Exercise Enhancement

Physical inactivity is the fourth leading risk factor for **premature death** worldwide. Being physically active is one of the most important things you can do for your health. Everyone, regardless of age, gender, and ability, can benefit from regular exercise.

Accordingly, the evidence linking better cardiorespiratory fitness to improved health and longevity is overwhelming. In fact, **maintaining cardiorespiratory fitness** reduces risk of chronic diseases and death more than any pharmaceutical drug. Regular exercise slows down how quickly the body ages, and reduces the risk of cancer, dementia, osteoporosis, heart disease, stroke, depression, obesity, type 2 diabetes, and high blood pressure.

Exercise and physical fitness training is one of the most powerful anti-aging strategies there is. Exercise powerfully activates a major longevity factor called **AMPK (AMP-activated protein kinase)**—a key regulator of energy metabolism that is linked to longevity.

Emerging research now shows that targeted natural interventions, such as **creatine**, **carnitine**, **branched chain amino acids**, **glutamine**, and **vitamin D,** can help maximize the health and longevity benefits of exercise.

How Much Exercise Do I Need?

The most recent report of the United States Department of Health and Human Services, updated in 2018, recommends that healthy adults engage in:

- **150 to 300 minutes** of **moderate-intensity** aerobic activity or **75 to 150 minutes** of **vigorous aerobic activity** per week, or an equivalent combination; and
- **Strength** or **resistance training** on two or more days per week.

Children aged three to five should get lots of regular activity each day. Children age 6 to 17 should get 60 minutes of moderate-to-vigorous activity each day, including aerobic activity and bone and muscle strengthening activities. Older adults should be as active as their health and abilities allow.

Additional benefits are conferred by engaging in more than 300 minutes of moderate-intensity exercise per week. Aerobic activity should be spread out throughout the week. It is important to engage in more than one type of exercise. Unless physical capacity is a limiting factor, everyone should engage in **aerobic** exercises (eg, brisk walking or cycling), **strength** exercises (eg, lifting weights), **flexibility** training, and **balance** exercises.

High intensity interval training (HIIT) is a training approach that relies on short bursts of anaerobic training followed by recovery periods. While there is compelling evidence that HIIT conveys substantial fitness and health benefits, it may be too extreme for people with pre-existing health conditions. Inexperienced exercisers should consult a trainer or healthcare provider before starting a HIIT program.

Integrative Strategies for Enhancing Exercise

- **Hormone restoration for men and women.** Studies in healthy older men have shown that hormone replacement therapy (HRT) increases exercise capacity and muscle strength. Post-menopausal women using conventional HRT had significantly greater improvements in exercise-induced insulin sensitivity than post-menopausal women who were not using HRT.
    - More information is available in the Female Hormone Restoration and Male Hormone Restoration protocols.
- **Dietary considerations.** Consuming a carbohydrate-containing meal four to six hours before exercise ensures adequate reserves of glycogen (stored carbohydrate energy) in the muscle and liver. The International Society for Sports Nutrition recommends protein and carbohydrate consumption within three hours after exercise.
- **Caffeine.** Studies suggest caffeine ingested before or during exercise enhances endurance exercise performance. For example, competitively trained males who ingested 5 mg/kg body weight, equivalent to two to four cups of coffee for a 170-pound individual, lifted more total weight on the chest press and generated greater anaerobic power.
- **Creatine.** In older adults, creatine supplementation, with or without resistance exercise, enhances muscle strength and mass, increases bone strength, and slows the rate of muscle mass and strength loss. Creatine doses used in studies typically ranged from 5–21 grams per day for a 150-pound individual.
- **L-carnitine.** Studies have demonstrated that supplementation with 2 grams of L-carnitine can improve exercise performance and recovery.
- **Branched chain amino acids (leucine, isoleucine, and valine).** In a double-blind, placebo-controlled study, branched chain amino acid supplementation for three days increased resistance to fatigue and enhanced fat burning for fuel during exhaustive endurance exercise.
- **Vitamin D.** Sufficient blood levels of vitamin D are important for musculoskeletal injury prevention and recovery, and are

associated with reduced inflammation and pain, stronger muscles, and better athletic performance.
- **Glutamine.** In a controlled two-week trial in male college-aged martial arts athletes, supplementation with 3 grams of glutamine daily for two weeks reduced muscle damage and prevented immune function declines, including during a strenuous training period.

Introduction

Physical inactivity is the **fourth leading** risk factor for *premature death* worldwide.[1] Throughout human history, survival necessitated physical activity. Daily physical work defined and shaped the way the human body functions.

Today, a general lack of physical activity directly contributes to many chronic diseases and reduces life expectancy by about as much as smoking or obesity. Physical inactivity may account for nearly 10% of all premature deaths.[2,3]

Evidence linking better *cardiorespiratory fitness* to improved health and longevity is overwhelming.[4-7] In fact, maintaining cardiorespiratory fitness reduces risk of chronic diseases and death more than any drug.[8-11]

Experts have called for a measurement of *cardiorespiratory fitness*, such as sub-maximal VO2 max estimates, to be added to routine cardiovascular health screening alongside more typical markers, such as cholesterol, blood pressure, and hemoglobin A1C.[4,6,7]

Physical activity can include a variety of enjoyable activities such as dancing, gardening, sightseeing, and other simple alternatives to sedentary behavior. Even 75 minutes of brisk walking per week has been linked to longevity and substantial health benefits.[12]

At the cellular level, exercise protects DNA against oxidative damage and rejuvenates energy-producing mitochondria.[13-15] Exercise also activates **AMPK** (AMP-activated protein kinase)—a crucial regulator of energy metabolism.[16]

In this protocol, you will discover innovative ways to maximize the longevity benefits of regular physical activity using an integrative approach. For instance, **hormone restoration**, including impressive exercise-potentiating effects of the adrenal hormone **DHEA**, will be reviewed. You will also learn about the performance-enhancing effects of various natural agents, including **creatine**, **carnitine**, **whey protein**, **omega-3 fatty acids**, and **vitamin D**.

