Nutrition: Nutrition Supplements for Exercise and Sport - Part I

Exercise Statistics

- CDC researchers - 77,000 people - interviews conducted between 2008 and 2010
- Only 20% of adults met federal guidelines for both aerobic and muscle-strengthening exercise
- >80% of adolescents do not do enough aerobic physical activity to meet the youth guidelines
- 33% of adults and 25% of adolescents are completely inactive in any leisure-time aerobic activity

2010 - Less than 5% of adults participate in 30 minutes of physical activity each day
- Physical Inactivity more common among women, blacks, Hispanics, elderly, and the less affluent
- Only 40% of Americans exercise enough to receive health benefits
• Only 35% - 44% of adults 75 years or older are physically active - 28-34% of adults ages 65-74 are physically active
• 2010 - Children now spend more than seven and a half hours a day in front of a screen (e.g., TV, videogames, computer)
• 2011 - Nearly one-third of high school students play video or computer games for 3 or more hours on an average school day

• 2013 - Adults living in the following states are most likely to report exercising 3 or more days a week for at least 30 minutes:
  • Vermont (65%), Hawaii (62%), Montana (60%), Alaska (60%)
  • Least likely were Delaware (46%), West Virginia (47%) and Alabama (47%)
  • National average for regular exercise is 52%

Common Supplements Taken in Mainstream Population
• U.S. Supplement sales - $11.5 billion in 2012
• NHANES Survey 2003 to 2006 - covered all types of supplements - 53% took at least one a day
• 2007 NHANES Survey - Most common - multivitamin/mineral (39%)
• 18% of adults use supplements (not including vitamins and minerals)
• Most popular - fish oil (37%), glucosamine (20%), Echinacea (20%), flaxseed oil (16%), ginseng (14%)
Survey of 2,000 people each year from 2007 - 2011
Average supplement use was 66% and average regular use was 50%
Multivitamins were the most commonly used supplement (71%), followed by omega-3/fish oil (33%), calcium (32%), vitamin D (32%) and vitamin C (32%)
Sport supplements were used by 17% of the people (2011)

Supplement Use in Sport and Exercise

- Study - Division I athletes - 89% use supplements (Froiland, 2004)
- Study - 88% use > 1 and 58% used >2 (Burns, 2004)
- Study - Canadian athletes (94%) use one or more at least once a month (Kristiansen, 2005) - Child/adolescent athletes - from 22% to 71% - Elite athletes use the most
- Study - 2,355 US adults >18 yr in 2011 - 46% took sports drinks, 32% protein bars, 27% energy drinks, 24% energy bars, and 12% energy shots

Most Common Sport Supplements from 2000 - 2008

- Vitamin/minerals (20-83)
- Sports drinks (56)
- Herbals (44-48)
- Energy drinks (42)
- Multivitamin only (42)
- Protein bars (38)
- Vitamin C (35)
- Iron (30)
- Meal replacement (22) and Protein (13-22)
- Creatine (16)
2015 Japanese Survey

- Surveys taken 1-5 months before the 2012 Olympic Games in London
- 552 Japanese athletes
- 82% used 1 or more supplements in the year prior
- 44% took at least 1 supplement daily
- Most common - amino acids (56%)
- Most common purpose - recovery from fatigue
- Information was from coaches, managers, and trainers

Exercise and Immunity

- Exercise causes stress - physical and psychological
- Neuroendocrine changes that occur with stress also occur with exercise - elevated epinephrine, cortisol, endogenous opiates, etc
- Acute physical stressors in animals and humans influence immune parameters

Exercise Causes

- Transient leukocytosis - Initial post exercise increase followed by decrease to pre exercise levels within 2-6 hours
- Largest increase is in neutrophils
- Increase in relative and absolute amounts of NK cells - 2-5x pre-exercise base levels
- NK Cell Cytotoxic activity increases
• Short vigorous (intense) exercise enhances several aspects of neutrophil and macrophage phagocytic activity
• STUDY - Neutrophil activation increased after short (<10min) vigorous ergometry exercise
• STUDY - Reduced growth of experimental tumors in animals given long term exercise training

Dark Side of Exercise

• Prolonged intense exercise = Immunosuppression
• STUDY - (Macneil, Hoffman-Goetz) - Reduced lymphocyte proliferative responses (30%-40%) in response to mitogen stimulation after cycling at intensities up to 75% max
• No difference in untrained or trained people

Infectious Diseases and Exercise

• Benefit with moderate exercise - Fewer respiratory infections in people who exercise
• STUDY - (Nieman et al) - brisk walking - 45min - 5 days per week - 15 weeks
• 5.1 symptoms/day in exercise group - 10.8 symptoms/day in sedentary women
• Greater incidence of infectious diseases particularly upper respiratory in marathon runners during intense training/overtraining
Conclusion

