Chapter 9

Nutritional Supplementation

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Introduction

The nutritional requirements of every person may differ in some capacity due to the broad number of factors that affect the nutritional needs of an individual. When greater physiological and psychological stress acts upon the body, the need for supportive nutrients increases. The specific type of demand dictates the change in nutritional needs. When the increased stress is from physical activity, the mode, intensity, and duration all become relevant factors in determining the correct nutritional make up of the diet. For instance, heavy resistance training requires different nutritional adjustments than long distance running. The amount of energy used during activity and the physiological recovery and repair mechanisms differentiate the nutrition for optimal performance.

Glycogen Storage

During high-volume, heavy resistance training, glycogen stores in the muscle provides the largest portion of calories for work. For this reason, it is important to maximize glycogen stores before engaging in this type of exercise bout. Cellular glycogen saturation is best initiated immediately following the previous exercise bout. The heightened metabolic environment created from physical exertion causes the depleted cells to more efficiently absorb nutrients. During the three hours immediately post-exercise, cells have an increased permeability to cellular nutrients and an increased sensitivity to anabolic hormones, including insulin (77; 135; 152). Consuming a mixture of protein (6-10 grams) and carbohydrates increases both glycogen saturation and protein synthesis in the muscle tissue under optimal conditions (18; 78).

The quantity of carbohydrates consumed should reflect the caloric expenditure of the previous exercise bout (76). Research suggests that within the first hour following exercise, 1-2 grams of carbohydrate should be consumed for each kilogram of body weight (75; 78). Several studies suggest that during intense training programs, the total replenishment of carbohydrates should reach up to 10 g of carbohydrate per kilogram of body weight and be consumed over the course of several hours following each exercise bout (23; 80). A key factor in glycogen replenishment is the total energy utilized from carbohydrates versus other sources (i.e. fat, protein) during exercise. When glycogen is significantly depleted, it becomes more difficult to fully refuel for the next event.

Immediately following an exercise bout, high glycemic foods (foods with a carbohydrate component that is quickly absorbed into the blood stream) are an ideal choice for carbohydrate replenishment (25). The internal biological environment makes better use of the energy, which quickly enters circulation. Cellular availability of nutrients is very important to the post-exercise metabolic process. This is true for both stop-and-go anaerobic activities typical of resistance training, as well as sustained aerobic exercise events (24; 102; 131). Research trials consistently found that inadequate carbohydrate consumption in the hours following exercise led to reduced performance in subsequent training bouts. Based on these findings, many athletes and high intensity exercisers utilize post-exercise recovery drinks. Carbohydrate-electrolyte solutions can contribute to replenishment, but are often inadequate in calories to fully satisfy the recovery demands. Additional carbohydrate sources should be consumed to reflect adequate caloric intake of the appropriate nutrients.

Recovery beverages or commercially blended meal replacement drinks can be ideal alternatives to regular food due to their easy digestibility and convenience. The actual energy breakdown of the beverages varies by manufacturer and the particular intention of the product. Protein drinks consumed immediately after exercise can contribute to tissue recovery, but are generally too low in carbohydrates to replenish glycogen stores and are excessive for protein synthesis stimulation. Fluid energy mixtures which provide both carbohydrates and protein can be an ideal solution for post-exercise energy consumption when appropriate food sources are not available. Possible benefits include increased digestibility and absorption rates compared to many whole food choices and the convenience of the supplemental energy, providing a practical alternative to the labor and time requirements of meal preparation.

Glycogen storage can also be enhanced by pre-exercise food consumption. Following sleep or any 8-12 hour period when eating does not occur, glycogen stores become reduced. Pre-activity fuel should be mainly in the form of carbohydrates to encourage adequate energy for intense work. Consuming a meal high in protein or fat does not satisfy the energy needs of working tissue during heavy training and slows the digestion process when mixed with carbohydrates. Carbohydrates consumed approximately 3 hours before the exercise bout provide adequate time for digestion and absorption of the nutrients. Adequate fluid should also be consumed during this period to prepare the body for activity participation.
Supplements and Ergogenic Aids

To further enhance physical performance, many exercisers and athletes use supplements in addition to their dietary intake of nutrients. The term **supplement** simply means replacing nutrients that are required for proper nutrition but are not being met through normal dietary intake. When supplements are taken above what is necessary for normal homeostasis with the intention of performance enhancement, they are classified as **ergogenic aids**. Dietary ergogenic aids are supplemental nutrients or compounds that are consumed for the purpose of enhancing a physiological or psychological effect via improvements by one or more functions of the body. The most common dietary supplements are multi-vitamin mineral pills. They represent the largest portion of the dietary supplement industry and are estimated to cover 70-90% of all supplements marketed (3; 91; 136). According to the American Dietetic Association, more than 50% of adults have taken or currently take vitamin pills in addition to their normal dietary intakes. Many exercisers also believe that taking additional vitamins is necessary for improved performance and health (119).

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**Key Terms**

**Supplement**- A substance added to the diet to make up for a deficiency.

**Ergogenic Aids**- Any external influences which can positively affect physical performance or mental focus.

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Goals of Fluid Replacement Drinks

Blood glucose levels are maintained by carbohydrate absorption in the small intestines. This helps offset decreased glycogen stores and can prolong work.
For many people, the hardest concept to accept is that “more is not always better.” If adequate nutrition is attained in the diet, additional intake of supplements simply adds chemical agents to the body. Over 50 years of research concludes that additional supplementation above adequate nutritional intake values for the individual will not provide exercise performance enhancement. For most people, ingesting additional vitamin and minerals above the recommended dietary upper limit required by the body will simply cause any excess to be excreted in the urine or become processed by the liver and add an increase risk of toxicity poisoning in tissues (2; 4; 74; 157; 165). Will a single multi-vitamin hurt? Certainly not, but caution should be taken when consuming megavitamins, particularly when also consuming other supplements (27; 139; 166).

Exercise does increase the nutrient demands of the body, so intense exercisers should be mindful to track their intake of vitamins and minerals, particularly antioxidants (141; 160). Again, the Upper Tolerable Intake Limit should provide the ceiling for prudent ingestion. A variety of food sources, particularly plant-based foods, should be used to meet the majority of vitamin and mineral needs of the body (34; 161).