Types of Exercise

A comprehensive exercise program includes aerobic, muscle strengthening, flexibility, and balance exercises.[17,18]

Aerobic Exercise

Aerobic exercise is rhythmic and prolonged physical activity that elevates the heart and breathing rates. Examples of aerobic activity include fast walking, running, bicycling, and swimming. Aerobic training increases cardiorespiratory fitness, improves cerebral blood flow, and reduces the risk of death due to heart disease and all causes.[17,19-21]

"Aerobic exercise" refers to aerobic metabolism, in which oxygen is used to regenerate the energy-storing molecule ATP (adenosine triphosphate) in the mitochondria. Glucose in the blood, glycogen (stored carbohydrate) in muscle cells, and free fatty acids in blood and muscle cells provide fuel for ATP production.[22]

Muscle-Strengthening Exercise

Muscle-strengthening or resistance exercise involves forceful muscle contraction against external resistance.[17] This type of exercise increases muscle strength, size, and endurance, and prevents sarcopenia, or age-related loss of muscle mass and strength. Strength training, when undertaken at an adequate pace, also improves cardiovascular endurance. Examples of muscle-strengthening exercise include weight training using free or machine weights, resistance bands, or body weight.[17,18,23]

Flexibility Exercise

Flexibility or stretching exercises entail slow and steady stretching of muscle groups. Stretches should be held for 10 to 60 seconds without jerking or bouncing, and repeated two or three times, progressively increasing the stretch. While mild discomfort is expected, flexibility exercises should not be painful, as pain may indicate minor muscle tearing. Flexibility exercise combined with muscle-strengthening exercises improve range of motion and relax muscles. Stretching before exercise may increase mental preparedness, but there is conflicting evidence as to whether it prevents injury. Stretching after exercise, when muscles are warm, may be more effective.[17,24-26]

Balance Exercise

Balance exercises, such as holding positions on one leg or using balance boards, may help individuals with awareness of motion and relative position problems and may also help prevent falls.[17,27] The American Heart Association and American College of Sports Medicine recommend balance exercises for individuals who fall often or have mobility problems. The guidelines include recommendations for the following types of activities[18]:

- Increasing the difficulty of postures and decreasing the base of support, such as progressing from two-legged postures to one-legged postures
- Movements that disturb the center of gravity, such as heel-to-toe walking and turning in place
- Postures that stress certain muscle groups, such as standing on toes or heels
- Reducing sensory input, such as standing with eyes closed

Muscle strengthening exercise also improves balance by strengthening the muscles and tendons that support joints.[17]

Recent research has examined how different methods of exercise training affect various aspects of cellular biology, including telomerase activity and telomere length. Telomeres are structural components at the end of chromosomes that play a role in cellular aging and regeneration. During each cell division cycle, telomeres shorten. When they reach a critical length, the cell enters senescence. Shorter telomeres are associated with cardiovascular disease, obesity, and diabetes, as well as a reduced life expectancy. A healthy diet, non-sedentary lifestyle, and regular exercise may be associated with longer telomeres.[28]

Telomerases are enzymes that add nucleotides to telomeres, thus regulating telomere length. Research indicates telomeres may shorten in a progressive, age-related manner, but telomerase activity decreases steadily from age 4 to 39. After age 40, approximately 65% of people have low but stable telomerase activity levels, while approximately 35% have no detectable activity levels. Studies indicate active adults have an upregulation of telomeric binding factors, which protect telomeres from shortening, as compared to those that do not regularly exercise.[29]

Other observational studies suggest higher levels of physical activity are associated with longer telomeres, particularly in older individuals. This may be because exercise combats oxidative stress and inflammation, alters telomerase activity, and increases the number of skeletal muscle satellite cells (skeletal muscle precursor cells that help regenerate muscles after an injury).[29]

In one study, 124 healthy, previously inactive men were randomized into an aerobic endurance exercise group, a high-intensity interval group, a resistance training group, or a control group that did not exercise. Each intervention involved three 45-minute training sessions per week for six months.

VO2max was increased by all three training methods. Telomerase activity was up-regulated two- to three-fold in the endurance and interval training groups, but not the resistance group. White blood cell levels increased in the endurance and interval groups as well. A single bout of endurance training, but not resistance training, increased telomerase activity in certain leucocytes. Thus, aerobic activity may promote cellular health and healthy aging.[30]

More interventional studies are required to confirm the specific effects of exercise intensity and frequency on telomere length and telomerase activity.