• Consensus of human and animal studies -
• Intense exercise or overtraining depresses immune functions
• Regular, moderate exercise enhances certain immune functions

POLLING QUESTION

FLUIDS
Heat Removal

- Muscles release heat during exercise
- Blood is warmed with exercise and increases core temperature -
  - Stimulates hypothalamus to initiate the sweating mechanism
- Blood removes the heat by rushing to the skin so heat can be lost by sweating
- and thus evaporation
- 80% of all heat liberated is via evaporation

Regulation of Fluids

- When fluid is lost via sweat
- Plasma volume decreases
- Plasma osmolality increases ([Cl] and [Na])
- Vascular pressure receptors and hypothalamic osmoreceptors sense these changes
- Increases Vasopressin (ADH) - from pituitary
- Increases Renin - released from the kidneys
- Both of these will increase water and sodium retention by the kidneys - retains water
- Provokes an increase in thirst

- Under normal situations - Fluid intake will eventually exceed any fluid losses
- For athletes - difficult to get back to normal many do not ingest enough fluid to offset large losses during training
- Water replacement maintains core temperature
- Thirst mechanism is not reliable to maintain core balance
- If fluids are not replaced - dehydration will result and decrease performance
Daily Fluid Loss

- Total volume of fluid loss depends on -
  - Environmental conditions
  - Size and surface area of the person
  - Metabolic rate of person
  - Volume of excreted fluids

- Daily average losses without exercise (sedentary)
  - 2-3 liters/day
- Athlete who trains 2 hours per day can easily lose an additional 2 liters
- Resulting in total losses of up to 5 liters/day

Dehydration

- Many people are chronically dehydrated
- Without proper hydration - many chemical reactions within a cell may not occur
- Symptoms - elevated HR, muscle cramping, headache, fatigue, decreased appetite, dry mouth - can lead to tingling and numbness→ collapse
Fluid Intake - Adequate?

- 13 cross-sectional surveys in 13 countries (2015)
- 3,611 children (4-9 years) and 8,109 adolescents (10-18 years)
- Total fluid intake (water and beverages of all kinds) recorded over 7 consecutive days
- CONCLUSIONS: A high proportion of children and adolescents are at risk of an inadequate fluid intake. This risk is especially high in males and adolescents when compared with females or children categories

Voluntary Fluid Intake

- Voluntary fluid intake during physical activity usually replaces only 50% of the sweat loss
- Results in varying amounts of dehydration
- Often exceeds 3% of body weight
- Studies - of World War II soldiers found that they did not drink enough to replace all the water they lost by sweating - even when adequate supplies of drinking water was available

- It is not possible to adapt to dehydration
- Even small amounts of dehydration can be detrimental to an athlete's performance
- Marathon runners typically lose about 3% - 5% of their body weight
- Body water loss equal to 1% of body weight diminishes ability to perform a set task
- STudy - 4% dehydration can result in a 20-30% decrease in work performance
STUDIES

• STUDY - (Armstrong et al)
  Dehydration of 2% of body weight can impair exercise performance during competitive runs as short as 1,500m - as well as 5,000m and 10,000m

• STUDY - (Below et al)
  Cyclists - 50 minutes at 80%vo2max - then sprinted for 9-12 minutes
  when dehydration was prevented (replacing 80% sweat loss) performance improved 6%
  (with CHO drink - 12% improved)

Urine Output

• Need enough water per day to urinate every 2-4 hours
• Normal urine should be pale and there should be enough of it
• If Dehydrated -
  • Small volume of urine
  • Dark urine

Water Fluid Guidelines

• 24 hrs prior to exercise - drink in excess
• 2 hrs prior to exercise 16 - 24oz
• 15 minutes prior  8 - 16oz
• Immediately prior  3 - 6oz (100 -200ml)
• Every 15-20 minutes during exercise  6 - 8oz
• After exercise - enough to restore lost weight
• 20oz of fluid for every pound of BW lost
• In warm environment - additional 8-16oz of fluid in the 30 minutes prior to exercise
Electrolytes

- Sodium
- Chloride
- Potassium
- Primary way that most minerals are lost from the body is from urine
- Exception is sodium and chloride
- Sodium and Chloride are the key minerals that can be lost through sweat in substantial amounts

Electrolyte Need

- No need for K supplementation
- STUDY - (Costill et al) - low potassium diet - heavy exercise that induced high sweat volumes for short periods of time (4 days)
- No significant decrease in total body K
- Na and Cl may need to be supplemented
- 50-100 meq Na would cover any losses
- 1/4 teaspoon of salt (50 meq)

POLLING QUESTION
Sport Drinks

Sports Drink Recipe

• 1/4 cup sugar in dissolved hot water
• 1/4 teaspoon of salt
• 1/4 cup orange juice (others)
• Fill up to make 1 quart
• Same calories and salt as Gatorade - 50cal/8oz