Vitamins and minerals are not the only supplements used for performance enhancement. Numerous nutrients, compounds, and chemical agents are purported to enhance most performance-related physiological functions. They are generally categorized by the specific “claimed” effect the supplement is supposed to have on the body. The following list includes the most popular categories found in most nutrition stores.

### Common Sports Drinks

<table>
<thead>
<tr>
<th>Drink</th>
<th>Carbohydrate Type</th>
<th>Carbohydrate Grams</th>
<th>Calories</th>
<th>Sodium</th>
<th>Potassium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gatorade</td>
<td>Sucrose, Glucose, &amp; Fructose</td>
<td>14</td>
<td>50</td>
<td>110</td>
<td>30</td>
</tr>
<tr>
<td>Powerade</td>
<td>High fructose corn syrup &amp; Glucose Polymers (Maltodextrins)</td>
<td>19</td>
<td>70</td>
<td>55</td>
<td>30</td>
</tr>
<tr>
<td>All-Sport</td>
<td>High fructose corn syrup</td>
<td>19</td>
<td>70</td>
<td>55</td>
<td>55</td>
</tr>
<tr>
<td>Hydrafuel</td>
<td>Glucose, Glucose polymers, &amp; Fructose</td>
<td>16</td>
<td>66</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>1st Ade</td>
<td>High fructose corn syrup, Glucose, Fructose, &amp; Sucrose</td>
<td>16</td>
<td>60</td>
<td>55</td>
<td>25</td>
</tr>
<tr>
<td>Coca-Cola</td>
<td>High fructose corn syrup</td>
<td>27</td>
<td>103</td>
<td>69</td>
<td>0</td>
</tr>
<tr>
<td>Orange Juice</td>
<td>Sucrose, Fructose, &amp; Glucose</td>
<td>25</td>
<td>104</td>
<td>6</td>
<td>436</td>
</tr>
</tbody>
</table>
The supplement industry is a “buyer beware” market. The FDA regulates dietary supplements under a different set of regulations than those covering "conventional" foods and drug products (prescription and over-the-counter). Under the Dietary Supplement Health and Education Act of 1994 (DSHEA), the dietary supplement manufacturer is responsible for ensuring that a dietary supplement is safe before it is marketed. The FDA is responsible for taking action against any unsafe dietary supplement product after it reaches the market. Generally, manufacturers do not need to register their products with the FDA or get FDA approval before producing or selling dietary supplements. Manufacturers must make sure that product label information is truthful and not misleading.

The self-regulation of the supplement industry has created an environment where almost anything goes, just as long as the label of the product being sold does not make a medical claim or suggest that the product can cure or prevent a disease. These loose reins on the billion dollar supplement industry have opened the gates to unethical “health hustling.” A limited number of supplements reviewed by scientifically sound research trials have shown efficacy in performance enhancement or effective weight loss.

The labels are also of concern when buying supplements. Numerous well-controlled studies have found inconsistencies in the potency and implied or listed concentrations of the active ingredients on supplement labels. Companies manufacturing and selling supplements are not necessarily scrutinized for quality control practices. If supplements are purchased, they should come only from reputable companies.

Beware of advertising and marketing that uses testimonials, “independent research” trials, celebrity endorsements, guarantees of quick results, and “secret” ingredients. Other suspicious marketing buzzwords include “Doctor recommended” or “physician approved,” amazing results, pharmaceutical label appearances, or free trial give-away offers. Likewise, when the findings do not match the conventional wisdom of science or governmental recommendations and the research is not published in peer-reviewed journals, this evidence points directly at a questionable approach. Scientifically valid information is extremely welcome and exchanged amongst the top scientists and researchers. This lends itself to question why supplement “research” is often done independently of these prestigious circles if it is actually valid.

~Quick Insight~

Hundreds of products fall within these categories. The claims associated with the consumption of the dietary supplements range dramatically. Some products are purported to offer numerous health benefits, while others advertise that consumption will improve a single function of the body. Due to the vastness in product offerings and limited peer-reviewed literature supporting the claims, only the most popular supplements are reviewed below.

**Mass and Strength Gains**

When the emphasis of the training focuses on muscle hypertrophy, many exercisers and body builders ingest compounds that supposedly aid in the formation of new muscle mass. The most common ergogenic aids include creatine monohydrate, supplemental protein, branch chain amino acids, glutamine, nitric oxide, and HMB. The proposed mechanism for improving muscle mass is not the same in each of the dietary supplements. In many cases, individuals ingest several of these supplements to take advantage of a possible synergistic effect.

**Creatine**

Creatine was first identified by a French scientist in the 1800’s. It is a naturally occurring protein that serves as an anaerobic source of immediate energy. The majority (60%) of the creatine in the body is stored in the skeletal muscle as phosphocreatine, with the other 40% found in the free unphosphorylated creatine form.
Creatine is also found in the muscle of animals, so foods such as meat, poultry, and fish provide natural dietary sources. These foods contain approximately 4 to 5 g of creatine per kg of food.

In the human body, the liver, kidneys, and pancreas produce creatine from the non-essential amino acids arginine, glycine, and methionine. The body only synthesizes about 1 to 2 g of creatine a day, which is utilized during physical activity. The molecular structure of creatine makes it heavy; therefore, the body does not maintain large stores, preferring instead to re-phosphorylate the molecule into its active form as dictated by energy demands. Although creatine concentrations are greatest in fast-twitch fibers, slow-twitch fibers more efficiently re-phosphorylate the molecule. No significant differences distinguish the creatine in males and females nor does exercise increase one’s storage capacity. Creatine is the primary energy used for immediate high-force output exercise and is also involved in acid buffering, as well as glycolysis regulation.

Creatine monohydrate is the supplement form of creatine formed from sarcosine and cyanamide. Studies have shown that the supplementation of 20-25 g per day for 3-5 days increases intramuscular creatine (10-30%) and phosphocreatine (the phosphorylated active form) stores (10-40%) (14). The magnitude of the concentration enhancements correlate to initial levels of creatine in the body prior to supplementation. The increased concentrations are associated with improved short-term performance of intense exercise and rate of resynthesis back into the active form during rest intervals (13; 97; 123). In addition to improvements in immediate energy availability, creatine also associates with an increase in body mass, which may be due to increases of fat-free mass and/or fluid retention (100). Currently, there are mixed views as to the causes of the mass gains (150). No conclusive evidence suggests that creatine supplementation aids in long-duration activities, such as running (41). It is important to note that scientific investigations have reported equivocal results, with fairly equal numbers of significant and non-significant findings supporting creatine’s efficaciousness.