High-Intensity Interval Training

High-intensity interval training, or HIIT, is becoming increasingly popular. This type of exercise training consists of short, repeated bursts of intense exercise followed by periods of recovery.[31,32]

High-intensity interval workouts can be performed using several different protocols. The high-intensity exertion phase can last from five seconds to eight minutes, and is followed by recovery periods of no or low-intensity exercise that can last as long as the active phase. During exertion, the heart rate reaches 80–90% of maximum. Perhaps the most common protocol involves 30 seconds of maximal effort cycling followed by four minutes of recovery, with the cycle repeated four to six times per session, three times per week. Other less-demanding formats have also been devised.[32-34]

In a 12-week study in previously sedentary men, a total exercise time of 30 minutes per week, of which only three minutes was intense exertion, was compared with 150 minutes per week of moderate-intensity continuous training. Despite a five-fold-less time commitment, interval training was found to be equally effective as traditional endurance training at improving insulin sensitivity, cardiorespiratory fitness, and skeletal muscle mitochondrial content.[35]

Several other studies have indicated HIIT is superior to continuous moderate-intensity training at improving cardiorespiratory fitness, vascular endothelial function, insulin sensitivity, and arterial stiffness. HIIT also improves blood pressure and cholesterol profiles, promotes fat loss while maintaining muscle, and may be of particular benefit to those with or at risk of type 2 diabetes.[32,36-38]

In a review of studies in patients with lifestyle-induced chronic diseases, HIIT was nearly twice as effective as lower-intensity continuous exercise at improving cardiorespiratory fitness—a strong predictor of mortality.[38]

Despite perceptions that compliance with recommendations for more vigorous exercise is poor, a study in prediabetics found short-term adherence to HIIT was greater than traditional continuous workouts.[39] In another study, high-intensity interval running was perceived to be more enjoyable than continuous running. In addition, since a lack of time is a common excuse for avoiding exercise, the shorter duration of HIIT can be a major workout incentive.[32,39,40]

HIIT should be adjusted to a person's own fitness level. People with health conditions are advised to obtain medical clearance prior to starting a HIIT program.[32]

Benefits of Exercise

Anti-Aging Effects

Abundant evidence supports the anti-aging benefits of exercise. Even a modest amount of leisure time physical activity—just 75 minutes of brisk walking per week—has been associated with longer life expectancy.[12] Also, regular exercise correlated with independence in a study of Japanese centenarians.[41]

Exercise influences several hallmarks of aging, including DNA repair, cellular senescence, and mitochondrial function.[13] Resistance exercise decreases oxidative DNA damage in aging individuals[14] and increases ***mitochondrial biogenesis***—the creation of new mitochondria—in muscle and brain tissue.[15]

Exercise can help prevent cardiovascular disease during aging, and helps stave off sarcopenia, or age-related loss of muscle mass and strength.[42,43] Improvements in muscle strength resulting from resistance exercise can increase functional capacity and reduce risk of disease and disability in old age.[44] Physical activity, especially resistance strength training, also helps maintain healthy bone density during aging.[45]

Exercise also powerfully activates **AMPK**—a key regulator of energy metabolism and another major longevity factor.[16] AMPK is an enzyme that promotes the burning of glucose and fats to generate cellular energy. AMPK also inhibits aberrant cell growth (ie, cancer), promotes the creation of new mitochondria, and increases insulin sensitivity.[16,46,47]

AMPK activation may be responsible for many of the health benefits of exercise; conversely, lack of AMPK activation may contribute to the detrimental health effects of a sedentary lifestyle.[16,46]

The antidiabetic agent *metformin* also activates AMPK and may mitigate other chronic diseases linked to inactivity, such as heart disease and cancer.[46,48,49]

Preclinical evidence suggests the magnitude of AMPK activation in response to exercise diminishes with age.[50] Therefore, AMPK-activating agents, such as metformin and the plant extract *Gynostemma pentaphyllum,* may complement exercise in aging adults.

Protecting Against Immune Senescence

The progressive deterioration of the immune system that occurs with aging is termed *immune senescence.* Immune

senescence is associated with poor response to vaccinations and increased risk of infection, cancer, cardiovascular disease, diabetes, and other age-related chronic diseases.[51-53]

Emerging evidence indicates regular exercise protects against immune senescence and may rejuvenate the aging immune system.[51,54,55] In a study in healthy male subjects, those with better cardiorespiratory fitness had lower age-related accumulation of senescent and nonfunctional T cells—a signature feature of immune senescence.[56]

Human and animal studies have shown that regular exercise favorably affects other markers of immune senescence as well. These include an enhanced vaccination response, lower blood levels of inflammatory cytokines, greater natural killer (NK) cell activity, and better outcomes in viral infections and some cancers.[57]

Moderate-to-high intensity exercise (ie, 50% to 70% of maximal oxygen consumption) performed on a regular basis (eg, 30 minutes, five days per week) enhances immune function and lowers the incidence of chronic disease.[51,55,58]

Cardiovascular Protection

Exercise improves several cardiovascular risk parameters, including blood pressure, inflammation, glucose and insulin metabolism, endothelial function, cerebral blood flow, and blood lipids.[59,60]

A recent meta-analysis of nearly 400 randomized controlled trials with approximately 40,000 participants assessed the effects of endurance, dynamic resistance, isometric resistance, and combined endurance and resistance exercise interventions and antihypertensive medications (angiotensin-converting enzyme inhibitors, angiotensin-2 receptor blockers, β-blockers, calcium channel blockers, and diuretics) on systolic blood pressure levels in normal and hypertensive individuals.