Functions

• Increases delivery of water and electrolytes
• Increases delivery of CHO
• More concentrated the solution (more CHO) - more time it takes for gastric emptying
• Beverages at 6%-7% CHO empty from stomach at similar rates as water alone
• Carbonating the beverage appears to have no effect on gastric emptying rates
Glucose and Sodium - major constituents
Combination of sucrose, glucose, fructose, maltodextrins (corn starch - polymers of dextrose - dextrorotary form of glucose) promote similar water flux rates
Glucose polymers (repeating glucose units) offer no advantage over glucose
[CHO] less than 8% (fewer than 19g CHO per 8oz) - appear to maximize fluid absorption

Positive Study
- (Coyle) - 1 hour of intense exercise
- CHO and fluid ingestion alone or in combination
- Large volume of fluid or 79g CHO individually ingested - each improved performance compared to placebo by 6%
- When large volume of fluid and CHO were combined - performance was improved by 12%

2013 Positive Study
- 8 male tennis players
- Two, 3-match round-robin tournaments
- Sports drinks or placebos - before, during, and after each match
- Sports drinks maintained higher glycemia levels, higher stroke frequency and decreased rates of perceived exertion
Water vs. Sports Drink Intake

- **Sports Drink** - Need 5-10oz (150-300ml) with 4%-8% CHO every 15-20 minutes
- If exercise < 60 min - Water
- If exercise < 60 min (intense) - Sports drink
- If exercise > 60 min - Sports drink
- 0.5 - 0.7g of Na (1.2-1.8g of NaCl) per liter of solution

Why Take Sport Supplements?

- Do they effect performance
- Do they effect recovery
- Do they protect against muscle damage or free radicals
- Do they increase strength or Vo2max
- Do they change any exercise parameters
- Do they effect reversing a deficiency

MINERALS
Exercise does not appear to increase an athletes need for minerals (exceptions may be present)
Exercise does increase sweat and urinary losses of most minerals
However - unsure if the body can adapt to the loss by increasing retention or absorption - or perhaps minerals are redistributed during exercise - or perhaps mineral concentrations are lowered due to expansion of plasma volume that occurs with exercise

Boron
Claims - Br increases testosterone levels - thereby increasing growth and strength
Based on Nielsen study
Br - postmenopausal women - doubled their serum testosterone levels - problem - subjects were deprived Br for 4 months
Males did not have increase serum testosterone
Another study - bodybuilders given Br supplements
Serum Br levels increased - no significant increases in serum testosterone, lean body mass or strength

Calcium - Copper - Vanadium
Calcium - not studied for ergogenic potential - Inadequate calcium in female athletes - Leads to greater risk of stress fractures
Copper - part of superoxide dismutase - which increases with training - Most athletes consume enough - Supplements not necessary
Vanadium - No evidence of anabolic effects - might act like insulin or help to increase the effects of insulin - possible serious side effects
Chromium

- Active component of the glucose tolerance factor - potentiates the actions of Insulin in CHO - lipid - protein metabolism
- Promotes glucose transport
- May help bind insulin to receptors
- Insulin regulates and enhances protein synthesis by increasing uptake of amino acids

Theory

- Many Americans are deficient - up to 50%
- Exercise may affect Cr status - 24 hour Cr losses were 2x higher on the day of exercise - than on a rest day
- Benefit?
- Cr may increase insulin action and may increase lean body mass and decrease fat
- Conflicting Studies

Negative Studies

- STUDY - (Clancy et al)
  - Football players - spring training
  - Weight lifting - 4 days/wk - Running - 2 days/wk
  - 200mcg Cr picolinate or placebo for 9 weeks
  - No changes in strength or body composition
- STUDY - (Hallmark et al)
  - Weight lifted 3x/week for 12 weeks
  - Placebo or 200mcg Cr picolinate
  - No significant strength or body composition changes
Iron

- Many women athletes are deficient
- Incidence of GI bleeding in runners - 8%-85%
- Women runners are often in negative iron balance due to low meat and high fiber diet
- However -
- Incidence of IDA is no greater in female athletes than in the adult and adolescent female population (5%-6%)

Deficiency and Supplementation

- IDA has significant impact upon exercise and performance
- Iron depletion without anemia also has a negative impact on exercise
- Most studies have not found exercise improvements in non-anemic iron deficient women
- Also - exercise performance after iron supplements in athletes with normal iron status - no benefits

Magnesium

- Involved in energy production - plays a role in exercise performance due to effect on glucose mobilization/utilization in the periphery and CNS
- Exercise may lower Mg status
- 2 STUDIES - Mg blood levels are lower than baseline after 30 minutes of swimming, after a 120km hike, a marathon race, 12min of cycling at 80% max and after a treadmill 2 hour run at 65% vo2 max
2 Positive Animal Studies