Creatine is usually consumed in cycles of loading and maintenance phases. The loading phase usually requires an individual to consume 20 to 30 g of creatine for 5 to 6 days (132). It appears that an upper limit for total creatine is approximately 160 mmol/kg of dry muscle (4). After a specific amount of creatine storage is attained, the excess is excreted in the urine. The maintenance phase uses a smaller dosage to maintain creatine stores after the loading phase. This phase usually uses consumption rates of 2-5g per day, which reflect two times the turnover rate by the body (133).

Anecdotals reports of side effects associated with creatine supplementation have included abdominal cramping, cramping, stiffness, and strains. These case studies, though, do not represent well-controlled trials, so no causal relationship between creatine supplementation and these side effects has yet been established. Since activities associated with creatine as the primary fuel are short duration, high intensity, these types of activities alone may result in these types of symptoms. Abdominal cramping or diarrhea may also occur when consuming excessive amounts of creatine, particularly during the loading phases. The current research does not provide evidence of clinically significant side effects (62; 117; 140). Long-term studies may be necessary to determine if excessive amounts of creatine will have adverse effects on the liver, kidneys, or cardiac muscle. Individuals taking creatine should be educated regarding proper dosages. Additionally, caffeine ingestion with creatine has been shown to negate creatine’s ergogenic effects.

**Protein**

Without question, protein is the key component in forming and repairing muscle tissue. Protein plays an integral role in muscle growth and remodeling through protein synthesis. In muscle tissue, amino acids interact with one another to form structural and contractile proteins, aiding in the muscle’s production of force. These contractile proteins increase in size and number with appropriate resistance training, therefore causing an increase in the cross sectional area of the muscle, contributing to muscle hypertrophy.

The Recommended Daily Allowance (RDA) for protein and amino acids is 0.9 gram of protein per kilogram of body weight in sedentary populations or 12-15 % of the calories in the total daily diet. The average American diet easily supplies this amount of protein, with most people exceeding their requirements.
Whey is a high-quality protein with vast nutritional properties that occurs naturally in cow’s milk. Whey protein is a complete protein containing all eight essential amino acids. It is extracted and purified in the cheese making process. Protein synthesis is positively affected by the fast-absorbing whey protein, yielding the greatest benefits (32). Consumption should occur within an hour of an exercise bout due to the rapid absorption and permeability of the cell membrane. Whey also contains glutathione, a powerful antioxidant that boosts immune function. This may provide an additional benefit for strength training athletes, who may compromise their immune systems through intense training (22; 31; 64). Whey protein in its pure form contains very little fat, cholesterol, or lactose (making it an excellent milk substitute for lactose-intolerant individuals).

**Casein Protein**

Casein is also a high quality protein and represents the highest percentage of protein found in milk. Casein has a slower release of amino acids and is not ideal for rapid protein replacement post-exercise. Glutamine, an anti-catabolic amino acid, is found in high concentrations in casein. Due to the body’s slow digestion rate of casein, it should be consumed in the evening during rest. Casein does contain a small amount of lactose or milk sugar that could cause a problem for lactose-intolerant individuals. The theory that consuming excess protein facilitates greater gains in muscle size is false, as is the theory that bodybuilders require 1 g of protein per pound of body weight to support muscle function during heavy...
training. Energy intakes are activity and body size specific. In general, activities which employ intense resistance training or prolonged, intense aerobic exercise warrant increased protein consumption (38; 61; 108). Most dietitians suggest that 1.6 grams per kilogram of body weight will adequately meet any protein demand, but higher quantities of protein can be tolerated for competitive strength athletes; approximately 2 grams per kilogram of body weight (60; 109). Individuals who exceed this value are likely consuming additional calories, which may lead to unwanted weight gain and in some cases, cause renal distress due to the increase demand on the kidneys from excess nitrogen.

**Branched Chain Amino Acids—Subunits of Proteins**

Amino acids are the building blocks of proteins. The body requires approximately 20 amino acids, of which eight (nine in infants and sometimes older adults) are classified as essential amino acids that cannot be synthesized by the body. The branched chain amino acids (BCAA) are essential amino acids that must be consumed in the diet. Valine, isoleucine, and leucine are the BCAAs that account for one third of the protein in muscle tissue. This significant contribution makes them important for muscle remodeling and functioning of the muscle cells.

Long duration endurance activities use protein as a fuel source when glucose is depleted. Branched chain amino acids easily convert to fuel, sparing other amino acids (53; 104). This process decreases the catabolic effect by sparing other proteins (16).

Whey protein contains a high concentration of BCAAs. This group of amino acids also serves as precursors to other muscle building amino acids such as glutamine and alanine (70; 103). Glutamine is a non-essential amino acid that aids in the recovery and rebuilding of muscle. Strength training depletes the concentrations of glutamine and alanine, but due to the fact that these amino acids are non-essential, they are resynthesized within the body from the BCAA.

Additional consumption or supplementation of amino acids over what the body requires does not increase strength or endurance (54). If an activity decreases the concentration of essential amino acids, replenishment is necessary, but excessive amounts do not have an added benefit, other than contributing to a positive caloric balance.

Increased amounts of amino acids in the body can actually cause adverse effects (52). Similar to the discussion regarding minerals, balance is the key to function. Excessive amounts of one type of amino acid can cause biochemical competition for other amino acids. Any imbalance can lead to a deficiency. Digestion of excessive amounts of BCAA may cause gastrointestinal discomfort and/or place added stress on the liver or kidneys (51).

**Glutamine**

Glutamine is a non-essential, naturally occurring amino acid found within the muscle cell. During prolonged exercise, proteins are used as a fuel source for muscle contractions. Amino acids, such as glutamine, are used as precursors for gluconeogenesis in the formation of glycogen. Muscular contractions release glutamine into the bloodstream, which is taken to the liver to form glucose for energy during exercise. This process reduces the catabolic effect or protein degradation during exercise recovery (162).
Supplementing glutamine is thought to increase post-exercise glycogen stores and reduce the amount of protein degradation from glucocorticoids, positively affecting muscle size (7). Other claims include protein sparing and increased buffering capacity of lactic acid, consequently increasing the time until fatigue. This would allow for a longer and more intense training session and greater gains with decreased recovery times. Furthermore, some evidence exists to support glutamine in the reduction of upper respiratory infections during long duration activities (144).