Endurance and resistance exercise and all classes of antihypertensives lowered systolic blood pressure, as compared with controls. This effect was greater with anti-hypertensive medications across all populations. Among those with hypertension, there was no difference between medication use and endurance or resistance exercise in lowering blood pressure levels. Further research is needed to understand more fully how exercise lowers systolic blood pressure.[61]

Exercise is also beneficial in the treatment of existing cardiovascular diseases.[60,62] According to a review of 63 randomized controlled trials that enrolled nearly 15,000 patients with established coronary heart disease, exercise-based cardiac rehabilitation programs reduced mortality and hospitalizations due to heart disease. In the majority of these studies, exercise also improved patient quality of life.[63]

***Note**: Individuals with pre-existing cardiovascular disease should consult a qualified healthcare provider before embarking on an exercise program.*

Cognitive Health

Physical activity can prevent cognitive decline in older adults and reduce the risk of neurological diseases, such as Alzheimer disease and Parkinson disease. Aerobic exercise reduces the loss of brain tissue that occurs with aging.[64-68]

Abundant evidence indicates physical activity and exercise enhance cognitive functioning and wellbeing across the human lifespan.[64,69,70] In a study in 2,747 young adults aged 18–30 years, greater aerobic fitness was associated with better verbal memory and faster psychomotor speed in middle age.[70] Similarly, another study found middle-aged participants who engaged in the most leisure time physical activity were less likely to develop dementia 28 years later as compared with less-active participants.[69]

Exercise improves cognitive health by enhancing the transmission of information between nerve cells. ***Brain-derived neurotrophic factor***, a signaling protein, appears to play a critical role in this process. Exercise increases the production of brain-derived neurotrophic factor in an area of the brain called the hippocampus, which is vital to learning and memory. Intriguingly, exercise may even increase the size of the hippocampus.[64,65]

Weight Management

According to recommendations from the American Heart Association and American College of Cardiology, long-term weight loss is best attained with lifestyle change that includes both a low-calorie diet and increased physical activity.[71,72]

Protection Against Diabetes

Exercise increases insulin sensitivity, helps control blood glucose levels, and improves cardiovascular risk factors, such as high blood pressure and elevated blood fats. Even a single exercise session induces many of these beneficial effects.[73-75]

Randomized trials have shown that combining physical activity with modest weight loss lowers type 2 diabetes risk by up to 58% in high-risk populations.[73,74] In a four-year randomized controlled lifestyle-intervention trial, increased physical activity along with reduced caloric intake resulted in partial or complete remission of diabetes in 11.5% of participants during the first year; 7.3% of participants remained in partial or complete remission after four years.[76]

Chronic Pain Management

A detailed analysis of 264 published studies, which included nearly 20,000 participants, found that exercise and physical activity is associated with modest improvements in pain, functional capacity, and quality of life. Another review of published studies found that high-intensity strength exercises performed in the workplace three times weekly for 20 minutes markedly reduced pain in the shoulders and spine.[77] In a separate analysis, supervised and home-based progressive shoulder strengthening and stretching exercises relieved shoulder pain. For low-grade shoulder pain, exercise provided short-term benefits similar in magnitude to a single steroid injection.[78]

Preventing Functional Decline with Age: Sarcopenia and Osteoporosis

Sarcopenia refers to progressive loss of muscle mass and strength with age. *Osteoporosis* is a condition marked by low bone mass, increased bone fragility, and greater fracture risk. Sarcopenia and osteoporosis are both common in older adults; increase risk of falls and fractures; and are linked to frailty, decreased mobility, and a higher risk of death.[42,79-85]

Physical activity and exercise training, including aerobic activity and strength training, increase bone mass, muscular strength, balance, and mobility.[86-88] A review of the scientific literature found regular physical activity is the only intervention that consistently improves frailty and sarcopenia as well as functional performance in older adults.[43]

Improvements in physical function resulting from exercise have been demonstrated even in the frail elderly, including those living in institutional settings.[89,90] A regular program of both ***aerobic*** and ***strength*** exercise is recommended for adults as well as frail older persons.[43]

Gut Microbiome Modulation

Microbes in the gastrointestinal tract play a critical role in human health. Increased microbial diversity has been associated with improved metabolism, immune function, and overall health. Disturbances to the balance of these microbes, including reduced diversity of the gut microbiome, have been linked to a wide range of diseases, including obesity, metabolic syndrome, and inflammatory bowel disease.[91-94]

While a range of factors, such as diet and antibiotic usage, influence the gut microbiome, early evidence suggests exercise may have a positive influence on the gut flora.[91] In one study, professional athletes had a significantly higher diversity of gut microorganisms than control groups. Dietary differences between the athletes and control groups may have accounted for some of these effects.[93,95]

A study in mice found exercise altered gut microbial composition, improved intestinal structural integrity, and reduced gastrointestinal inflammation.[96] In another study in mice, exercise increased abundance and diversity of the gut microbiome and protected against a toxin-induced reduction in microbial abundance.[97]

How Much Exercise Do I Need?

Any level of physical activity is preferable to no activity. People who engage in even low levels of physical activity appear to have a 20% reduced risk of death compared with those who are sedentary.[18,24,98-100]

Every 10 years, the United States Department of Health and Human Services publishes updated Physical Activity Guidelines for Americans.[101] Their most recent report recommends adults get 150 minutes of moderate-intensity aerobic activity or 75 minutes of vigorous aerobic activity per week, or an equivalent combination. In addition, strength or resistance training should be performed at least twice per week.

The report also indicates that more substantial health benefits can be obtained with 300 minutes of moderate-intensity activity or 150 minutes of vigorous-intensity activity each week.