- Study - (Chen, HY 2014) - Rats - saline or Mg sulfate - Mg enhanced glucose availability in the peripheral and central systems - Increased muscle lactate clearance in the muscle during exercise
- Study - (Cheng, SM 2010) - Gerbils - Mg sulfate Improved duration time of forced swimming - also raised glucose levels and attenuated lactate levels

Positive Human Studies

- In general -
- Mg has been shown to increase physical capacity of endurance athletes
- Strength Study - (Brilla and Haley)
- 2 groups - Mg oxide or placebo
- Mg group had twice the strength in leg extension exercise compared to placebos

Phosphate

- High energy - Some athletes phosphate load
- 3-5g/day of oral phosphate salts (capsules) - taken for 3 to 6 days - or immediately before sport event
- Study - 8 cyclists - 3 days exercise - 3.6g NaP
- VO2 max significantly higher in phosphate group
- Study - 1g NaP (qid) - 3 days exercise
- Increased VO2 max
- Decreased blood lactate levels
Benefits of Phosphates

- Increased aerobic capacity
- Increased peak power output
- Increased anaerobic threshold
- Improved myocardial and cardiovascular responses to exercise

Zinc

- Excreted in the urine, feces, and sweat
- Increased excretion of zinc with exercise
- Athletes are often deficient
- STUDY - (Haralambe) - 23% men and 43% women athletes had below normal range
- STUDY - >40% of elite women marathon runners consume less than 10mg/day (RDI 7-10 based on age)(Deuster et al)

Positive and Negative Studies

- STUDIES - show Increases in muscle endurance in rats and humans
- STUDY - double blind - 16 women - 135mg/day of zinc
- Increased muscle strength and endurance
- NEGATIVE STUDY - 33.6mg and 50mg for 1 month of exercise of 6 days/week -
- No effect on heart rate or lactate or time to exhaustion during 75% VO2 max run
Problem??

• > 50mg/day may be immunosuppressive - more likely at >100mg
• Large zinc supplements (150mg/day) will decrease HDL cholesterol and leukocyte and lymphocyte activity
• Copper absorption inhibited when zinc is >50mg/day
Appears that supplements are not necessary unless a deficiency state exists.
No increased requirement from physical training.
Possible exceptions -
- B2, B6, Niacin and choline?
- High CHO diets - increase need of B vitamins

Multi-Vitamins

- In General -
- At or near RDA - No benefit
- Moderate to high - Positive effects
- Increased strength
- Increased race times
- Faster recovery
- Decreased infections and injuries
- Feelings of well-being

B1 (Thiamine)

- Increases Energy
- Coenzyme in conversion of pyruvate—> ACoA
- De-carboxylation of BCAA
- Most athletes have adequate intake
- Weight restricted athletes have 66% of RDA
- Studies are mixed
B2 (Riboflavin)

- Metabolism of fats, CHO, CHON for energy
- Cell growth/respiration
- Protects against free radical damage in people who exercise (part of antioxidant chain)
- In general - No benefit if have adequate status
- However - Sedentary people who begin exercising acquire a decreased B2 status - STUDY - 50-67 yr olds had decreased B2 after 4 weeks of exercise
- Heat exposure may increase need of B2

B3 (Niacin)

- Energy metabolism - nicotinamide is precursor to NAD and NADP
- Beneficial in lowering body core temperature
- No effects on performance - positive or negative - with nicotinic acid or niacin
- Bodybuilders use nicotinic acid - causes flushing reaction due to histamine release - enlarges surface blood vessels prior to competition - bodybuilder looks more “ripped”

B6 (Pyridoxine)

- Amino Acid metabolism
- Many athletes have low levels
- STUDY - (Guilland et al) - 66% of male college athletes consumed only 69% RDA
- Need extra B6 if on high CHO and Protein diet
- B6 appears to enhance GH release after maximal exercise - Possible benefit for short term anaerobic exercise - (weightlifting)
B5 - Inositol - Biotin - Folic Acid - B12

- B12
- DNA and RBC formation - growth
- May improve endurance by enhancing oxygen carrying capacity of the RBC?
- No significant data showing increase of performance
- B5 - Inositol - Biotin - Folic Acid
- Very little research - exercise

B-complex Marksmen Study

- STUDY - (Bonke and Nickel, 1989)
- 90mg B1 - 60mg B6 - 120mg B12 per day
- 8 weeks
- Given to a group of marksmen
- Improved firing accuracy
- Decreased tremors
- Why? - unknown

Choline

- Precursor of acetylcholine and phosphatidylcholine (lecithin)
- Fat and Cholesterol metabolism
- No dietary requirement
- An amine - body can make it from methionine
- Hypothesis -
  Affects nerve transmission
  Increase strength and Reduce body fat
• Levels can decrease after exercise
• STUDY - Running 20 miles or swimming 2 hours resulted in 40%-50% decreased plasma choline level
• STUDY - (Spector et al)
• 2g of free choline before exercise prevented a decrease in choline levels (25%-40%)
• Running times improved (next slide)
• A timed swim test improved (next slide)

