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Sports Nutrition Part 2

Dr. James Meschino DC, MS, ROHP

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Reference Texts for this Subject

1. Sports and Exercise Nutrition (fourth edition)- Required Textbook

- William D. McArdle
- Frank I. Katch
- Victor L. Katch
- Wolters Kluwer/Lippincott & Wilkins (2013)

2. Exercise Physiology: Energy, Nutrition and Human Performance (second edition)

- William D. McArdle
- Frank I. Katch
- Victor L. Katch
- Lea & Febiger (1986)

3. Physiology of Exercise: Responses & Adaptations (second edition)

- David R. Lamb
- MacMillan Publishing Company (1984)

4. Essentials of Strength Training and Conditioning: National Strength and Conditioning Association

- Thomas R. Baechle (Editor)
- Human Kinetics (1994)

Also see Additional Research Review Papers in Course Materials

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Topics Covered in Sports Nutrition Part 2

- Thermoregulation
- Wet-bulb Global Temperature and Assessing Heat Injury Risk by Ambient Temperature
- Fluid Requirements (and CHO during exercise)
- Hyponatremia (and sodium requirement)
- Affect of Clothing ands Climate on Thermoregulation
- Heat Illness: Signs, Symptoms and Treatment
- Minerals Lost in Sweat
- Oxidative Stress and Antioxidants
- Exercise and Immunity
- Creatine
- Sodium Bicarbonate
- Growth Hormone Secretagogues
- Beetroot Juice

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Topics Continued:

- HMB
- Caffeine and Ephedra
- Coenzyme Q10
- Chromium
- HCA
- Catechins
- Coleus Forskolin
- L-Carnitine
- Ginseng
- B-Vitamins
- Iron
- Magnesium

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Topics Continued:

- Vitamin D
- DHA (docosahexaenoic acid)
- MCT oil
- Pyruvate
- Glycerol
- Glucosamine
- MSM
- Anti-inflammatory Herbs and Natural Agents
- Androstenedione and DHEA
- Alcohol

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Thermoregulation and Fluid Balance

- A person can tolerate a drop in body temperature of 10 degree C, but an increase of only 5 degree C (hyperthermia – in past 30 yrs more than 100 times a football player has died from excessive heat stress during practice or games)

- College wrestlers, military exercises and longer duration athletic events also see increased risk of dehydration-induced hyperthermia (with risk of death)

- Athletes using EPO (erythropoietin) have greater risk of heat injury due to increased blood viscosity as dehydration progresses while exercising in heat.

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Environmental Stressors (heat, cold, hypoxia, noise, darkness, trauma, pathogens):

These all challenge the body's adaptation capacity. Most people can accommodate or acclimatize to earth's stressful environments in about 8-14 days, whereas loss of acclimatization occurs in about 14-28 days, but varies based on individual factors:

- Genetic characteristics
- Available resources
- Age (compromised during adolescence and old age)
- Nature and duration of previous experiences
- Number of similar experiences
- Emotional and psychological response (worry, fear, panic, self-assurance) to environmental stress.

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- Because aerobic exercising men and women often elevate their metabolic rate 20-25 times resting metabolic rate, heat production of this magnitude could theoretically increase core temperature by 1 degree C every 5-7 mins.

- The body also absorbs heat from the environment by solar radiation and from objects warmer than the body.

- Heat loss occurs by the physical mechanisms of radiation, conduction, convection. However**, water evaporation from the skin and respiratory passages provide the most important avenue for heat loss**. **Evaporative cooing under optimal conditions accounts for a heat loss of about 18 kcal/min.**

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- In a cold environment heat conservation occurs by rapidly shunting blood deep to the cranial, thoracic and abdominal cavities, including portions of muscle mass. This optimizes insulation from subcutaneous fat and other areas of the body's shell.
- Conversely, excessive internal heat buildup dilates peripheral vessels that channel warm blood to the cooler periphery. During exercise in the heat, the strong drive for thermal balance can increase sweat rate to as high as 3.5 L/hr (1-2 L/h is customary).
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- Hypothalamus contains central neural coordinating center for temperature regulation. These specialized nerve cells regulate temperature at 37 degrees C (+ or – 1 degree C). It can't turn off heat but can help body dissipate heat.

- The skin also has thermal receptors that feed into hypothalamus.

- Cold receptors in the skin are more numerous than thermal receptors, which feed input to hypothalamus and cerebral cortex – so individual can also consciously seek relief from extreme cold or extreme heat.

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4 Thermoregulation Mechanisms:

1. Radiation: Warmer objects in the environment emit electromagnetic heat waves that are warmer that the body. As such the body absorbs some heat through the air but does not need to be in direct contact with object. As such, even on a very cold day, a person can gain heat from direct sun exposure or wave-lengths reflected from the snow, sand or water. The body absorbs radiant heat energy when an objects temperature in the environment exceeds skin temperature.

2. Conduction: Heat loss by conduction transfers heat directly through a liquid, solid or gas from one molecule to another. As such, a hiker can lye on a cool rock that is shielded from the sun to dissipate some heat via conduction. As well, if the environment is cooler than the body, some heat from the body dissipates into the cooler air that is in contact with the body surface or any other cooler surface in contact with the body.

3. Convection: The effectiveness of heat loss via conduction to air depends on how rapidly the air near the body exchanges once it warms. With little or no air movement or convection, warmed air next to the skin acts as a heat insulator, but if cooler air continuously replaces warmer air (breezy day, or room with a fan, or during running or outdoor cycling), heat loss increases because convection currents carry heat away.

- For example – air currents moving at 4 mph cool twice as effective as air movement at 1 mph.

4. Heat Loss Via Evaporative Sweating: Evaporation of sweat provides the major physiologic mechanism for heat loss and thus defense against overheating**.** Water vaporization from respiratory passages and skin surface continually transfer heat to the environment. Each liter of vaporized water transfers 580 kcal of heat energy from the body to the environment.

- In response to heat stress 2-4 million sweat glands (eccrine) secrete large quantities of hypotonic saline solution (0.2-0.4% NaCl). **Cooling occurs when sweat evaporates from the skin surfaces**. Cooled skin then cools blood shunted from the interior to the surface.

- Along with heat loss through sweating, approximately 350 mL of water seeps through the skin each day (insensible perspiration) and evaporates to the environment. Also, approximately 300 mL of water vaporizes daily from the respiratory passages moist mucous membrane.

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Increased Ambient Temperature

- Increased ambient temperature reduces effectiveness of heat loss by conduction, convection and radiation. **When ambient temperature exceeds body temperature these thermal transfer mechanisms actually contribute to heat gain.** When this occurs only evaporation of sweat and vaporization from the respiratory tract provide ability for heat dissipation. Sweat increases directly with ambient temperature.

- For someone relaxing on a hot, humid environment the normal 2-L daily fluid requirement often doubles or triples from evaporative fluid loss.

- With exercise, sweat rate increases right away and reaches equilibrium about 30 mins into exercise based on exercise load. A large cutaneous blood flow coupled with evaporative cooling generally produces an effective defense against hyperthermia (provided fluid intact). The cooled peripheral blood then returns to deeper tissues to pick up (absorb) additional heat on its return to the heart.

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Three Factors Determine Sweat Evaporation from the Skin:

1. Surface area exposed to environment
2. Temperature and relative humidity of ambient air
3. Convective air currents around the body

- **By far, relative humidity exerts the greatest impact on the effectiveness of evaporative heat loss.** Relative humidity refers to percentage of water in the ambient air at a particular temperature compared with the total quantity of moisture the air could carry. For example at 40% relative humidity the ambient air contains only 40% of the airs moisture-carrying capacity at that specific temperature. With increasing humidity ambient airs vapor pressure approaches that of moist skin (approximately 40 mmHg). Consequently, evaporative heat loss becomes thwarted even though a large quantity of sweat beads on the skin and eventually rolls off. This represents a useless water loss that can lead to dehydration and overheating.

- Continually drying the skin with a towel before sweat evaporates also thwarts evaporative cooling. Sweat does not cool the skin; rather skin cooing occurs only when sweat evaporates.

- One can tolerate relatively higher temperatures provided relative humidity remains lower, allowing sweat to evaporate. So, dry desert climate can feel easier to exercise than cooler but more humid tropical climates

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Circulatory Adjustments

- In hot weather, pulse speeds up and peripheral vessels dilate to bring warm blood to surface for heat dissipation to environment. May see flushed face or reddened face in some individuals as a result. With extreme heat stress 15-25% of cardiac output passes through the skin, greatly increasing thermal conductance of peripheral tissues. Increased peripheral blood flow favors radiative heat loss, particularly, from the hands, forehead, forearms, ears, and tibia areas of lower leg.

Hormonal Adjustments

- Heat stress increases release of ADH (anti-diuretic hormone – vasopressin) from hypothalamus, which increases water resorption in the kidney tubules making the urine more concentrated.

- With repeated bouts of exercise on consecutive days kidneys also secrete aldosterone to increase water and sodium resorption. Aldosterone also decreases sodium concentration in sweat (reduces sweat osmolality), which aids in electrolyte conservation, helping to prevent hyponatremia.

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Evaluating Environmental Heat Stress:

Five factors other than air temperature determine the physical strain imposed by heat

1. Body size and fatness
2. Level of training
3. Acclimatization
4. Adequacy of hydration
5. External factors (convective air currents, radiant heat gain, intensity of exercise, amount, type and color of clothing and most importantly, relative humidity). Football players have died exercising at 75 degrees F, when relative humidity exceeded 95%.

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American College of Sports Medicine Temperature Recommendations:

- Very High-Risk: above 28 degree C (82 degrees F) postpone race
- High Risk: 23-28 degrees C (73-82 degrees F) heat-sensitive individuals (obese, low physical fitness, unacclimatized, dehydrated, previous history of heat injury) should not compete
- Moderate Risk: 18-23 degrees C (65-73 degrees F)
- Low Risk: below 18 degrees C (65 degrees F)

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The Wet-bulb Globe Temperature

- The **wet-bulb globe temperature** (WBGT) is a type of apparent temperature used to estimate the effect of temperature, humidity, wind speed (wind chill), and visible and infrared radiation (usually sunlight) on humans.

- A **wet bulb** thermometer **measures** the extent of cooling as moisture dries from a surface (evaporative cooling). The **wet bulb temperature** is always lower than the dry **bulb temperature** except when there is 100% relative humidity, making the **wet bulb temperature** a more accurate **measurement** of product **temperature**.

- Wet and dry bulb - an instrument used to **measure** the relative humidity of the atmosphere. It consists of a **thermometer** with a **bulb** that is **wet** or moist and one that is kept **dry**. The relative humidity is calculated from the difference in readings of the **thermometers** when water evaporates from the **wet bulb**, decreasing its temperature.

- The **wet-bulb globe temperature** (**WBGT**) It is used by industrial hygienists, athletes, and the military to determine appropriate exposure levels to high temperatures. It is derived from the following formula:

$$WBGT = 0.7T_w + 0.2T_g + 0.1T_d$$

where

- T_w = Natural wet-bulb temperature (combined with dry-bulb temperature indicates humidity)
- T_g = Globe thermometer temperature (measured with a globe thermometer, also known as a black globe thermometer)
- T_d = Dry-bulb temperature (actual air temperature)

Temperatures may be in either Celsius or Fahrenheit

- Indoors, or when solar radiation is negligible, the following formula is often used: $WBGT = 0.7T_w + 0.3T_g$

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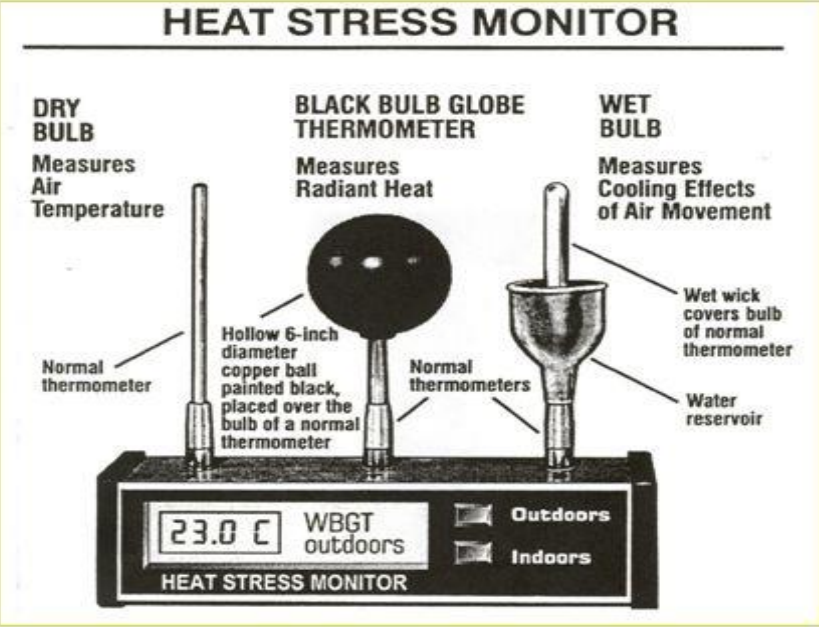
Wet-bulb Global Temperature

What is WBGT ?



- Wet Bulb Globe Temperature Index (WBGT)– Measures Human Heat Stress Exposure
- Dry Bulb (DB) – Measures Ambient Air Temperature
- Wet Bulb (WB) – Measures Cooling Effect of Air Movement
- Black Bulb Globe (GT) – Measures Radiant Heat

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Wet Bulb Globe Temperature Category Work/Rest and Water Intake

08/07/15

Unacclimated and Acclimated Work/Rest and Water Intake Chart

Heat Risk Category		Wet Bulb Globe Temp	Light Work		Moderate Work		Heavy Work	
			Work/Rest	Water Intake (quart/hr)	Work/Rest	Water Intake (quart/hr)	Work/Rest	Water Intake (quart/hr)
No Risk	Unacclimated	78 – 79.9	50/10 min	½	40/20 min	¾	30/30 min	¾
	Acclimated	78 – 79.9	continuous	½	continuous	¾	50/10 min	¾
Low	Unacclimated	80 – 84.9	40/20 min	½	30/30 min	¾	20/40 min	1
	Acclimated	80 – 84.9	continuous	½	50/10 min	¾	40/20 min	1
Moderate	Unacclimated	85 – 87.9	30/30 min	¾	20/40 min	¾	10/50 min	1
	Acclimated	85 – 87.9	continuous	¾	40/20 min	¾	30/30 min	1
High	Unacclimated	88 – 90	20/40 min	¾	10/50 min	¾	avoid	1
	Acclimated	88 – 90	continuous	¾	30/30 min	¾	20/40 min	1
Extreme	Unacclimated	> 90	10/50 min	1	avoid	1	avoid	1
	Acclimated	> 90	50/10 min	1	20/40 min	1	10/50 min	1

Adapted from: 1) USGS Survey Manual, Management of Occupational Heat Stress, Chapter 45, Appendix A. 2) Manual of Naval Preventive Medicine, Chapter 3: Prevention of Heat and Cold Stress Injuries. 3) OSHA Technical Manual Section III: Chapter 4 Heat Stress. 4) National Weather Service Tulsa Forecast Office, Wet Bulb Globe Temperature.

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Fluid Replacement Guide

Heat Category	WBGT Index, (°F)	Easy Work Walking on hard surface, 2.5 mph, <30 lb. load; weapon maintenance, marksmanship training.	Moderate Work Patrolling, walking in sand, 2.5 mph, no load; calisthenics.	Hard Work Walking in sand, 2.5 mph, with load; field assaults.
		Fluid Intake (quarts/hour)	***Fluid Intake (quarts/hour)***	***Fluid Intake (quarts/hour)***
1	78° - 81.9°	½	¾	¾ (1)*
2	82° - 84.9°	½	¾ (1)*	1 (1¼)*
3	85° - 87.9°	¾	¾ (1)*	1 (1¼)*
4	88° - 89.9°	¾	¾ (1¼)*	1 (1¼)*
5	> 90°	1	1 (1¼)*	1 (1½)*

*Use the amounts in parentheses for continuous work when rest breaks are not possible. Leaders should ensure several hours of rest and rehydration time after continuous work. This guidance will sustain performance and hydration for at least 4 hours of work in the specified heat category. Fluid needs can vary based on individual differences (± ¼ qt/hr) and exposure to full sun or full shade (± ¼ qt/hr). Rest means minimal physical activity (sitting or standing) in the shade if possible. Body armor - add 5°F to WBGT index in humid climates. NBC (MOPP 4) - Add 10°F (Easy Work) or 20°F (Moderate or Hard Work) to WBGT index. **CAUTION:** Hourly fluid intake should not exceed 1½ qts. Daily fluid intake should not exceed 12 qts.

USAPHC 1-800-222-9698 http://phc.amedd.army.mil

TA-091-0615 (Also available as a poster.)

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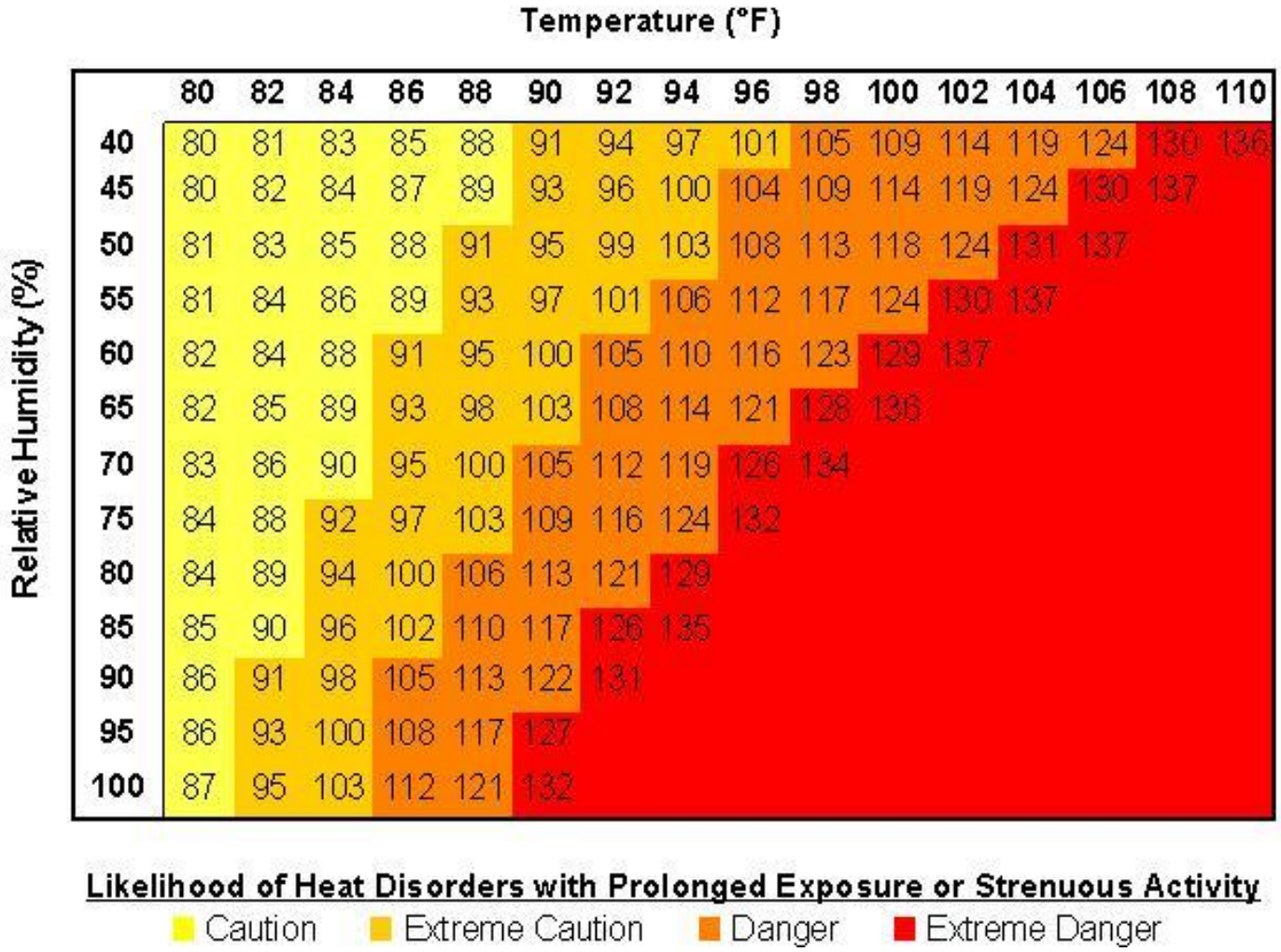
Likelihood of Heat Disorders with Prolonged or Strenuous Exercise



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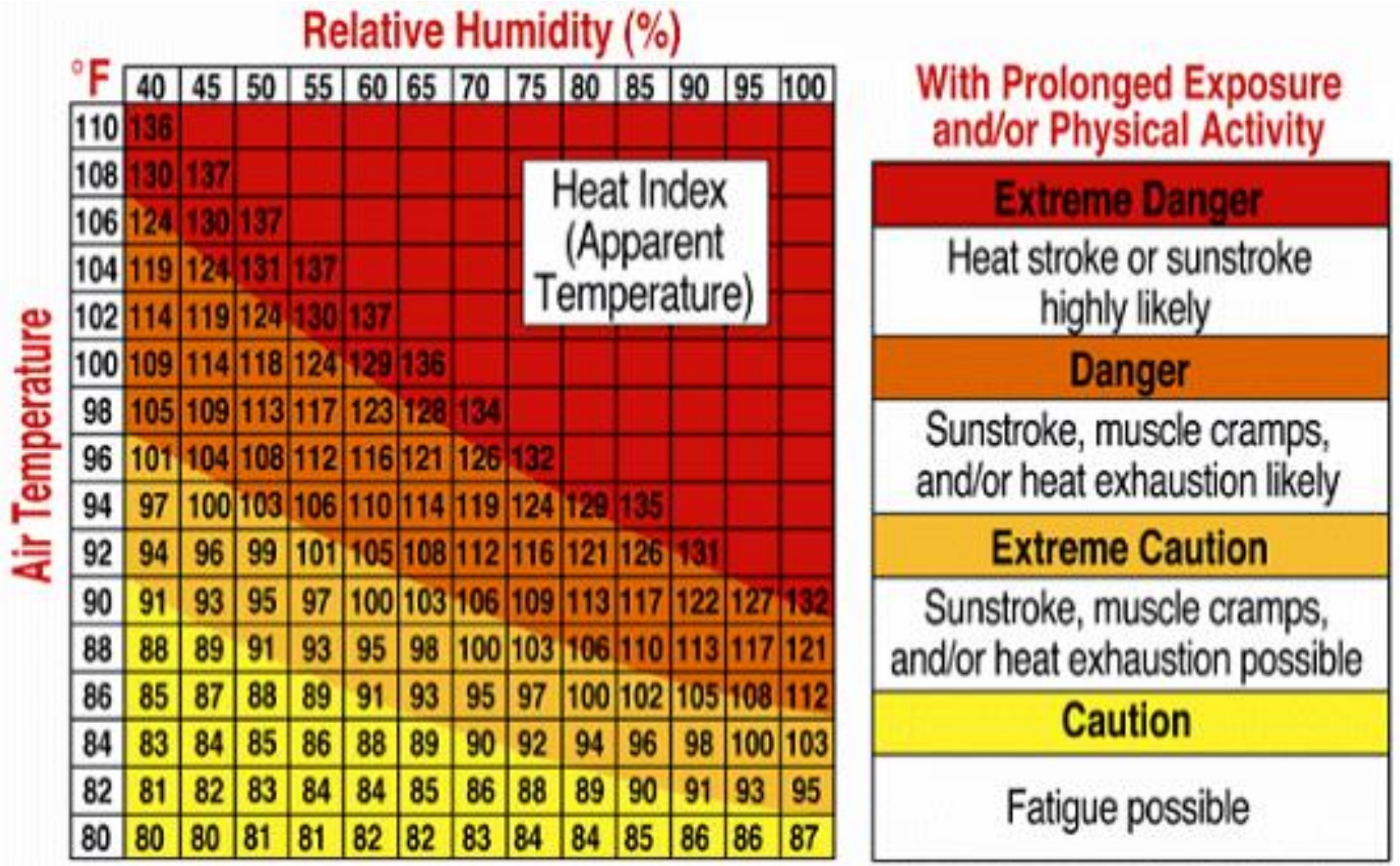

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WBGT READING	ACTIVITY GUIDELINES & REST BREAK GUIDELINES
Under 82.0	Normal activities--Provide at least three separate rest breaks each hour of minimum duration of 3 minutes each during workout
82.0 - 86.9	Use discretion for intense or prolonged exercise; watch at-risk players carefully; Provide at least three separate rest breaks each hour of a minimum of four minutes duration each
87.0 - 89.9	Maximum practice time is two hours. For Football: players restricted to helmet, shoulder pads, and shorts during practice. All protective equipment must be removed for conditioning activities. For all sports: Provide at least four separate rest breaks each hour of a minimum of four minutes each
90.0 - 92.0	Maximum length of practice is one hour, no protective equipment may be worn during practice and there may be no conditioning activities. There must be 20-minutes of rest breaks provided during the hour of practice
Over 92.1	No outdoor workouts; Cancel exercise; delay practices until a cooler WBGT reading occurs

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GUIDANCE FOR HIGH SCHOOL ATHLETICS	
WBGT READING	**ACTIVITY GUIDELINES & REST BREAK GUIDELINES**
UNDER 82.0	Normal activities - Provide at least three separate rest breaks each hour of minimum duration of 3 minutes each during workout.
82.0 - 86.9	Use discretion for intense or prolonged exercise; watch at-risk players carefully; Provide at least three separate rest breaks each hour of a minimum of four minutes duration each.
87.0 - 89.9	Maximum practice time is two hours! For football: players restricted to helmet, shoulder pads and shorts during practice. All protective equipment must be removed for conditioning activities. For all sports: Provide at least four separate rest breaks each hour of a minimum of four minutes each.
90.0 - 92.0	Maximum length of practice is one hour, no protective equipment may be worn during practice and there may be no conditioning activities. There must be 20 minutes of rest breaks provided during the hour of practice.
OVER 92	NO OUTDOOR WORKOUTS! Cancel exercise; delay practice until a cooler WBGT reading occurs.

GHSA Heat Index Record Sheet. Georgia High School Athletic Association Heat Index Measurement and Record. 2012:1.

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Sweat Loss and Dehydration

- A moderate exercise workout generally produces a 0.5-1.5 L sweat loss over a 1-hr period. Even in swimming and cross-country skiing on cold day, sweating still occurs. The cooler temperature of water for swimmers also increases water loss through increased urine output.

- Intentional water losses used by certain weight class athletes, such increased sweating from saunas, steam room, hot whirlpool, shower, fluid and food restriction, diuretic and laxative drugs, or vomiting, an all increase risk of dehydration (boxers, wrestlers, weight lifters, rowers – to decrease weight in boat). These practices decrease body's heat dissipation capacity and increase risk of dehydration, compromise performance, and can lead to heat stroke, compromised cardiovascular function and hyperthermia during competition and training.

- Dehydration associated with a 3% decrease in body weight slows gastric emptying rate, thus triggering epigastric cramps and feelings of nausea. Because sweat is hypotonic, the fluid loss during sweating increases blood plasma osmolality. Losing disproportionately more water than NaCl.

- In a practical sense, rapid weight loss through dehydration does not impair maximal exercise performance of short duration up to 60 secs, but when exercise exceeds one-minute dehydration profoundly impairs physiological function and compromises optimal ability to train and compete.

- Water loss via sweating in an acclimatized person peaks at 3-L per hour during intense exercise in the heat and averages nearly 12-L (26 pounds) on a daily basis (roofer on hot summer day).

- Several hours of intense sweating can cause sweat gland fatigue, which ultimately impairs core temperature regulation.

- Elite marathon runners can lose in excess of 5-L of water during competition, which equals 6-10% of their body mass.

- Slower paced marathoners and ultramarathoners usually lose about 500 ml fluid per hour.

- Soccer players playing in temperate climate (10 degrees C, 50 degrees F) lose 2-L fluid during 90-minute soccer game.

- Other sports with large fluid losses include football, basketball, hockey.

- Any degree of dehydration impairs capacity of circulatory and temperature-regulating mechanisms to adjust to exercise demands.

- Dehydration of 2% (of body mass) impairs physical work capacity and physiological function predisposing to heat injury when exercising in a hot environment.