Older adults should target 150 minutes of moderate-intensity physical activity per week, or as much as their health will allow. Balance exercises may also help prevent falls in older adults.

Activities, such as yoga, that develop flexibility, agility, balance, and coordination are also encouraged for all age groups.[18,24,98-100]

Assessing Cardiorespiratory Fitness

Despite its vital importance, cardiorespiratory fitness is not included in ordinary clinical assessment. An urgent need exists to incorporate aerobic exercise testing alongside traditional measurements of blood pressure, glucose, and cholesterol in individual cardiovascular risk assessments.[4,7]

Cardiorespiratory fitness can be assessed by measuring maximal oxygen uptake, also known as **VO2max**—the maximum ability of the body to utilize oxygen during exercise. However, direct measurement of VO2max requires maximal physical effort, which is often difficult and may be unsafe for some aging individuals.[102,103]

Submaximal exercise testing is a popular and more practical alternative to assess aerobic fitness. This approach estimates VO2max by determining the heart rate response to submaximal intensity exercise, such as stair stepping, cycling, or running (or walking) on a treadmill.[102-104] These types of tests are accessible through fitness centers or sports medicine facilities. If you are interested in having a submaximal exercise test, check with your healthcare provider.

In most people, cardiorespiratory fitness can be improved by performing moderate-to-intense physical activity on a consistent basis.[3,7]

Strategies for Enhancing Exercise

Hormone Restoration (Men and Woman)

Age-related decline in levels of testosterone and growth hormone are associated with loss of muscle mass and strength, exercise capacity, and mobility in elderly men. In addition, aging is associated with accumulation of body fat and insulin resistance.[105] Diminished muscle mass and strength in the elderly are also accompanied by the rapid age-related decline in the hormone DHEA (dehydroepiandrosterone).[106]

Testosterone and growth hormone are potent anabolic (tissue-building) agents that increase muscle mass, but they act through different mechanisms. The combination of testosterone and growth hormone has a greater anabolic effect than either hormone alone. In fact, studies in healthy older men have shown that hormone replacement therapy (HRT) with a combined regimen of testosterone and growth hormone, but not either one alone, increased exercise capacity and muscle strength.

Collectively, these studies indicate treatment with moderate doses of testosterone and growth hormone is safe over a six-month period.[105] However, long-term use of growth hormone therapy may increase the risk of some cancers.[107] People at risk for cancer should consult a healthcare provider before initiating growth hormone therapy, and long-term use may be unwise.

For more information about HRT, see Life Extension's Male Hormone Restoration protocol.

In women, HRT using estrogen and progesterone may also enhance the effects of exercise. In one study, post-menopausal women using conventional HRT had significantly greater improvements in exercise-induced insulin sensitivity than post-menopausal women not using HRT.[108]

Bioidentical hormone replacement therapy (BHT)—including progesterone, estradiol, and estriol—has become a popular alternative to traditional HRT for the treatment of menopausal symptoms. Bioidentical hormones are structurally identical to human hormones.[109-111]

Data from a review of studies found the use of bioidentical hormones carries a lower risk of breast cancer and cardiovascular disease, and treatment with BHT has been as effective as conventional HRT for the treatment of menopausal symptoms.[112,113] For more information on BHT, see the Life Extension's Female Hormone Restoration protocol.

Dietary Considerations

Proper timing of meals can enhance exercise capacity and aid recovery and tissue repair following exercise.[114-116]

Consuming a carbohydrate-containing meal four to six hours ***before*** exercise ensures adequate reserves of glycogen (stored carbohydrate energy) in muscle and liver. An additional carbohydrate plus protein snack, consumed 30 to 60 minutes prior to exercise, may protect against energy depletion towards the end of an intense exercise session, as well as help prevent breakdown of protein in muscle tissue.[115]

During prolonged intense exercise (ie, greater than 60 minutes), beverages (10–15 fl. oz.) containing carbohydrate and electrolytes should be ingested every 15–20 minutes to prevent low blood sugar levels.[115]

Post-exercise nutrition is important to help replenish glycogen stores and repair muscle tissue damaged during exercise. The International Society for Sports Nutrition recommends protein and carbohydrate consumption within three hours after exercise.[115,117]

Elderly individuals may require greater post-exercise protein intake to maximize recovery.[117] One study showed 20 grams of post-exercise supplemental protein maximally stimulated muscle protein synthesis in young men[118]; another study found that in elderly men, 40 grams of post-exercise whey protein enhanced muscle protein synthesis more than 20 grams of whey protein.[119]

Caffeine

Studies suggest caffeine ingested before or during exercise enhances endurance exercise performance. Emerging research also suggests caffeine aids in short-term, high-intensity burst activity performance. For example, competitively trained males who ingested 5 mg/kg body weight of caffeine lifted more total weight on the chest press and generated greater anaerobic power.[120] This dose of caffeine corresponds to about 2–4 cups of coffee for a 170-pound individual.[121,122] Approximately 150 to 300 mg of caffeine, or about one to three cups of coffee, has been shown to improve concentration and decision making during and after exhausting exercise.[121]

Possible mechanisms for the ergogenic effects of caffeine include increased fat burning, reduced fatigue, central nervous system stimulation, and reduced perception of pain.[121,123,124] The stimulant effect of caffeine is primarily due to its ability to block adenosine receptors in the brain.[125,126]