The premise behind glutamine supplementation is to reduce functional changes in muscle tissue and negative nitrogen metabolism. Increasing glutamine is intended to decrease the use of protein for fuel, decreasing the catabolic effect of muscle wasting (11). Some data on animals shows that glutamine infusion effectively counteracts glucocorticoid-induced muscle atrophy. Atrophy attenuation appears related to the maintenance of muscle glutamine levels, which in turn, may limit the glucocorticoid-mediated down regulation of myosin heavy chain synthesis (116; 138). However, studies have not shown that glutamine supplementation has a direct effect on protein sparing and/or decreases in muscle wasting in humans in response to normal exercise. It has shown some promise in excessive stress states, such as burn victims and later stage HIV (AIDS) patients, but not in normally trained individuals consuming adequate nutrients (1; 28). Glutamine supplementation and resistance training during a six week study showed no difference in strength, torque, or lean body mass compared to a placebo (26; 42).

Although glutamine seems to be ineffective when consumed by healthy individuals that meet their protein requirements, it may have merit when mixed with other amino acids (30). One study examining the use of supplemental protein, a mixture of whey protein and glutamine, showed an increase in muscle strength with consumption (29). When mixed with creatine similar benefits were found (105). This data suggest that a supplement containing key amino acids may contribute positively to an improvement in training efficiency through positive effects on muscle integrity and hematopoiesis. The key question is the role glutamine plays, when used within a supplement mixture.

**L-arginine**

L-arginine (arginine) is a semi-essential or conditional amino acid produced naturally in the body that is purported to have numerous beneficial effects. The normal functions of arginine include aiding in protein synthesis, increasing immune and nervous system function, increasing oxygen delivery to the heart, and regulating growth hormone levels. For athletes and body builders, the claim that arginine plays a role in growth hormone stimulation is of particular interest. Increasing growth hormone levels promotes strength, lean body mass, and the reduction of body fat. Laboratory results do show an increase in growth hormone with very large doses of arginine. However, arginine does not have the same effects when used at the recommended over-the-counter dosages as it does with laboratory dosages that would be clearly unsafe for use by the general population. Therefore, L-arginine remains a non-essential amino acid, falsely promoted as enhancing the secretion of growth hormone, the breakdown of fat, and the development of muscle when dietary intakes are sufficient.

Another claim that is of interest to athletes is that arginine may have a positive impact on protein synthesis when coupled with other amino acids (126). The evidence that arginine supplementation increases strength gains and lean body mass are inconclusive. Abel et al. reported increases in strength gains...
and lean body mass, whereas Marcell et al. stated that arginine did not increase growth hormone levels at rest or with resistance training (6; 112). Supplementation did not increase plasma concentrations of glucagon, urea, and somatotropic hormone with ingestion of 15 g of arginine daily for 14 days prior to a marathon. This study did not show any increase in plasma creatine kinase activity, insulin, ammonia, or respiratory exchange ratio accompanying arginine use (124). Research also has shown that arginine supplementation in some clinical settings involving trauma, such as burn injuries and sepsis, may maintain lean muscle mass and functional capacity (125). However, there is little data to support that arginine has the same effect in healthy individuals. Though arginine is a precursor for nitric oxide and creatine, the effects of supplemental arginine as an ergogenic aid have been inconclusive (5).

As mentioned above, arginine serves as a precursor to the vasodilator, nitric oxide. The function of nitric oxide allows for increased oxygen delivery to the myocardium of the heart. Scientific evidence exists supporting arginine’s role in increased myocardial blood flow associated with nitric oxide. Arginine’s vasodilating and decreased atherosclerotic properties seem to improve the exercise abilities in patients with coronary blood flow issues such as coronary artery disease (9; 113). Ingestion of 6 g of arginine per day for 3 days has been shown to increase exercise tolerance due to increased coronary blood flow in patients with compromised coronary arteries (12). Improved immune function may occur with supplementation in diseased subjects (8; 43). The key is to remember these are patients in a clinical setting with cardiovascular diseases and that similar evidence does not exist connecting these effects with healthy individuals consuming adequate nutrients.

Arginine can be synthesized in sufficient amounts from the average diet. The recommended daily intake of arginine is 3.5 to 5 grams, and the average diet contains approximately 3-6 g of arginine. High amounts of arginine can be found in walnuts, peanuts, and even chocolate. Foods high in protein also contain significant amounts of arginine. There are no significant adverse effects with consumption levels under 25 g per day. Diabetics should not consume high amounts of arginine due to its effect on insulin production.

**Nitric Oxide**

The vasodilator nitric oxide is synthesized from L-arginine in almost all cells in the body. Nitric oxide is a strong vasodilator and has been shown to assist in the metabolic regulation of glucose, fatty acids, and amino acids. Nitric oxide signals smooth muscle to relax, causing the arteries to dilate, thereby increasing blood flow. Nitric oxide is the most potent muscle relaxant in the body. It is released from the endothelium or the inner lining of the blood vessels, increasing blood flow capabilities. The endothelium increases the release of vasodilating substances, such as nitric oxide with aerobic training to accommodate increased blood flow and oxygen delivery to muscle (59).

Training improves the tissues’ ability to secrete nitric oxide (58; 93; 143). This training adaptation has also been shown to occur in cardiac patients who experience increases in nitric oxide release with aerobic training participation (57; 94; 142). In fact, cardiac medications dependent upon nitrate, such as nitroglycerin, work on the principle of blood vessel dilation. In the case of nitroglycerin, dilation is aimed specifically at the coronary artery to increase blood flow to the myocardial tissue.

**~Key Terms~**

**Glucocorticoids**- A group of anti-inflammatory steroid-like compounds, such as hydrocortisone, that are produced by the adrenal cortex.