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- **For each liter of sweat loss, exercise heart rate increases 8 bt/min with a corresponding 1.0 L/min decrease in cardiac output.**

- Studies show that dehydration of 4.3% of body mass decreases endurance performance by 18% (walking endurance) and VO2 max decreased by 22%.

- With dehydration of only 1.9% of body mass, see 22% decline in endurance performance and 10% decrease in VO2 max.

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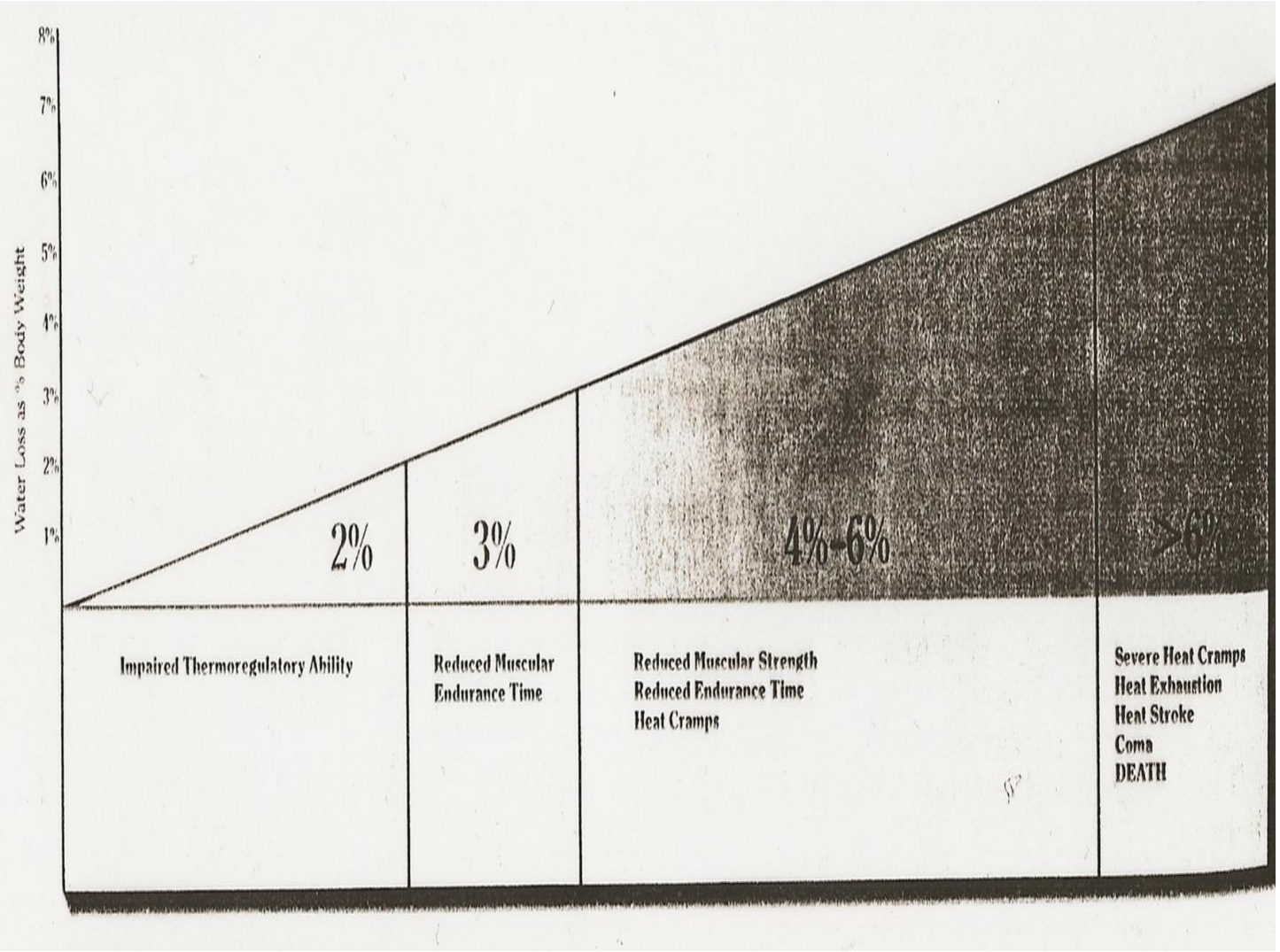
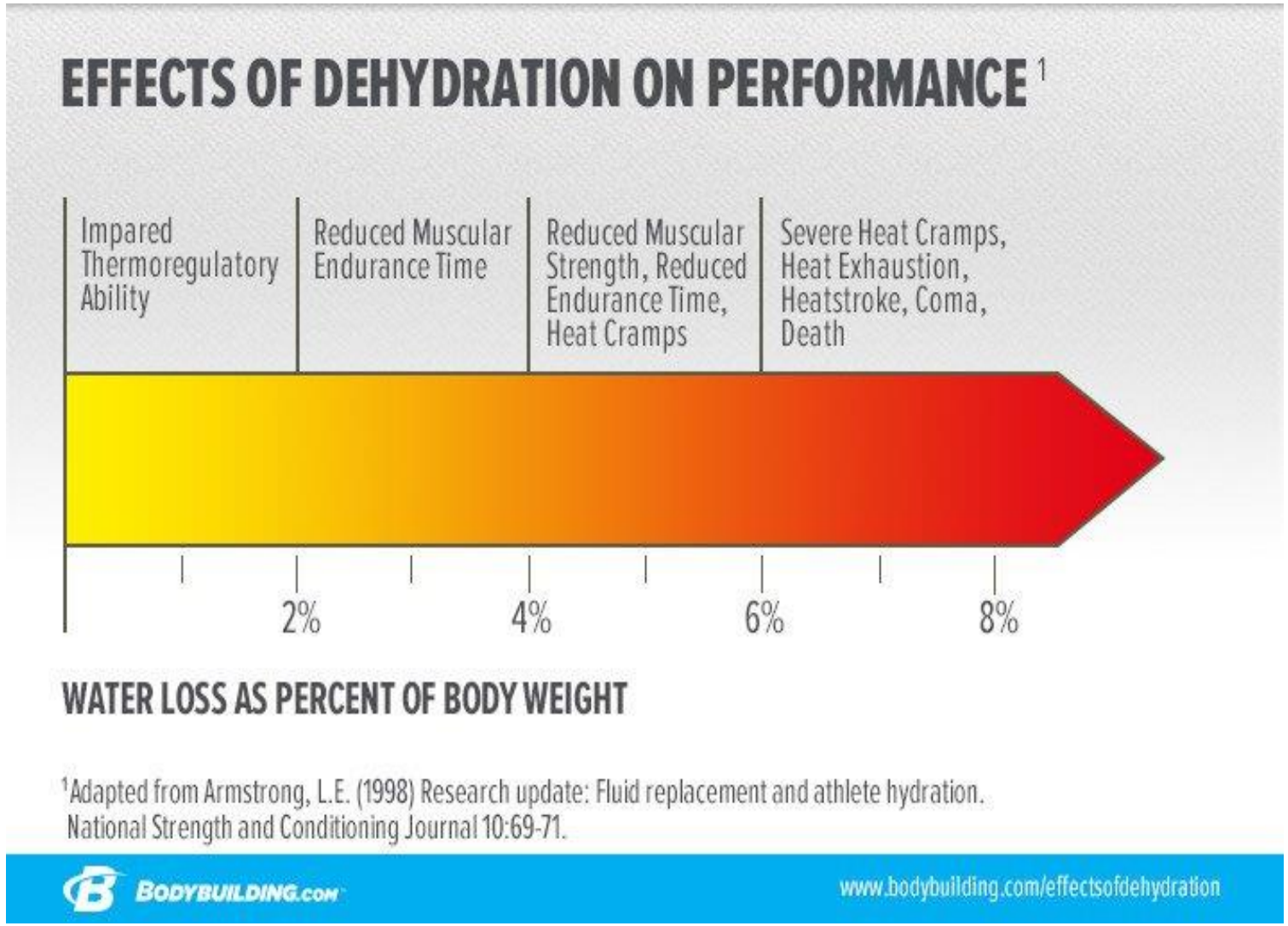
Consequences of Dehydration During Exercise




EFFECTS OF DEHYDRATION ON PERFORMANCE 1
Impared Thermoregulatory Ability
Reduced Muscular Endurance Time
Reduced Muscular Strength, Reduced Endurance Time, Heat Cramps
Severe Heat Cramps, Heat Exhaustion, Heatstroke, Coma, Death
2%
4%
6%
8%
WATER LOSS AS PERCENT OF BODY WEIGHT
1Adapted from Armstrong, L.E. (1998) Research update: Fluid replacement and athlete hydration. National Strength and Conditioning Journal 10:69-71.
BODYBUILDING.COM
www.bodybuilding.com/effectsofdehydration

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Cold Air Sports Increase Risk of Dehydration

- Due to colder air being dryer (contains less moisture), especially at high altitudes, risk of dehydration increases during vigorous cold-weather exercise as greater fluid loss occurs during respiration as incoming cold, dry air fully humidifies and warm to body temperature. This air-conditioning process can create a 1-L daily fluid loss.

- Cold stress also increases urine production, which adds to water loss. As well, many people overdress for outdoor winter activities, enabling heat gain to outpace heat loss resulting in sweating. The heavy clothing also impairs evaporative cooling. Many people exercising on cold winter days are not cognisant of fluid needs to the degree of that appreciated by warm-weather exercise participants.

- Left on their own most individuals voluntarily replace only about ½ of the water (less than 500 ml/hr) during exercise. Thus, education is important and vigilance by sports nutrition coach.

- Note that cold-treatments do not work to cool the body – cold wet towel to forehead or abdomen. **The only way to cool core temperature is consumption of fluids at 4 degrees C during exercise**.

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Pre-Exercise Fluids

- In addition to drinking adequate amounts of fluid in the 24 hours leading up to exercise or competition the recommendation is also to consume 400-600 ml (13-20 oz) of cool water about 20 mins before exercise (may add pure fructose for endurance events). Pre-exercise fluid intake increases stomach volume, helping to optimize gastric emptying during exercise.

- A systematic regime of hyperhydration by consuming 4.5-L of fluid daily 1 week before soccer competition by acclimated elite young players in Puerto Rico increased body water reserves (despite greater urine output) and improved temperature regulation during a soccer match in warm weather. This protocol produced a body fluid volume 1.1-L greater than prior protocol of usual water and fluid intake with hyperhydration.

- Pre-exercise hydration does not replace need to continually replace fluids during exercise.

- **Crushed Ice** - 2017 Study showed that precooling with oral intake of crushed ice led to improved gross efficiency with cycling due to an increased heat storage capacity, which was the result of lower core temperature (Int J Sport Nutr Exerc Metab. 2017 Jun;27(3):220-227. doi: 10.1123/ijsnem.2016-0215. Epub 2017 Jan 4. https://www.ncbi.nlm.nih.gov/pubmed/28050930)

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- Remember that the **max volume of fluids absorbed from gut to bloodstream is 1,000 ml per hour (1-L/hr)** whereas exercising in extreme heat can produce a **sweat rate of 2,000 ml per hour (2-L/hr**). As such, even athletes drinking regularly during competition need to be monitored for signs of dehydration and heat stress.

- Voiding small amounts of dark, yellow urine with a strong odor provides a qualitative indication of inadequate hydration. (remember that vitamin B2 also produces bright yellow urine).

- Well hydrated persons normally produce large volume of urine that is light colored and without a strong smell. (Remember that supplementation with N-acetylcysteine and alpha lipoic acid – sulfur-containing supplements can also produce a strong sulfur-smelling urine).

- With team sports each athlete should be provided with their own squeeze bottle for fluids.

- Menstrual cycles do not adversely affect rehydration.

- The elderly usually require greater time to rehydrate after dehydration period.

- Weighing athletes before and after practice or competition helps assess hydration, as **1 lb of weight loss represents 450 ml (15 fl oz) of dehydration.**

- If rehydration after exercise are left entirely to thirst mechanism then it usually takes several days to re-establish normal hydration. Thus, the recommendation is to drink at least 125-150% of the existing body fluid loss (body weight loss) as quickly as possible after exercising. The 25-50% extra water accounts for the portion of ingested water lost in the urine. The kidneys continually form urine, so the volume of ingested fluid following exercise should exceed exercise sweat loss by 25-50% to restore fluid balance. Unless the beverage has sufficient high sodium content, excess fluid intake merely increases urine output with no benefit to rehydration. Thus, sports drinks contain higher amounts of sodium (and potassium) than regular sodas and juices.

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- Flavoured Drinks Help – consuming highly palatable flavored beverages with added salt facilitates voluntary rehydration in children and young and older adults.

- The American College of Sports Nutrition (ACSM) recommends that sports drinks contain 0.5-0.7 gm of sodium per liter of fluid consumed during exercise lasting more than one hour. Moderate exercise produces negligible losses of potassium in sweat.

- Even with intensive exercise potassium loss does not pose a serious health threat. Potassium-rich foods after training is a good way to replenish potassium (citrus fruits, bananas). A glass of orange juice or tomato juice replaces all the potassium, calcium and magnesium excreted in 3-L of sweat.

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Hyponatremia – occurs when serum sodium concentration falls below 135 mEq/L, a serum sodium concentration below 125 mEq/L triggers severe symptoms. Low extracellular sodium creates an osmotic imbalance across the blood-brain barrier that causes rapid water influx into the brain. This causes swelling of the brain tissues resulting is S and S of: headache, confusion, malaise, nausea, cramping and may progress to seizures, coma, pulmonary edema, cardiac arrest and death.

- In 2002 13% of Boston marathoners were shown to have some degree of hyponatremia at end of race (low serum sodium).

- Ultra-marathoners at greatest risk for hyponatremia but events lasting less than 4 hours can also produce hyponatremia in athletes not consuming adequate amounts of sodium in their fluid replenishment protocol during the event. Typically, the athlete consumes large volumes of water (with insufficient sodium), which increases water volume but produces decreases plasma osmolality. This promotes movement of sodium from extracellular to intracellular space, resulting in tissue swelling of lungs, brain tissue – adversely affecting nervous system function.

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Heat Acclimatization Affects Sodium Lost in Sweat – athletes who are not acclimatized to exercise in the heat lose 40-100 mmol/L (920-2300 mg/L) of sodium in sweat, whereas heat acclimatized athletes lose only 5-30 mmol/L (115-690 mg/L) of sodium during exercise in the heat. This reduces their risk of hyponatremia.

To prevent over-hydration and related hyponatremia these are the **five recommended steps:**

1. 2-3 hours before exercise, drink 400-600 ml (14-22 oz) of fluid
2. Drink 150-300 ml (5-10 oz) of fluid about 30 mins before exercise
3. Drink no more than 1,000 ml/hr (32 oz) of plain water spread over 15 min intervals during or after exercise
4. Add a small amount of sodium (approx. ¼ to ½ tsp of salt per 32 oz to ingested fluid). Commercial sports drinks are also effective in providing water, CHO and electrolytes.
5. Do not restrict dietary salt

The presence of CHO in the sports drink may also help protect against exercise-associated hyponatremia, possibly via the glucose-sodium transporter required for glucose absorption.

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Improving Heat Tolerance: Step-by-Step Guide

- Use 15-20 mins of light-intensity exercise in first several exercise sessions when starting to train in hotter climate. It takes 7-10 days for complete heat acclimatization to occur, so first week of workouts have to be lighter while body is undergoing adaptations.

- After first few days, exercise intensity and duration can increase systematically to reach normal duration and intensity by day 7-10.

- After 10 days of heat exposure sweating capacity nearly doubles and sweat become more dilute (less sodium loss) and more evenly distributed on the skin surface.

- Loss of heat acclimatization occurs within 2-3 weeks upon returning to a more temperate climate.

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- **Prepubescent Children** – although they have more heat-activated sweat glands than adults require more time to acclimate to hotter environment.

- No gender differences regarding heat tolerance ability between men and women, although women contain more heat-activated sweat glands per unit skin than men, yet they sweat less prolifically. Women relay more circulatory mechanisms for heat dissipation, whereas greater evaporative cooling occurs in men.

- Women posses a relatively large body surface area to body mass ratio, a favorable dimensional characteristic for heat dissipation and are able to cool faster for the same reason.

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Body Fat and Heat Exchange

- Excess body fat negatively affects exercise performance in hot environments primarily due to increased insulation effect. Excess body fat also adds to metabolic cost of weight bearing exercises, causing generation of even more internal heat while retarding effective heat exchange.

- The additional demands of equipment weight (such as football gear), intense competition, and a hot-humid environment compound these effects.

- Fatal heat stroke occurs 3.56 times more frequently in obese young adults than in individuals whose body mass falls within reasonable limits.

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Effects of Clothing:

- Different materials absorb water at different rates. **Cottons and linens readily absorb moisture.** In contrast heavy sweat shirts and rubber or plastic garments produce high relative humidity close to the skin and retard the vaporization of moisture. This inhibits or even prevents evaporative cooling. Color also plays an important role; dark colors absorb light rays and add to radiant heat gain, whereas clothing of light colors reflect heat rays from the body.

- **Moisture-wicking fabrics (polypropylene, Cool-max, Drylite, DRI-FIT) that adhere close to the skin's surface** provide optimal heat transfer and moisture from skin to the environment, particularly during high intensity exercise in hot weather. These fabrics wick moisture away from the skin, they also offer benefits during exercise in cold environments because dry clothing, in contrast to sweat-drenched clothing, greatly reduces risk of hypothermia.

- **Football Uniforms**: they present a considerable barrier to heat dissipation. Even with loose fitting, porous jerseys, wrappings, padding (with plastic coverings), helmet, and other objects of armor effectively **seal off 50% of the body's surface from the benefits of evaporative cooling**. And the 6-7 kg weight of equipment also increases the metabolic load not to mention the thermal challenge from a hot, artificial playing surface and the body heat-retaining qualities of the equipment. The large body size of these athletes further magnifies heat load, particularly for linemen who posses a relatively small body surface area to body mass ratio and a higher percentage of insulating body fat than other players.

- Coaches and athletes must remain vigilant during games and practices played in hot, humid environments to protect athletes from uncompromising physiologic and perceptual issues related to excessive heat stress.

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Cycling Helmets – although the head provides an important avenue of heat loss, wearing a cycling helmet does not restrict heat loss from the body more so than cycling without a helmet. The helmet protects the head from injury and thus, is a key protective strategy.

- Much of what researchers know about the effects of hot environment on human exercise performance and related nutritional concerns stems from research performed on military personnel from the 1930's to 1960's.

- Individuals tend to eat less as temperature rises. Protein intake usually stays the same with reductions in CHO and fat intake. This reduces the thermogenic effect of food, helping to lower heat load.

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Types and Severity of Heat Illness:

- Heat Cramps – Heat Exhaustion – Heat Stroke (no clear demarcation separates these three stages of increasing heat illness severities). The accumulation of their multiple adverse interacting stimuli can produce exercise-induced heat injury. When heat injury occurs only immediate corrective action using rehydration can reduce heat stress until medical help arrives.

A. Heat Cramps: (involuntary muscle spasms) – likely results from imbalance of hydration level and electrolyte concentrations. Crampers tend to have high sweat rates and sweat sodium concentrations. With heat cramps the body temperature does not necessarily increase. Prevention involves using sodium-containing sports drinks and adding a pinch of salt to meals routinely.

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B. Heat Exhaustion: usually occurs in dehydrated, untrained and unacclimatized people; often during the first summer heat wave or first hard training in hot weather. The cause is ineffective circulatory adjustments compounded by depletion of extracellular fluid (plasma volume) from excessive sweating. Blood pools in the dilated peripheral vessels, which drastically reduces the central blood volume required to maintain cardiac output.

- **S and S include:** weak pulse, low blood pressure in upright position, headache, nausea, dizziness, goose bumps, and general weakness. Body temperature DOES NOT RISE to dangerous levels (above 104 degrees F or 40 degrees C). The person with these symptoms should stop exercising and seek a cooler environment; fluids should be administered orally or via intravenous therapy with 5% dextrose sugar in either 0.45% NaCl or 0.9% NaCl.

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C. Exertional Heat Stroke: (medical emergency) – reflects a failure of heat-regulating mechanisms induced by excessively high body temperature. With thermoregulation failure sweating usually ceases, the skin becomes dry and hot, body temperature rises to 41.5 degrees C or higher, and the circulatory system becomes excessively strained.

- If left untreated the disability becomes fatal from circulatory collapse, oxidative damage, systemic inflammatory response, and damage to the CNS and other organs (cook heart, brain, liver etc.)

- Heat stroke is a medical emergency state and while awaiting medical care only aggressive treatment to rapidly lower core temperature can avert death.

- Immediate treatment entails **alcohol rubs and ice packs; whole body cold or ice water immersion remains the most effective treatment for collapsed hyperthermic individuals,** especially those who are unfit, poorly acclimatized to the heat, and excessively fat. But this disorder can also occur in fit young individuals.

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Oral vs Rectal Thermometer Assessment of Core Temperature:

- Oral temperature underestimated core temperature as evaporative cooling from the mouth and airways occurs during high-levels of pulmonary ventilation.

- However, a rectal thermometer and an ingestible thermometer pill that measures gastrointestinal temperature each provide an accurate measure of core body temperature.

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Fluid Requirement and Strategy

- As larger stomach fluid volume increases the gastric emptying, maintaining a relatively large stomach fluid volume represents a major factor that speeds gastric emptying to compensate for any inhibitory effects of the beverage's CHO content.

- Consuming 400-600 ml (13-20 oz) of fluid 20 mins before exercise optimizes the benefits of increased stomach volume on fluid and nutrient passage into the small intestine.

- Then, regularly consuming 150-250 ml (5-8 oz) of fluids every 10-15 mins throughout exercise maintains gastric fluid volume and helps move fluids into small intestine, enhancing absorption into blood stream.

- This protocol delivers 1 liter of water per hour during moderate and intensive exercise, which meets the needs of most athletes. Cold water at 5-degrees C may speed gastric emptying, absorption and help prevent rise in core temperature.

- Alcohol and caffeine during exercise increase diuresis (water loss via urine) with alcohol having the most pronounced effect. These are contra-indicated as they can lead to dehydration and resulting hyperthermia.

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Types of CHO in Sports Beverage:

- Drinks containing glucose polymers between 3-20 glucose units derived from cornstarch breakdown, reduce the number of particles in solution and thus lower the osmolality of the sports drink, helping to prevent slowing of gastric emptying. Then adding a small amount of glucose and sodium (glucose being the more important factor) does not negatively affect gastric emptying. It also facilitates fluid uptake by the intestinal lumen because rapid cotransporter of glucose-sodium across the intestinal mucosa stimulates water's passive uptake by osmotic action.

- Also note that – rehydration solutions that combine two different transportable CHO substrates (glucose, fructose, sucrose, or maltodextrins) produce greater water uptake at a particular intestinal lumen osmolality than solutions containing only one substrate from enhanced solute flux and thus water flux, from the intestine. The second substrate stimulates more intestinal transport mechanisms, thus facilitating net water absorption by osmosis.

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Addition of Sodium to Sports Drinks:

- Prevents Hyponatremia – that can occur if only plain water is consumed.
- Increases thirst mechanism and sodium-dependent osmotic drive to drink – promoting continued fluid intake
- Reduces urine output, keeping more water in bloodstream
- Maintains plasma osmolality and fluid retention

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Ideal Sport Drink Criteria:

- CHO – 5-8% solution – even when consumed in the heat has been shown to regulate temperature and fluid balance as well as plain water, but has the advantage of delivering exogenous CHO to muscles.

- Consuming a 5-8% CHO solution beverage in post-recovery period in warm environments also improves endurance capacity for subsequent exercise.

- To determine the percentage CHO in a drink – divide CHO content (in gm) by fluid volume (in mL) and multiply by 100.

- Gatorade – 6% CHO solution
- Powerade – 8% CHO solution

- In very hot weather a more dilute CHO drink is recommended – less than 5% CHO solution – to prevent hyperthermia
- In cooler weather sports drinks at 15% CHO solution may be used.

- With consumption of most sports drink the gastric emptying rate for fluids is 1700 mL water per hour, even when drinking an 8% CHO solution beverage. The goal is 1,000 mL water consumed per hour. If exceed this amount can result in GI distress symptoms and discomfort.

Table 2 **Recommended Carbohydrate Intakes for Runners**

Recommended Carbohydrate Intake (g/kg/day)	Activity Duration	Activity Intensity
5 to 7	60 minutes	Moderate*
6 to 10	1 to 3 hours	Moderate to high**
10 to 12	4 to 5 hours	Moderate to high**

*Brisk walking at 3.5 mph

**Running at 5 mph

RESOURCES

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2. PHYSICAL ACTIVITY. CHOOSEMYPLATE.GOV WEBSITE. HTTP://WWW.CHOOSEMYPLATE.GOV/PHYSICAL-ACTIVITY-WHAT-IS. UPDATED JUNE 10, 2015. ACCESSED JANUARY 6, 2016.

Estimating Fluid Needs During Exercise

- Sweat rate
  - Fluid loss per hour of exercise
  - Sum of body weight loss plus fluid intake

- Calculate sweat rate:
  - Weigh yourself 1 hour before/after workout
  - Subtract post-workout weight from pre-
  - 1 pound lost = 16 oz

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Fluid Requirements: Some Summary Points

- Sweat rate of 1-2 liters per hr is usual (up to 4 L/hr- Salazar)
- Water absorbs heat of muscle work (not used to re-couple ADP plus phosphate to form ATP) and transports it the skin and lungs
- Via respiration (lungs) convection, radiation, evaporation and conduction, heat is lost to the environment (refrigeration system to keep core temp below 42 degrees C or 108 degrees F)

- With 2% water loss – impairs heat regulation, but not performance
- With 3-4% water loss – 30% impairment of performance
- At 6% water loss – heat stroke and prostration. The core temp. rises above 42 degrees C, cooking the brain, lungs, and heart, with failure in each of these organs. (On average, 4 deaths per year occur in high school football players)

- The American College of Sports Medicine – 5-8 ounces of fluids, every 10-15 mins (depending on the ambient temp and humidity), for events lasting more than 40-60 mins.

- Recall that cold water is absorbed faster than fluids at room temp and that sports drinks should not contain more than ~8% CHO solution as a rule, as higher concentrations slow gastric emptying and reduce absorption of water from GI to blood stream (due to hyperosmolarity)

Hyponatremia:

- Sodium (from extracellular fluids) is lost in sweat more than any other mineral – 1500 mg of sodium per 1 liter sweat

- With prolonged exercise (3-4 hrs) higher intracellular sodium levels may prevail relative to extracellular sodium

- This is known as hyponatremia and results in a drawing of water into the cells of the brain and lungs, producing disorientation, shortness of breath, coma and possibly death

- Thus, for prolonged exercise (more than 90 mins) an athlete should consume 1 gm sodium chloride for every liter of fluids consumed. (sports drinks meet this criteria)

- **Potassium** : it can be replaced through the consumption of fruit or fruit juices post exercise, and is not an absolute requirement for sports drinks (unless its an ultra-marathon event, whereby athletes consume food and/or food bars)

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Other Minerals Lost In Sweat:

- Calcium, zinc and iron: although not lost in sweat to an appreciable degree, these nutrients are commonly found to be under-consumed (marginal deficiencies), increasing risk of osteoporosis, poor wound healing, reduced taste acuity weakened immune function, reduced IGF-I levels, and weakness.