Possible side effects of caffeine consumption include increased heart rate, disturbed sleep, and nervousness; these are generally less pronounced with lower doses.[121] The response to caffeine varies considerably from person-to-person.[127-129] A recent review suggested older adults may be more susceptible to the sleep-disrupting effects of caffeine than younger individuals, so awareness of sleep quality and modifying caffeine use appropriately is important.[130]

Integrative Interventions

Primary Support

Creatine. Creatine is a compound naturally produced in the body that can also be obtained through the diet, predominantly meats and fish. Not only is supplemental creatine one of the most popular and well-researched ergogenic (performance-enhancing) aids used by athletes,[131,132] it is also an effective agent for preventing or slowing age-related muscle loss—known as *sarcopenia*—and has improved cognitive performance in the elderly.[133-135] Mouse studies indicate creatine may hold potential *anti-aging* effects.[136]

Numerous studies have shown that creatine supplements can increase muscle mass and enhance athletic performance.[132,135] Creatine is most effective as an aid to high-intensity, short-duration activities (eg, sprinting or weight lifting), which derive energy from creatine phosphate.[22,131,137]

In older adults, creatine supplementation, with or without resistance exercise, has enhanced muscle strength and mass, increased bone strength, and slowed the rate of sarcopenia.[134,138] Furthermore, according to one analysis, combining creatine supplementation with muscle strengthening exercise is more effective than exercise alone in increasing muscle mass, strength, and functional performance in older men and women.[133]

Creatine doses used in studies that enrolled aging subjects typically ranged from 5–21 grams per day, for a 150-pound individual, for limited periods of time.[138] Taking creatine supplements with carbohydrate, or protein and carbohydrate, may increase creatine muscle retention.[132]

L-carnitine. L-carnitine is a compound obtained from food and synthesized in the body from the essential amino acids lysine and methionine. It is required for burning fat for energy production within the mitochondria, and can act as a free radical scavenger.[139]

Studies have demonstrated that L-carnitine supplementation can improve exercise performance and recovery.[139,140] In a randomized, double-blind, placebo-controlled trial, healthy male volunteers who ingested 2 grams of L-carnitine along with 80 grams of carbohydrate twice daily for 24 weeks exhibited 21% increased muscle carnitine content, compared with no change in the control group. This was associated with reduced perception of effort and improvement in exercise performance.[140]

By reducing free radical generation and muscle soreness, L-carnitine supplementation supports muscle recovery after strenuous exercise.[141,142] In a placebo-controlled trial in healthy young men, oral supplementation with 2 grams of L-carnitine for two weeks resulted in significantly reduced markers of oxidative stress and muscle damage following an acute bout of exercise.[139]

Branched chain amino acids. The essential branched chain amino acids (BCAAs) leucine, isoleucine, and valine are important for the synthesis of muscle protein and are burned by muscle cells for energy.[143-147]

Human and animal studies have shown that supplemental intake of BCAAs increases exercise endurance.[148-150] In a double-blind placebo-controlled study, BCAA supplementation for three days increased fatigue resistance and enhanced fat burning for fuel during an exhaustive bout of endurance exercise that caused glycogen (stored carbohydrate) depletion.[151]

Like other essential amino acids, BCAAs function as precursors (building blocks) for muscle protein synthesis.[152] Importantly, BCAAs, especially leucine, also exert anabolic effects by directly stimulating muscle growth and inhibiting muscle protein

degradation.[143,153,154]

By reducing breakdown of muscle proteins and promoting protein synthesis, BCAAs improve exercise recovery.[143,154] In a study in long-distance runners undergoing intense training, BCAA supplementation reduced soreness and fatigue, as well as markers of inflammation and muscle damage.[155]

Vitamin D. Vitamin D plays an essential role in bone metabolism, muscle function, and immune health. Sufficient blood levels of vitamin D are important for musculoskeletal injury prevention and recovery, and are associated with reduced inflammation and pain, stronger muscles, and better athletic performance.[156,157]

Apart from its role in preventing fractures and muscle injuries, research also suggests vitamin D may have performance-enhancing effects. Unfortunately, many athletes are vitamin D deficient.[156,158] Trials of supplemental vitamin D at dosages of 3,300 to 5,000 IU daily have found improvements in sprinting and jumping performance as well as increased circulating testosterone.[156,158,159]

One team of scientists suggested supplementing with 4,000 to 5,000 IU per day of vitamin D3, along with 50 to 1,000 mcg per day of a mixture of vitamins K1 and K2 to complement vitamin D's role in bone and calcium metabolism, could support athletic performance by improving recovery time and muscle function.[158]

Glutamine. Glutamine, because it is synthesized in the body, is a non-essential amino acid. However, glutamine becomes "conditionally essential" when blood levels are reduced in times of illness and stress.[160-163]

Glutamine plays a role in immune response to muscle damage.162,164,165 In a controlled two-week trial in male college-aged martial arts athletes, supplementation with 3 grams of glutamine daily for two weeks reduced muscle damage and prevented immune function decline, including during a strenuous training period.166 A controlled clinical trial that used 10 grams of glutamine daily for three weeks in athletes undergoing intensive training found an improvement in immunity as evidenced by white blood cell profiles, including an increase in NK cell activity.[167] Another controlled clinical trial found athletes given 5 grams of glutamine immediately after and two hours after intense, prolonged exercise reported roughly 40% fewer upper respiratory infections than those given placebo.[168]

