not promote a significant increase in strength and lean body mass, or a significant decrease in percent body fat.[76]

Trent et al conducted a double-blind, placebo-controlled protocol for 16 weeks. Chromium as picolinate (400 mcg) or a placebo were distributed to designated individuals. At the end of 16 weeks, the chromium group failed to show a significantly greater reduction in either percent body fat or body weight, or a greater increase in lean body mass, than did the placebo group. It was concluded chromium picolinate was ineffective in enhancing body fat reduction in this group.[77]

Lukaski et al investigated the effects of eight weeks of daily chromium supplementation in 36 men in a double-blind design. Strength, mesomorphy, fat-free mass, and muscle mass increased with resistance training independently of chromium supplementation ($P < 0.0001$). These findings suggest routine chromium supplementation has no beneficial effects on body composition or strength gain in men, although it must be noted the placebo group received a trace level of chromium.[78]

Evidence strongly indicates supplementation of chromium will not enhance strength or body composition. Similar to boron, chromium-rich foods or a supplement containing chromium should be included in the diet to avoid deficiency; however, it is unrealistic to expect gains in strength or improvement in body composition.

## Selenium

Selenium is a trace mineral which is utilized as a cofactor in several enzymes. It is commonly found in antioxidant formulas because of its role as a cofactor in the enzyme glutathione peroxidase. Evidence suggests the administration of organic selenium partially compensates for and decreases the intensity of oxidative stress in athletes.[79] While optimal antioxidant status is critical to athletes, selenium might have an additional role in the determination of body composition. Selenium deficiency can affect the metabolism of thyroid hormones. Iodothyronine 5'-deiodinase, which is mainly responsible for peripheral T3 production, has been demonstrated to be a selenium-containing enzyme.[80] In rats fed a selenium-deficient diet, hepatic iodothyronine 5'-deiodinase is decreased by 47%. Lower concentrations of T3 and T4 have also been demonstrated in selenium-deficient animals.[81] Reduced peripheral conversion of T4 to T3 secondary to a selenium deficiency might create a functional hypothyroidism which would be expected to adversely impact body composition.

## Vanadium (Vanadyl Sulfate)

Vanadium as vanadyl sulfate is widely utilized by athletes seeking to improve body composition. It is generally promoted as

having an anabolic effect which enhances the transport of amino acids into cells. Several studies have indicated its ability to reduce fasting glucose and improve hepatic and peripheral insulin sensitivity in non-insulin-dependent diabetic humans.[82-84] However, vanadyl sulfate does not appear to alter insulin sensitivity in nondiabetic subjects.[84] A single study reported the effect of oral vanadyl sulfate (0.5 mg/kg/day) on anthropometry, body composition, and performance in a 12-week, double-blind, placebo-controlled trial involving 31 weight-training volunteers. No significant treatment effects for anthropometric parameters and body composition were observed. Both groups had similar improvements in performance in most exercises; however, a significant improvement in one repetition-maximum leg extension was found in the treatment group. The authors concluded that although vanadyl sulfate was ineffective in changing body composition in weight-training athletes, its performance-enhancing effect required further investigation.[85] Anecdotal reports indicate bodybuilders often supplement 15 mg t.i.d., however, this practice is ill-advised due to both the lack of demonstrated efficacy and the lack of information regarding long-term toxicity of high doses of vanadium.

## Zinc

Dietary deficiency of zinc is prevalent. Because of this, zinc supplements have been widely advocated for athletes. While it might not be wise to indiscriminately administer zinc, suggestive evidence indicates zinc might impact body composition due to its interaction with a variety of hormones.

It is thought intense exercise can result in changes in zinc metabolism. Zinc has been demonstrated to be lowered in trained adolescent gymnasts and even lower in females in the general population. Brun et al suggested this reduction might play a role in abnormalities of puberty, growth, or muscular performance.[86]

Some investigators have concluded zinc might play an important role in modulating serum testosterone levels in normal men. Prasad et al observed dietary zinc restriction in normal young men is associated with a significant decrease in serum testosterone concentrations. They also reported zinc supplementation of marginally zinc-deficient normal elderly men resulted in an increase in serum testosterone from 8.3 +/- 6.3 to 16.0 +/- 4.4 nmol/L ($p = 0.02$).[87] It is important to remember, while zinc deficiency might inhibit testosterone production, zinc supplementation to an individual with adequate levels has not been shown to produce excess testosterone.

Zinc deficiency might result in reduced production of growth hormone (GH) and/or insulin-like growth factor-I (IGF-I).[88] Oral zinc replacement has normalized growth hormone levels and increased growth rate in teenagers found to be GH deficient.[89] Zinc supplementation causes a significant increase in liver synthesis of IGF-I (somatomedin C). In chronic zinc deficiency, reduced liver production of IGF-I is responsible for reduced physical growth; moreover, in this situation, receptor resistance to IGF-I (in addition to GH) has been demonstrated. Receptor sensitivity is reestablished after supplementation with zinc. Zinc also might play a role in increasing the number of receptors.[90]

Zinc deficiency might affect the metabolism of thyroid hormones. The structure of nuclear thyroid hormone receptors contains zinc ions, crucial for the functional properties of the protein.[80] In experimental animals, zinc deficiency decreases concentrations of triiodothyronine (T3) and free thyroxine (fT4) in serum by approximately 30% when compared with zinc-adequate controls. The concentration of thyroxine (T4) in serum was not affected by zinc deficiency. In these animals, zinc deficiency also decreased the activity of hepatic iodothyronine 5'-deiodinase by 67%.[81]

Because of the multiple interactions of zinc with hormones critical to strength and body composition, it is recommended athletes get a determination of zinc nutriture and supplement if required.

## Conclusion

Based upon available information, strength athletes are likely to obtain improved results by following a supplementation routine which includes creatine monohydrate (at least 3 g/d), a post-workout protein shake (40 g of protein), vitamin C (1-3 g/d), and a multivitamin/mineral formulation which contains approximately 3 mg of boron, 200 mcg of chromium, 200 mcg of selenium, 100 mcg of vanadium, and 15 mg of zinc. The published results to date on HMB are impressive; however, because of its high price, it should be tried only if results either plateau or are not obtained with the above supplementation protocol. I do not currently recommend phosphatidylserine for several reasons. It has not been demonstrated yet to produce bottom-line results of improved strength or body composition, and it is very expensive to dose at 800 mg/d. I also do not routinely recommend isolated amino acids, with the exception of glutamine. Although compelling evidence could be used to make an argument for many of the isolated amino acids, my bias is that a high-quality protein supplement, such as whey, provides adequate levels of all of the amino acids for the majority of athletes. Because of the correlation of low glutamine levels and over-training, supplementation with two grams per day of glutamine, in addition to a protein supplement, should be considered in individuals whose training regimen places them at risk for over-training.

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