- Exercise can further exacerbate marginal deficiencies of any of these nutrients, and thus assessment of dietary status should be performed

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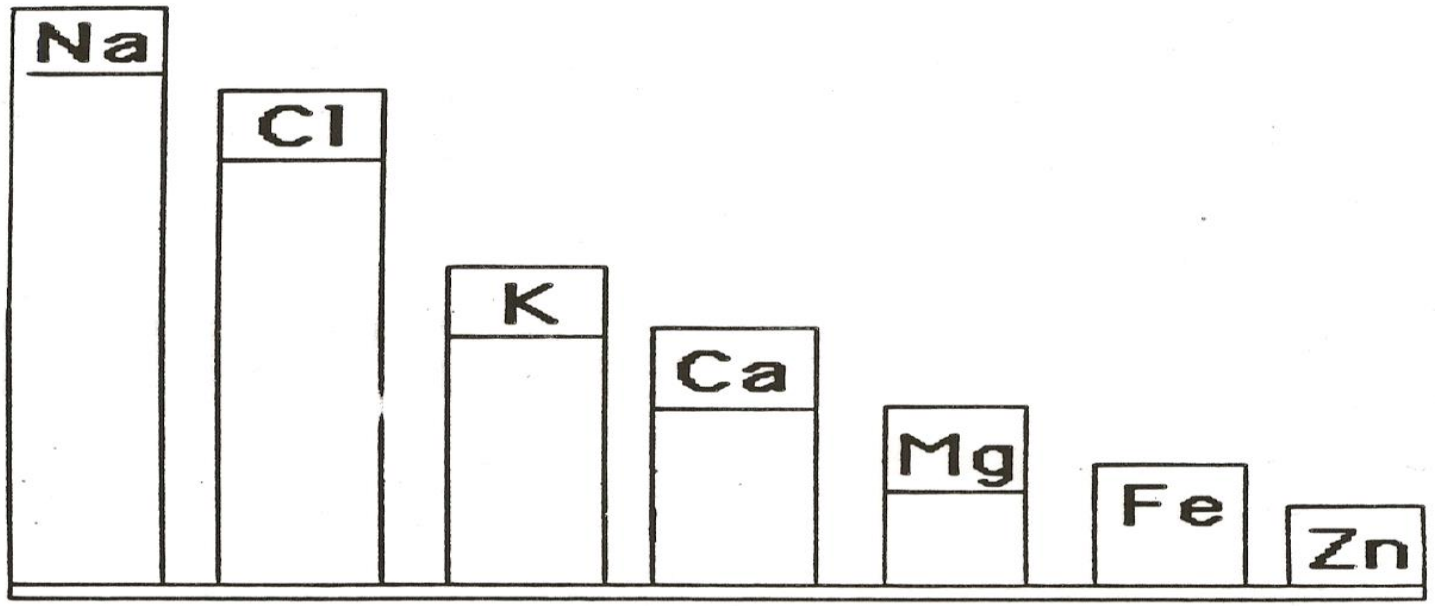
Proportions Of Minerals Lost In Sweat



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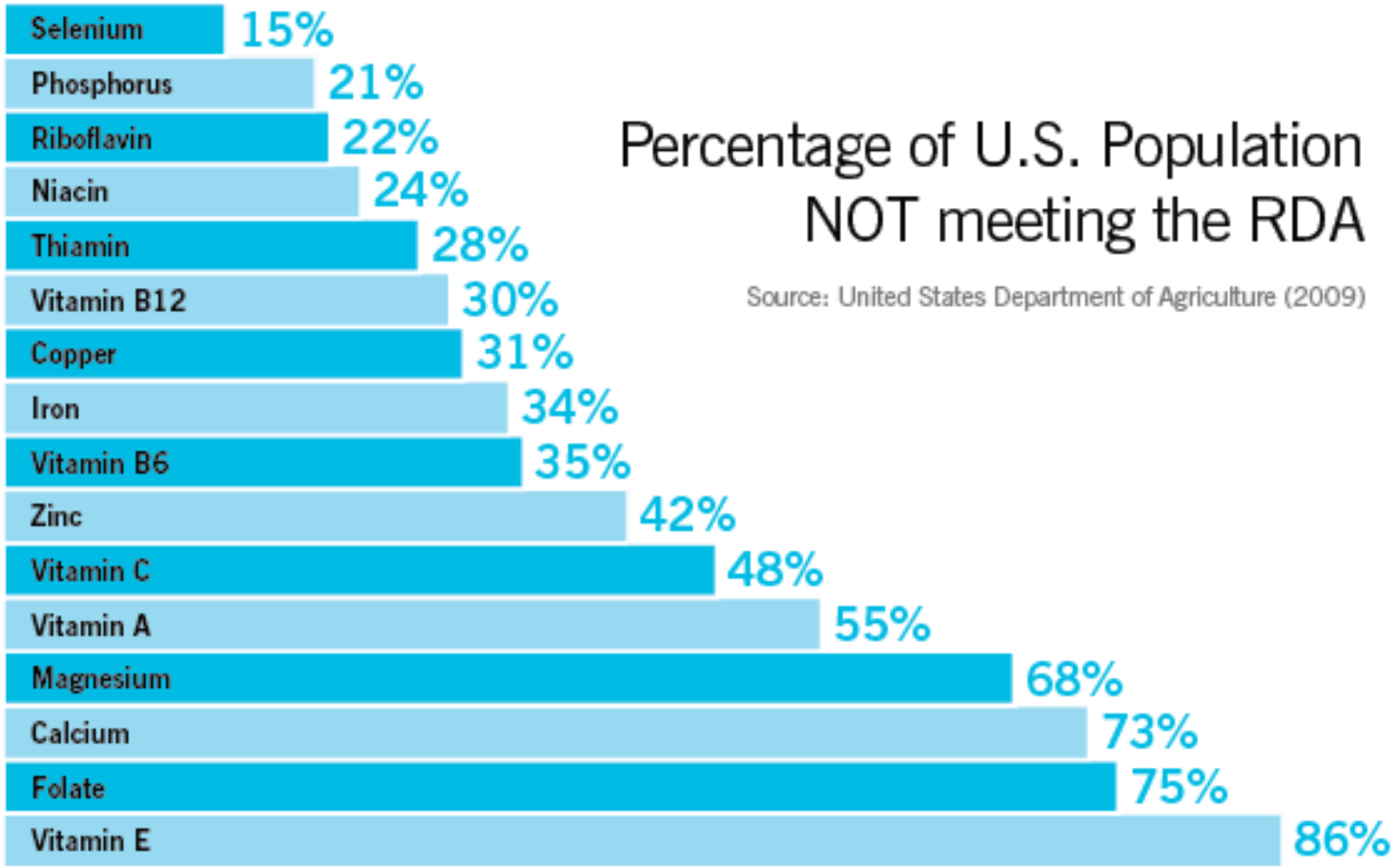
Iron, Zinc, Magnesium, Calcium: Percentage of Americans already on the margins of deficiency. Regular exercise can worsen this profile via increased loss of minerals with sweat



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Oxidative Stress Induced By Aerobic Exercise and Antioxidant Supplements

Overview

Increased aerobic metabolism generates an increased number of ROS (reactive oxygen species), which can lead to increased muscle inflammation, soreness and damage to local or distal tissue structures.

- ROS include:
  - 1. Superoxide anion
  - 2. Hydroxy radical (from hydrogen peroxide)
  - 3. Singlet oxygen (sun beats down on skin)

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Biomarkers for ROS include:

1. Malondialdehyde (dimethylmalondialdehyde- DMA) – blood levels
2. Breath Pentane

Supplementation with antioxidants (Vitamin C 500-2,000 mg, Vitamin E 200-1,000 IU, Beta-carotene 10,000-50,000 IU) shown to greatly reduce ROS biomarkers and minimize muscle damage and soreness

Next Slide Show Work of Goldfarb – Medicine and Science in Sports and Exercise Journal

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Free Radicals and Vitamin E (Goldfarb)

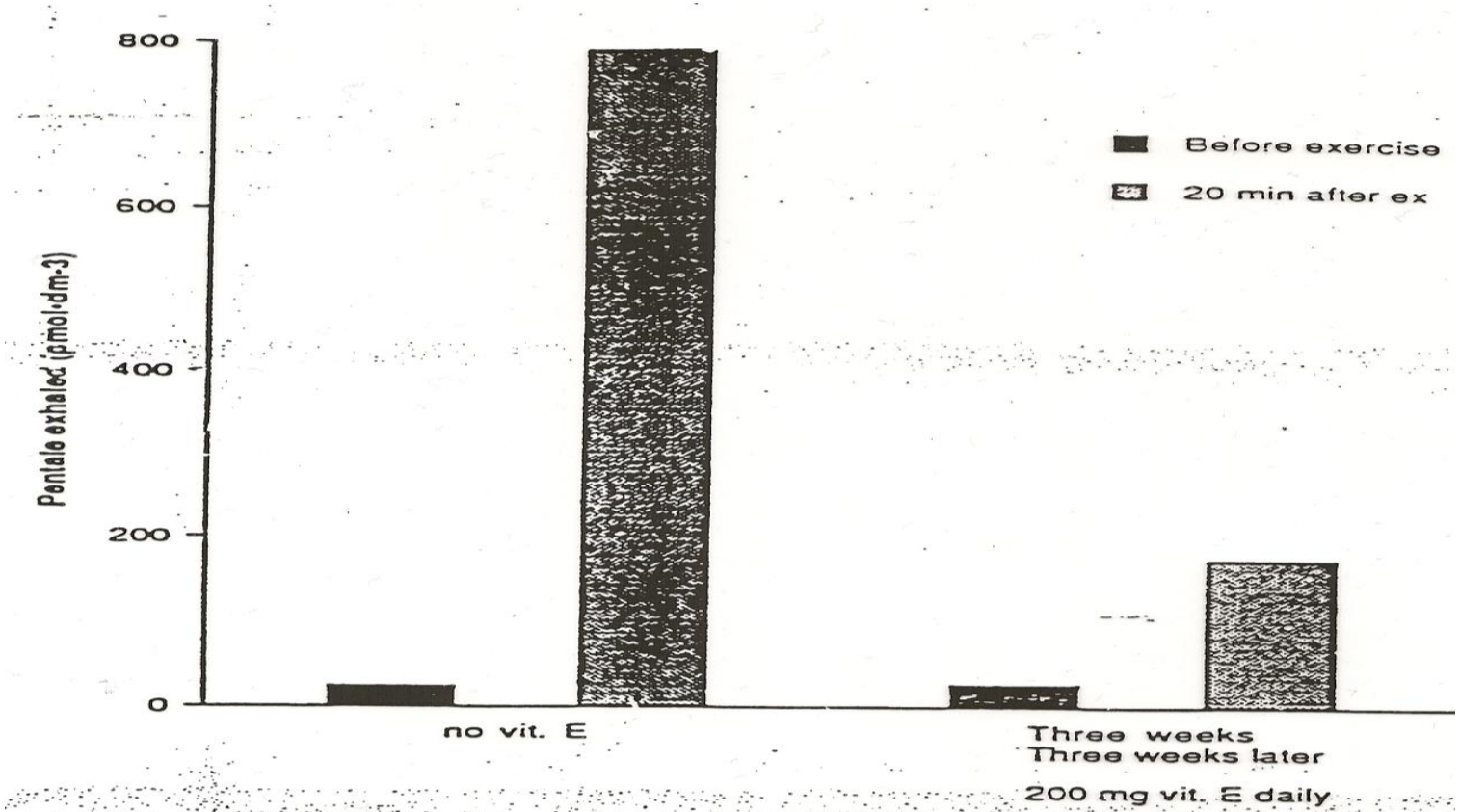

Figure 5—Pentane levels in expired breath of one subject before an
20 min after 5 min of exercise at 100% $VO_{2\,max}$ with and witho
Vitamin E supplement (ref. 40).

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Antioxidants Referenced Research

- Strenuous exercise has been shown to increase the production of reactive oxygen species (free radicals) due to increased oxygen utilization. Free radicals can damage muscle tissue, leading to inflammation and soreness, as well as increased oxidative stress to body in general. Exercising in the presence of air pollution (nitrous oxide etc.) has also been shown to increase oxidative stress to lung tissues and the general circulation. (1,2)

- Studies reveal that supplementation with various antioxidants lowers indirect markers of oxidative stress (e.g. blood levels of dimethylmalonaldehyde and breath pentane in expired air). Vitamin E (400 – 1,200 IU per day) has been shown to provide this benefit, and to protect lung tissue as well. (3,4,5) Vitamin C and Beta-carotene supplementation at 400 – 3,000 mg and 25,000 IU, respectively, have also been shown to minimize oxidative stress induced by exercise. (1) (additional reading - Kenneth Cooper, The Antioxidant Revolution).

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Several studies (double-blind) indicate that antioxidant supplementation in the above noted ranges may also reduce pain and speed up muscle recovery after intense exercise by reducing free radical damage to muscles.(6,7)

Vitamin C supplementation (600 mg per day) was also shown to reduce the incidence of upper respiratory tract infections in marathon runners within 14 days of completing a 90 km race (33% incidence) compared to the placebo group (68% incidence).

Marathon runners have also been shown to have lower blood levels of Vitamin C (by 20%) after completing a 21 km run, and demonstrate increased excretion of Vitamin C in their sweat and urine (Peters et al AJCN, 1993).

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- Another study, using a combination of Vitamin E, Vitamin C and Beta-carotene supplementation, revealed that exercising individuals taking the daily antioxidant supplement cocktail for 90 days had significantly higher levels of blood glutathione and increased superoxide dismutase and catalase enzyme activity in circulating neutrophils, than did the placebo group. (8)

- Recent studies also confirm that supplementation with vitamin E, vitamin C, and beta-carotene, reduce free radical damage to skin cells induced by exposure to ultra-violet light. During their development in the deeper layers of the epidermis, epidermal cells absorb antioxidants from the blood stream, which provides them with added antioxidant protection against sun-light induced photo-aging and against the free radical damage that causes mutations to their genetic material, which are linked to skin cancers, including melanoma, squamous cell, and basal cell carcinoma.

- It should also be noted that ultra-violet light depletes antioxidants within the skin, which increases demand for higher intake levels of nutritional antioxidants to replenish these stores.

- Skin surface lipids, a mixture of lipids excreted from epidermal cells in combination with secretions from sebaceous glands, also contain antioxidants that are derived from dietary and supplemental sources. (9,10,11,12,13,14,15,16,17,18,19,20)

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Reference 1: Antioxidants and URTIs

Daily supplementation of 500-1500 mg of vitamin C may confer benefit to individuals engaged in strenuous exercise who experience frequent URTIs

Moderate exercise heightens immune function, whereas prolonged period of intense exercise suppress and stress the body's first line of defense against infectious agents.

Additional Vitamin C and Vitamin E shown to be helpful to reduce URTIs in these cases, as well as CHO ingestion before, during and after a training period - all boost immune mechanisms

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- Although the body responds to exercise-induced oxidative stress by naturally up-regulating synthesis of its own endogenous antioxidant enzymes, exercise has been shown to increase biomarkers of oxidative stress.

- In humans supplementation with Beta-carotene, Vitamin C, and Vitamin E have lowered breath markers of lipid peroxidation at rest and following exercise compared to non-supplemented control subjects.

- 5-months of Vitamin E supplementation in racing cyclists produced a protective effect on markers of oxidative stress induced by extreme endurance exercise.

- Two weeks of Vitamin E supplementation (120 IU) decreased free radical interaction with cellular membranes and slowed muscle tissue disruption from heavy resistance training.

- Some studies have not shown a benefit from Vitamin E supplementation, which may be accounted for by differences in exercise severity and oxidative stress load.

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Exercise and the Immune System

Moderate exercise (run 20-30 km per wk) increases immune function, but intensive training can weaken immune function. (1)

After 3 hrs of endurance training:

Epinephrine and cortisol levels 59% above baseline (catabolism). This weakens immune system (high cortisone levels)

25-46% decline in natural killer cells (NKC) at 1.5-6 hrs post ex

NKC responsible for 10-15% of all lymphocytes (1st line defense against viral infections)

NKC also destroy cancer cells and mutated cells

Increased WBC count (leukocytosis) lasting for 21 hrs post ex, likely due to inflammation and elevated cortisol levels (1)

Marathon runners show higher incidence of URTIs post-race than non competitors. Vitamin C at 600 mg per day shown to reduce URTIs in this group. (Also glutamine supplementation) (2-11)

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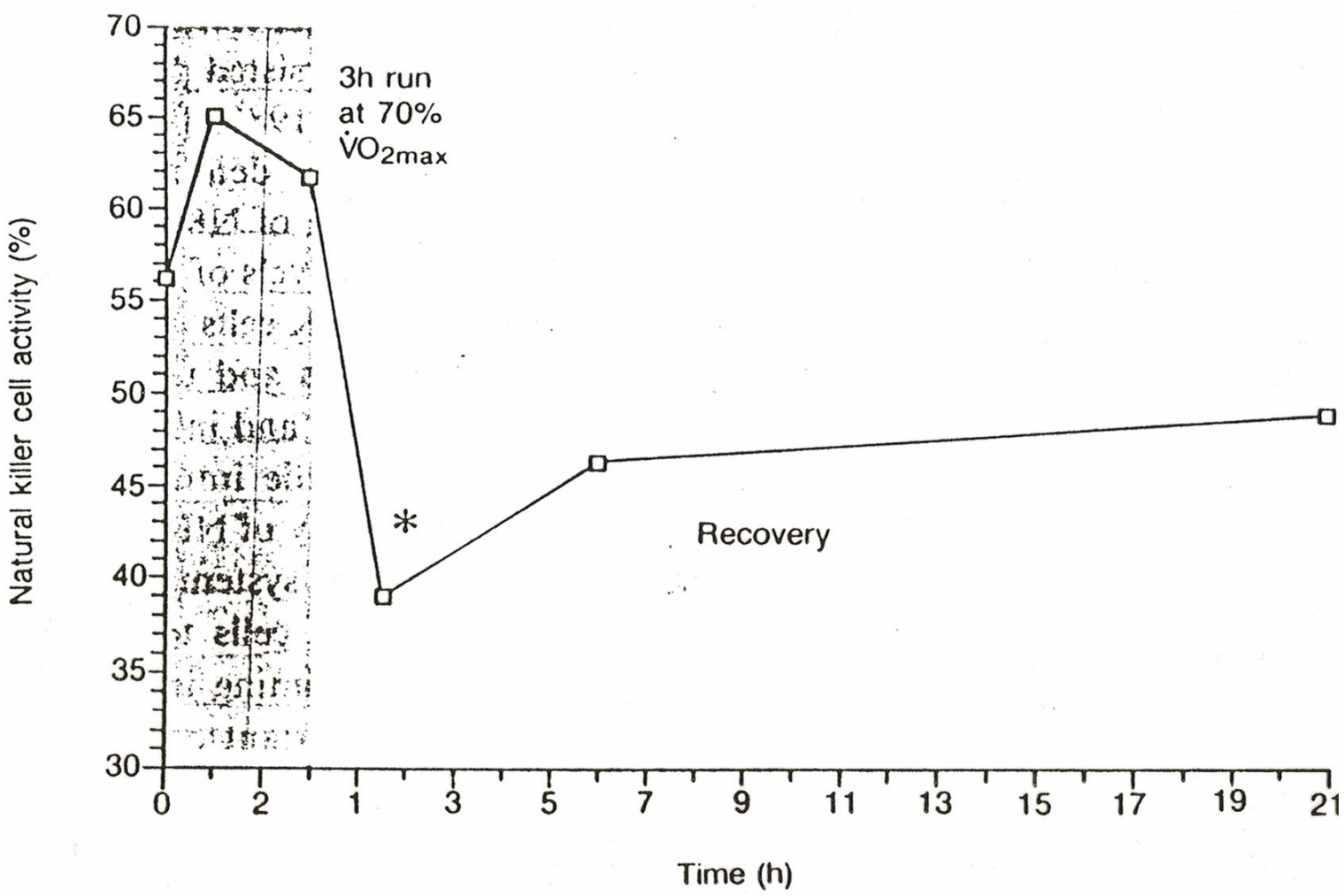
Exhaustive Exercise and Natural Killer Cells



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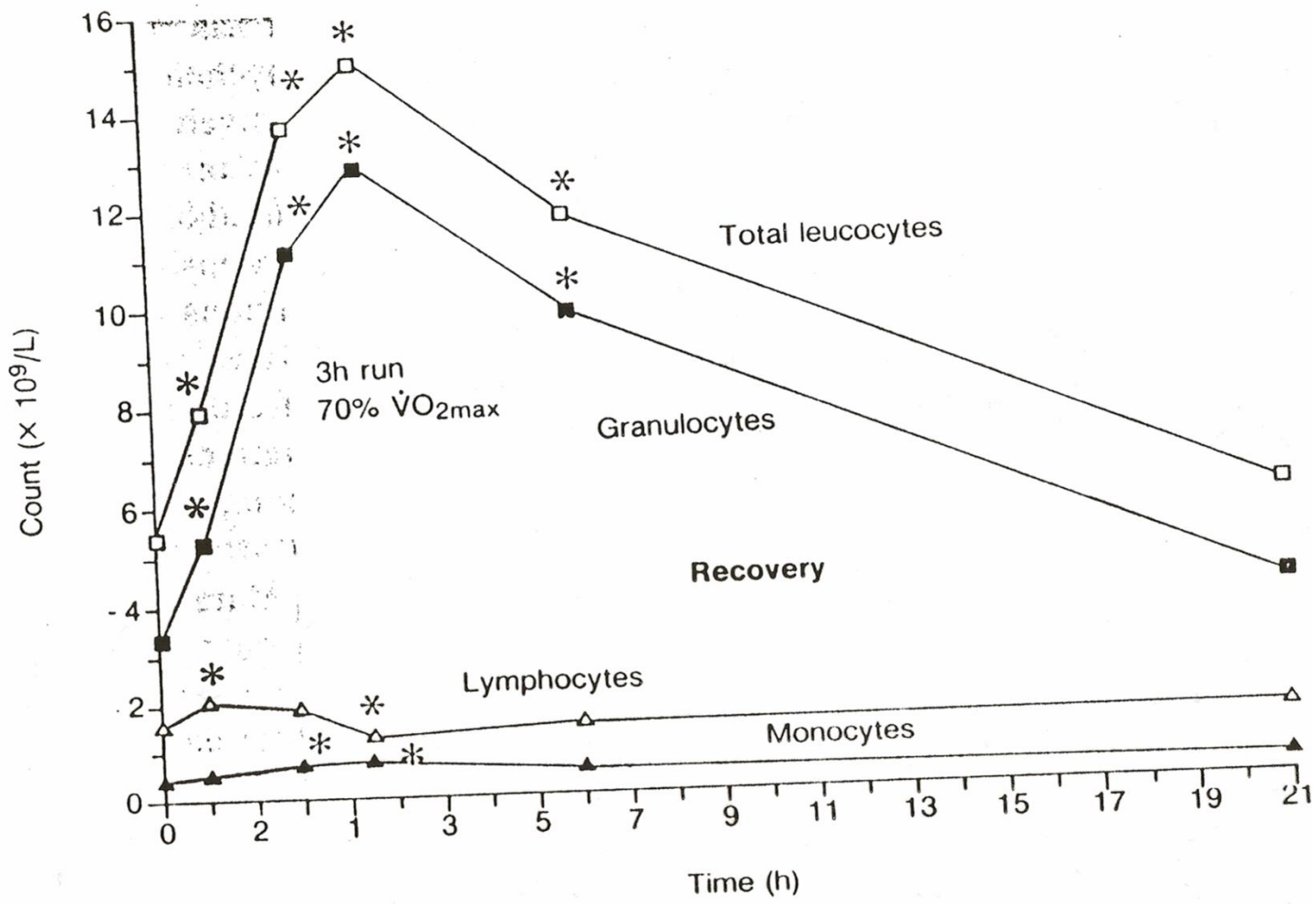
Exhaustive Exercise and WBC Response (inflammation)



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Study By Peters et al (1993 –Am J Clin Nutr):

- 14 days after a 90 km road race on foot, the vitamin C group (600 mg per day during training and after) showed 33% incidence of URT infections vs 68% in the placebo group, who's symptoms were more severe and lasted longer

- A 21 km run produced a 20% decline in plasma Vitamin C, (on average) with increased Vitamin C excretion in urine and sweat.

- Vitamin C used to quench oxygen free radicals generated during aerobic metabolism, hence its requirement increases (12-14)

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Vitamin C (600 mg) decreases URT In Runners

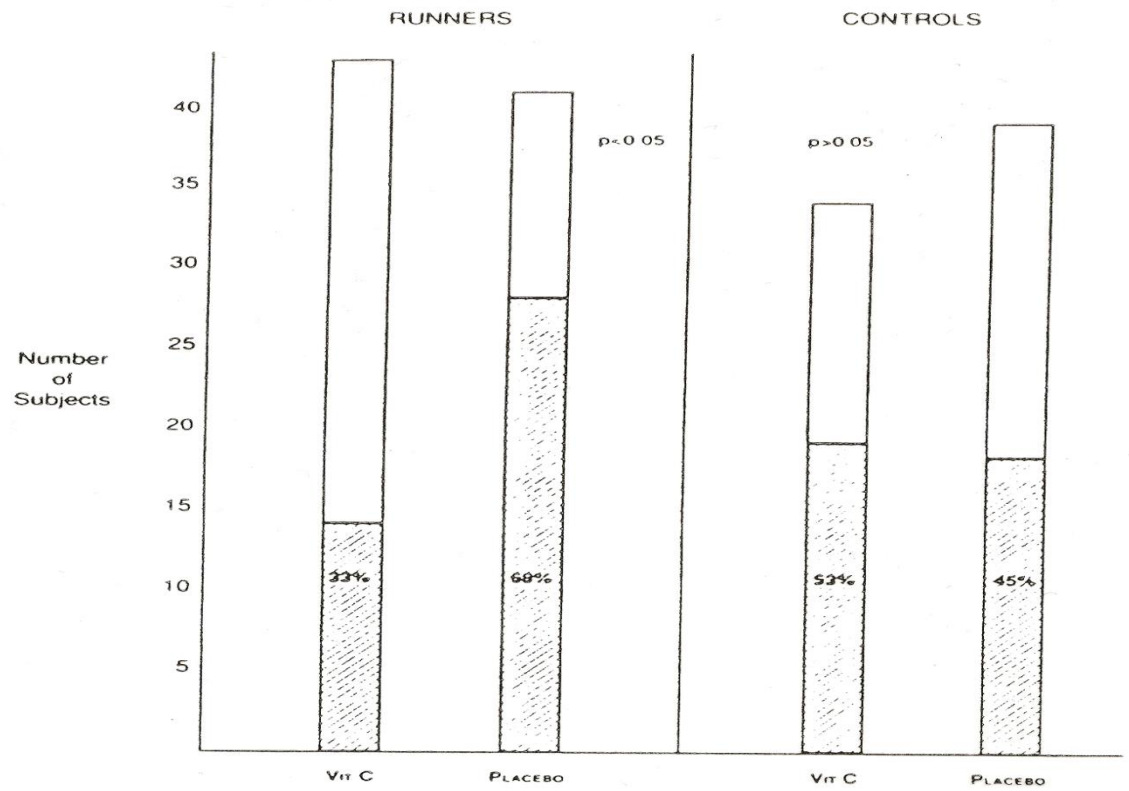

FIG 1. The incidence of symptoms of upper-respiratory-tract infection in groups of runners and control subjects receiving either 600 mg vitamin C/d or a placebo. Note that the incidence of symptoms was significantly less in runners ingesting vitamin C (□, symptomatic; □, asymptomatic).