DHEA. Produced by the adrenal glands, dehydroepiandrosterone (DHEA), along with its sulfated form, DHEA-S, is the most abundant steroid hormone in circulation.[169,170] DHEA is a precursor of sex hormones, such as estrogens and androgens. DHEA levels peak around age 25 and decline by roughly 80% by age 75.[106,171]

Studies show DHEA supplementation has exercise-enhancing effects.[106,172] In a study in elderly men and women, DHEA supplementation significantly enhanced muscle growth and strength in response to resistance exercise.[106]

In a randomized controlled trial, a single dose of 50 mg DHEA increased free testosterone levels above baseline in middle-aged men. This dosing was followed by a bout of HIIT, after which free testosterone remained elevated in the DHEA-supplemented middle-aged individuals.[172]

Whey protein. Whey protein, a group of milk-derived proteins with a high concentration of essential amino acids and BCAAs, activates muscle protein synthesis and recovery in response to resistance exercise.[173] Whey protein supplementation significantly decreases body weight and body fat and increases lean body mass when combined with resistance training.[173-176]

Whey protein is rapidly digested and absorbed. Leucine, one of the BCAAs in which whey protein is especially rich, plays an important role in muscle protein metabolism, healthy glucose metabolism, and body weight maintenance.[147,173,177]

In one study, whey protein given to healthy subjects during recovery from maximal-effort exercise significantly increased the amount of muscle satellite cells. These satellite cells, or stem cells, are essential for muscle regeneration.[176,178] In another study, high-leucine whey protein hydrolysate was more effective than placebo at increasing muscle and tendon growth after 12 weeks of leg resistance exercise (knee extensor training).[179]

Additional Support

D-ribose. D-ribose is the biologically active form of the naturally occurring sugar, ribose, and is produced in the body from glucose. Ribose is involved in the synthesis of ATP, which provides energy to muscle cells during exercise. Supplementation with ribose has accelerated ATP synthesis following its depletion during intense exercise.[180-182]

A controlled trial in 12 male recreational body builders found that supplementation with 10 grams of ribose per day for four weeks resulted in greater gains in muscle strength and endurance than placebo.[183] D-ribose may also help combat fatigue and improve mood and vitality in aging adults,[184] which may allow for increased exercise frequency. A dosing study found taking D-ribose on an empty stomach leads to more efficient absorption than taking it with food.[185]

Periodically, concerns arise regarding the potential of D-ribose to promote damaging glycation reactions. While ribose can contribute to glycation reactions when present in high concentrations, the amount of D-ribose attained through supplementation is not worrisome. These concerns have been addressed thoroughly in an article titled *Restoring Cellular Energy Metabolism* in the October 2012 issue of Life Extension Magazine.

Omega-3 fatty acids. A growing body of evidence supports the use of omega-3 fats to improve recovery from strenuous exercise.[186,187] Omega-3 fatty acids, particularly eicosapentaenoic acid (EPA), can be beneficial in the prevention and treatment of sarcopenia.[188,189] In a controlled study in older adults, daily supplementation with omega-3 fatty acids containing over 1.8 grams of EPA and 1.5 grams of docosahexaenoic acid (DHA) increased the rate of muscle protein synthesis compared with a corn oil, which provided no benefit.[189]

Coenzyme Q10. Coenzyme Q10 (CoQ10) is an essential component of the series of biochemical reactions that generate energy in the cell's mitochondria. CoQ10 also functions as a free radical scavenger, protecting cells against oxidative damage.[190-192] Clinical studies have demonstrated an exercise-enhancing effect of CoQ10 supplementation.[193,194] In a study in trained and untrained individuals, supplementation with 100 mg of CoQ10 for 14 days increased the length of time participants could exercise before reaching exhaustion.[194]

A randomized controlled study in male runners found that 14 days of CoQ10 supplementation reduced the spike in blood levels of lactate, interleukin-6, tumor necrosis factor-alpha, and C-reactive protein induced by a bout of middle-distance competitive running.[195] The dose of CoQ10 used in the study was 5 mg/kg/day, or about 350 mg per day for a 155-pound person.

In an animal study, rats were supplemented with CoQ10 for six weeks during exercise training. This produced beneficial changes in levels of key regulatory proteins, including nuclear factor-kappaB and Nrf2, both of which defend against inflammation and oxidative stress.[191]

Arginine. Arginine is a conditionally essential amino acid that participates in a variety of metabolic pathways, including protein synthesis. Importantly, arginine is a precursor of nitric oxide (NO), a potent vasodilator. Arginine supplementation may increase blood flow to muscles.[196-198]

In a controlled clinical trial in competitive male cyclists, supplementation with 6 grams of L-arginine daily for three days increased 20 kilometer time trial performance, reduced oxygen consumption, and reduced systolic and diastolic blood pressure.[199] In another controlled clinical trial in untrained college-aged men, supplementation with a product containing 1.5 grams or 3 grams of arginine (along with grape seed extract) for four weeks reduced the time to onset of cycling-induced fatigue as compared with placebo.[196]

Animal studies indicate arginine supplementation may be beneficial for exercise recovery.200,201 In one study, L-arginine supplementation before a single bout of exercise reduced muscle fiber damage and maintained exercise performance capacity in rats. These effects were attributed to increased muscle nitric oxide content.[200]

Resveratrol. Resveratrol is a polyphenol compound found in plants and plant foods such as grapes, red wine, peanuts, and Japanese knotweed.[202,203] Resveratrol has been shown to favorably influence several factors involved in chronic degenerative diseases, including inflammation, insulin sensitivity, oxidative stress, and endothelial dysfunction.[204-208]