**Atrophy**- A wasting away or decrease in the size of an organ or tissue of the body.

**Hematopoiesis**- The formation of blood or blood cells in the living body.

**L-arginine**- An amino acid obtained from the hydrolysis or digestion of protein.

**Vasodilator**- Something such as a nerve or drug that causes the blood vessels in the body to become wider following the relaxation of the smooth muscle in the vessel wall.
breakdown of protein resulting from intense exercise. High levels of nitric oxide as a supplement may be hazardous due to the numerous other roles that this substance plays in the body.

**Beta-hydroxy Beta-Methylbutyrate (HMB)**

Beta-hydroxy beta-methylbutyrate (HMB) is a bioactive metabolite of the amino acid leucine. HMB is thought to be anti-catabolic, decreasing the breakdown of protein resulting from intense exercise (54; 54; 146; 149). The body naturally produces small amounts of HMB depending on diet. The normal bodily synthesis is between 0.3-1.0 g daily. The recommended daily dosage for the supplement is 3 g/day taken in doses of 1 g, three times a day.

Research concerning the benefits of HMB is inconclusive (54; 148; 149). A literature review of the ergogenic effects of HMB showed minimal or no gains with supplementation (122; 128). One study suggests that delayed onset muscle soreness (DOMS) is reduced after 14 days of consecutive HMB supplementation in untrained exercisers (158), whereas another contradicts these findings (127). It has been suggested that creatine and HMB can increase lean body mass and strength and that the effects are additive (83; 84). Although not definitive, these results suggest that creatine and HMB act by different mechanisms, which may complement each other. Again, more research is necessary to verify these results.

The research is inconclusive as to any actual decreases in protein breakdown in trained individuals. Limited data has shown a decrease in catabolism in untrained individuals. The fact that untrained individuals experience reduced catabolism with HMB supplementation but trained individuals do not could be due to the fact that trained individuals may already suppress protein breakdown as an adaptation to exercise. In conclusion, there have been a variety of studies that have been inconclusive for change in body composition or strength with HMB supplementation in trained individuals (98; 145; 147). To date, there have been no adverse effects associated with HMB.

**Androgenic-Anabolic Steroids**

Androgenic-anabolic steroids (AAS) is an official definition for all male sex steroid hormones, their synthetic derivatives, and their active metabolites. Although anabolic steroids are drugs with specific therapeutic purposes, they are more commonly used for non-therapeutic effects in a large number of healthy individuals. Steroids have reached the public spotlight due to their heavy presence in professional and Olympic sports. Athletes use steroids to enhance performance and increase recovery from high volumes of physical exertion due to training, practice, and competitions. The use of steroids is well documented in body building and power sports, but there has been a significant rise in the use of anabolic steroids by recreational exercisers for the purposes of vanity. Additionally, steroid use in adolescent populations has risen significantly with estimates climbing to nearly 3 million users (47; 55; 81).

The lure of the drug is fairly obvious. Increases in mass, reductions in body fat, and notable increases in strength are all very desirable for athletes, those that are vanity-driven, and individuals who experience issues related to insecurity or low self-confidence. Dissatisfaction with the body and low self-esteem are associated with the so-called reverse anorexia syndrome that often predisposes some individuals to use steroids. Early research trials suggested that anabolic steroids offered little benefit as an ergogenic aid, likely due to low dose administration. Today, supra-dosage analysis shows conclusive evidence of several-measure efficacy. Scientific literature has documented that short-term administration can increase strength and bodyweight when used in conjunction with resistance training. Strength gains between 5-20% above starting value and lean mass gains of 2-5 kg have been observed. Increases in red blood cell counts and hemoglobin concentrations have been documented with anabolic steroid use. However, no effect on endurance performance has been observed. Although limited research exists, it is quite likely that anabolic steroids will yield improvements in recovery and subsequent performance in response to any event that stresses tissue to the point of micro-trauma. Endurance events, including the Tour de France, have shown that steroids have found their place in all sports, regardless of the related metabolic energy system employed.

The abuse of anabolic steroids is linked with various adverse effects. The degree of the side effects seems to be dose related. High level doses commonly used for body building and athletic enhancement can lead to serious and irreversible organ damage, primarily to the liver and cardiovascular system (163). These adverse effects stem from documented increased rates of hypertension and atherosclerosis, blood clotting dysfunction, jaundice, hepatic neoplasms and carcinoma, tendon damage, as well as psychiatric and behavioral disorders (86; 120). The primary negative effects of short- and long-term anabolic steroid abuse self-reported by males include the occurrence of acne vulgaris, increased body hair, gynecomastia, as well as anger and aggressive behavior (130). Women and
Psychological and personality adjustments are well documented with steroid abuse. Anabolic steroids can cause aggression, hostility, and anger as well as depression. Mood disturbances are likely to be dose and drug dependent. Other adverse effects include disturbances within the endocrine and immune systems, liver dysfunction and damage, alterations of the urogenital tract, and the sebaceous system of the skin. It is likely that additional effects occur but are not documented or are underestimated because scientific studies use administrations of relatively low dosages. The mechanism of action is specific to the steroid molecule and its affinity to androgen receptors. Therefore, side effects can differ between compounds.

Anabolic androgenic steroids are illegal in the United States, and therefore, users must buy them illegally, like any illicit drug. In attempts to get the steroid effect without the risk of a jail sentence, many exercisers have used prohormone supplements. Androstenedione is an anabolic androgenic steroid used to increase blood testosterone levels for the purposes of increasing strength, lean body mass, and sexual performance. Research on androstenedione and its related compounds, including androstenediol, have not shown any evidence that the supplementation of prohormones works to increase strength or lean body mass in humans (54; 115). The long-term health effects of prolonged androstenedione supplementation are unknown and prohormones are linked with some of the same negative side effects as steroids. Dehydroepiandrosterone (DHEA) has also been used to elevate testosterone levels in attempts to enhance muscle mass and strength. DHEA is a weak androgen purported to provide anti-aging effects, including improved libido, vitality, and immunity levels. Research demonstrates that DHEA supplementation does not increase serum testosterone, nor provide any of the touted effects. In fact, prohormones are often converted to estradiol, increasing male estrogen levels (21; 35).