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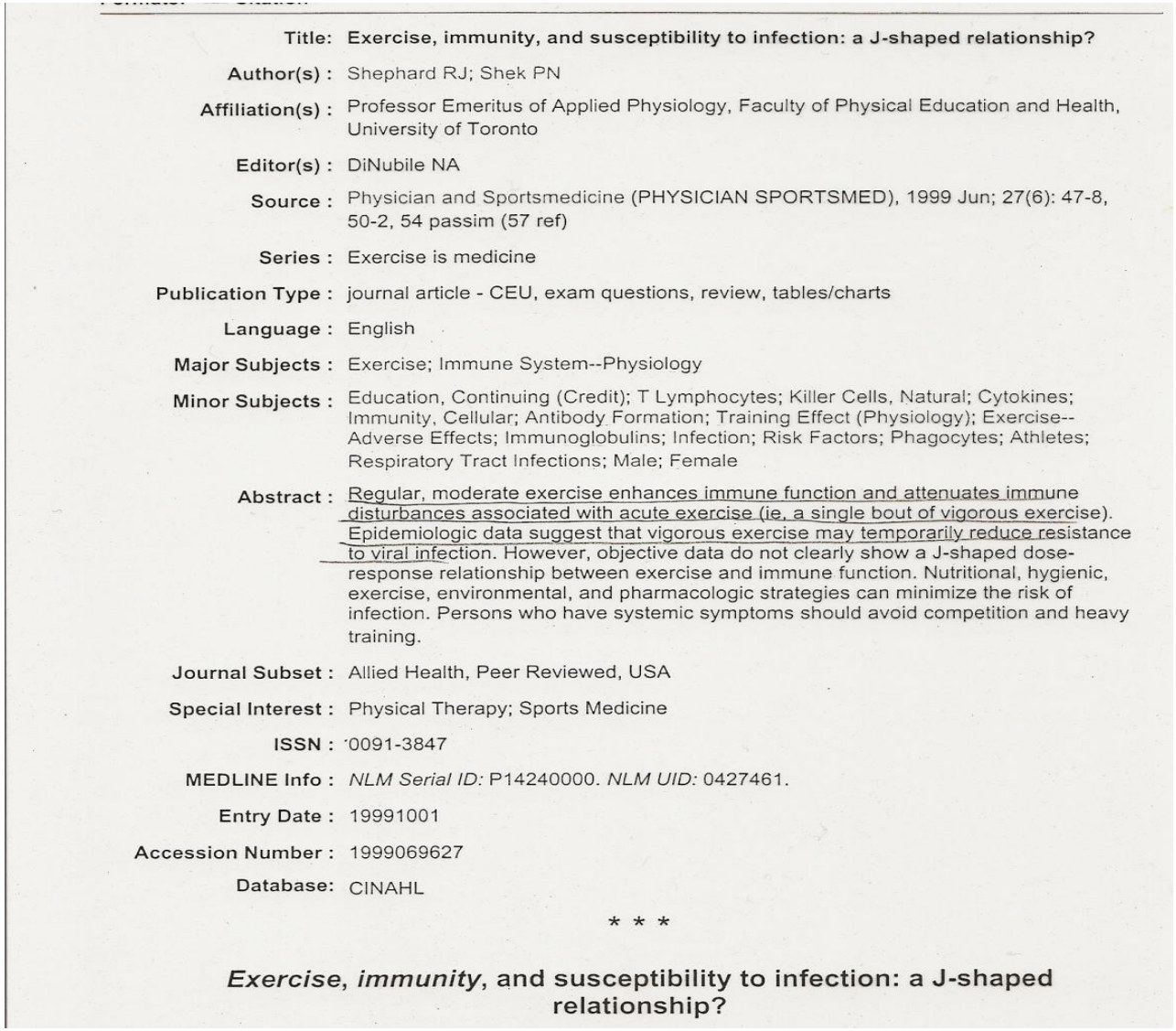
Moderate Exercise Enhances Immune Function (J-Shaped Curve)



Title: **Exercise, immunity, and susceptibility to infection: a J-shaped relationship?**

Author(s) : Shephard RJ; Shek PN

Affiliation(s) : Professor Emeritus of Applied Physiology, Faculty of Physical Education and Health, University of Toronto

Editor(s) : DiNubile NA

Source : Physician and Sportsmedicine (PHYSICIAN SPORTSMED), 1999 Jun; 27(6): 47-8, 50-2, 54 passim (57 ref)

Series : Exercise is medicine

Publication Type : journal article - CEU, exam questions, review, tables/charts

Language : English

Major Subjects : Exercise; Immune System--Physiology

Minor Subjects : Education, Continuing (Credit); T Lymphocytes; Killer Cells, Natural; Cytokines; Immunity, Cellular; Antibody Formation; Training Effect (Physiology); Exercise--Adverse Effects; Immunoglobulins; Infection; Risk Factors; Phagocytes; Athletes; Respiratory Tract Infections; Male; Female

Abstract : Regular, moderate exercise enhances immune function and attenuates immune disturbances associated with acute exercise (ie, a single bout of vigorous exercise). Epidemiologic data suggest that vigorous exercise may temporarily reduce resistance to viral infection. However, objective data do not clearly show a J-shaped dose-response relationship between exercise and immune function. Nutritional, hygienic, exercise, environmental, and pharmacologic strategies can minimize the risk of infection. Persons who have systemic symptoms should avoid competition and heavy training.

Journal Subset : Allied Health, Peer Reviewed, USA

Special Interest : Physical Therapy; Sports Medicine

ISSN : 0091-3847

MEDLINE Info : *NLM Serial ID:* P14240000. *NLM UID:* 0427461.

Entry Date : 19991001

Accession Number : 1999069627

Database: CINAHL

* * *

***Exercise*, *immunity*, and susceptibility to infection: a J-shaped relationship?**

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Reference 1: Strenuous Exercise and Impaired Immunity

Strenuous exercise (marathon run, intense training session) provides an “open window” (3-72 hours) of decreased antiviral and antibacterial resistance and increased risk of URT infection (by two to six times) that manifests itself within 1 or 2 weeks.

For example, at least 13% of the participants in the Los Angeles marathon reported an episode of URTI during the week following the race. For runners of comparable ability who did not run the race, the URTI incidence was 2%.

A bout of moderate exercise boosts natural immune functions and host defenses for up to seven hours, such as increase NK cell activity. They are part of innate immunes system which requires no prompting to destroy viruses and emerging cancer cells.

A prolonged bout of exhaustive exercise (or other forms of extreme stress or increased training) severely impairs the body’s first line of defense against infection, decreasing activity of neutrophils, lymphocytes and select CD-cells. Elevated temperature, cytokines, and various stress-related hormones (epinephrine, GH, cortisol, certain beta-endorphins) may mediate depression of innate immune system (NK cells and neutrophil activity) and adaptive T and B lymphocyte immune defenses with exhaustive exercise and worsened by second bout of exercise on same day.

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Regular aerobic exercise of moderate duration (20-45 minutes) has a positive effect on immune function, increasing resistance to stress in young and older individuals and in the obese during periods of weight loss.

Areas of improvement include enhanced cytotoxic immune mechanisms (i.e. antitumor actions of NK cell activity) **and slowing of the age-related decline in T-cell function and associated cytokine production.**

Cytotoxic T-cells defend against viruses and fungal infections

Natural Killer Cells increase 225% following an **acute bout of resistance training**, a response similar to the immediate effect of moderate aerobic exercise.

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In conjunction with strenuous exercise - A high fat diet (62% fat) negatively affects immune function compared with a CHO-rich diet (65%).

Consuming CHO prior, during and after exercise shown to keep the immune system functioning at more optimal level – similar intake of CHO as for optimizing athletic performance. This strategy helps to **suppress cortisol** and induce immune response (increased phagocytosis by immune cells and increased anti-inflammatory cytokine release) regardless of age and gender.

Combined supplementation with Vitamin C and Vitamin E produce more prominent immunopotentiating effects (enhanced cytokine production) in young healthy adults than supplementation with either of them alone.

More than likely the presence of other stressors – lack of sleep, mental stress, poor nutrition, or weight loss – magnifies the stress on the immune system from a single but of (or repeated bouts) of exhaustive exercise.

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Vitamins C, E and Beta-Carotene Supplementation Enhances Neutrophil Antioxidant Function In Athletes

Title: **Diet supplementation with vitamin E, vitamin C and beta-carotene cocktail enhances basal neutrophil antioxidant enzymes in athletes.**

Author(s) : Tauler P; Aguiló A; Fuentespina E; Tur JA; Pons A

Author's Address : Laboratori de Ciències de l'Activitat Física and Departament de Biologia Fonamental i Ciències de la Salut, Edifici Guillem Colom. Facultat de Ciències, Universitat de les Illes Balears, Campus Universitari, 07071, Palma de Mallorca, Balears, Spain.

Source : Pflugers Archiv : European journal of physiology [Pflugers Arch] 2002 Mar; 443 (5-6), pp. 791-7.

Pub. Type : Clinical Trial; Journal Article; Randomized Controlled Trial

Language : English

Journal Info : *Country of Publication:* Germany *NLM ID:* 0154720 *ISSN:* 0031-6768 *Subsets:* IM

MeSH Terms : Antioxidants/*administration & dosage
Ascorbic Acid/*administration & dosage
Neutrophils/*enzymology
Vitamin E/*administration & dosage
beta Carotene/*administration & dosage
Adult; Catalase/metabolism; Diet; Double-Blind Method; Drug Synergism; Exercise/physiology; Glutathione Disulfide/metabolism; Glutathione Peroxidase/metabolism; Glutathione Reductase/metabolism; Human; Male; Neutrophils/drug effects; Oxidative Stress/drug effects; Sports; Superoxide Dismutase/metabolism

Abstract : Exercise increases oxygen consumption and causes a disturbance of intracellular pro-oxidant-antioxidant homeostasis. Few data are available as to the cumulative effects of exercise on the antioxidant defenses of the neutrophil. We studied the effects of 90 days' supplementation with placebo or an antioxidant cocktail of vitamin E (500 mg/day) and beta-carotene (30 mg/day) and the last 15 days also with vitamin C (1 g/day) on sportsmen's basal neutrophil antioxidant defenses. We analyzed the activities of catalase, glutathione peroxidase, glutathione reductase and the activities and levels of superoxide dismutase, glutathione and glutathione disulfide in neutrophils purified from antecubital vein blood of sportsmen before and after diet supplementation. Plasma vitamin E, beta-carotene and vitamin C concentrations in the antioxidant-supplemented group were approximately 1.6, 10, and 1.2 times higher respectively than those of the placebo group. The antioxidant-supplemented group presented a significantly higher glutathione versus glutathione disulfide ratio in neutrophils (about 20%) than the placebo one. Antioxidant supplementation enhances the antioxidant enzyme activity of superoxide dismutase and catalase in neutrophils.

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Glutamine: Overview

- The adventures of glutamine were reviewed previously
- Studies show blood glutamine levels declines with exercise
- Two short term double-blind studies with athletes failed to show an anti-catabolic effect or anabolic effect of glutamine supplementation (athletes base their use on burn victim and other studies)

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- Glutamine supplementation (5gm taken at end of each work out) reduced incidence of URT infections in athletes to 19% vs 51% (non supplement users) during study period (primary fuel for immune cells)

- Glutamine supplementation (2,000-4,000 mg per day) shown to increase GH and IGF-I levels after age 35-40. Unknown effect on younger groups. (Also ornithine alpha-ketoglutarate)

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Positive Immune Effects Of Glutamine Supplementation

Title: **The relation between glutamine and the immunodepression observed in exercise.**

Author(s) : Castell LM; Newsholme EA

Author's Address : University Department of Biochemistry, Oxford, United Kingdom.

Source : Amino acids [Amino Acids] 2001; 20 (1), pp. 49-61.

Pub. Type : Journal Article; Review; Review, Tutorial

Language : English

Journal Info : *Country of Publication:* Austria *NLM ID:* 9200312 *ISSN:* 0939-4451 *Subsets:* IM

MeSH Terms : Exercise*
Immune Tolerance*
Glutamine/*metabolism
Amino Acids/physiology; Animal; Fatigue; Glutamine/blood; Human; Immune System/physiology; Models, Biological; Neutrophils/metabolism; Respiratory Tract Infections/metabolism

Abstract : Glutamine is the most abundant amino acid in the body. It is an important fuel for some key cells of the immune system. Both the plasma concentration of glutamine and the functional ability of immune cells in the blood are decreased after prolonged, exhaustive exercise. Glutamine feeding has had beneficial effects in clinical situations, and the provision of glutamine after intensive exercise has decreased the incidence of infections, particularly of upper respiratory tract infections. However, the precise effect of glutamine on immunodepression in this situation is not yet established.

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Anti-Catabolic Effects Of Glutamine Supplementation

Title: **Glutamine: a potentially useful supplement for athletes.**

Author(s) : Antonio J; Street C

Author's Address : Dept. of HPERLS, Human Performance Laboratory, University of Nebraska-Kearney, Kearney, NE 68849, USA.

Source : Canadian journal of applied physiology = Revue canadienne de physiologie appliquee [Can J Appl Physiol] 1999 Feb; 24 (1), pp. 1-14.

Pub. Type : Journal Article; Review; Review, Tutorial

Language : English

Journal Info : *Country of Publication:* UNITED STATES *NLM ID:* 9306274 *ISSN:* 1066-7814 *Subsets:* IM

MeSH Terms : Dietary Supplements*
Glutamine/*metabolism
Glutamine/*pharmacology
Immune System/*drug effects
Muscle, Skeletal/*metabolism
Sports/*physiology
Animal; Blood Glucose/metabolism; Human; Muscle Proteins/metabolism

Abstract : The role of glutamine as a possible ergogenic aid has not been posited in the scientific literature. Although there is an abundance of clinical evidence supporting the need for exogenous glutamine in the maintenance of muscle protein mass and immune system function in critically ill patients, little work has been done that examines the potential utility of glutamine for athletes engaged in heavy exercise training. This brief review will describe a number of studies on the effects of glutamine supplementation on muscle protein mass, immune system function, and glucose regulation. Based on the available clinical evidence, we would speculate that glutamine has potential utility as a dietary supplement for athletes engaged in heavy exercise training.

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L-Glutamine

- Glutamine is a non–essential amino acid in that the body can synthesize it from glutamic acid via glutamine synthase enzyme. However, during periods of fasting, starvation, critical illness, cancer, AIDS and following trauma, radiation treatment, surgery, bone marrow transplantation or in patients with a weakened immune system or undergoing catabolic stress (burn victim), extra glutamine replenishment has been shown to be beneficial to help re-establish homeostasis.

- Glutamine is the main anti-catabolic agent in muscle, which helps preserve muscle tissue (preventing its breakdown). The heavier one trains, the greater the stress on the muscle and the greater the use of glutamine. As such, some athletes use glutamine as an anti-catabolic supplement to reduce the amount of muscle catabolism that occurs during a work out.

- During and following exercise or trauma, large amounts of alanine and glutamine are released from muscle. The loss of alanine and glutamine induced by exercise is above the amounts available and represents more than 50% of the total loss of muscle amino acids. Thus, other amino acids (branched-chain amino acids) are used to make alanine and glutamine under these conditions, which then results in catabolism of muscle protein.

- Support for the use of glutamine supplementation is derived from studies that show that it can be used to maintain muscle mass in catabolic patients (e.g., burn victims). However, two small double-blind placebo-controlled trials involving individuals (18 – 24 year old subjects) performing resistance training failed to show improvement in performance, composition or muscle protein degradation over the short term (six weeks), using doses of 0.9 gm and 0.3 gm per kg of body weight, respectively.

- It is known that intense exercise lowers blood levels of glutamine, which can remain persistently low with over training.

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- Glutamine supplementation may increase ammonia levels and add to the ammonia burden of certain patients and athletes, jeopardizing recovery and performance, respectively.

- However, supplementation with ornithine alpha-ketoglutarate has been shown to act as a glutamine precursor, without contributing to ammonia build up, and thus may be a better choice.

- As well, ornithine alpha-ketoglutarate reduces muscle catabolism in burn and surgery patients and is known to increase muscle glutamine levels.

- Both glutamine supplementation (2 grams per day) and ornithine alpha-ketoglutarate (2 – 4 gms per day) supplementation have been shown to increase the release of growth hormone, which may be useful in the long run to help maintain and build additional lean mass, in conjunction with resisted exercise training. This may be a greater importance to older individuals than young athletes, as younger athletes already have high circulating levels of growth hormone.

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- It should also be noted that glutamine is the primary energy source for intestinal epithelial cells and is a vital nutrient for immune cells. Glutamine supplementation in endurance athletes has been shown to reduce the incidence of infections in this population, who are known to have their immune system suppressed by excess training of this nature.

- A double blind placebo-controlled study showed that glutamine supplementation at a dose of 5 gm, taken after the end of exercise, in 151 endurance athletes resulted in a significantly lower incidence of infections (19%) compared to the placebo group (51%) during the study period.
-

  It is has been suggested that the immune system suppression associated with endurance exercise, may be in part, due to reduction in glutamine that results from intensive training. Another study, using the same protocol, demonstrated that 81% of athletes taking glutamine had no subsequent infection during the study period compared to 49% in the placebo group.

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- For those who wish to use glutamine, experts suggest that it is generally regarded as a safe supplement at doses up to 2 gm per day.

- However, those who are sensitive to monosodium glutamate should use it with caution, as glutamine is metabolized into glutamate in the body.

- Glutamine may also trigger epileptic seizures in epileptics, and there are two case reports linking glutamine supplementation (more than 2 gm per day) to episodes of mania, in patients with no previous history of bipolar disorder.

Reference: Glutamine: http://www.dynamicchiropractic.com/mpacms/dc/article.php?id=52041

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Glutamine Referenced Research

- Glutamine can also serve as precursor to glucose synthesis in the liver, and if available in high concentrations, has been shown to reduce the reliance upon alanine formation.

- Hence, increased ingestion of glutamine or increased glutamine stores can reduce the catabolic effect on the structural amino acids in muscles (leucine, isoleucine and valine). These three amino acids comprise 30% of all the structural amino acids in skeletal muscle.

- For this reason, glutamine supplementation has been shown to be anti-catabolic in patients experiencing catabolic conditions (burn victims, post-surgery, possibly intensive exercise etc. – see glutamine).

- In the body, glutamine constitutes the largest single component of the free amino acid pool. Glutamine is the amino acid that is found in highest concentrations in the blood and it also serves as a free amino acid in peripheral tissues, including muscle. Although it contains two amide groups, **it is very non-toxic.** In fact, one of its roles is to shuttle amide groups to the liver from peripheral tissues, which are in turn converted to urea and discarded by the body.

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- The deamination of amino acid releases ammonia (NH3, NH4), which is a highly toxic compound to the human body. To guard against ammonia toxicity the body attaches these amide (NH2 and NH3) groups to glutamate in peripheral tissues to form glutamine. In this form, these amide groups are non-toxic.

- Once glutamine travels to the liver from these peripheral tissues, including muscle tissue, the amide groups are extracted forming urea, and the carbon skeleton can be used to make glucose if the body is in a low energy state.

- Thus, one of the endogenous sources of glutamine is the transfer of amide groups to glutamate (to form glutamine), which occurs in the deamination (catabolism) of various amino acids during catabolic states (including exercise)

- In review, glutamine formed in peripheral tissues can travel to the liver. After discarding the amide groups to form urea, the carbon skeleton can be used to form glucose if the body is in a low energy state. This occurs as glutamine is first converted to alpha –ketoglutarate (deamination of NH2 and NH3 groups use to form urea).

- From there, alpha- ketoglutarate is converted to oxaloacetate, then to phosphoenolpyrvate, which can back peddle to glucose. Dietary and supplemental glutamine can also serve as source of glucose in the liver, sparing the catabolism of branched-chain amino acids in skeletal muscle, by reducing the demand for alanine as a glucose precursor. This is one way in which, glutamine supplementation has been shown to be anti-catabolic.

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- Glutamine supplementation has also been shown to stimulate the release of growth hormone from the pituitary gland, which in turn stimulates the release of insulin-like growth factor-I (IGF-I) from the liver. This hormone (IGF-I) is known to stimulate anabolic processes, including protein synthesis within skeletal muscle.

- Thus, in older patients, who exhibit lower circulating levels of growth hormone and IGF-I, glutamine supplementation can act to preserve or increase lean mass, in conjunction with adequate protein intake and resisted exercise training, by raising serum levels of IGF-I as much as 30%.

- As such, 2,000 to 4,000 mg of glutamine supplementation (usually in conjunction with other amino acids that act as growth hormone releasing factors, or secretagogues), may spare the breakdown of branched-chain and other structural muscle amino acids, and stimulate the further synthesis of myofilaments (muscle protein contractile bands), within the muscle, helping to preserve and increase lean mass.

- Note that ornithine alpha-ketoglutarate, which the body can convert into glutamine, has been shown to be an even more potent stimulator of growth hormone and IGF- I release upon supplementation at a dose of 10 gm per day. This molecule consists of ornithine bound to two molecules of alpha-ketoglutarate (Grow Young With HGH. R. Klatz. 1997).

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Protein and Amino Acid Daily Turnover and Multi-Modal Function

- The large free amino acid pool (blood and tissue) in the body ensures the continuous availability of individual amino acids to tissues for the synthesis of proteins, neurotransmitters, and other nitrogen-containing compounds. **A well-nourished individual experiences a 300-600 gm protein degradation per day, and about a 100 gm ingestion of dietary protein.**

- **From this pool, tissues utilize amino acids for the continuous synthesis of new proteins (300-600 gm) to replace those degraded.** The continuous turnover of proteins in the body makes the complete complement of amino acids available for the synthesis of new and different proteins, such as antibodies.

- It also provides a complete pool of specific amino acids which can be utilized as oxidizable substrates: precursors for gluconeogenesis and the formation of ketones, and for heme, creatine phosphate, purine, pyrimidine, neurotransmitter synthesis, for ammonia-genesis to maintain blood pH (if acidity should increase as in acidosis), and for numerous other functions.

- The efflux of amino acids from skeletal muscle supports the essential amino acid pool in the blood. Skeletal muscle oxidizes the branched-chain amino acids to produce energy and the carbon skeleton from which muscles can make more glutamine. Alanine and glutamine account for about 50% of the total alpha-amino nitrogen released by skeletal muscle.

- The amino groups of branched-chain amino acids and of aspartate and glutamate are transferred out of skeletal muscle in alanine and glutamine. Hence, under hyper-catabolic conditions labile amino acids are degraded in this fashion to support blood sugar (alanine and glutamine converted to glucose in the liver).

- The formation of glutamine (also from the catabolism of branched-chain amino acids) is also required as a fuel by rapidly dividing immune cells (e.g., lymphocytes and macrophages), and for protein synthesis in cells involved in the immune response and wound healing, as is the case in burn victims and in other hyper-catabolic states.

- The hormones primarily involved in the degradation of structural muscle proteins are glucagon and cortisol (cortisol is released under periods of stress). Thus, athletes need to pay attention to the testosterone to cortisone ratio, as over-training increases cortisone release, which encourages the breakdown of muscle protein.

- **Branched-chain Amino Acids (leucine, isoleucine, valine)**

Within skeletal muscle the branched-chain amino acids are deaminated during exercise. Their amide group (NH2) is hooked on to pyruvate to form the amino acid alanine, which exits the muscle and travels to the liver through the blood stream to serve as a source of glucose. Their carbon backbone can also serve as an energy substrate for oxidation in the production of ATP. In the liver, alanine is first converted back to pyruvate (essentially, the amide group is remove from alanine and used to form urea). Pyruvate is then converted to oxaloacetate, and then to phosphoenolpyruvate, and then to glucose. The deamination of alanine increases the production of urea within the liver.

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References: Glutamine and BCAA

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3. Lamb D. Physiology of Exercise, second edition. Macmillan Publishing Company; 1984.
4. Baechle T, editor. Essentials of Strength Training and Conditioning. Hong Kong: Human Kinetics; 1994.
5. Klatz R. Grow Young With HGH. Harper Perennial (HarperCollins Publishers); 1997. p. 200 – 227
6. Kreider R. Effects of protein and amino-acids supplementation on athletic performance. Sportscience vol 3, number 2. 1999. Pages: 1-11

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Reference 1: Glutamine Update

Glutamine shown to counteract the catabolic effect of glucocorticoid drugs (i.e. prednisone). Cortisol, which is also elevated with intense training, decreases amino acid transport into the cell, which depresses protein synthesis, and stimulates protein catabolism – except in the liver which uses these available amino acids for glucose synthesis. (Using Adrenal Adaptogen Herbs that suppress cortisol release from intense training is employed by many weight lifters and other high-intensity training athletes to try to suppress over-secretion of cortisol)

Adaptogen Herbs that Suppress Cortisol Release:

Ashwaghanda

Rodiola

Schisandra

Glutamine supplementation modulates glucose homeostasis during and after exercise in a direction that facilitates post-exercise recovery**. It also promotes muscle glycogen accumulation in human muscle recovery – likely via gluconeogenic pathway**.

Glutamine plasma concentrations decrease following prolonged high-intensity exercise, so a glutamine deficiency has been linked to the immuno-suppression caused by strenuous exercise and increased risk of URT

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- Glutamine required by lymphocytes and macrophages for nucleotide synthesis, in disease-fighting process against infections

- Sepsis (infection), injury, burns, surgery, and endurance exercise lower glutamine levels in plasma and skeletal muscle, as glutamine get used up during exercise and increased metabolic rate to synthesize glucose and help rid body of ammonia from amino acid deamination (catabolism) seen under these conditions.

- **A lowered plasma glutamine concentration contributes to immune suppression that accompanies strenuous exercise.**

- Marathoners who ingested a glutamine drink (containing 5 gm glutamine) at the end of a race and then 2-hrs later reported fewer URTIs than unsupplemented runners.

- Glutamine ingested at time 0, 30min, 60min and 90min after marathon race prevented decline in plasma glutamine level, but no evidence of improved immune function as a result.

- Recall that glutamine may also have anti-catabolic effects, preserving muscle mass, **inhibit release of cortisol** (to guard against further muscle protein catabolism and weakened immunity) and **increase GH release** (anabolic effects), as well providing primary fuel to intestinal epithelial cells and many immune cells. Thus, optimizing glutamine nutritional status appears to be prudent, especially given the fact that exercise depletes plasma glutamine.

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Other Considerations in Strengthening The Immune system:

- In addition to a healthy diet, supplementation with antioxidants and zinc, as well as L-glutamine, daily supplementation with **Astragalus** and **Reishi mushroom extract** (**and Medicinal Mushroom Blends**) may be considered for athletes striving to prevent a weakening of immune function secondary to strenuous training.

- The prolonged use of echinacea is discouraged as it may trigger underlying autoimmune conditions or re-activate herpetic or other hyper-immune responses

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Astragalus:

- Astragalus used for at least 2,000 years to enhance immune function (China)
- The primary active ingredients, triterpene glycosides (including exclusive polysaccharides), and flavonoids have been shown to:
  - 1. Prevent the common cold in double-blind studies
  - 2. Significantly enhance lymphocyte proliferation
  - 3. Increase secretion of many cytokines required for optimal immune function
  - 4. Increase T-cell cytotoxicity
  - 5. Increase NKC cytotoxicity
  - 6. Provide direct anti-viral effects
- Dosage: 100-200 mg (2:1 extract) – for prevention of common cold (Up to 500 mg. 3X/day as Rx dose)

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Reishi Mushroom Extract:

- Reishi mushroom (the mushroom of immortality) used for > 2,000 years (China) as an anti-cancer and immune-enhancing supplement.

- Its unique polysaccharide agents and ganoderic acids provide the following benefits:
  - 1. Increase secretion of important cytokines for optimal immune function
  - 2. Raise IgA levels improving immunity in the URTI
  - 3. Direct anti-viral agents against herpes and other viruses
  - 4. Protect the liver against various toxins

- Dosage: General wellness - 30-120 mg per day (std to 10-12% polysaccharide content). Therapeutic use – up to 250 mg, 4X/day.

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Pelagonium sidoides

- Emerging evidence that Herbal Extract EPs7630, containing Pelagonium sidoides extract) improves immune parameters in exercising athletes, with studies showing decreased severity and time to recovery in individuals using this formula who had URTIs, including bronchitis and acute rhinosinusitis.

- It has potential to reduce URTI incidence as it improve immunity of upper respiratory tact.

- Reference: Abstracts From the December 2016 International Sports and Exercise Nutrition Conference in Newcastle upon Tyne. Human Kinetics Journals >International Journal of Sport Nutrition and Exercise Metabolism ; Volume 27, Issue Suppl 1:
- https://journals.humankinetics.com/doi/abs/10.1123/ijsnem.27.s1

- **Pelargonium sidoides** - Medicinal plant, native to South America – used traditionally to treat URTI and related infections

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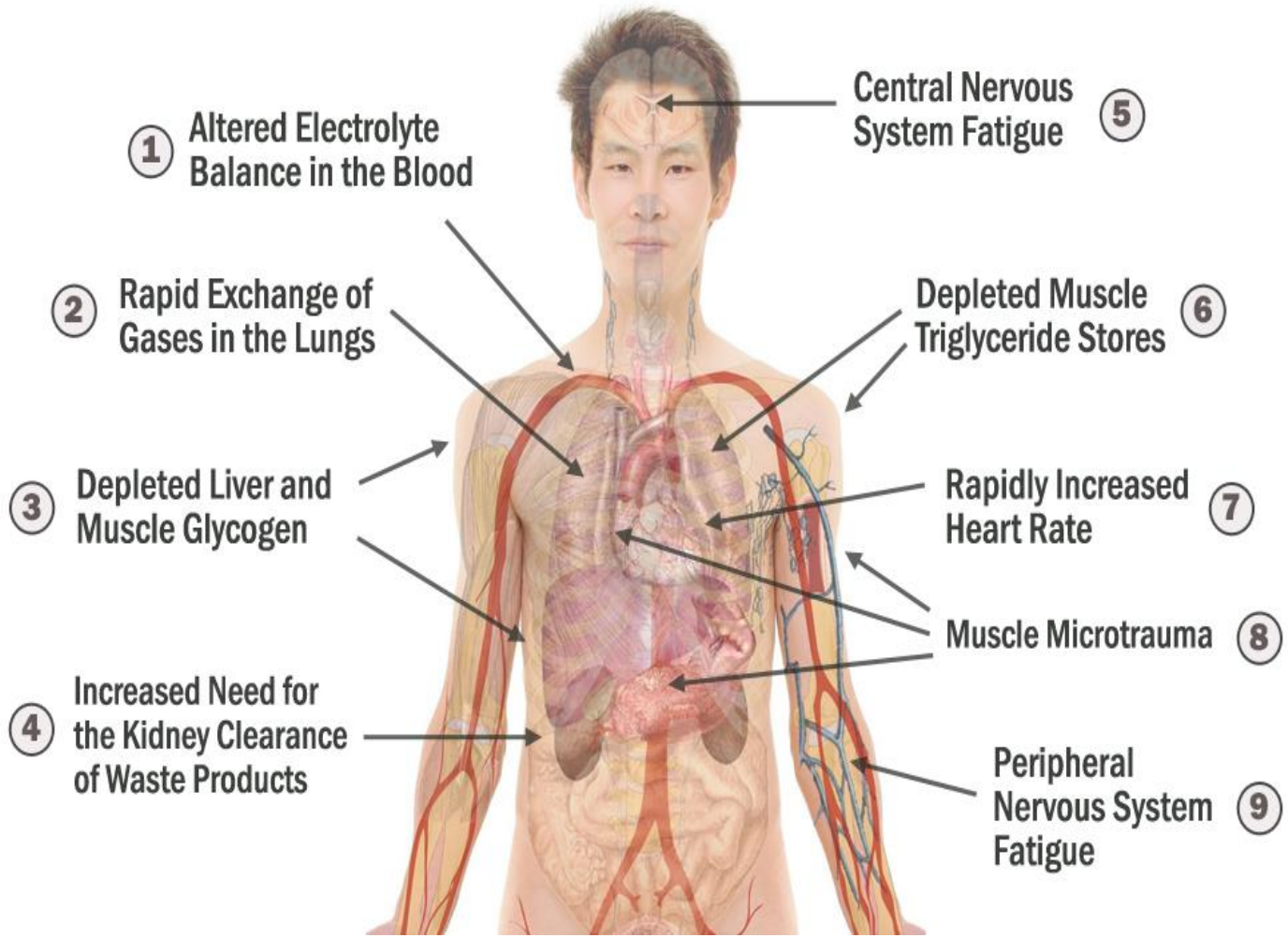
Post-Exercise Exhaustion Results From...