2 Positive Studies

• STUDY - higher percentage of swimmers who took choline before their swim had improved performance on a timed swim test compared to a placebo
• STUDY - long distance runners improved running times by 5 minutes over a 20 mile course compared to placebo group
• 2 - 8 grams of choline

Negative Studies

• STUDY - brief duration activities (2min) but highly intense or submaximal exercise for 70min - No decrease in plasma choline levels

• In General -
• No studies support choline increasing strength
• No studies support the loss of body fat
Vitamins A – D – K
No effects on exercise performance

Antioxidants

POLLING QUESTION
Free Radicals

- Single e- in outer shell
- Highly reactive - Very unstable
- Every part of the cell and almost every molecule is subjected to free radical attack including DNA, Proteins and PUFA residues of phospholipid cell membranes
- Excess exercise can lead to free radical formation

Exercise causes rate of whole body consumption of oxygen to increase 10-15x
- Oxygen flux in active skeletal muscle may increase 100x
- Significant increase in free radical production over the resting state

High intensity anaerobic work and weight training can lead to -
- Transient tissue hypoxia
- Can lead to increased H+ ions and react with superoxide anions - producing free radicals
- Can also lead to freeing of transitional metals (Iron and Copper) - involved in Fenton reaction - which increases formation of the very destructive hydroxyl radical
Other Ways Exercise Produces Free Radicals

• Increases catecholamines
• Increases lactic acid production
• Increases core temperature
• *All are associated with exercise and all can increase generation of free radicals*

In Addition

• Exercise causes →
• Tissue injury →
• Chemical mediators release →
• Phagocytic migration →
• Free radical formation and Inflammation

Antioxidants and Exercise

• Antioxidant enzyme activity increases in subjects who are trained
• Appears to be a protective adaptation to exercise stress
• *An intense bout of exercise may overwhelm the inherent capacity of the endogenous antioxidant system* -
• Particularly in a person who does not habitually exercise
Vitamin E

• Great free radical scavenging ability
• Improves insulin action and glucose tolerance
• Helps in recovery from exercise
• Foods high in CHO tend to be low in Vit E - Therefore - high CHO and low fat diets - may lead to vitamin E deficiency in athletes

2 Positive Animal Studies - Muscle Damage

• Animal (rat) STUDIES
• Vitamin E deficiency promotes decline in endurance performance
• Vitamin E deficient animals were more susceptible to tissue damage than controls
• STUDY - (Jackson et al)
• Rats - vitamin E 240mg/day - 42-45 days
• Less severe muscle damage in exercised rats and mice compared to control

3 Positive Human Studies - Muscle Damage

• 2 STUDIES - (Sumida et al) and (Cannon et al)
• Post exercise serum enzymes - indicative of muscle damage - were decreased in subjects who consumed 300-800IU of Vitamin E for 4-8 weeks
• STUDY - (Hartman et al)
• Vitamin E 800mg
• Taken 12 hours and 2 hours before exercise - and 22 hours after exercise
• Reduced DNA damage in peripheral WBCs after exhaustive exercise
2 More Positive Human Studies

- STUDY - (Meydani et al)
- 800IU/day - 7 weeks
- Exercise induced lipid peroxidation was significantly reduced with Vitamin E
- STUDY - (Kanter et al)
- 1,000IU/day - 1 week prior to exercise - Diminished LDL Oxidation rate was observed

Vitamin E Conclusions

- When a deficiency exists -
- Multiple studies demonstrate a decrease in physical performance

- Otherwise - Vitamin E only decreases free radical damage and muscle damage induced by exercise - probably does not directly improve performance

Vitamin C

- Free radical scavenger
- May reduce muscle damage and lipid peroxidation after exercise
- May reduce infections in athletes
- STUDY - (Peters et al) - 600mg/day for 3 weeks before a 42-km road race
- Fewer cases of upper respiratory infections in runners who took Vitamin C
Positive Human Studies

• STUDY - (Jakeman and Maxwell) - 400mg for 3 weeks
• More rapid recovery of maximal contraction
• Less fatigue and Less muscle damage
• STUDY - (Kaminski and Boals)
• 3 grams for 3 days before exercise - and 4 days after strenuous calf exercises
• Less muscle soreness of the calf

Conclusion

• Vitamin C has shown improvements in exercise physiology measurements -
• Increased peak work capacity
• Increased muscular strength
• Improved sub-maximal work loads
• Improved recovery time
• Less illness
• No improvements in exercise performance