The recent availability of the designer steroid tetrahydrogestrinone (THG) has brought the issue of performance enhancement to the forefront of the public

~Quick Insight~

Psychological and personality adjustments are well documented with steroid abuse. Anabolic steroids can cause aggression, hostility, and anger as well as depression. Mood disturbances are likely to be dose and drug dependent. Other adverse effects include disturbances within the endocrine and immune systems, liver dysfunction and damage, alterations of the urogenital tract, and the sebaceous system of the skin. It is likely that additional effects occur but are not documented or are underestimated because scientific studies use administrations of relatively low dosages. The mechanism of action is specific to the steroid molecule and its affinity to androgen receptors. Therefore, side effects can differ between compounds.
spotlight. Increased public awareness and questions as to implications in professional sports have caused more rigorous screening and more extensive bans on prohormones and related compounds in sanctioned competition. Supplements and drugs used to modify or replace endogenous endocrine activity are associated with disruption of normal hormone homeostasis, leading to subsequent dangerous adverse effects.

**Weight Loss Supplements**

Weight loss supplement sales generate well over one billion dollars annually. There are currently more than 50 individual dietary supplements and over 125 commercial formulas sold for weight loss purposes. Weight loss supplements appeal to consumers as a “quick fix” solution without the labors of exercise or dieting. Although very few products show any level of effectiveness, very few people investigate whether evidence-based efficacy exists beyond the claims of the manufacturer. Weight loss supplements are of particular popularity due to the social stigma associated with obesity and the difficulties most people experience when attempting to lose weight through diet and exercise. Weight loss supplements are classified by their purported biological mechanism. The five general categories of dietary weight loss supplements contain chemicals or compounds that function in one of the following ways:

- Increase energy expenditure
- Modulate carbohydrate metabolism
- Suppress appetite
- Increase fat oxidation or reduce fat synthesis
- Block dietary fat absorption

Clinical data to support the effectiveness of most weight loss supplements is limited. Chemical agents that affect the sympathetic nervous system seem to be the only type of supplements that have shown any level of effectiveness in research. The two most investigated sympathetic agents are caffeine and ephedra, both commonly consumed in a mixture with other compounds. The sale of ephedra alkaloids was banned by the FDA in 2004 due to reports of negative cardiovascular effects associated with its ingestion. Caffeine is currently a regulated chemical, tested for in many sports.

**Caffeine**

Caffeine is a naturally occurring substance that is widely consumed in a variety of forms. It is a common ingredient found in coffee, tea, soda, chocolate, and nutritional supplements. It produces multiple physiologic effects throughout the body which are likely mediated mainly through action at centrally-located adenosine receptors. Caffeine’s stimulant effects are used for both weight loss and performance enhancement.

Caffeine improves concentration, reduces fatigue, and enhances alertness. It has been studied for its potential use as an ergogenic aid. Several studies have demonstrated an improvement in exercise performance in submaximal endurance activities (89; 121; 129). Its potential ergogenic effect in acute, high-intensity exercise is supported by a number of clinical studies. Clinical data to support the effectiveness of most weight loss supplements is limited. Chemical agents that affect the sympathetic nervous system seem to be the only type of supplements that have shown any level of effectiveness in research. The two most investigated sympathetic agents are caffeine and ephedra, both commonly consumed in a mixture with other compounds. The sale of ephedra alkaloids was banned by the FDA in 2004 due to reports of negative cardiovascular effects associated with its ingestion. Caffeine is currently a regulated chemical, tested for in many sports.

**Caffeine Consumption**

<table>
<thead>
<tr>
<th>Over-Consumption Symptoms</th>
<th>Physiological Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweating</td>
<td>Increased heart rate</td>
</tr>
<tr>
<td>Nervousness</td>
<td>Increased blood pressure</td>
</tr>
<tr>
<td>Feeling of uneasiness</td>
<td>Vasodilation</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Increased fatty acids in blood</td>
</tr>
<tr>
<td></td>
<td>Increased production of gastric acid</td>
</tr>
</tbody>
</table>

**Delayed Onset Muscle Soreness (DOMS)** - The pain or discomfort often felt 24 to 72 hours after exercising, which subsides generally within 2 to 3 days.

**Androgenic Anabolic Steroids (AAS)** - A class of natural and synthetic steroid hormones that promote cell growth and division, resulting in growth of several types of tissues, especially muscle and bone.

**Jaundice** - Yellow discoloration of the whites of eyes, skin, and mucous membranes caused by deposits of bile salts in these tissues, occurring as a symptom of various diseases such as hepatitis, that affect the processing of bile.

**Hepatic Neoplasm and Carcinoma** - Damage and development or onset of liver cancer.

**Gynecomastia** - Abnormal enlargement of the male mammary glands.

**Gonadotrophin** - A hormone that stimulates the growth and activity of the gonads.

**Myocardial Hypertrophy** - An enlargement of the cardiac muscle.

~Key Terms~
exercise is less clear. It is relatively safe and has no known negative performance effects, nor does it cause significant dehydration or electrolyte imbalance during exercise. Because of its potential use as an ergogenic aid, its use in sports is regulated by most sanctioning bodies. Pre-competition quantities are regulated in athletes participating in IOC and NCAA sanctioned events (79).

The level of caffeine necessary to produce an ergogenic effect is 250 to 700 mg (88; 154). By comparison, a drip method cup of coffee has between 110 to 150 mg of caffeine. Anything above these levels could lead to disqualification from an NCAA or IOC event. Overconsumption of caffeine may lead to symptoms such as sweating, nervousness, and an overall feeling of uneasiness associated with anxiety. These side effects are due to increases in heart rate, blood pressure, vasoconstriction, increased amounts of fatty acids in the blood, and increased production of gastric acid. Excessive consumption may cause an upset stomach and even vomiting. Additionally, routine caffeine consumption may lead to tolerance or dependence, and abrupt discontinuation produces irritability, mood shifts, headache, drowsiness, or fatigue (155).

**Ephedra**

Ephedra alkaloids are commonly used for weight loss or enhanced athletic performance. They come from a plant containing sympathomimetic compounds. Ephedra is sold commercially as a bronchodilator, but is most commonly used as a weight loss supplement. Ephedra supplementation is usually coupled with caffeine or botanical caffeine from guarana and sometimes aspirin (69). The mixture is intended to cause stimulation of the sympathetic nervous system with subsequent vasodilation. Ephedra has been shown to work as an appetite suppressant, likely from the stimulant effects associated with its ingestion. Meta-analysis of research trials which used ephedra containing substances showed a consistent weight loss of 0.9 kg per month compared to placebo. Although its use for weight loss seems to be efficacious, the serious risks associated with its consumption were cited for its ban in 2004.