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Ergogenic Supplements and Other Nutrients:

1. Creatine Monohydrate : Overview
   - Increases m. CP by 10-40% at a dosage of 20-25 gm per day, taken in divided (5 gm) doses for 5-7 days, followed by a maintenance dosage of 10 gm per day (5 gm twice daily).
   - Often cycled, 1 month on, one month off (only once17 yrs old)
   - Produces significant gains in explosive strength, absolute strength, repeated max sprints and lean mass gains (80% studies positive)

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- **Emerging applications include:**
  - Neuromuscular diseases (ALS, Huntington's dis., Parkinson's dis., McArdles dis., Myasthenia gravis, Duchenne muscular dystrophy)
  - Heart Failure Patients
  - Musculoskeletal Rehabilitation (immobilized limbs in casts show less atrophy)
  - Anti-aging –in young seniors and seniors – increases strength, lean mass and endurance performance (reverses sarcopenia of aging)
- Absorption – improved with concurrent ingestion of simple CHO
- Adverse Effects – m. water retention (slow endurance athlete), and previous kidney damage re-activated (one-case report)

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Creatine's Multi-Purpose Applications

Title: **Clinical pharmacology of the dietary supplement creatine monohydrate.**

Author(s) : Persky AM; Brazeau GA

Author's Address : Department of Pharmaceutics, College of Pharmacy, University of Florida, Gainesville, Florida 32610, USA. apersky@ufl.edu

Source : Pharmacological reviews [Pharmacol Rev] 2001 Jun; 53 (2), pp. 161-76.

Pub. Type : Journal Article; Review; Review, Tutorial

Language : English

Journal Info : *Country of Publication:* United States *NLM ID:* 0421737 *ISSN:* 0031-6997 *Subsets:* IM

MeSH Terms :
Creatine*/biosynthesis
Creatine*/pharmacokinetics
Creatine*/pharmacology
Creatine*/therapeutic use
Dietary Supplements*
Animal; Area Under Curve; Energy Metabolism/drug effects; Heart Diseases/drug therapy; Human; Metabolic Clearance Rate; Mitochondrial Myopathies/drug therapy; Support, U.S. Gov't, P.H.S.; Tissue Distribution

Abstract : Creatine is a dietary supplement purported to improve exercise performance and increase fat-free mass. Recent research on creatine has demonstrated positive therapeutic results in various clinical applications. The purpose of this review is to focus on the clinical pharmacology and therapeutic application of creatine supplementation. Creatine is a naturally occurring compound obtained in humans from endogenous production and consumption through the diet. When supplemented with exogenous creatine, intramuscular and cerebral stores of creatine and its phosphorylated form, phosphocreatine, become elevated. The increase of these stores can offer therapeutic benefits by preventing ATP depletion, stimulating protein synthesis or reducing protein degradation, and stabilizing biological membranes. Evidence from the exercise literature has shown athletes benefit from supplementation by increasing muscular force and power, reducing fatigue in repeated bout activities, and increasing muscle mass. These benefits have been applied to disease models of Huntington's, Parkinson's, Duchenne muscular dystrophy, and applied clinically in patients with gyrate atrophy, various neuromuscular disorders, McArdle's disease, and congestive heart failure. This review covers the basics of creatine synthesis and transport, proposed mechanisms of action, pharmacokinetics of exogenous creatine administration, creatine use in disease models, side effects associated with use, and issues on product quality.

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Creatine: Referenced Studies

Creatine monohydrate is one of the sports supplements that has received much attention in this regard and has been shown to enjoy widespread use across the North American athletic population, with U.S. retail sales of the product reaching $200 million per year as of 1998. (1)

Creatine is one of the few supplements in the sports nutrition area, where extensive research exists to support its performance-enhancing claims. As such, practitioners should be aware of the research pertaining to its safe and effective application for athletes, as well as the newly emerging studies implicating its potential role as an adjunctive treatment in the management of certain cardiac conditions, neurodegenerative diseases, musculoskeletal rehabilitation and as an anti-aging intervention for older subjects.

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Physiological Considerations

- It is now widely accepted that creatine supplementation can increase muscle strength and mass. (1,2,3,4) Creatine is an amino acid that is stored in muscle in the form of creatine phosphate. During explosive or intensive exercise, creatine phosphate is broken down by a specific enzyme to yield creatine, plus phosphate, plus free energy. The free energy released from the breakdown of creatine phosphate is used to regenerate ATP, which is the fuel that powers muscle contraction. (2)

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- The normal daily requirement for creatine is about 2 grams for a person weighing 70 kg. Animal protein (especially meats) normally provides at least half that amount, with approximately one gram per day synthesized by the liver. A half-pound of raw meat contains about 1 gram of creatine, but fish is also a good source.

- A number of recent studies have demonstrated that short-term creatine supplementation increases creatine phosphate stores in skeletal muscle by 10% to 40% (3). In combination with proper training, creatine supplementation leads to an increase in muscle mass, which is thought to occur from increased protein synthesis, as the muscle lays down an increased number of contractile myofibrils (protein bands that contract and generate force). Increased muscular fluid retention may also participate in muscle volume gains with creatine use. (5,6,7) Creatine has also been shown to provide antioxidant properties. This may be of some significance as free radicals generated from exercise can affect muscle fatigue and protein turnover. (24)

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- It also appears that creatine supplementation may allow athletes to train harder (due to increased available energy for muscle concentration), which promotes strength gains, and increases muscle size due to hypertrophy (larger muscle fiber size). (2,3)

- The established protocol for creatine supplementation used by athletes involves a loading dosage of 20 to 25 grams per day for the first 5 to 7 days. Typically an athlete will mix a heaping teaspoon of creatine monohydrate crystals into a glass of juice to obtain about 5 grams of creatine.

- During the loading phase, the athlete does this on 4 or 5 occasions throughout the day to achieve an intake of 20-25 grams. After the loading phase is completed, the maintenance daily dosage is usually 5 to 10 grams per day. Recent reports suggest that taking creatine with glucose (a simple carbohydrate) may increase the amount of creatine absorbed by the muscles. As such, some manufacturers combine creatine with carbohydrates in a premix product to help improve creatine delivery to muscles (25).

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Clinical Applications and Mechanism of Action

I. Increased Strength and Performance In Athletes

- Several studies have shown that creatine supplementation improves performance in repeated bouts of high intensity strength work and repeated sprints, which are primary determinants and requirements for many sports. (8,9,10,11,12,13,14,16,17,18)

- In short, substantial evidence suggests that creatine supplementation can increase lean body mass, muscular strength, and sprint power. (24)

- Significant gains in strength and lean mass often occur in the first 6 weeks of creatine supplementation, when combined with proper training and diet. In one study, college football players who took creatine supplements for 28 days during resistance and agility training had significant gains in lean mass when compared to players who took the placebo. (15)

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- Individuals may vary in their response to creatine supplementation, but it is not uncommon to see a 5 to 10 lb. increase in body weight within the first six weeks.

- Approximately 80% of creatine studies have reported a performance-enhancing effect. This is quite impressive when you consider the fact that creatine is not structurally or functionally related to anabolic steroids, and creatine supplements are not banned by the International Olympic Committee or the National Collegiate Athletic Association.

- Creatine use is based on the same principle as carbohydrate loading, in that an athlete is manipulating their dietary intake to optimize muscle creatine phosphate stores for more explosive power and enhanced performance.

- Athletes requiring repeated bouts of explosive power may also benefit from creatine supplementation as demonstrated by M. Izquierdo, et al.

- Among other positive benefits revealed in their study of nineteen trained athletes, they showed that short-term creatine supplementation (20 gms per day for 5 days) enhanced repeated sprint performance and attenuated decline in jumping ability after repetitive high-power-output exercise bouts (MRPB). (22) Similar results have been documented by G.

- Cottrell, et al, in subjects performing repeated sprint cycling. (23) These studies have important implications for many sports such as hockey, basketball, soccer, volleyball, lacrosse, football, tennis and any sport requiring repeated bouts of all-out lower extremity explosive power and/or jumps.

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II. Neuromuscular Diseases

- Creatine supplementation in humans has been reported to enhance power and strength both in normal subjects and in patients with various neuromuscular diseases. (14,34,35)

- Clinical studies in patients with ALS (amyotrophic lateral sclerosis) (14), Huntington's disease, Parkinson's disease, Duchenne muscular dystrophy, McArdles disease (15), and myasthenia gravis (16) have shown that creatine supplementation can produce an increase in strength and thus, provide symptomatic treatment and improved quality of life for many of these patients. (14,15,16,39,40)

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III. Heart Failure

- Creatine supplementation has been shown to improve exercise capacity in patients with heart failure in some studies.

- Along with Coenzyme Q10, hawthorn extract and L-carnitine, creatine is one of few natural health products that has been shown to reverse certain parameters of heart failure. (36,37)

- As reported by K. Witte, et al, there is evidence for a possible role for micronutrient deficiency in heart failure, of which creatine may be one of the principle factors. (10,11,17)

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IV. Musculoskeletal Rehabilitation

- Creatine was shown to speed recovery of muscular power in a double-blind, placebo-controlled study involving 20 male and female students whose right legs were immobilized in casts for a period of two weeks.

- Those given creatine supplementation during and after leg immobilization displayed more muscular power and greater muscle size after three to ten weeks of physical rehabilitation than did subjects who took the placebo. (18)

- Finally, this study also suggested that the anabolic strength and size gains associated with creatine supplementation were likely due to increased activity of myogenic transcription factors. Previously, rat studies have shown that creatine intake affected myogenic transcription factors, but the study by Hespel (2001) was the first to suggest that same effect occurs in humans.(Hespel P et al. Oral creatine supplementation facilitates the rehabilitation of disuse atrophy and alters the expression of muscle myogenic factors in humans. The Journal of Physiology. Vol 536, (2): 625–633. October 2001)

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V. Anti-aging in Older Subjects

- Creatine supplementation provided to active subjects over 70 years of age, and subjects 59-72 years of age, have resulted in significant gains in several indices of muscle performance including, increased maximal dynamic and isometric strength, lower body mean power, lower extremity functional capacity, increased fat-free mass, increased lean mass and endurance power.

- These studies suggest that creatine supplementation may help to forestall or reverse muscular atrophy and progressive weakness that occurs during aging, and that creatine may be useful as an intervention to improve the ability of certain elderly individuals to perform functional living tasks, decreasing dependency and, enhancing their quality of life. (19,20)

- Other studies have noted that younger individuals respond to creatine supplementation more efficiently than do older subjects in that muscular phosphocreatine stores were shown to increase on average by 35% in young subjects (~24 years of age) and 7% in older subjects (~ 70 years of age) after five days of creatine supplementation (20 gms per day). As such, it may take a longer period to maximize creatine stores in older subjects on creatine supplementation. (21)

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Absorption and Utilization

- Creatine absorption from the intestinal tract is very efficient. Studies show that a 6-8 gm oral load of creatine results in approximately 50% of the ingested creatine being excreted in the urine.

- Thus, researchers are still working to identify the ideal single, daily and cumulative doses of creatine for various applications. (26)

- Other studies demonstrate that a 5 gm oral load of creatine, followed by 93 gm oral load of simple carbohydrate in solution (water) at 30 minutes post-creatine intake (4-times per day), resulted in a 60% increase in total muscle creatine compared to subjects ingesting the same amount of creatine in the absence of a simple carbohydrate drink.

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- Subjects ingesting creatine and the simple carbohydrate drink, had higher insulin levels and significantly less creatine lost in their urine, indicating that higher insulin levels is likely a key to greater muscle uptake and utilization of creatine, and a reduction on urinary loss. Thus, it is accepted that creatine utilization is enhanced by concurrent ingestion of a simple carbohydrate drink (e.g., fruit juice). (25)

- Additionally, concurrent administration of creatine and glycogen reveal that creatine supplementation enhances muscle levels of glycogen (glycogen supercompensation) beyond that attainable from glycogen loading alone. As supercompensation of muscle glycogen is also an ergogenic factor in exercise performance, the combination of creatine and carbohydrate loading appear to improve performance by increasing muscle creatine and muscle glycogen. (27)

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Adverse Side Effects and Toxicity

- As for the safety of creatine supplementation, a 1997 study showed that short-term creatine use (20 grams per day for 5 days) did not increase markers of kidney stress in five healthy men. (13) A study comparing creatine users, for up to five years duration, to control subjects has shown that creatine users have no remarkable differences in their creatinine, urea, and plasma albumin clearances compared to controls.

- The researchers conclude that neither short-term, medium-term, nor long-term oral creatine supplements induce detrimental effects in the kidney of healthy individuals. (29,30,31)

- To date, no liver abnormalities have been evident in short-term creatine challenge studies. (30)

- However, individuals with pre-existing kidney disease should be cautious, as evidenced by the development of kidney dysfunction in a 25 year old soccer player taking creatine who previously had been treated for focal segmental glomerulosclerosis of the kidney. His kidney function returned to normal after discontinuing creatine supplementation. (28)

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- Some experts suggest that compulsory regular kidney and liver monitoring should accompany the use of creatine due to the increased burden placed upon the liver and kidneys. (30)

- As pointed out by other experts, creatine is normally found in cardiac muscle, brain, and testes, as well as skeletal muscle, and these former tissues have been largely unstudied with respect to the effects of creatine supplementation. (32)

- The Food and Drug Administration (FDA) has advised athletes to consult a physician or a health care professional before embarking on any scheme of creatine loading or supplementation. (28) Nevertheless, few reported adverse side effects from creatine use have been reported despite its widespread use among young athletes. (1)

- Other infrequently reported side effects include gastrointestinal disturbances and muscle cramps. (30)

- In regards to children and younger athletes, the safety of creatine supplementation has not yet been investigated in these individuals. Until all safety issues have been evaluated, experts strongly recommend against use of creatine among adolescent athletes. (33)

- Overall, creatine supplementation appears to be safe for healthy adults. It's a low molecular weight compound that is excreted in the kidneys by simple diffusion. In the maintenance phase, athletes consume only slightly more creatine (3-5 gm per day) than is generally found in the diet, which is usually about 2 gm per day. (10, 11)

- There are no well-known drug-nutrient interactions for creatine at this time. (38)

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Summary

- Supplementation within creatine has been shown to improve various parameters of athletic performance and body composition in athletic subjects.

- It may also be of therapeutic value for a number of health conditions and used as an anti-aging intervention in older individuals. Debate continues over issues of long-term safety, whether or not there should be pre-screening kidney filtration evaluation prior to introducing creatine supplementation, and minimum of age at which creatine supplementation can be safely administered.

- It is important to ensure that patients with a history of kidney disease or impairment avoid the use of creatine, and practitioners should be sure to address this question when creatine supplementation is being discussed.

- In my own practice, I discourage the use of creatine supplementation in athletic patients under the age of 16 or 17 years of age, who are seeking to improve their strength, muscle size and/or performance. This is a position I intend to maintain until further safety and toxicity studies are in place to show that a young, developing body can safely handle this intervention without undue side effects, including evaluation of renal and liver damage.

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Reference 1: Creatine Update

Meat, poultry and fish provide rich sources of creatine. The body synthesizes about 1-2 gm creatine daily, primarily in liver, kidney and pancreas, from the amino acids arginine, glycine, and methionine.

Vegetarians tend to have lower levels due to avoidance of animal protein foods, rich in creatine. Vegetarians showed greatest increases in muscle creatine and phosphocreatine than omnivores, when creatine supplementation is introduced

Supplementation with 20-30 gm per day (creatine) shown to increase intramuscular free creatine and phosphocreatine (PC) by 10-30% in just 2-weeks. These levels remain high for a few weeks after only a few days of supplementation.

Creatine is a legal ergogenic aid (IOC).

Just about all ingested creatine incorporates into skeletal muscle via insulin-mediated active transport. About 40% exists as free creatine and the remainder forms PC.

Fast twitch fibers store 4-6 times more PC than ATP.

PC regenerates ATP, but may also shuttle intramuscular high-energy phosphate between the mitochondria and the cross-bridge sites that initiate muscle action- aiding all-out performance events.

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Studies continue to show the positive ergogenic effects of creatine loading on total work accomplished during repetitive sprint cycling performance (interval sports)

In football players doing resistance training creatine has increased body mass, lean body mass, cellular hydration, muscular strength and performance.

Increases myosin heavy-chain synthesis in conjunction with resistance training (protein synthesis via myogenic transcription factor up-regulation)

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Variations of Creatine Supplementation:

1. 20 gm per day for 6 days, followed by 2 gm per day to maintain elevated muscle creatine for 28 days

2. Or 3 gm creatine supplementation for 28 days provides equal benefit of muscle creatine levels

Creatine not shown to improve aerobic performance and little effect on isometric muscular strength or a brief single movement like a golf swing.

Older subjects (70 yrs old) have seen greater lean mass gains, leg strength, muscular endurance and average power on the legs during resistance training compared to those doing resistance training without creatine.

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Studies on healthy subjects continue to show no deleterious effects of creatine on kidney or liver function or other health parameters.

In cases of existing kidney disease it should not be used.

Creatine supplementation shown to enhance muscle hypertrophy in resistance training individuals via increases MPS. This may largely be due to ability to work harder (lift more weight) stimulating greater lean mass gains

If discontinue creatine supplementation muscle creatine returns to baseline levels in about 35 days.

2 gm per day appears to be sufficient to maintain elevated muscle creatine levels once loading phase is complete. Many experts suggest 5gm per day, however.

Consuming CHO (simple sugars) with creatine enhances creatine absorption, likely due to insulin-mediated glucose absorption by skeletal muscle, which also facilitates transport of creatine into muscle fibers

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Stop Caffeine when Using Creatine – Caffeine diminishes the ergogenic effect of creatine supplementation. Creatine with our without caffeine shown to increase intramuscular PC by 4-6% after 6 days of supplementation. Dynamic torque production also increased by 10-23% with creatine-only treatment compared to placebo. Consuming caffeine totally negated creatine's ergogenic effect.

Caffeine may prevent skeletal muscle from retaining the creatine it takes in from the bloodstream, losing the ergogenic effect. It is recommended that athletes using creatine should refrain from ingesting any caffeine for several days before competition.

There are some studies that no benefit from creatine supplementation, but overall the evidence points to a significant ergogenic effect in most case.

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Sodium Bicarbonate and Sodium Citrate:

Overview: Accumulation of lactic acid leads to fatigue during exercise primarily as a result of hydrogen ions (H+), which lower pH of muscle, which in turn decreases binding of calcium to troponin, reducing the activation of actin-myosin cross-bridges required for muscle contraction. Acidity also inhibits glycolytic enzymes, resulting in less ATP formation.

High intensity activity increases the acidity in the blood and other tissues due to the build up of lactic acid. It is known that increased acidity impairs muscle contraction ability, which in turn hinders performance. (1) Studies have shown that the oral ingestion of an alkalizing agent, such as sodium bicarbonate can reduce the build up of acidity, enabling muscles to work at higher intensity levels, thereby enhancing performance in some events.

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The ingestion of sodium bicarbonate (135 mg/lb body wt) or sodium citrate (225 mg/lb/body wt) dissolved in at least 2 cups of water and ingested one hour prior to an exercise lasting 1-7 minutes, can significantly improve performance by buffering acidity.

These buffering agents **do not** improve performance in events less than one minute or longer than 7 minutes

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- Placebo-controlled trials indicate that sodium bicarbonate improves exercise performance for events lasting one to seven minutes when 135 mg per pound of body weight, of sodium bicarbonate, is dissolved in at least two cups of fluid and is either ingested **as a single dose at least one hour before exercise, or divided into smaller amounts and taken several hours before exercise.(2)**

- As well, exercise performance of short to intermediate duration (1 –7 minutes) has been reported for sodium citrate ingestion at 225 mg per pound of body weight in placebo-controlled studies. (3,4,5,6)

- However, exercise events of less than one minute or more than seven minutes are not improved by taking alkalizing agents. (7,8,9,10,11) Note that sodium citrate may be preferable over sodium bicarbonate because it caused less gastrointestinal upset. (12)

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Reference 1: Buffering Solutions Update

800-m race, trained athletes ingested 300 mg/kg body mass of sodium bicarbonate vs calcium carbonate placebo, the alkaline drink raised pH and standard alkaline levels before exercise.

Subjects ran an average of 2.9 seconds faster under alkalosis, and achieved higher post-exercise values for blood lactate, pH and extracellular H+ concentrations than compared to placebo

These benefits have been shown in women and men

Both sodium bicarbonate and sodium citrate have shown similar results

The extracellular buffering from exogenous bicarbonate or citrate facilitates coupled transport of lactate and H+ across the muscle cell membrane during anaerobic exercise. This delays the fall in intracellular pH and its subsequent negative effects on muscle function.

Nearly 3 seconds represents a dramatic improvement in 800-m race time; it transposes to a distance of about 19-meters at race pace, bringing a last place finisher to first place.

But no improvement in resistance training events or low-intensity, aerobic exercise. But if the aerobic event involves intense exercise, such as 30-km time trial by cyclists, a 0.5 gm/kg body mass ingested before time trial improved performance vs placebo. So, not just 1-7 minute duration inclusion criteria to gain benefit – intense aerobic exercise athletes of longer duration may also see ergogenic effect.

Side Effects: Some athletes experience exercise inhibiting **-** abdominal cramps and diarrhea about 1-hr after ingestion. Substituting sodium citrate for sodium bicarbonate can reduce or eliminate adverse GI symptoms

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Sodium Bicarbonate Over 6 Days Prior to Event

Title: Acute versus chronic sodium bicarbonate ingestion and anaerobic work and power output

Author(s) : Mc Naughton L; Thompson D

Affiliation(s) : University of Bath, Department of Sport and Exercise Science, Bath BA2 7AY, England. E-mail: l.mcnaughton@bath.ac.uk

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Major Subjects : Sodium Bicarbonate; Ergogenic Products; Dietary Supplementation--Methods; Hydrogen-Ion Concentration; Exercise Physiology; Physical Performance

Minor Subjects : Male; Adult; Descriptive Statistics; Body Weights and Measures; Ergometry; Exercise Test, Cardiopulmonary; Random Assignment; Exercise Intensity--Evaluation; Data Analysis Software; Analysis of Variance; Repeated Measures; T-Tests; Sodium--Blood; Funding Source

Abstract : BACKGROUND: The aim of this study was to compare and contrast the effects of acute versus chronic sodium bicarbonate ingestion. METHODS: PARTICIPANTS: Eight male, (mean+/-SE): age, 20.8+/-0.4 yrs; height, 179.6+/-0.6 cm; body mass, 79.4+/-0.85 kg, Sigma7skf, 48.6+/-4.8 mm, VO2max=55.9+/-0.8 ml x kg(-1) x min(-1)) volunteer subjects, ingested NaHCO3 in either a dose of 0.5 g x kg(-1) body mass acutely or the same dose daily over a period of six days in order to determine whether there were any differences in performance of 90 sec maximal cycling ergometry. INTERVENTION: After subjects undertook an initial control (C) test session, all were then randomly assigned to one of two groups, acute or chronic NaHCO3 ingestion. Subjects in the acute ingestion (AI) group completed their supplemented test on day one, and then on the following day. Chronic ingestion (CI) subjects completed the test after one day of chronic ingestion as well as following six days of bicarbonate ingestion. Following ten days rest, subjects repeated the protocol in the opposite group. MEASURES: Blood samples were taken pre- and postingestion, daily, and pre- and postexercise and were analysed for, pH, Base excess (BE), HCO3-, PO2, PCO2, Na+, K+, Cl-, and lactate. RESULTS: Both the chronic (CI) and acute ingestion (AI) groups were significantly different to the control (C) value ($p<0.001$ and $p<0.05$, respectively). CONCLUSIONS: We would suggest using chronic ingestion as a means to improve high intensity work rather than the acute ingestion of sodium bicarbonate. The ingestion of sodium bicarbonate, over a period of six days, significantly improved work output two days after bicarbonate ingestion ceased.

Journal Subset : Allied Health, Europe, Peer Reviewed

Special Interest : Nutrition; Physical Therapy; Sports Medicine

ISSN : 0022-4707

MEDLINE Info : *NLM Serial ID:* J39540000. *NLM UID:* 0376337.

Dose = 0.5 g/kg per day - 6 days prior to Explosive Event

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- 2017 Study- showed that after high-intensity cycling to exhaustion the subsequent ingestion of 0.3 g/kg body wt (sodium bicarbonate) improved recovery time for second bout of cycling to exhaustion (improved performance compared to placebo group), and showed higher blood pH levels and bicarbonate ion concentrations (HCO_3^-).

- In my case= 27 gm of sodium bicarbonate (90kg x 0.3)

- Recovery period between exercise bouts to exhaustion was 90 mins

- Human Kinetics Journals : International Journal of Sport Nutrition and Exercise Metabolism
- Volume 27, Issue 5 : https://journals.humankinetics.com/doi/abs/10.1123/ijsnem.2017-0065

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Growth Hormone Secretagogues: Arginine and Ornithine

- Arginine and Ornithine are amino acids that have been shown to increase the release of growth hormone (growth hormone secretagogues) when supplemented at a dose of 500 mg each, twice per day, five times per week. (1,2) Arginine on its own at dose of 250 mg per kg of body weight, per day (e.g., 20 gm per day) or ornithine on its own at 170 mg per kg body weight, per day, have also been shown to increase growth hormone blood levels in some athletes. (3,4)
- However, these are extremely high doses and the long-term safety of doses in this range needs to be evaluated. (7) Two well-designed, double-blind study with athletes demonstrated that 500 mg of both arginine and ornithine, taken twice per day, five days per week, for only five weeks (in conjunction with weight training), resulted in decreased body fat, higher total strength and lean mass gains, and reduced evidence of muscle catabolism compared to the placebo group. (1,2)

- It should be noted that arginine is also a precursor to the synthesis of nitric oxide, which induces vasodilation of central and peripheral arteries. As such, it has been used successfully to treat male impotence, angina, and congestive heart failure. (5,6,7) Arginine may fuel the replication of herpetic viruses, and therefore, may be contraindicated in patients with recurrent herpes 1 or 2 outbreaks, and patients with post-herpetic syndrome. (7)

- Growth Hormone Secretagogues – In general, taking individual amino acids, or combining various amino acids together as an amino acid stack, has been shown to increase the release of growth hormone **(taken one hour before bedtime)**. The growth hormone releasing amino acids include, glutamine, ornithine alpha-ketoglutarate, glycine, lysine, ornithine and arginine. Anti-aging doctors often attempt to bring the insulin-like growth factor-I (IGF-I) levels back to 350-375 ng/ml, which may be of concern in terms of promoting the growth of a latent cancer (e.g., prostate, breast colon). More reasonable levels for individuals over 40 yrs would be a level of 225-275 ng/ml.