Selenium

• Co-factor in glutathione peroxidase
• Training decreases levels by a small amount
• Limited studies exist
• Reduces oxidative damage during exercise
• STUDY - 100-240mcg/day
• Decreased oxidative damage after exercise
• Time to exhaustion on treadmill was unchanged
Free Form Amino Acids

POLLING QUESTION

Some single amino acids may improve exercise performance - typically for endurance exercise over many hours and/or when training volume is increased

- Arginine
- Ornithine
- BCAA
- L-Carnitine (discussed in part II)
- Glutamine (discussed in part II)
Arginine

- Made in the body naturally - Deficiencies are rare
- Foods - red meat, fish, poultry, wheat germ, grains, nuts/seeds, dairy products
- Arginine converted to nitric oxide (NO)
- Nitric oxide is a powerful neurotransmitter that helps blood vessels relax and improves circulation

Functions

- Relaxes blood vessels (vasodilator) - cardiovascular benefit
- Wound healing
- Helps kidneys remove waste products and ammonia from the body
- Maintains immune function
- Promotes Glucagon, Insulin, GH secretion

Positive Studies

- L-arginine infusion at rest increases plasma insulin, growth hormone, glucagon, catecholamines and prolactin
- L-arginine infusion increases nitric oxide (NO) and alters skeletal-muscle metabolism during exercise
- L-arginine augments the effects of exercise training on insulin sensitivity and capillary growth in muscles
• At very high intakes - 250mg per 2.2 pounds of body weight (10-30 grams)
• GH levels increase
• At lower amounts - exp - 5 grams taken 30 minutes before exercise
• GH levels do not increase
• There are great individual differences in the effectiveness of arginine as a growth hormone releaser - the effect can decrease with certain things

GH release effect is reduced by -
• Increasing Age - minimal after 40
• Taking it continuously - Breaks are needed (perhaps 4 weeks of continuous use followed by a two week break)
• Taking it with food - other amino acids and insulin can reduce effect
• Needs to be taken on an empty stomach (one hour before or three hours after a meal)

DOSE
• No recommended daily amount
• Because body normally makes enough
• Studies have used different amounts
• Common dosage is 2 to 3 grams three times a day
Side Effects and Safety

- Safe up to three months
- No long term studies for safety
- Minor side effects - Abdominal pain, nausea, cramps, bloating, diarrhea
- May aggravate gout and asthma
- May lead to liver and kidney disease

Nitric Oxide

- Regulates vasodilatation, blood flow, platelet function, mitochondrial respiration - may increase exercise capacity
- Certain foods promote NO production from the reduction of nitrate to nitrite to NO
- NO production is hampered by free radicals - antioxidants may be helpful
- Production is reduced as we age

Nitric Oxide Synthesis

- At least two physiological pathways
- NOS synthase dependent
- NOS synthase independent
- NOS dependent - L-arginine is oxidized to NO by the action of the NOS enzymes
- L-citrulline can be converted to L-arginine and is a secondary NO donor in the NOS-dependent pathway
• NOS-independent pathway -
• Nitrate and nitrite are the main substrates
• Are reduced to NO and other bioactive nitrogen oxides
• Nitrate sources - 80% of dietary nitrates are derived from vegetable consumption
• Nitrite sources - vegetables, fruit, and processed meats

• Other molecules -
• dietary supplement glycine propionyl-L-carnitine (GPLC), has also been suggested to increase levels of NO
• Unclear

NO Theory with Exercise
• NO may enhance oxygen and nutrient delivery to active muscles
• Thus improve tolerance to physical exercise
• Improve recovery mechanisms
• Mixed study results
Positive Sport Study - 2010

- 16 male cyclists aged 50 to 73
- 5.2 grams of L-arginine, L-citrulline and antioxidants
- 16.7% increase in anaerobic threshold at 3 weeks
- Placebo group - no increase in thresholds
- Anaerobic threshold = point at which lactic acid starts to accumulate in the muscles - a predictor of performance in aerobic exercise

Trained or Untrained?

- (Bescos, R et al, 2012)
- Training status of subjects is important
- Studies - NO donors could improve tolerance to aerobic and anaerobic exercise of untrained or moderately trained healthy subjects -
- Highly trained subjects - no positive effect
- Also - positive results is from mostly young male population

NO and Triglycerides

- STUDY - Zand, J et al, 2011
- Neo40 - Product of nitrate rich beetroot and Hawthorn berry (nitrite reductase activity)
- double-blinded, placebo-controlled
- Subjects > 40 yrs with 3 or more CV risk factors
- Neo40 - reduced triglycerides in 72% of patients with elevated triglycerides
Citrulline

• May improve exercise performance
• May help detoxify ammonia via the urea cycle and inhibit additional glycolysis
• STUDY - (Takeda, 2011) - Mice
  • Increased swimming time until exhaustion
  • Exercise-induced blood ammonia elevation and blood lactate was repressed/lowered