Data collected from 50 trials of the supplementation of ephedra yielded estimates of 2.2- to 3.6-fold increases in the likelihood of psychiatric, autonomic, or gastrointestinal symptoms, and heart palpitations (90). It is estimated that a consequential response occurs in one in every thousand people that use the supplement (56). Reports of adverse events associated with the use of this non-prescription supplement raised concerns in the United States regulatory community (15). A review of FDA-collected data of adverse effects from ephedra between 1997 and 1999 identified episodes of hypertension, arrhythmias, myocardial infarction, stroke, and seizures (10). At least ten deaths and thirteen permanent disabilities stemmed from these episodes, and 40% of the incidences occurred at recommended dosages in persons without pre-existing cardiovascular conditions.

Although ephedra sales represented less than 1% of all supplement sales in the U.S. in 2001, 64% of all adverse effects from herbal supplements were linked to its use. Many studies have shown positive effects without harm, but the reported risks are sufficient to shift the risk-benefit ratio against ephedra use (20; 164).

**Bitter Orange**

Following the ban of ephedra-containing supplements in February 2004, many manufacturers were forced to change the chemical formulas of their weight loss supplements. Most quickly substituted the herb bitter orange (citrus aurantium) for ephedra and marketed the products as "ephedra-free" supplements, suggesting that these supplements promote the same desired effects, including energy enhancement, weight loss, and appetite suppression (134). Citrus aurantium extract contains the botanical adrenergic amines synephrine and octopamine. Synephrine is structurally similar to epinephrine, and like ephedra, it is a sympathomimetic alkaloid. There is little evidence that products containing bitter orange are an effective aid to weight loss, which may be due to the limited research on the product (67). Some authorities question the likelihood of bitter orange working as an effective weight loss supplement at all because synephrine has lipolytic effects in human fat cells only at high doses, and octopamine does not yield lipolytic effects in human adipocytes (49; 66).

Like ephedra, bitter orange may also have the potential to cause adverse health effects (96). Due to the fact that synephrine increases blood pressure in humans and has the potential to increase cardiovascular events, the supplement likely comes with the same risks as ephedra (50; 65). The few reports of individuals experiencing an adverse event that they attributed to the supplement came from interviews and most indications suggest that the severity of the event was fairly mild. One research trial indicated that ephedra-free weight-loss supplements have significant cardiovascular stimulant actions, similar to ephedra but concluded that these effects are not likely caused by citrus aurantium alone (134). The conclusion was
based on the fact that an eight-fold higher dose of synephrine (Advanta Z) had no effect on blood pressure. The increased risk for cardiovascular incident is likely attributed to the synergistic effects of bitter orange and caffeine along with the other stimulants in the multi-component formulation.

**Weight Loss Drugs**
The prevalence of obesity in America has caused physicians to turn to pharmacological therapy to manage cases of significant obesity. Weight loss drugs differ from over-the-counter supplements in that they require a doctor’s prescription for their use. In most cases, a person must have a BMI above 30, or greater than 27, with the addition of coronary risk factors to qualify for medication. Obesity medications primarily have three goals: weight loss, the maintenance of weight loss, and reductions in cardiovascular and metabolic disease risk. Drug interventions focus specifically on weight loss, with changes in body fat composition and a reduction of health risks as secondary endpoints.

Several drugs and pharmacologic interventions have been used to fight obesity, including thyroid hormone, amphetamines, phentermine, amfepramone (diethylpropion), phenylpropanolamine, mazindol, fenfluramines, sibutramine, and orlistat. The purposed mechanisms for the weight loss agents include decreased appetite, reduced absorption of fat, or increased energy expenditure (111). Most pharmacotherapies have shown to be effective at reducing body weight compared to placebo when used in conjunction with a calorie-controlled diet or lifestyle intervention in short-term trials (99; 111). Only
~Key Terms~

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiomyopathies</strong></td>
<td>Diseases or disorders of the heart muscle, especially of unknown cause.</td>
</tr>
<tr>
<td><strong>Fibrinolysis</strong></td>
<td>The process where a fibrin clot, the product of coagulation, is broken down.</td>
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<tr>
<td><strong>Prohormones</strong></td>
<td>An intraglandular precursor of a hormone.</td>
</tr>
<tr>
<td><strong>Dehydroepiandrosterone (DHEA)</strong></td>
<td>A natural steroid hormone produced from cholesterol by the adrenal glands.</td>
</tr>
<tr>
<td><strong>Tetra-hydro-gestrinone</strong></td>
<td>A designer anabolic steroid banned by The Food and Drug Administration.</td>
</tr>
<tr>
<td><strong>Caffeine</strong></td>
<td>An alkaloid often found in tea or coffee, and used chiefly as a stimulant.</td>
</tr>
<tr>
<td><strong>Bronchodilator</strong></td>
<td>A drug that widens the air passages of the lungs and eases breathing by relaxing bronchial smooth muscle.</td>
</tr>
<tr>
<td><strong>Guarana</strong></td>
<td>A natural substance similar to caffeine.</td>
</tr>
<tr>
<td><strong>Sympathomimetics</strong></td>
<td>A dietary supplement aimed at encouraging fat loss.</td>
</tr>
<tr>
<td><strong>Octopamine</strong></td>
<td>A compound used as an adrenergic drug.</td>
</tr>
<tr>
<td><strong>Lipolytic Effects</strong></td>
<td>Breakdown of fats.</td>
</tr>
<tr>
<td><strong>Adipocytes</strong></td>
<td>Any of various connective tissue cells found in the adipose tissue, specialized for the storage of fat.</td>
</tr>
<tr>
<td><strong>Amphetamines</strong></td>
<td>Any one of a group of drugs that are powerful central nervous system stimulants.</td>
</tr>
<tr>
<td><strong>Phentermine</strong></td>
<td>A drug that suppresses the appetite by altering the body’s metabolism.</td>
</tr>
<tr>
<td><strong>Amfepramone</strong></td>
<td>Comparable to amphetamine with similar effects.</td>
</tr>
<tr>
<td><strong>Phenylpropanolamine</strong></td>
<td>An androgenic drug that acts as a vasoconstrictor and is used as a nasal decongestant, a bronchodilator, an appetite suppressant, and mild stimulant.</td>
</tr>
<tr>
<td><strong>Mazindol</strong></td>
<td>A drug used to control appetite and decrease weight.</td>
</tr>
<tr>
<td><strong>Fenfluramines</strong></td>
<td>A drug that is used in the treatment of obesity.</td>
</tr>
<tr>
<td><strong>Sibutramine</strong></td>
<td>A drug that suppresses appetite by inhibiting the reuptake of the neuro-transmitters norepinephrine and serotonin.</td>
</tr>
<tr>
<td><strong>Orlistat</strong></td>
<td>A drug that prevents the digestion and absorption of dietary fats.</td>
</tr>
<tr>
<td><strong>Dopamine</strong></td>
<td>A neurotransmitter formed in the brain by the decarboxylation of dopa, which is essential to the normal functioning of the central nervous system.</td>
</tr>
<tr>
<td><strong>Norepinephrine</strong></td>
<td>A substance, both a hormone and neurotransmitter, secreted by the adrenal medulla and the nerve endings of the sympathetic nervous system to cause vasoconstriction and increases in heart rate, blood pressure, and the sugar level of the blood.</td>
</tr>
<tr>
<td><strong>Serotonin</strong></td>
<td>An organic compound formed in the tissue, especially the brain, blood serum, and gastric mucous membranes, and active in vasoconstriction, stimulation of the smooth muscles, transmission of impulses between nerve cells, and regulation of cyclic body processes.</td>
</tr>
</tbody>
</table>
sibutramine and orlistat have shown evidence of long-term efficacy with acceptable levels of adverse effects (63). Consequently, these are the only currently approved drugs for the long-term management of obesity in adults.