There is clinical and preclinical evidence that resveratrol can augment the effects of exercise on muscle mitochondrial capacity, increasing energy production and utilization.[204,209] In a double-blind placebo-controlled trial in healthy young adults, daily supplementation with 500 mg of resveratrol, plus 10 mg of piperine, a black pepper extract, combined with low-intensity endurance exercise for four weeks significantly increased muscle mitochondrial capacity.[204]

Two animal studies found resveratrol supplementation improved exercise performance compared with exercise alone.[210,211] In one study, rats fed a diet supplemented with resveratrol during 12 weeks of exercise training were able to run longer and further than rats trained without resveratrol. Improved muscle strength was also noted in resveratrol-treated rats.[211]

Gynostemma pentaphyllum. *Gynostemma pentaphyllum* is an herb with a long history of use in Chinese medicine as a health tonic. Components of Gynostemma have been shown in preclinical research to activate AMPK—a major regulator of glucose, fat, and energy metabolism in the body.[212,213]

Animal studies have demonstrated the anti-fatigue effects of Gynostemma.[212,214] In one of these studies, polysaccharides derived from Gynostemma extended the exhaustive swimming time of rats. The Gynostemma polysaccharide extracts also lowered blood lactic acid levels and increased liver and muscle glycogen concentrations.[212]

A study in mice found that the prolonged time to exhaustion from exercise after administration of Gynostemma polysaccharides was linked to reduced oxidative stress and enhanced muscle glycogen levels.[214]

***Cordyceps sinensis*.** *Cordyceps sinensis* is a medicinal mushroom used for centuries in China and India to promote vigor, endurance, and longevity.[215-217] Scientific studies have found that Cordyceps mycelia boosts exercise performance.[216,218]

In a double-blind placebo-controlled trial in adults aged 50 to 75 years, 12 weeks of supplementation with an extract of *Cordyceps sinensis* fermented mycelium delayed fatigue and resulted in improved aerobic performance on an exercise test.[215]

Another animal study found *Cordyceps sinensis* mycelia may mimic some of the metabolic benefits of exercise. Supplementation with *Cordyceps sinensis* in rats increased exercise endurance, despite a lack of training. Significant AMPK activation was thought to be partly responsible for this effect.[218] Potential mechanisms for the exercise-enhancing effects of

Cordyceps include improved blood sugar regulation, increased insulin sensitivity, and greater production of ATP—the cell's energy source.[215,218]

Panax ginseng. Panax ginseng (also called Chinese or Korean ginseng) is a popular herbal medicine used worldwide to increase physical strength and reduce fatigue.[219-221] Potential mechanisms for the performance-enhancing effects of ginseng root include improved fat utilization for energy (while sparing glycogen), increased levels of the vasodilating molecule nitric oxide, and mild central nervous system stimulation.[219,220,222-226] Multiple clinical trials and animal studies have shown ginseng improves exercise performance and prevents fatigue. It may have stronger effects in older and recreational athletes.[220,222,224,226-228]

Ginseng appears to delay exercise-induced fatigue.[220,221,225,229] In a controlled study in healthy male subjects, eight weeks of supplemental Panax ginseng root extract prior to exercise on a treadmill decreased formation of malondialdehyde—a marker of oxidative stress. Exercise time to exhaustion was significantly prolonged.[226]

Two types of compounds in ginseng—polysaccharides and ginsenosides—are thought to contribute to its fatigue-fighting properties.[219,223,224]

Ginsenosides are converted to bioactive compounds, such as compound K, by intestinal bacteria.[230] Compound K possesses anticancer, anti-inflammatory, and anti-allergic properties, and contributes to the health-enhancing effects of ginseng.[230,231] Fermented ginseng contains compound K, making fermentation one method of enhancing bioavailability.[232,233]

***Rhodiola rosea*.** Found in mountainous areas of Europe, Asia, and North America, *Rhodiola rosea* is an herb with a long history of use in traditional medicine as an anti-fatigue, anti-stress, and mood-enhancing agent. Studies have also shown that Rhodiola has positive effects on exercise performance and endurance in humans and animals.[234-237] Rhodiola is an adaptogen, increasing the body's ability to adapt to the stress of physical exercise.[238,239] Rhodiola also increases utilization of fat for energy, improves mitochondrial function, and suppresses free radicals.[216,238,239]

In one controlled trial in active young women, rhodiola improved endurance exercise performance by reducing perceived effort. Subjects given a single oral dose (3 mg/kg body weight, or about 200 mg for a 150-pound person) of rhodiola completed a six-mile time trial on a stationary bicycle significantly faster that subjects given placebo. Rhodiola also lowered the heart rate response to submaximal exercise in this study.[234]

Another placebo-controlled trial measured the effect of a rhodiola extract standardized to contain 3% *rosavins* and 1% *salidroside* in 24 participants. Researchers noted endurance exercise capacity improved one hour after an acute dose of 200 mg of rhodiola extract.[237]

Rhodiola may lessen exercise-induced muscle damage. In a study in male athletes, four weeks of rhodiola supplementation prior to exhaustive endurance exercise significantly decreased markers of muscle damage. Notably, serum levels of creatine kinase, which rise after vigorous exercise, substantially decreased after rhodiola ingestion.[238]

Exercise Enhancement

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