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References: Growth Hormone Secretatgogues

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- Anti-aging physicians often use a growth hormone secretagogue initially, and then add an individualized dose of growth hormone injection to patient management, as growth hormone secretagogues can only raise IGF-I levels to 250-275 ng/ml, which is the level normally seen in a 25-30 year old healthy person.

- This level (250-275 ng/ml) is more than adequate for an athlete who is 35 plus years of age in regards to providing an anabolic effect. It is best to first assess the athlete's IGF-I blood level to see if a secretagogue would be of value.

- If the athlete's IGF-I level is already at or above 250-275 ng/ml, then a secretagogue will be of no value. To date the literature suggests that an IGF-I level in the range of 250-275 ng/ml is not associated with an increased risk of cancer.

- Note that IGF-I also enhances immune function and may thus, help to reduce cancer risk as well as combat immune decline seen in over training and aging.

- IGF-I blood levels are a good surrogate marker for growth hormone status as the half-life of growth hormone is only 20 minutes, whereas the half-life of IGF-I is 20 hours. (8,9,10,11,12,13,14,15,16,17)

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Growth Hormone Secretagogues

Arginine and Ornithine: (Effects on IGF-1)

- Like glutamine, glycine, alpha-ketoglutarate and lysine, these two amino acids taken at 500 mg each, twice daily, five times per week, increase the release of GH. In athletes it produced the following effects in five weeks:

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Arginine and Ornithine continued:

- 1.Decreased body fat
- 2. Increased strength gains
- 3. Increased lean mass
- 4. Reduced muscle catabolism
- This study included a control group, who also performed weight training, but took a placebo instead of arginine and ornithine

- Many anti-aging Drs. suggest that a blood level of Insulin-like Growth Factor-I of ~ 350-375 ng/ml is ideal. Growth hormone secretagaogues can only raise IGF-I levels to a max. of 250-275 ng/ml, which is the normal level for a 25-30 year old person, and is quite adequate to enable a 30 yr old plus athlete to enhance anabolic lean mass gains, and appears to be safer in terms of cancer risk

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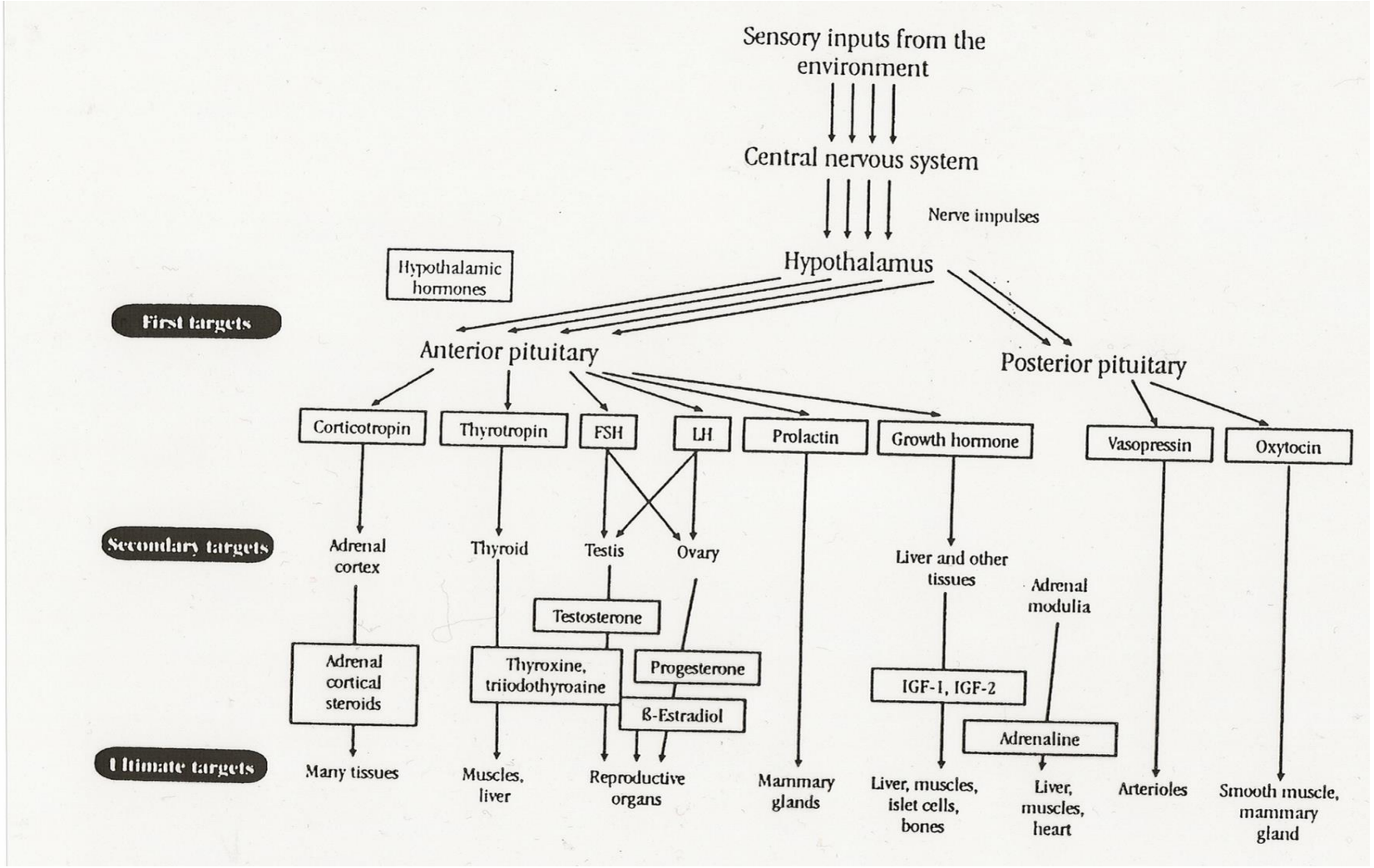
Growth Hormone And IGF-1 Cascade



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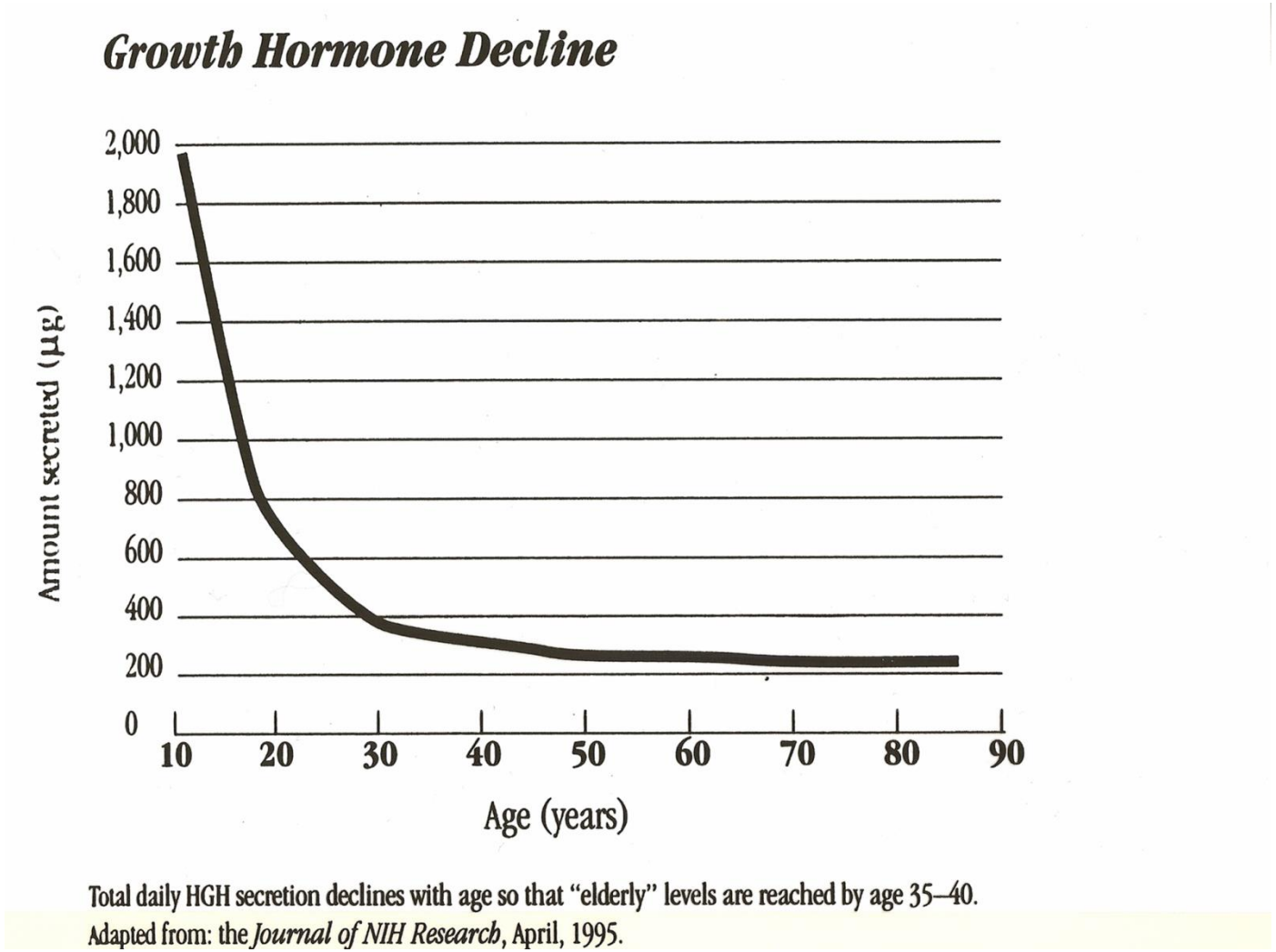
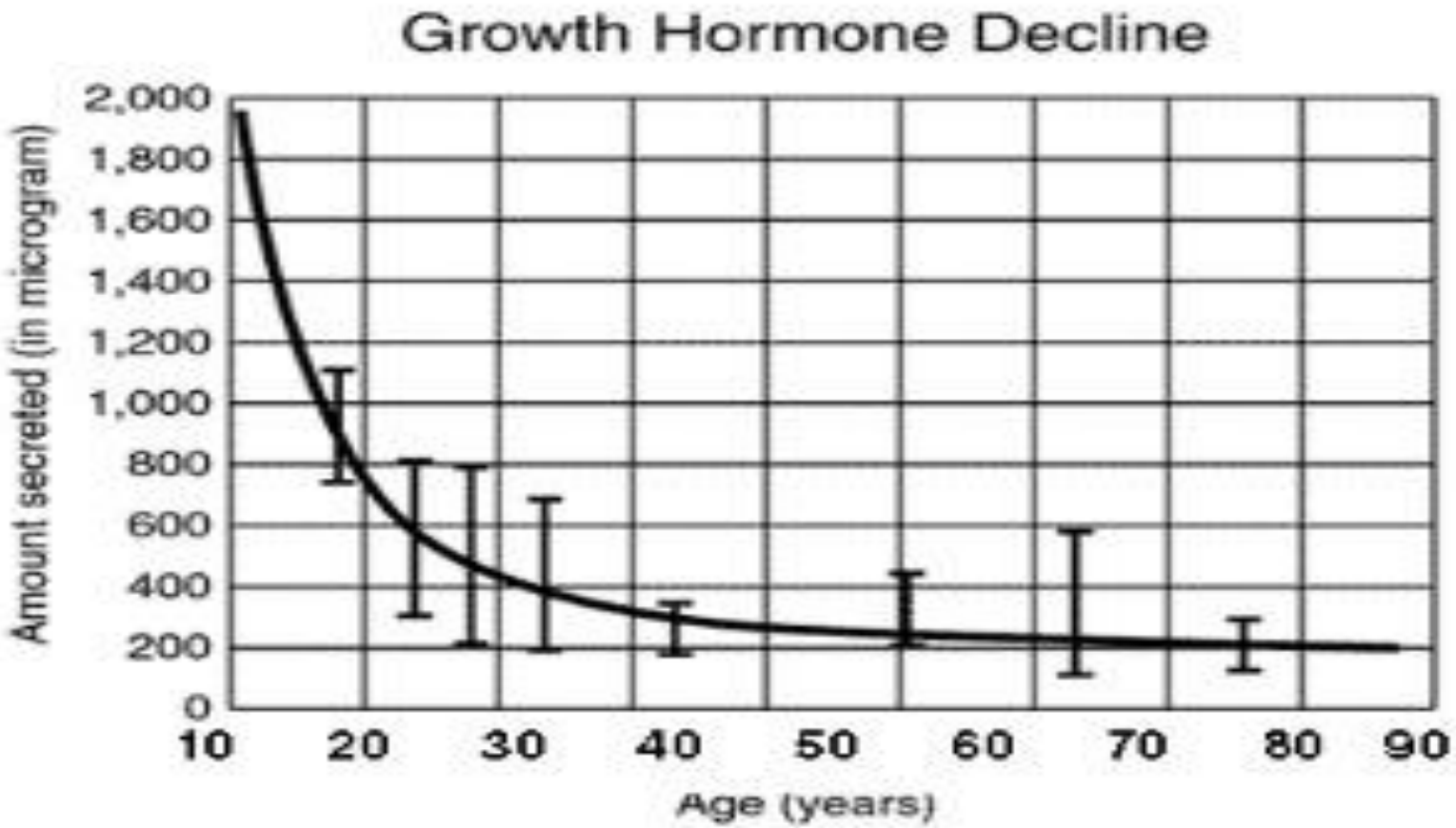
Age-Related GH Decline



Total daily HGH secretion declines with age so that "elderly" levels are reached by age 35–40.
Adapted from: the *Journal of NIH Research*, April, 1995.


Growth Hormone Decline
Amount secreted (in microgram)
2,000
1,800
1,600
1,400
1,200
1,000
800
600
400
200
0
10
20
30
40
50
60
70
80
90
Age (years)

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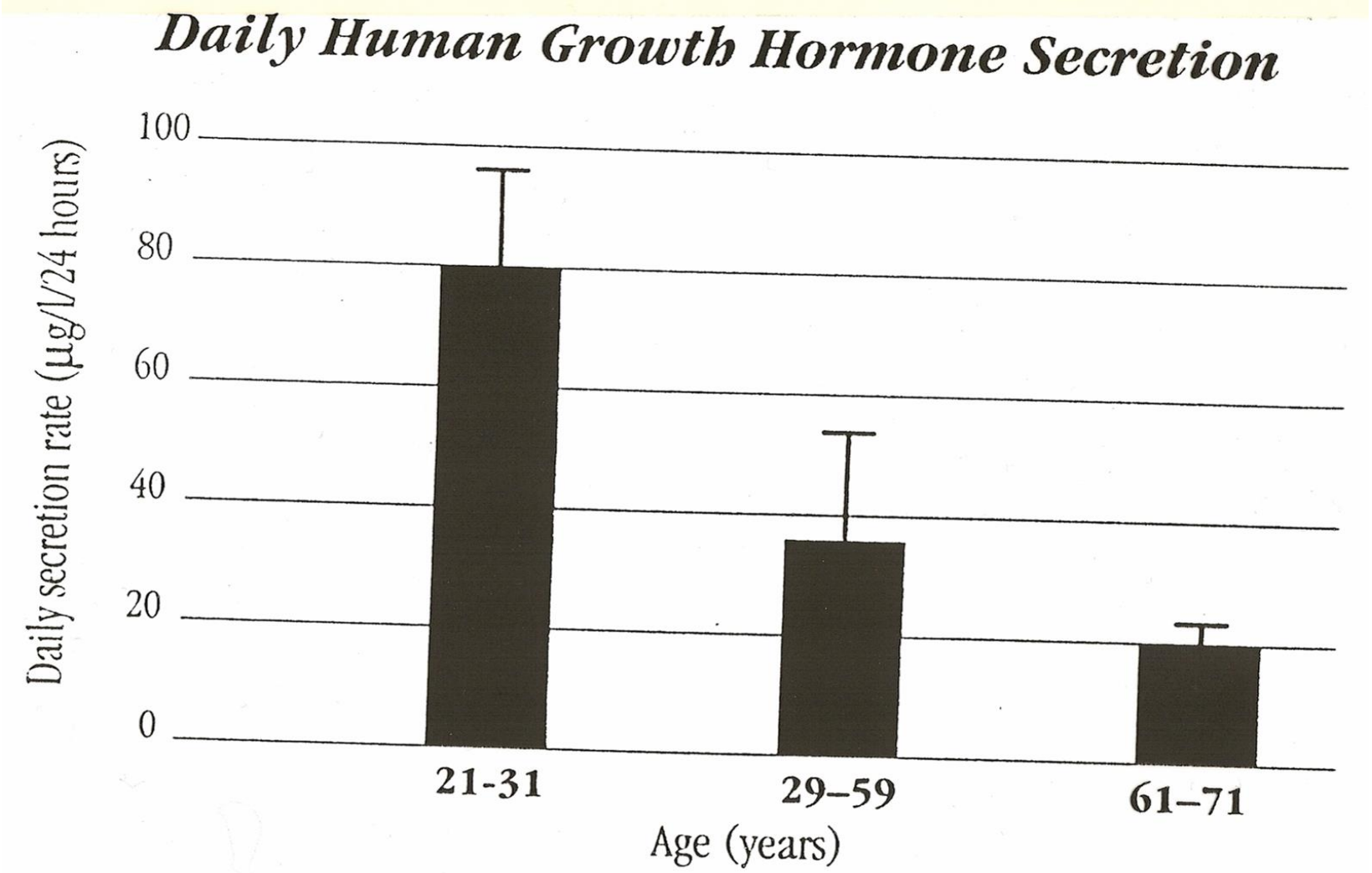
GH Decline With Age Continued



Daily HGH secretion rate is reduced progressively with increasing age

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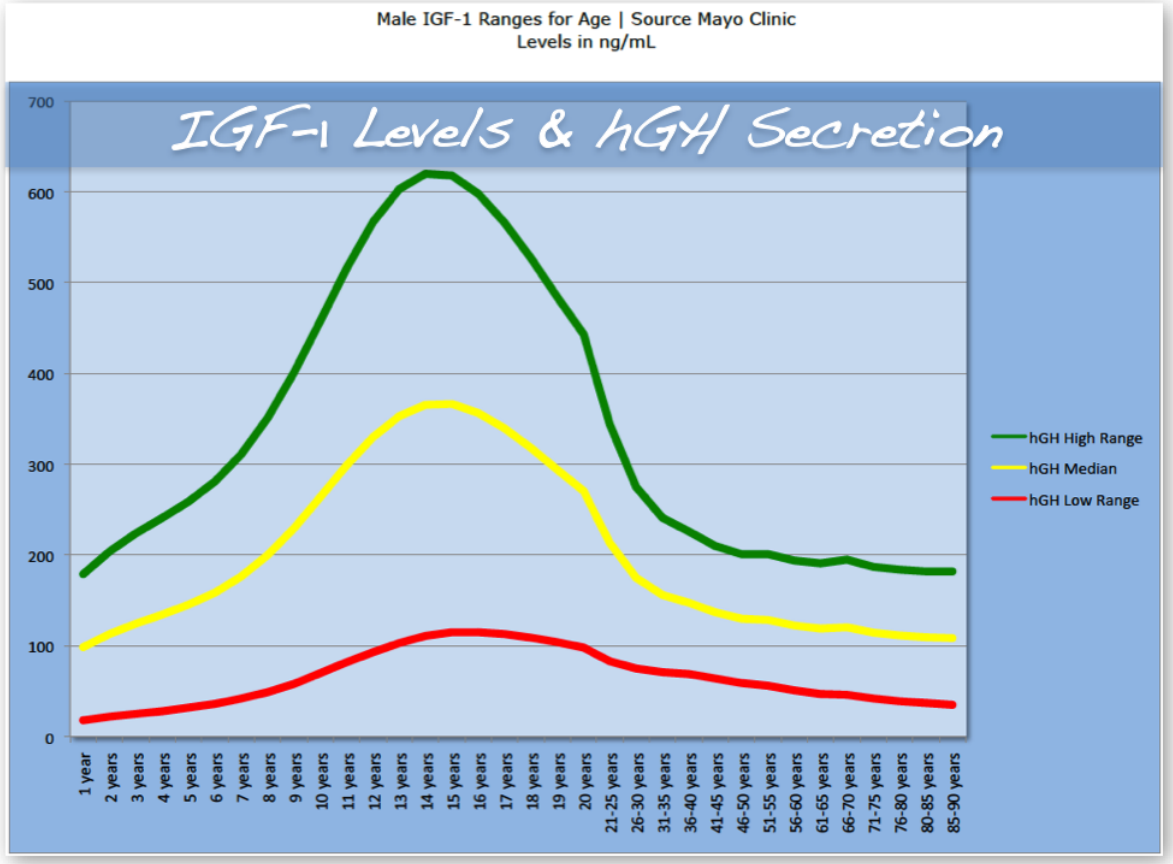
IGF-1 Levels Decline in Aging



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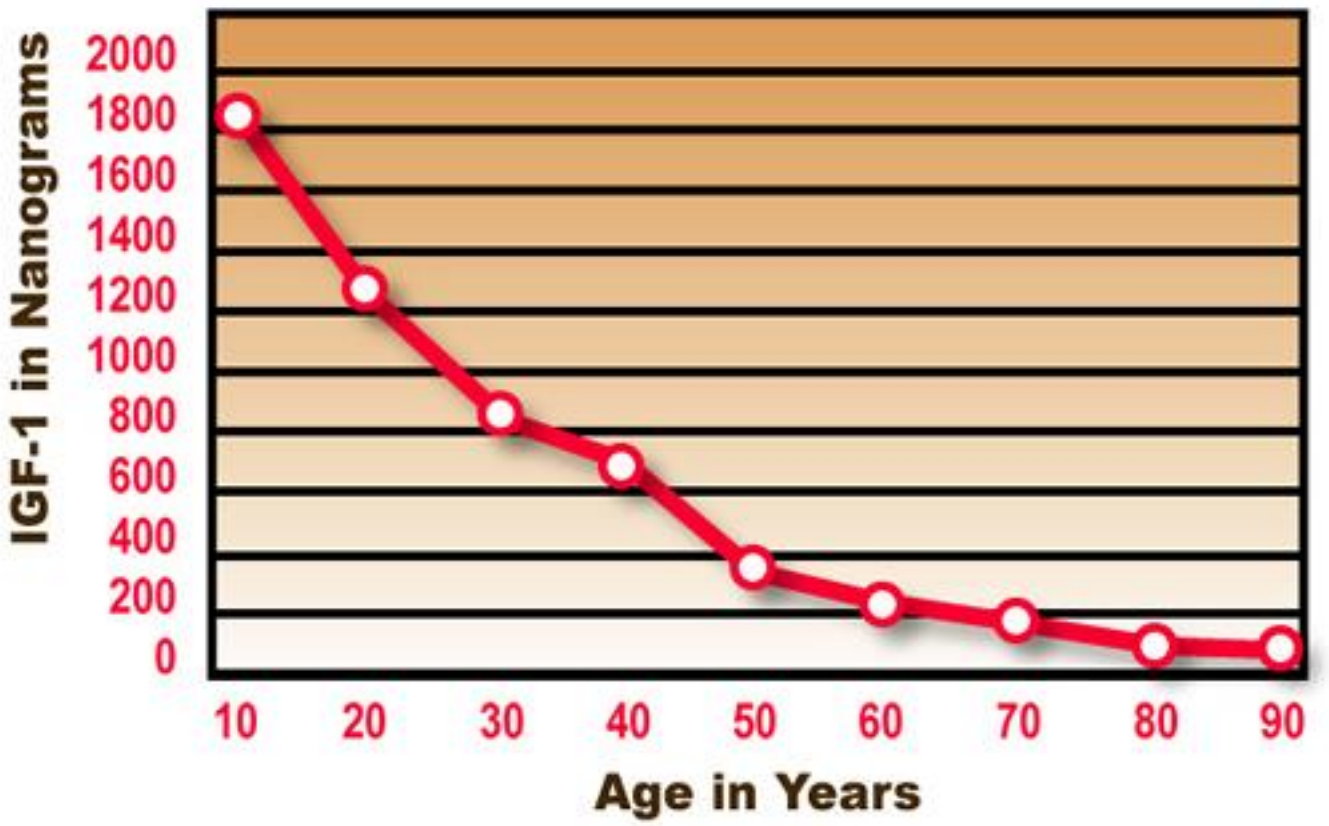
IGF-1 Decline in Aging



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Oral GH Secretagogues and Athletes

Title: **Use of amino acids as growth hormone-releasing agents by athletes.**

Author(s) : Chromiak JA; Antonio J

Author's Address : Department of Health, Physical Education, Recreation and Sport, Mississippi State University, PO Box 6186, Mississippi State, MS 39762-6186, USA.
jchrom@colled.msstate.edu

Source : Nutrition [Nutrition] 2002 Jul-Aug; 18 (7-8), pp. 657-61.

Pub. Type : Journal Article; Review; Review, Tutorial

Language : English

Journal Info : *Country of Publication:* United States *NLM ID:* 8802712 *ISSN:* 0899-9007 *Subsets:* IM

MeSH Terms : Sports*
Amino Acids/*administration & dosage
Somatropin/*secretion
Adolescence; Adult; Exercise; Female; Human; Male; Muscle, Skeletal/anatomy & histology; Muscle, Skeletal/drug effects; Muscle, Skeletal/physiology; Somatropin/blood

Abstract : Specific amino acids, such as arginine, lysine and ornithine, can stimulate growth hormone (GH) release when infused intravenously or administered orally. Many individuals consume amino acids before strength training workouts, believing this practice accentuates the exercise-induced GH release, thereby promoting greater gains in muscle mass and strength. The GH response to amino acid administration has a high degree of interindividual variability and may be altered by training status, sex, age, and diet. Although parenteral administration consistently leads to increased circulating GH concentration, oral doses that are great enough to induce significant GH release are likely to cause stomach discomfort and diarrhea. During exercise, intensity is a major determinant of GH release. Although one study showed that arginine infusion can heighten the GH response to exercise, no studies found that pre-exercise oral amino acid supplementation augments GH release. Further, no appropriately conducted scientific studies found that oral supplementation with amino acids, which are capable of inducing GH release, before strength training increases muscle mass and strength to a greater extent than strength training alone. The use of specific amino acids to stimulate GH release by athletes is not recommended.

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Exercise Increases IGF-1 Levels

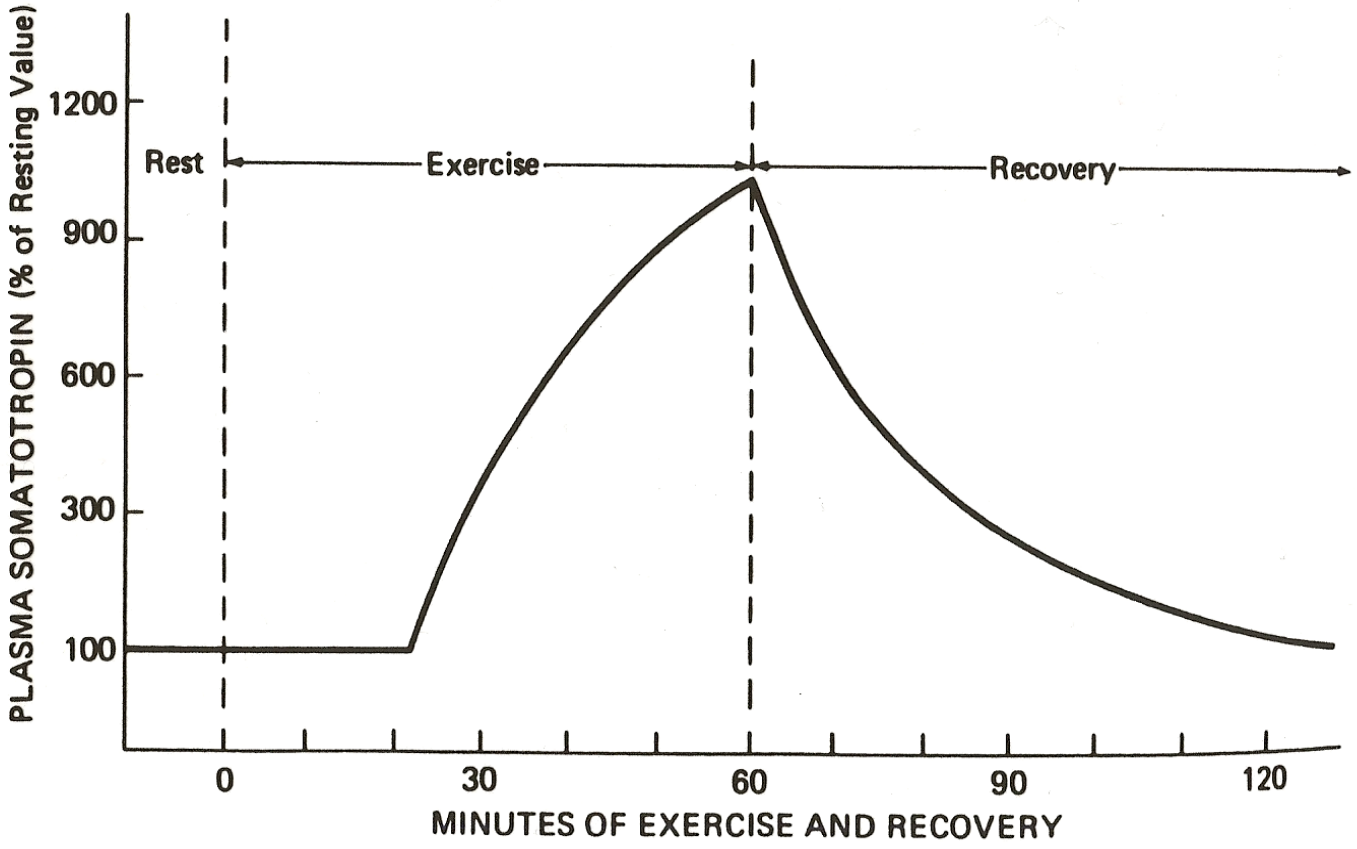

FIGURE 17.2. Diagram of growth hormone concentration in blood plasma during exercise and recovery.