Sibutramine is sold under the name Meridia. It works as an appetite suppressant by inhibiting the re-uptake of dopamine, norepinephrine, and serotonin. In doing so, it enhances satiety and reduces the appetite in users.

Compared to placebo use in clinical trials, sibutramine (10-15 mg daily) users experienced an average weight loss of 4.3 kg after one year (68; 110; 156). Increases in blood pressure and resting heart rates were reported in clinical trials and makers suggest that individuals with risks for cardiovascular complications should not take the drug (156). Other side effects may include headache, insomnia, dry mouth, and constipation.

**Orlistat** is a fat absorption blocker sold under the

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### Common Weight-Loss Drugs

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade name(s)</th>
<th>Action</th>
<th>Possible side effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine</td>
<td>Adipex-P®, Fastin®, Obenix®, Obefen®, Obermine®, Obesin®, Phenamine®, Phentride®, T-Diet®, Zantrex®</td>
<td>Appetite Supressant (catecholaminergic)</td>
<td>Nervousness, irritability, insomnia, headache</td>
<td>May increase risk of primary pulmonary hypertension</td>
</tr>
<tr>
<td>Diethylpropion hydrochloride</td>
<td>Tenuate®, Tenuate Dospian®</td>
<td>Appetite Supressant (catecholaminergic)</td>
<td>Nervousness, irritability, insomnia</td>
<td>Safer than other drugs for people with moderate hypertension</td>
</tr>
<tr>
<td>Mazindol</td>
<td>Mazanor®, Sanorex®</td>
<td>Appetite Supressant (catecholaminergic)</td>
<td>Nervousness, irritability, insomnia, dry mouth, constipation</td>
<td></td>
</tr>
<tr>
<td>Phenylpropanol-amine</td>
<td>Active ingredient in many products, including Acurtrim®, and Dexatrim®</td>
<td>Appetite Supressant (catecholaminergic)</td>
<td>Nervousness, insomnia, headache, dry mouth, dizziness</td>
<td>Should be used cautiously in coronary artery disease and high blood pressure</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Prozac®</td>
<td>Antidepressant with anorectic effects (serotonergic)</td>
<td>Lack of energy, insomnia, nausea, diarrhea</td>
<td>May adversely react with herbal supplements, such as St. John’s Wort and tryptophan</td>
</tr>
<tr>
<td>Sibutramine</td>
<td>Meridia®</td>
<td>Appetite Supressant (catecholaminergic and serotonergic)</td>
<td>Headache, insomnia, dry mouth, constipation, elevated blood pressure</td>
<td>Risk of physical and psychological dependence; blood pressure must be checked regularly</td>
</tr>
<tr>
<td>Orlistat</td>
<td>Xenical®</td>
<td>Fat absorption blocker (lipase inhibitor)</td>
<td>Gas, rectal leaking, diarrhea, fecal urgency</td>
<td>Vitamin supplementation recommended to prevent fat-soluble vitamin deficiency</td>
</tr>
</tbody>
</table>
name Xenical. Its weight loss mechanism works by blocking up to 30% of the fat in the diet from entering circulation through the intestines. Meta-analysis showed individuals that consumed Orlistat lost an average of 2.7 kg compared to placebo (71; 110). Other positive outcomes associated with Orlistat treatments include lower systolic blood pressure, decreased waist circumference, and a reduction of LDL cholesterol, fasting serum glucose, and insulin levels (73; 95). Due to its function, Orlistat causes unpleasant gastrointestinal side effects including gas, rectal discharge, fatty bowel movements, and fecal urgency (72; 156). Over-consuming fat when using Orlistat causes diarrhea and rectal leakage, which often teaches users to follow a reduced-fat diet. Additionally, users must consume adequate fat-soluble vitamins because the fat-blocking mechanism prevents some absorption of the vitamins A, D, E, and K, which are transported by lipids.

Weight loss drugs are not a desirable choice as the first intervention to losing body fat due to the possible acute side effects and lack of information pertaining to long-term use. For individuals experiencing moderate to severe obesity, the drugs may be effective in the reduction of their body weight, subsequently reducing their risk for disease. The use of weight loss medications should be closely monitored by a physician and should only be used in conjunction with a healthy diet and lifestyle. Due to the risk for injury, personal trainers should be familiar with the side effects of the medications their clients use and closely monitor their exercise participation.

Chapter Nine References


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