2016 Study

• Double-blind randomized placebo-controlled
• 22 trained males - 2.4 g/day of L-citrulline or placebo for 7 days - On Day 8 they took 2.4 g of L-citrulline or placebo 1 h before a 4-km cycling time trial
• L-Citrulline increased plasma L-arginine levels
• L-citrulline reduced the time taken to complete cycle ergometer exercise by 1.5 % compared with placebo
• L-citrulline improved subjective feelings of muscle fatigue and concentration immediately after exercise

• Some believe - oral l-arginine does not increase circulating nitric oxide or blood flow
• New molecule (2-[nitrooxy]ethyl 2-amino-3-methylbutanoate) marketed as “real nitric oxide”
• STUDY 2010 - 10 resistance trained men
• (2-[nitrooxy]ethyl 2-amino-3-methylbutanoate) or placebo
• Had a small effect on increasing circulating nitrate/nitrite (6.7%)
• 2012 STUDY - 2-nitrooxy ethyl 2-amino 3-methylbutanoate topical gel
• Fourteen resistance trained men (aged 24)
• exercise testing (arm curl isometric force and muscular endurance)
• 2-nitrooxy ethyl 2-amino 3-methylbutanoate gel had a modest (6.2%), non-statistically significant effect on exercise performance

Arginine Works with Ornithine in the
Synthesis of Growth Hormone

2 Positive Studies
• STUDY - Middle aged males - Weight training 5x/week - 500mg (bid) of each (double blind)
  • Decreased body fat
  • Increased total strength
  • Increased lean body mass
  • Results in only 5 weeks
• STUDY - Rats
  • Improved endurance exercise in rats
Ornithine

- Made in the body when arginine is metabolized during production of urea
- Foods = meat - dairy - eggs - fish
- Western diets supply 5 grams/day
- Increases Insulin
- May increase GH

Positive Studies

- STUDY - (Sugino 2008) - L-ornithine hydrochloride
  17 people - 2g/d for 7 days and 6g/d for 1 day
  Decreased fatigue
- STUDY - Ornithine hydrochloride
  170 mg/kg - 12 bodybuilders
  4x increase in serum somatotropin levels
- STUDY - 13 grams per day
  Increased growth hormone

Dose and Safety

- No known interactions
- Safety??
- Not pregnancy/lactating
- Dose - unknown range (many supplements contain 6 grams or so)
- 30 grams is used for burn patients
**Branched Chain Amino Acids**

- 3 of the 8 essential amino acids
- Leucine - Isoleucine - Valine
- Combo of 3 makes up 33% of skeletal muscle
- *Exercising muscle can increase uptake of BCAA fourfold*
- Exercise, Trauma, starvation - BCAA are oxidized for energy in the skeletal muscles

**Functions of BCAA**

- Enhances energy
- Increases endurance
- Increases Insulin secretion
- Aids in GH production
- Helps heal and repair muscle tissue
- Improve post exercise mood and cognitive performance during initial hour of recovery

- When energy is needed -
  - Body can break down muscle to get BCAAs
- Taken during or after a workout -
  - Muscles and other tissues are spared from breakdown
2 Positive Studies

- STUDY - healthy subjects
- One intravenous infusion of BCAAs
- Tissue breakdown that normally occurs overnight decreased by 50%

- STUDY - marathoners and cross-country runners
- Muscles were spared completely with a daily dose of BCAAS

2 Additional Positive Studies

- STUDY - (Shimomura and Murakami, 2004)
- BCAA taken before and after exercise
- Decreases exercise-induced muscle damage and promotes muscle protein synthesis

- STUDY - (Anthony, 1999)
- Rats - Leucine stimulates muscle protein synthesis following exercise

Another Positive Study (2010)

- Eight previously resistance trained males
- Received either BCAA or placebo for 3 weeks before commencing a fourth week of supplementation with concomitant high-intensity total-body resistance training
- Serum testosterone levels were significantly higher and cortisol levels were significantly lower in the BCAA group during and following resistance training
2016 Power Study

- 11 resistance-trained males performed a seated shot-put throw (SSPT) and a countermovement jump (CMJ)
- 20-g of BCAA or a placebo
- Following training there were significant decrements in CMJ and SSPT
- However - BCAA was shown to attenuate the decrements in CMJ and SSPT performance compared to placebo
- Conclusion - BCAA attenuate a decrease in power-producing ability

BCAA Negative Studies

- STUDY - (Areces, 2014) - 5g/day
  - Did not increase running performance
  - Did not prevent muscle power loss, muscle damage or pain during a marathon race
- Other Studies - 10 to 20 grams/day
  - Did not change body composition
  - Did not improve exercise performance
  - Did not enhance physical training

Summary of BCAA

- Effective - reducing muscle breakdown during exercise
- Ineffective - enhancing athletic performance
- Special Uses - prevents muscle loss at high altitudes and prolongs endurance in heat
Dose