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Age-Related Strength Gain Potential

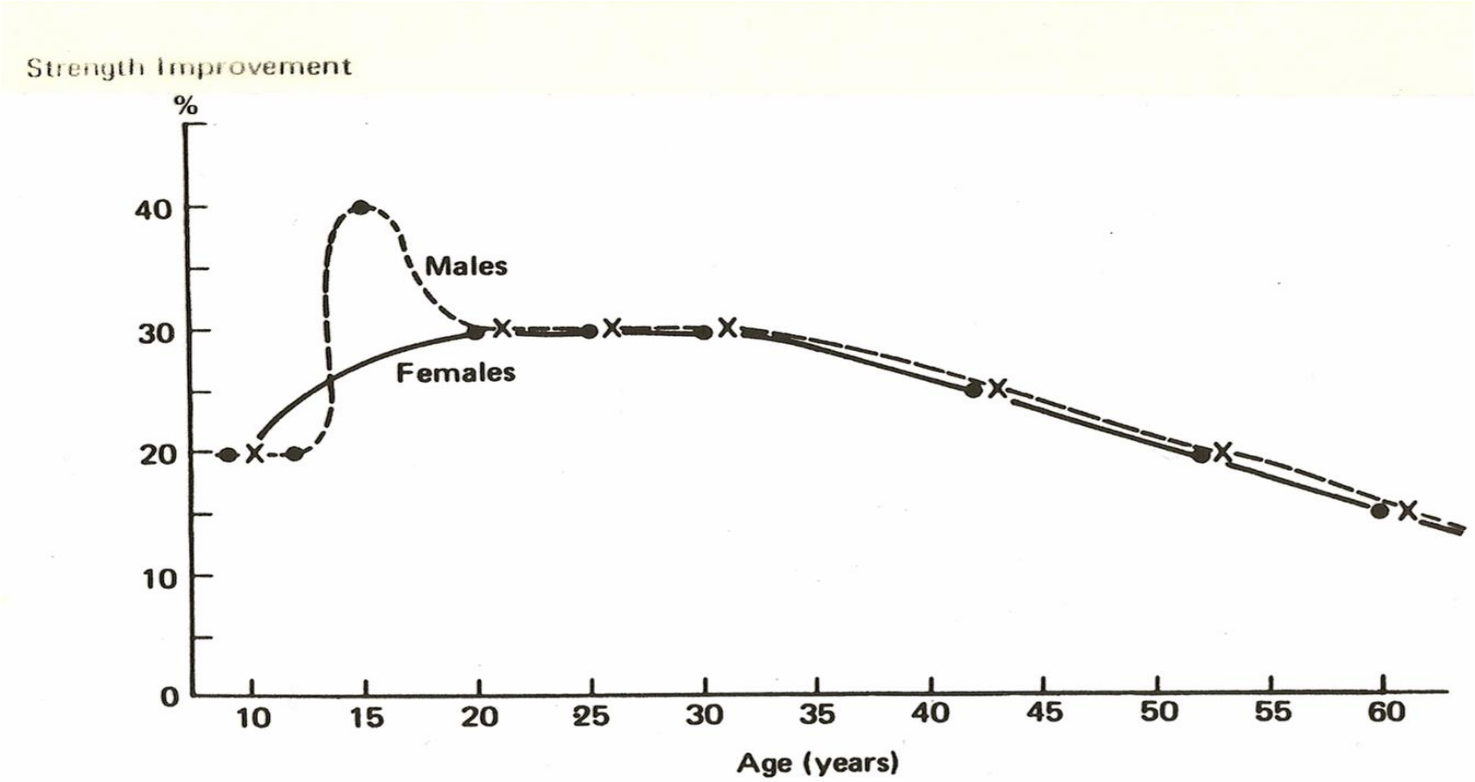

FIGURE 13.2. Hypothetical adaptations of males and females to 10 weeks of strength training. Note the effect of pubertal changes in both males and females.

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Arginine Effects On Performance:

1. Increased IGF-1

2. As precursor to Nitric Oxide – increases blood flow to muscles via vasodilation – studies show mixed effects on performance, but good results shown in patients with cardiovascular issues (congestive heart failure, healed myocardial infarction, and pulmonary hypertension)

3. Increases creatine synthesis in body. Arginine, glycine, and methionine are the three amino acids involved in the synthesis of creatine.

Daily food ingestion of arginine is approx. 3.5-5.0 gm/day

Supplementation Studies Have Used Dosages between 2-9 gm per day (reference: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2129157)

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Potential Side Effects of Arginine Supplementation:

- Arginine may aggravate herpetic viruses

- Arginine has mild anti-coagulant effect. This has been shown to be a positive effect in patients with hypercholesterolemia, by improving blood flow to coronary and other vessels (improved endothelial function)

- Reference: http://www.ncbi.nlm.nih.gov/pubmed/9060881

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Supplement I Take

Ingredients:

- Each serving contains the following:

1. Micronized Creatine Monohydrate – 5 grams
2. L-Glutamine – 0.5 grams
3. L-Arginine – 0.5 grams
4. L-Ornithine – 0.5 grams

One serving (one scoop) = 6.5 gms

60 servings per bottle (390 grams)

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Daily Dosage:

- **Loading Phase:** For the first 5-7 days, ingest two scoops (2 servings) in the morning, mixed into juice or shake mix, two scoops in the afternoon (mixed with juice or shake), and one additional scoop towards the end of the day (mixed into juice or shake mix)
- **Maintenance Phase:** ingest two scoops (servings) per day mixed into any juice or shake.

Clinical Applications:

- Athletic Performance: strength, explosive power, speed endurance, anabolic muscle gains
- Anti-aging: maintain strength, power, muscle mass, and energy in person's over 40
- Other Medical: adjunctive supplement in Multiple Sclerosis, Parkinson's disease, other neurodegenerative conditions, congestive heart failure, rehabilitation after fracture or limb immobilization (to prevent atrophy)
- Immune Support: in high performance athletes and individuals under chronic stress

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Beetroot Juice as Nitric Oxide Precursor:

2011 Study With Beetroot Juice

LANSLEY, KATHERINE E, et al. Acute Dietary Nitrate Supplementation Improves Cycling Time Trial Performance**. Medicine & Science in Sports & Exercise**. June 2011 - Volume 43 - Issue 6 - pp 1125-1131.

- **Purpose:** Dietary **nitrate supplementation** has been shown to reduce the O_2 cost of submaximal exercise and to improve high-intensity exercise tolerance. The present study investigated effects of acute dietary nitrate supplementation on power output (PO), $\dot{V}O_2$, and performance during 4- and 16.1-km cycling time trials (TT).

- **Methods:** After familiarization, nine club-level competitive male cyclists were assigned in a randomized, crossover design to consume 0.5 L of beetroot juice (BR; containing ~6.2 mmol of nitrate) or 0.5 L of nitrate-depleted BR (placebo, PL; containing ~0.0047 mmol of nitrate), **~2.5 h before the completion** of a 4- and a 16.1-km TT.

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Results: BR supplementation more than doubled plasma nitrate levels - Placebo = 241. 5 vs BR = 575nM.

BRJ improved 4-km performance by 2.8%, and 16.1-km performance by 2.7%

Conclusions: Results suggest that **acute dietary nitrate supplementation** with 0.5 L of BRJ improves cycling economy, as demonstrated by a higher PO for the same VO_2 and enhances both 4- and 16.1-km cycling Time Trial performance.

(Link to Reference: http://journals.lww.com/acsmmsse/pages/articleviewer.aspx?year=2011&issue=06000&article=00027&type=abstract)

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HMB (beta-hydroxy-beta methylbutyrate:

Overview:

- HMB is a breakdown product of leucine, glutamine and arginine

- HMB acts as signaling agent to up-regulate synthesis of muscle growth factors (autocrine) with protein synthesis

- A four week double-blind study – increased lean mass, strength, and decreased fat mass in fit and unfit men taking 3,000 mg per day of HMB in divided doses. Both groups performed exercise three times per week

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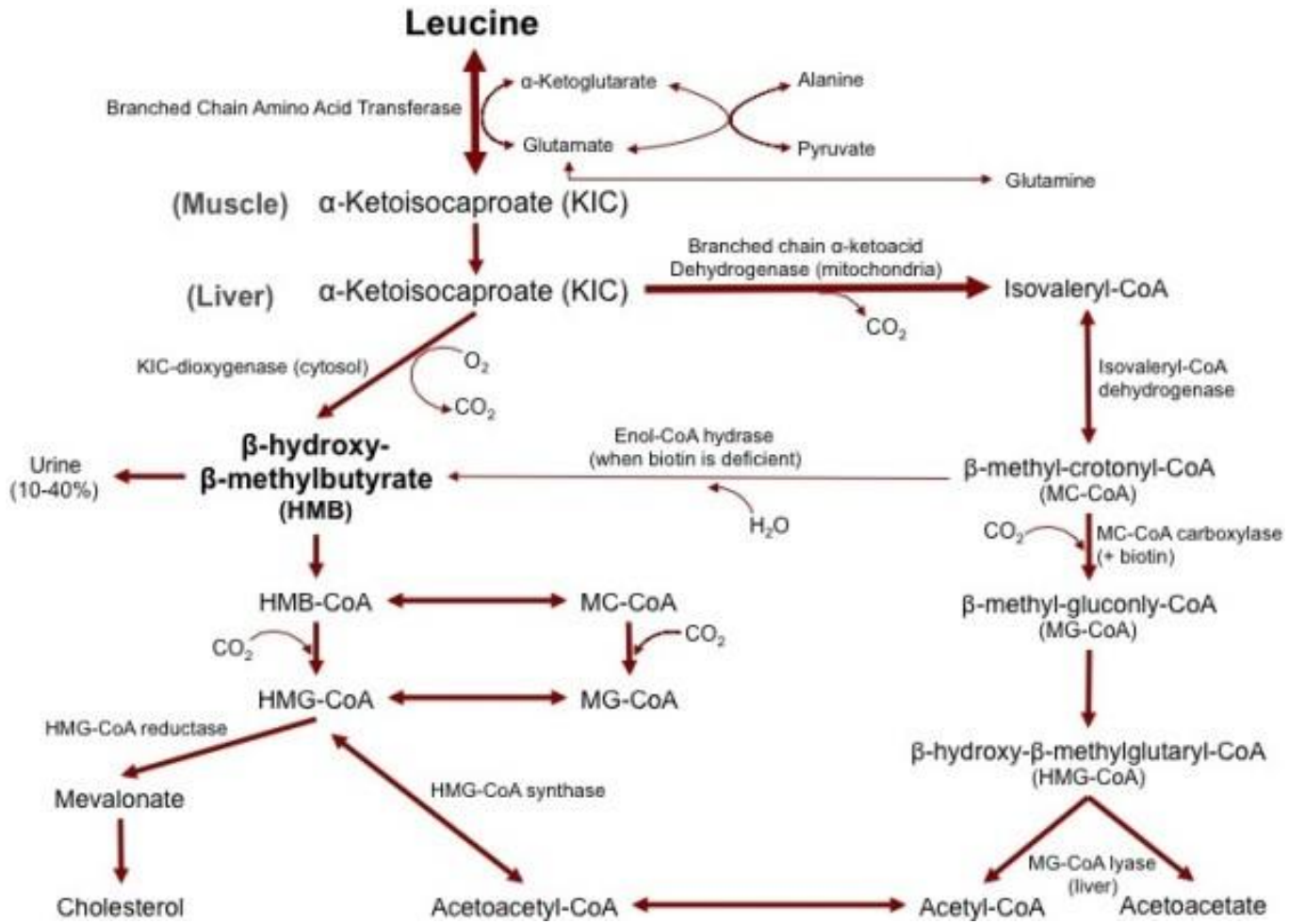
Breakdown of Leucine to HMB



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- Animal studies are also positive for these outcomes
- HMB has improved lean mass in AIDS patients
- However, a number of well- designed human studies have shown negative results in athletes (remains questionable)

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HMB And Lean Mass

Title: **Reversal of cancer-related wasting using oral supplementation with a combination of beta-hydroxy-beta-methylbutyrate, arginine, and glutamine.**

Author(s) : May PE; Barber A; D'Olimpio JT; Hourihane A; Abumrad NN

Author's Address : Department of Surgery/112, Veterans Affair Medical Center, 1000 Locust St., Reno, NV 85920, USA. peubanks@med.unr.edu

Source : American journal of surgery [Am J Surg] 2002 Apr; 183 (4), pp. 471-9.

Pub. Type : Clinical Trial; Journal Article; Randomized Controlled Trial

Language : English

Journal Info : *Country of Publication:* United States *NLM ID:* 0370473 *ISSN:* 0002-9610 *Subsets:* AIM; IM

MeSH Terms : Dietary Supplements*
Arginine/*therapeutic use
Body Composition/*drug effects
Cachexia/*drug therapy
Glutamine/*therapeutic use
Neoplasms/*complications
Valerates/*therapeutic use
Aged; Arginine/administration & dosage; Cachexia/etiology; Double-Blind Method; Drug Combinations; Female; Glutamine/administration & dosage; Human; Male; Middle Age; Muscle, Skeletal/drug effects; Neoplasms/pathology; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.; Treatment Outcome; Valerates/administration & dosage

Abstract : BACKGROUND: Cancer-related cachexia is caused by a diverse combination of accelerated protein breakdown and slowed protein synthesis. The hypothesis proposed in this study is that supplementation of specific nutrients known to positively support protein synthesis and reduce protein breakdown will reverse the cachexia process in advanced cancer patients. METHODS: Patients with solid tumors who had demonstrated a weight loss of at least 5% were considered for the study. Patients were randomly assigned in a double-blind fashion to either an isonitrogenous control mixture of nonessential amino acids or an experimental treatment containing beta-hydroxy-beta-methylbutyrate (3 g/d), L-arginine (14 g/d), and L-glutamine (14 g/d [HMB/Arg/Gln]). The primary outcomes measured were the change in body mass and fat-free mass (FFM), which were assessed at 0, 4, 8, 12, 16, 20, and 24 weeks. RESULTS: Thirty-two patients (14 control, 18 HMB/Arg/Gln) were evaluated at the 4-week visit. The patients supplemented with HMB/Arg/Gln gained 0.95 +/- 0.66 kg of body mass in 4 weeks, whereas control subjects lost 0.26 +/- 0.78 kg during the same time period. This gain was the result of a significant increase in FFM in the HMB/Arg/Gln-supplemented group (1.12 +/- 0.68 kg), whereas the subjects supplemented with the control lost 1.34 +/- 0.78 kg of FFM (P = 0.02). The response to 24-weeks of supplementation was evaluated by an intent-to-treat statistical analysis. The effect of HMB/Arg/Gln on FFM increase was maintained over the 24 weeks (1.60 +/- 0.98 kg; quadratic contrast over time, P <0.05). There was no negative effect of treatment on the incidence of adverse effects or quality of life measures. CONCLUSIONS: The mixture of HMB/Arg/Gln was effective in increasing FFM of advanced (stage IV) cancer. The exact reasons for this improvement

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HMB Increased Lean Mass With Resistance Training

Title: Conversion of beta-methylbutyric acid to beta-hydroxy-beta-methylbutyric acid by Galactomyces reessii.

Author(s) : Lee IY; Nissen SL; Rosazza JP

Author's Address : Division of Medicinal and Natural Products Chemistry, College of Pharmacy, University of Iowa, Iowa City 52242-5000, USA.

Source : Applied and environmental microbiology [Appl Environ Microbiol] 1997 Nov; 63 (11), pp. 4191-5.

Pub. Type : Journal Article

Language : English

Journal Info : *Country of Publication:* UNITED STATES *NLM ID:* 7605801 *ISSN:* 0099-2240 *Subsets:* IM

MeSH Terms : Butyric Acids/*metabolism
Saccharomycetales/*metabolism
Fermentation; Hydrogen-Ion Concentration; Magnesium/pharmacology; Support, Non-U.S. Gov't

Abstract : beta-Hydroxy-beta-methylbutyric acid (HMB) has been shown to increase strength and lean mass gains in humans undergoing resistance-exercise training. HMB is currently marketed as a calcium salt of HMB, and thus, environmentally sound and inexpensive methods of manufacture are being sought. This study investigates the microbial conversion of beta-methylbutyric acid (MBA) to HMB by cultures of Galactomyces reessii. Optimal concentrations of MBA were in the range of 5 to 20 g/liter for HMB production. Preliminary shake flask experiments indicated that HMB yields were sensitive to dissolved oxygen levels and that cell growth decreased significantly as MBA concentrations increased. Degradation of HMB was faster at acidic pH, and pH 7.0 was optimal for HMB production. Resting cells obtained from media without MBA could efficiently convert MBA to HMB. Thus, a two-step, fed-batch fermentation procedure in which biomass was first produced, followed by coaddition of MBA and glucose, while dissolved oxygen was maintained at 20% of saturation, was designed. A maximum HMB concentration of 38 g/liter was obtained after 136 h, and the molar conversion yield was more than 0.50 mol of HMB/mol of MBA during the fermentation.

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Referenced Studies with HMB

- HMB supplementation has been shown to increase the level of muscle cell growth factors (signaling agents), which in turn, promote protein synthesis and an increase in lean mass.

- A four-week double-blind trial involving 40 men showed that 3,000 mg of HMB supplementation per day plus exercise (three days per week) increased lean mass by 3.10%, compared to 1.92% increase in the placebo group, as well as a decrease in fat mass of 7.2% in the HMB group, compared to only 2.2% in the placebo group.

- The HMB users also showed greater strength gains than the placebo group. This study recruited both fit and unfit men, who were randomly assigned to the HMB or placebo group. (1,2).

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- A second study by the same researcher revealed that HMB supplementation can also improve endurance performance in athletes. (3)

- Animal studies also suggest that HMB supplementation can improve lean mass gains and some evidence suggests that in patients with AIDS, HMB supplementation can reduce muscle wasting. (4,5)

- However, a number of well-designed double-blind trials have found no effect of 3,000 to 6,000 mg of HMB per day on body composition or exercise performance in athletes, after four-weeks of supplementation. (6,7,8)

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References: HMB

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Reference 1 HMB Update

The body synthesizes between 0.3 and 1.0 gm of HMB daily, about 50% derived from leucine catabolism.

New studies show that HMB supplementation reduced urinary 3-methylhistidine and plasma creatine phosphokinase (CPK) during the first 2-weeks of training. These biomarkers of muscle damage ranged between 20-60% lower in the HMB-supplemented group, suggesting less muscle damage and catabolism with HMB supplementation. This group also lifted more total weight than unsupplemented group.

There was increase in muscle strength by 8% in unsupplemented group and 13% in group supplemented with 1500 mg (1.5 gm) HMB per day, and 18% increase in group supplementing with 3,000 mg (3.0 gm) per day

Other studies have shown similar effects on preventing muscle catabolism during training with increased strength gains, while other have not shown an effect.

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Mechanism of Action – research suggests that HMB inhibits normal proteolytic processes that accompany intense muscular overload. This effect may be short-lived and physiology appears to revert back to unsupplemented state as training progresses, even if keep taking HMB.

Thus, long-term effects on body composition and strength gains are unknown at this time. However, even in studies not showing improvement in strength, lower urinary 3-methyhistidine and plasma CPK was still evident, showing reduced muscle damage and catabolism.

Toxicity: Even at daily dosage at 8,000 mg (8gm) per day, during 8-weeks of resistance training no elevated hepatic enzymes or altered lipid profile, renal dynamics or immune function was noted. Age does not affect responsiveness to HMB supplementation.

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Caffeine:

- Caffeine stimulates release of fatty acids and glycerol from fat cells
- This occurs through an increase of cAMP (inhibits phosphodiesterase) which in turn stimulates HSL to hydrolyze trigylceride
- With increased fats in the blood stream early into exercise, the exercising muscle can slow glycogen burning, enhancing performance in **endurance events** primarily
- The usual dose of caffeine is 330 mg ingested one hour before exercise (~2 cups of coffee)

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- Caffeine also increases epinephrine and other catecholamines in blood, which act as stimulants

- Doses of 6 mg/kg body wt enhances performance and results in urine conc. below 12 mg/dL (The IOC restricted level)

References: Caffeine

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Reference 1 Update: Caffeine

The average American consumes 250 mg of caffeine daily, about 70% from coffee; 15% soft drinks; 2% chocolate.

It is the most widely consumed behavioral active substance worldwide.

Caffeine belongs to class of lipid-soluble purines

Depending on preparation one cup of coffee contains 60-150mg of caffeine (Instant coffee about 100mg; brewed tea 20-50 mg; caffeinated soft drinks about 50mg)

For competition 2-3 cups of percolated coffee contains 250-400mg of caffeine or between 3-6 mg/kg body mass, which produces urinary caffeine concentrations within the established IOC acceptable limit of 12 ug/ml and NCAA limit of 15 ug/ml or restricted substances.

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The intestinal tract absorbs caffeine rapidly with peak plasma concentrations reached within 1-hour. Caffeine clears from the body fairly rapidly taking about 3-6-hrs for blood caffeine concentrations to reduce by 50%. By comparison it takes about 10 hours for clearance of other stimulants like methamphetamine.

Drinking 2-3 cups of regularly percolated coffee 1-hour before exercise extends endurance in strenuous aerobic exercise and short duration maximal effort and repeated exercise bouts typically of high-intensity sports, under laboratory and field conditions.

The ergogenic effect of this dose is maintained for a 5-hour period, thus no need to ingest more caffeine on tournament days between games, matches or heats, if the next challenge falls within the 5-hour time frame.

An ergogenic effect can also occur by ingesting caffeine just minutes before exercise onset.

Studies show that caffeine ingested 60-minutes before exercise increases fatty acid oxidation and reduced glucose oxidation, thus slowing glycogen depletion, extended exercise time to exhaustion significantly at given similar heart rate and oxygen uptake as subjects not ingesting caffeine.

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- Even in events like maximal swimming effort for less than 25-minutes caffeine improves performance, and shown to improve split times in 500 meter swim. Higher blood glucose was also noted, suggesting increased glucose availability than without caffeine intake.

- For tasks requiring physical and mental performance (firefighter in action, or military operation) – the combination of 50gm glucose plus 40mg caffeine in a drink shown to reduce anxiety, and feelings of stress, improved performance and grip strength following fire fighter training.

- Caffeine is thought to act directly on adipose and peripheral tissues to stimulate the release of fatty acids into the bloodstream and/or by increasing epinephrine release, which stimulates beta-adrenergic receptors for hydrolysis of triglycerides and subsequent release of free fatty acids into the bloodstream. In both cases this increases fatty acid oxidation and spared depletion of liver and muscle glycogen.

- Caffeine and its metabolites also cross the blood-brain barrier, producing analgesic effects which block perception of muscle pain during exercise. It also increases motor neuron excitability, thus facilitating greater motor unit recruitment

- In the CNS caffeine does not act directly, but rather blocks the effects of adenosine – a substance that calms the brain and spinal cord neurons.

- Caffeine also acts directly on muscles to enhance exercise capacity in tests of repeated short-term anaerobic power, but not in tests of maximal strength.

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Precautionary Note: Younger persons (under 50 yr) who metabolize caffeine slowly (P450 1A2 detox enzymes – can test using nutrigenomics assessment) have increased risk for heart attack .

Caffeine consumption showed a 64% increased risk of heart attack in these individuals with 4 cups/coffee per day compared to 1 cup/day

Individuals over 50, who metabolize caffeine slowly should also be careful with caffeine consumption

Those who metabolize caffeine quickly have no increased heart attack risk

Most people know if caffeine affects them adversely and should avoid its use if that is the case.

Caffeinism – caffeine intoxication characterized by restlessness, tremulousness, nervousness, excitement, insomnia, flushed face, diuresis, GI complaints, rambling flow of thought and speech, tachycardia or cardiac arrhythmia, periods of inexhaustibility and/or psychomotor agitation.

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Caffeine Intoxication can increase risk of seizures, acid-base balance disorders, acute hepatitis, and CVD events.

In quantities of **1500 mg daily** it can produce the following 9 symptoms:

1. Restlessness
2. Headaches
3. Insomnia
4. Nervous Irritability
5. Muscle Twitching
6. Muscle Tremor
7. Psychomotor Agitation
8. Increased Heart Rate and Blood Pressure
9. Premature Left Ventricular Contractions

Death from caffeine overdose has occurred

Caffeine has an LD_{50} of 10gm (or 150 mg/kg body wt).

For a 50-kg woman acute health risk occurs at a caffeine intake of 7500 mg (7.5 gm) as an example

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Caffeine and Weight Loss and Fat-Burning

- Caffeine intake of 100 mg increases Resting Metabolic Rate (RMR) by 3-4% over 150 min time frame
- 200 mg caffeine increases RMR by 8.5% over 3-hr period, but caffeine tolerance can occur over time.
- 1 cups Starbucks Coffee – 112 mg caffeine
- It inhibits breakdown of cAMP, which in turn, perpetuates stimulation of hormone sensitive lipase for fatty acid release into bloodstream – upregulating fatty acid oxidation (thus weight-loss effect)

Reference: Int J Sport Nutr Exerc Metab. 2012 Apr;22(2):139-54. https://www.ncbi.nlm.nih.gov/pubmed/22465867

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Ephedra and Related Alkaloids:

- Ma huang (ephedra) is banned by IOC, as well as the herb's alkaloids, ephedrine and pseudoephedrine

- Ephedra is a CNS stimulant, increases the release of fatty acids and glycerol via HSL in fat cell (stimulates *B*-adrenergic receptors on fat cells - like adrenaline), which in turn increases cAMP, which stimulates HSL activity.

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- Combining 375 mg of caffeine with 75 mg of ephedrine increases high-intensity , aerobic exercise performance in young athletes

- Ephedra is the leader in reported adverse events of all natural health products (17% of all reported adverse events) – side effects include, sudden death, cardiac arrest, stroke, hypertension, seizures, nervousness, anxiety, insomnia

I Ephedrine

- Ephedrine has similar pharmacological action as epinephrine, but is less potent. Ephedrine is also absorbed more slowly than epinephrine, but is longer acting with more sustained effects on the brain and central nervous system, but again is much less potent.4

- Both ephedrine and pseudoephedrine cross the blood brain barrier resulting in stimulation of the nervous system.

The physiological effects of ephedrine are similar to those of epinephrine and include:

- Increases blood pressure
- Increases cardiac output
- Increases heart rate
- Increases blood flow to the heart, brain, and skeletal muscle
- Decreases blood flow to the intestinal tract and kidneys
- Relaxation of bronchial muscles and uterine muscles

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II. Pseudoephedrine

- Pseudoeohedrine also relaxes bronchial muscles like ephedra, but exerts weaker effects on the heart and central nervous system.