- Estimated average requirement - 68 mg/kg/day (leucine 34 mg, isoleucine 15 mg, valine 19 mg) for adults
- Newer thoughts - 144 mg/kg/day
- Need balance between the 3 amino acids
- 2mg of leucine and valine for each milligram of isoleucine

Safety and Side Effects

- Safe for most people up to 6 months
- Fatigue
- Loss of coordination - (be careful driving)
- High valine - crawling sensation in the skin - possible hallucinations
- High leucine - lead to pellagra (niacin def) and may increase ammonia in the body

Contraindications

- Avoid during pregnancy/lactation - unknown
- ALS - lung failure and higher death rates
- Branched chain ketoaciduria
- Alcoholism - increases liver damage
- Do not use 2 weeks prior to surgery
- Decreases absorption of levodopa - do not take together
- Decreases blood sugar - combo of diabetic medications may decrease too much
Creatine

- 95% is located in skeletal muscles
- Made by the body - synthesized from amino acids - arginine, glycine, methionine
- Primarily produced in the kidney - but also by the liver and pancreas
- Dietary intake - meats and fish in quantities of 5g Cr/kg of meat
- Allowed by IOC, NCAA and professional sports

POLLING QUESTION
Benefits of PCr

- May delay fatigue
- Improves muscle performance in high intensity work
- Enhances strength in weightlifters
- Increases lean body mass
- Improves muscle protein synthesis

Best for High Intensity Sports

- Short term exhaustive anaerobic exercise with minimal recovery periods
- Sprinting - Field events - Throwing
- Weight lifting
- Does not improve performance in aerobic exercises - older people (>60) - highly trained athletes

Two Direct Functions

- Energy source to replenish ATP
- Buffer to maintain muscle ph

- $\text{PCr} + \text{ADP} + \text{H}^+ \rightarrow \text{Cr} + \text{ATP}$
- Enzyme is Creatine Kinase
- Once ATP is generated - Cr is re-synthesized into PCr
- Most likely by oxidation in the mitochondria
During high intensity exercise - muscle stores of ATP are quickly used up

Rapid re-synthesis is needed

Impaired PCr re-synthesis has been linked to impaired performance

Studies - Depletion of PCr can occur within 5-7 seconds after sprints of 40, 60, 80, and 100 meters

STUDY - PCr Re-synthesis

(Greenhaff et al) - unilateral knee extension

at 0, 20, 60, 120 seconds

During first 40 seconds - rate of recovery was identical between placebo and Cr group

After that - PCr re-synthesis was greater in the supplemented group

Muscle concentration of Cr at end of recovery was 30% higher in supplemented group

Study - Absorption

Biopsy studies have shown increases of muscle PCr and total Creatine with Cr monohydrate supplementation

By as much as 33%

However - ATP stores were unaffected

There appears to be no nutritional or training programs that will increase amount of ATP to be stored (unless increase size of muscle)
Loading DOSE

- Results in a 20%-40% increase of PCr stores
- Different ways to LOAD -
  - 1. Load with 20 - 30 grams/day (or 0.3 grams per kg) for 5 days followed by a maintenance dose of 2 or more grams (0.03 grams per kg) daily - Two days of loading has also been used
  - 2. Load dose of 9 grams/day for 6 days

Is Loading Necessary?

- Similar results can be obtained with 3 grams per day for 28 days - no loading necessary
- STUDY - (Swedish Karolinska Institute) - group that loaded and group that did not
- No difference was observed
- 20% increase in muscle Cr
- Loading phase probably unnecessary
- 3g/day was effective

Creatine and CHO

- STUDY - (Green, et al)
- Ingestion of carbohydrate with Cr augments Cr accumulation in the muscle tissue
- 60% greater when 5g Cr was followed by 93g simple CHO (qid)
- Decreased urinary excretion of Cr
- Elevated serum insulin
- Increase in body mass - from 0.9-3.2kg
**Safety/Side Effects**

- Safe at recommended doses
- Stomach pain, diarrhea, nausea and muscle cramping
- May cause skin pigmented purpuric dermatosis
- High doses > 5g per day - may damage kidney, liver or heart

**Risks/Contraindications**

- Need extra water - 64 ounces per day
- Cr causes muscles to draw water from the rest of the body - dehydration
- Be careful in the heat
- Weight gain - due to muscles holding water
- Long term effects - unknown

- Do not use if you have diabetes, kidney disease or are pregnant/breast feeding
- Do not take with meds that can harm the kidneys
  NSAIDs - ibuprofen (advil, motrin, nuprin, others), indomethacin (indocin), naproxen (aleve, anaprox, etc), piroxicam (feldene) cyclosporine (neoral, sandimmune); aminoglycosides (amikacin (amikin), gentamicin (garamycin, gentak, etc), and tobramycin (nebcin, etc)
THE END