- Therefore, it is often recommended in the treatment of chronic asthma instead of ephedrine. 4

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Clinical Application and Mechanism of Action

Weight Loss Aid

- Ephedra has been shown to increase the metabolic rate and encourage the release of fatty acids from adipose tissue to the bloodstream, where they may be taken up and used as a metabolic fuel by skeletal muscle and other tissues. Ephedra acts as a sympathetic nervous system stimulant, enhancing the release of adrenaline and providing a direct thermogenic effect.

- The thermogenic effect can be enhanced by methylxanthines (i.e., caffeine) and salicylates. As such, combinations of these ingredients have been used in studies with athletes and have been shown to produce ergogenic performance-enhancing effects.

- For weight loss patients, most of the studies have used a combination of 20 mg of ephedrine and 200 mg of caffeine, three times daily. Although significant weight loss results have been achieved using this approach (i.e., 36 lbs of weight loss in 24 weeks compared to 29 lbs in the placebo group), health practitioners and consumers should be aware of the dangerous side effects that can result (see Adverse Side Effects and Toxicity) from the use of ephedrine or ephedra-containing supplements.

Dosage Range and Standardized Grade
Weight Loss Aid

As a weight loss aid, a common dosage is 12.5 – 25.0 mg of ephedrine, taken twice or three times per day. Most ephedra species (i.e., ephedra sinica or Ma Huang) are 1 – 3 percent alkaloid content, but a 10 percent standardized extract is now available.

Therefore, the dosage of a 10 percent alkaloid content (Ma Huang) extract would be 125 to 250 mg, three times daily.

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Adverse Side Effects, Toxicity and Contraindications

- As reported by the FDA (U.S.) Special Nutritionals Adverse Event Monitoring System, 17 percent of all adverse reactions related to dietary supplements were a result of ephedra-containing products in 1998 (more than 800 reports).
- The list of adverse side effects include:

▪ Nervousness	▪ Insomnia
▪ Irritability	▪ Psychosis
▪ Headache	▪ Dizziness
▪ Seizures	▪ Stroke
▪ Premature ventricular contractions	▪ Increased blood pressure
▪ Myocardial infarction (heart attack)	▪ Sudden death

- The Food and Drug Administration advisory review panel on non-prescription drugs recommended that ephedrine not be taken by patients with heart disease, high blood pressure, thyroid disease, diabetes, or difficulty in urination due to enlarged prostate or by patients taking antihypertensive or antidepressant drugs.

- Other contra-indications include anxiety, glaucoma, pheochromocytoma.

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Drug-Nutrient Interactions

Ephedra-containing products should not be used concurrently by patients taking the following medications:

▪ Caffeine containing drugs	▪ Cardec DM
▪ Epinephrine containing drugs	▪ Nadolol
▪ Pheneizine	▪ Phenylpropanolamine
▪ Monoamine oxidase inhibitors (MAO-inhibitors)	▪ Any Oral or Inhaled Anti-asthmatic medication
▪ Digoxin – digitalis	▪ Antihypertensive drugs
▪ Guanethidine	▪ Antidepressants

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Dangers Of Ephedra

Title: **Ephedra and its application to sport performance: another concern for the athletic trainer?**

Author(s) : Powers ME

Affiliation(s) : University of Florida, Gainesville, FL. E-mail: mpowers@hhp.ufl.edu

Source : Journal of Athletic Training (J ATHLETIC TRAIN), 2001 Oct-Dec; 36(4): 420-4 (38 ref)

Publication Type : journal article - CEU, review, tables/charts

Language : English

Major Subjects : Sports; Physical Performance; Ergogenic Products; Ephedrine; Herbs

Minor Subjects : Education, Continuing (Credit); Weight Loss; Herbs--Adverse Effects; Ephedrine--Adverse Effects; Ephedrine--Pharmacokinetics; Caffeine; Energy Metabolism

Abstract : Objective: The ma huang herb, otherwise known as ephedra, has gained widespread popularity as an ergogenic supplement. With the sympathomimetic alkaloid ephedrine as its primary active ingredient, ma huang is marketed to reduce fatigue; increase strength, power, and speed; decrease reaction time; and improve body composition. Although numerous side effects have been associated with the use of ma huang, its popularity in athletes continues to grow. This review provides rationale for the ergogenic claims regarding ma huang and compares and contrasts those claims with data from scientifically controlled investigations.

Data Sources: MEDLINE and SPORT Discus were searched from 1970 to 2000 using the key words ma huang, ephedra, and ephedrine in combination with humans, exercise, performance, and side effects.

Data Synthesis: Ephedrine has been used alone or in combination with other drugs as an effective weight-loss agent. The weight loss has been attributed to thermogenic and lipolytic effects which, in combination with the central nervous system stimulating effects, have also resulted in its use as an ergogenic aid. Most of the scientific data, however, do not support manufacturers' ergogenic claims, and numerous side effects have been associated with ephedrine use. Thus, the safety and efficacy of ma huang as an ergogenic supplement must be questioned.

Conclusions/Recommendations: It appears that the risks associated with the use of ma huang far outweigh any possible ergogenic benefits. Thus, it is extremely important that athletic trainers educate athletes on these issues so they can continue to perform at an optimum level in a safe and healthy manner.

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Reference 1 Ephedra Update

In April 2004 the FDA announced a ban on ephedra

Physician stopped prescribing ephedrine as a decongestant back in the 1930's, but the more mild pseudoephedrine is still present in OTC flu and cold medications and is used to treat mucosal congestion occurring hay fever, allergic rhinitis, sinusitis and other respiratory conditions.

Studies with athletes have shown increased muscular endurance during the first set of traditional resistance training exercise

As well, improved 1500 m running performance in male athletes ingesting 2.5mg/kg body mass compared maltodextrin placebo 90-mins before all-out run trial. Ergogenic effects were attributable to CNS effects rather than altered metabolism.

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Ephedra Plus Caffeine

- Ma huang (ephedra) is banned by the International Olympic Committee (IOC) as well as the herb's alkaloids, ephedrine and pseudoephedrine.

- Studies with young athletes show that the combination of caffeine (375 mg) plus ephedrine (75 mg) increases energy during high-intensity, aerobic-exercise performance.

- Note that caffeine is also banned by the IOC, at urinary levels at or above 12 mg/ml. (1,2)

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- Ephedra acts as an ergogenic aid by directly stimulating the central nervous system and by increasing the release of free fatty acids from fat cells. Its direct stimulatory action on the central nervous system enables athletes to recruit a greater number of muscle fibers into the process of muscle contraction, boosting the maximum output of muscle force.

- In regards to free fatty acids, ephedra stimulates the beta-adrenergic receptors on fat cells, which like adrenaline, increase the concentrations of cyclic AMP within fat cells, and thereby stimulates the action of hormone sensitive lipase (HSL). In turn, HSL hydrolyzes triglycerides within fat cells, permitting free fatty acids and glycerol to diffuse into the bloodstream.

- Once in the bloodstream free fatty acids combine with the protein carrier albumin, and circulate to the exercising muscle, which extract free fatty acids from the bloodstream and use them in their aerobic energy pathway (beta-oxidation to acetyl CoA, leading to oxidative phosphorylation) to synthesize ATP energy for muscle contraction.

- Thus, ephedra, like caffeine and the herb coleus forskohlii, can release free fatty acids into the circulation before exercise begins, providing an immediate fuel for aerobic metabolism and thereby slowing the depletion of muscle glycogen.

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- As the muscle glycogen depletion is a rate-determining factor in regards to how long an aerobic activity can be maintained at an optimal pace, any intervention that slows muscle glycogen depletion gives an athlete an advantage in many endurance events.

- Therefore, ephedra is an ergogenic aid for both high intensity, explosive events (via CNS stimulation) and endurance events (via the slowing of glycogen depletion). These effects can be further enhanced by combining ephedra with caffeine, at the above stated doses. (3-14)

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References: Ephedra Plus Caffeine

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Chromium

Overview

- Most adults shown to consume only 25-50 mcg of chromium per day (50-200 mcg is recommended)

- Chromium potentiates action of insulin, thus:
  1. Chromium has been shown to lower blood insulin (increasing glucose utilization, less lipogenesis, less sodium resorption)
  2. Chromium enhances amino acid uptake into muscles in trained athletes employing 12 wk weight training (men and women), with significant lean mass gains (Evans & Hasten)
  3 Chromium shown to reduce body fat (elevated RMR and less lipogenesis)
  4. Also, Chromium has been shown to lower cholesterol and triglycerides in diabetic and non-diabetic subjects - and reverses corticosteroid-induced diabetes (200-1,000 mcg daily) Non Toxic up to 1,000 mcg
  5. Also, Exercise increases urinary excretion of chromium (Anderson)

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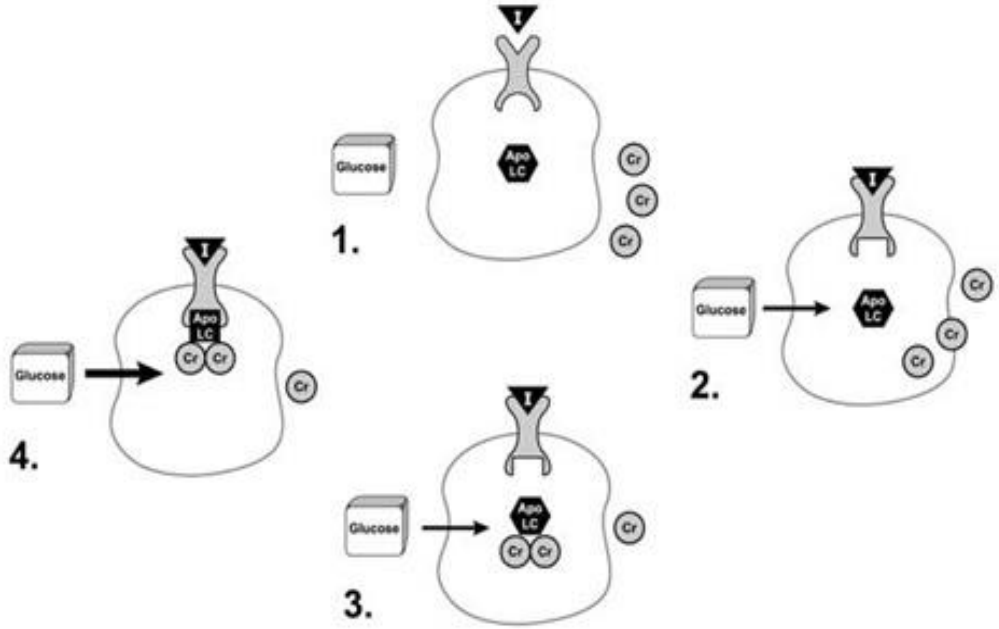
Chromium Enhances Insulin Function on Insulin Receptor



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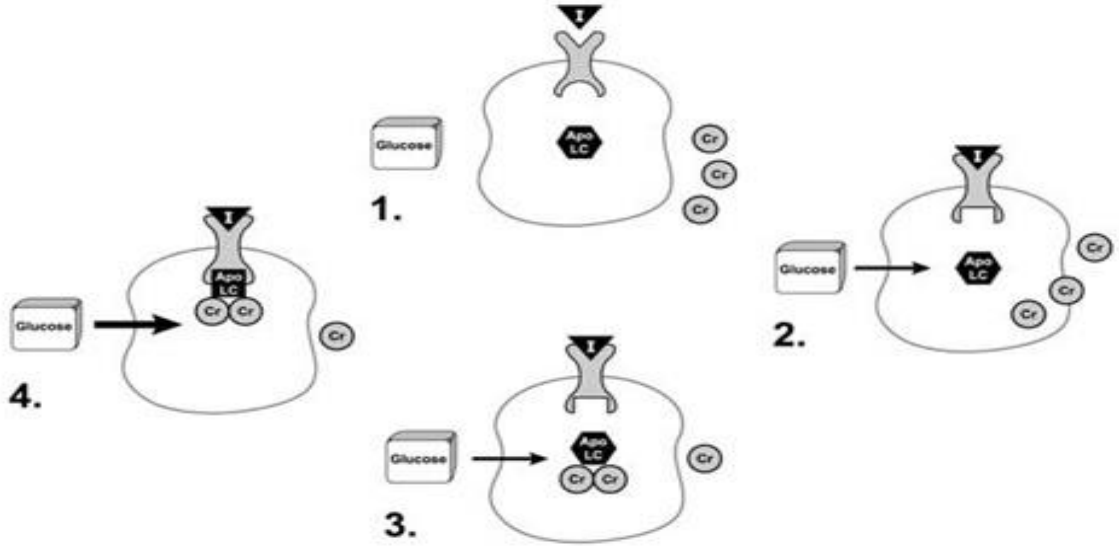
Chromium binds to LMWcr-peptide to increase action of insulin

- Insulin binds to and activates the insulin receptor.
- Insulin receptor activation stimulates the movement of chromium into the cell.
- Chromium binds to a peptide known as Apo-LMWCr* (Apo-LC).
- Functional LMWCr (LC) binds to the insulin receptor and enhances its activity.
- **LMWCr = low-molecular weight chromium-binding substance*
- *Adapted from Vincent, J.B. Quest for the molecular mechanism of chromium action and its relationship to diabetes. Nutr Rev. 2000; 58:67-72. (as found on line from the Linus Pauling Institute; Oregon State University).*



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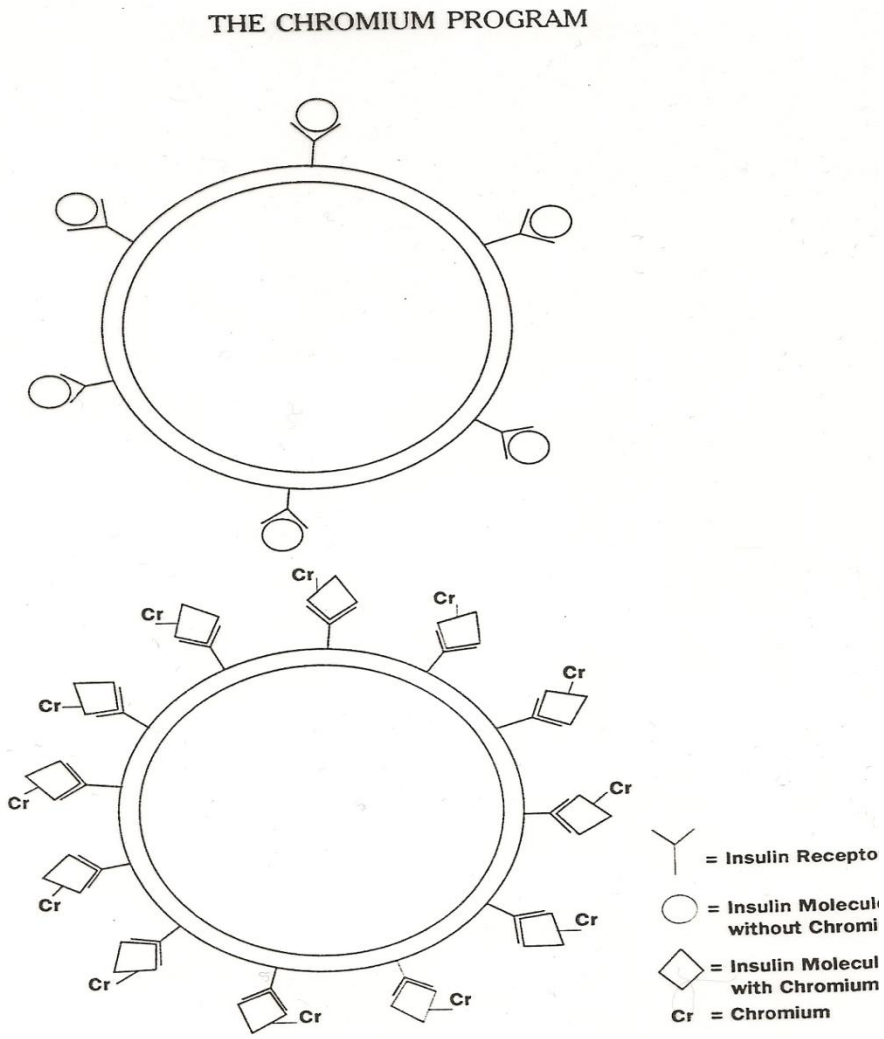
Chromium Enhances Insulin Sensitivity



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Chromium Increases Lean Mass

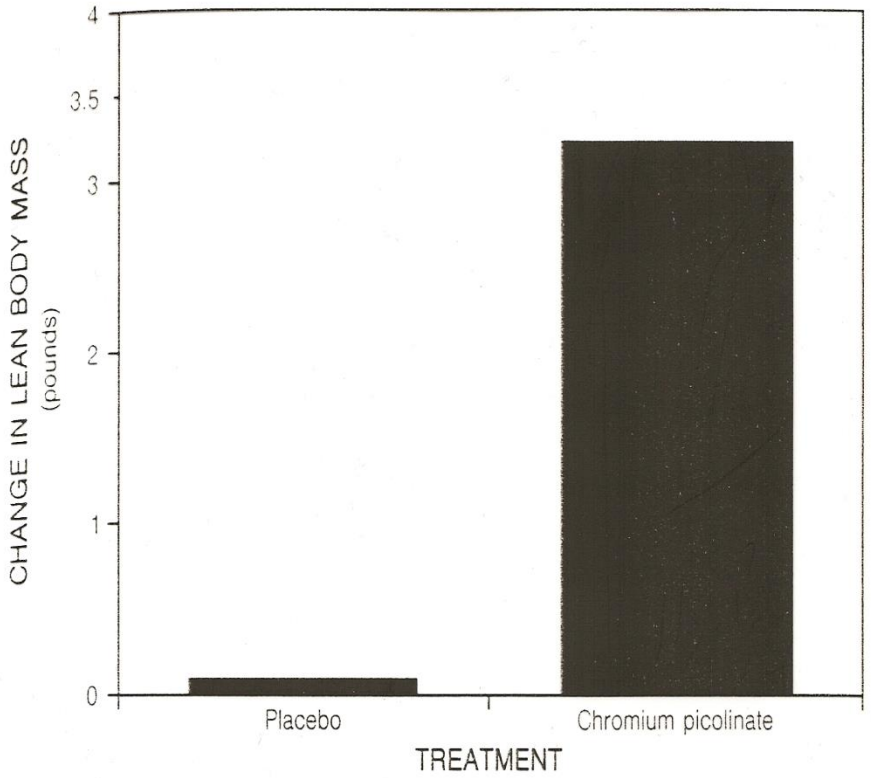

Figure 1. Effect of supplemental chromium on lean body mass in Evans's first study. Ten volunteers supplemented their usual diets with either 200 micrograms of chromium (chromium picolinate) or placebo daily for six weeks. During that time they followed a prescribed weight training program (see Appendix D). At the end of the six weeks, the lean body mass of those on chromium had increased by 3.5 lbs, whereas there was only a 0.08 lb change in lean body mass in those on the placebo. (From G. W. Evans and others, submitted for publication.)

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Chromium and Lean Mass – Football Players

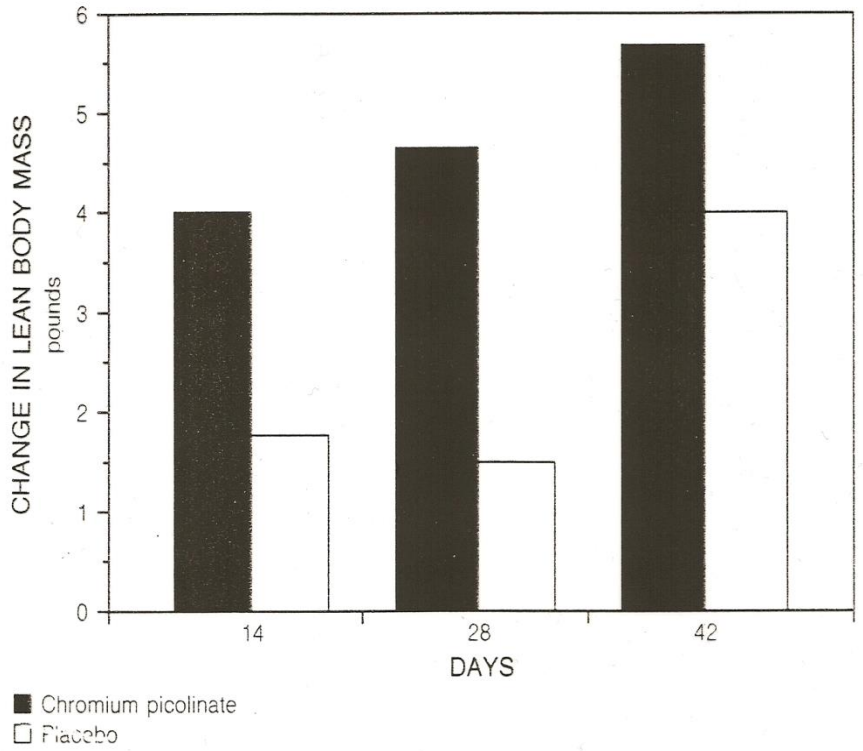

Figure 2. Effect of supplemental chromium on lean body mass in Evans's second study. Thirty-one football players took supplements of either 200 micrograms of chromium (chromium picolinate) or placebo for six weeks while participating in a supervised weight training program (see Appendix D). The group on chromium increased lean body mass by 4 pounds after two weeks and by 5.69 pounds by the end of the six weeks. In the group on placebo, there was less than a 2 lb increase after 14 days and only 4 lbs at the end of 6 weeks. 42% less than the group on chromium. (From G. W. Evans and others, submitted for publication.)

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Chromium Decreases Body Fat

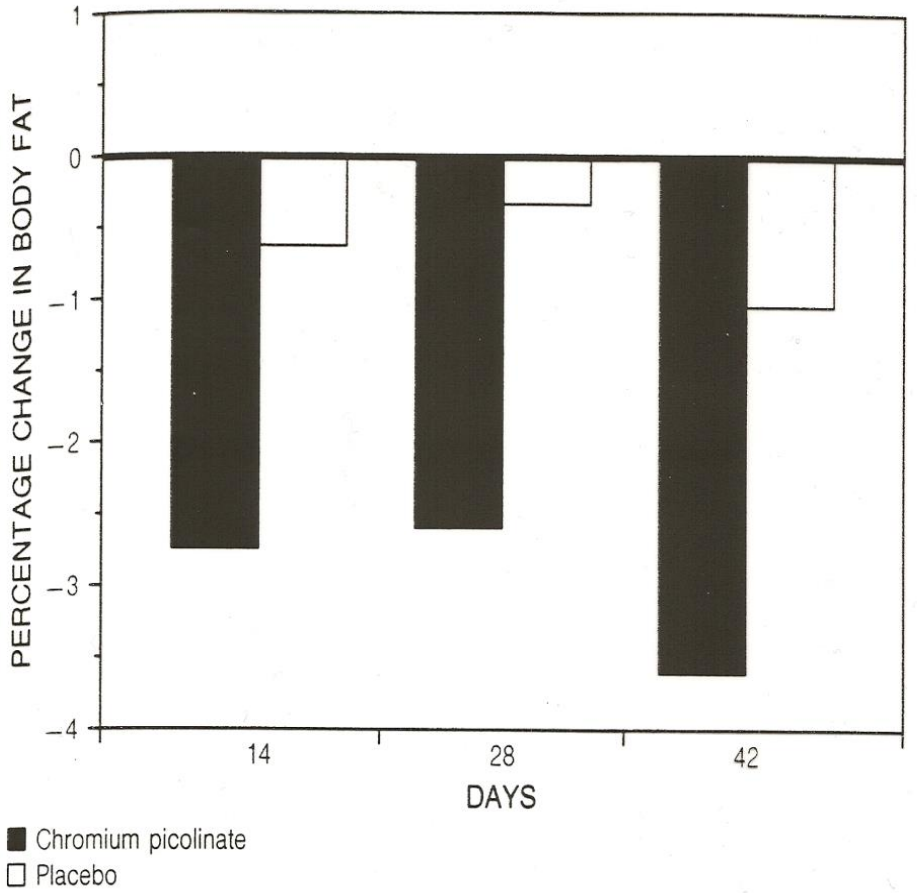

Figure 3. Effect of supplemental chromium on body fat.

In the thirty-one football players who participated in Dr. Evans's second study, there was a significant loss of body fat in the group on chromium. At the completion of the six-week study, those on chromium had lost 7.5 lbs (3.6 percent) of body fat. This was a highly significant result, compared with the group on placebo, which lost only 2 lbs (1 percent) of body fat. (From G. W. Evans and others, submitted for publication.)

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Summary of Chromium and Body Fat Reduction

Title: **Effects of chromium on body composition and weight loss.**

Author(s) : Anderson RA

Author's Address : Nutrient Requirements and Functions Laboratory, Beltsville Human Nutrition Research Center, U.S. Department of Agriculture, Beltsville, Maryland 20705, USA.

Source : Nutrition reviews [Nutr Rev] 1998 Sep; 56 (9), pp. 266-70.

Pub. Type : Journal Article; Review; Review, Tutorial

Language : English

Journal Info : *Country of Publication:* UNITED STATES *NLM ID:* 0376405 *ISSN:* 0029-6643 *Subsets:* IM

MeSH Terms : Body Composition/*drug effects
Chromium/*pharmacology
Weight Loss/*drug effects
Chromium/administration & dosage; Chromium/adverse effects; Dietary Supplements; Human; Nutrition Policy

Abstract : Chromium is an essential nutrient involved in the regulation of carbohydrate and lipid metabolism. Normal dietary intake of chromium in humans and farm animals is often suboptimal. In addition to its effects on glucose, insulin, and lipid metabolism, chromium has been reported to increase lean body mass and decrease percentage body fat, which may lead to weight loss in humans. The effects of chromium on body composition are controversial but are supported by animal studies, which increase their validity. A subject's response to chromium depends on his or her chromium status, diet consumed, type and amount of supplemental chromium, and study duration. There have been no confirmed negative effects of chromium in nutritional studies. Chromium is only a small part of the puzzle in the control of weight loss and body composition, and its effects, if present, will be small compared with those of exercise and a well-balanced diet.

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Chromium Referenced Studies

General Features

- Chromium is an essential trace element required for maintenance of normal glucose metabolism. The function of chromium is directly related to the function of insulin, as chromium enhances (potentiates) the activity of insulin. Some human studies demonstrate that chromium supplementation results in improvement of glucose intolerance. Thus, it may have important applications for diabetics, hypoglycemic patients, and in Syndrome X (the metabolic syndrome).

- Insulin-chromium interactions are not restricted to glucose metabolism. Animal and human studies indicate that chromium stimulates amino acid transport into the cells with a corresponding increase in protein synthesis.

- Only the trivalent state of chromium is biologically active (nutritional chromium). By contrast the hexavalent form of chromium used as metal alloys by industry (industrial chromium) can be extremely toxic.

- The chromium concentration of most body tissue decreases steadily as we age. As well, increasing impairment of glucose tolerance throughout normal pregnancy has been amply documented, and the changes in chromium concentration in the plasma may reflect decreased glucose tolerance or may actually reflect deficiency.

- Concentration of chromium in the hair is ten times higher than in blood, and hair concentration has been suggested as a means of assessing chromium status.

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Absorption and Metabolism

- The exact mechanism of chromium absorption is not known, but it is not simple diffusion. Chromium is transported in the plasma in combination with transferrin. Unlike other metals, once chromium is absorbed, it is almost entirely excreted in the urine. Thus, daily intake is important to optimize chromium's functions in the body.

- Generally speaking, absorption of inorganic chromium found in food and water appears to be only about one percent. Organically-bound chromium (e.g., GTF-chromium, chromium-chelates found in many supplements) permits a bioavailability of 10-25 percent. The total amount of chromium found in the body averages less than 6 mgs. The hair, spleen, kidney and testes contain the highest concentrations.1,2

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Supplementation Studies and Clinical Applications

Glucose Intolerance

- More than 15 controlled studies demonstrate that chromium supplementation has a positive effect on impaired glucose tolerance, by potentiating the action of insulin. This has important implications for hypoglycemics and Type II diabetics.4

- In clinical studies in non-insulin dependent diabetes mellitus (NIDDM), supplementation with chromium has been shown to decrease fasting glucose levels, improve glucose tolerance, lower insulin levels, decrease total cholesterol and triglycerides, and increase HDL-cholesterol levels.5-8 In most of these studies, subjects ingested a minimum of 200 mcg of chromium from a supplement, daily.

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Cholesterol and Triglyceride Lowering

- Chromium supplementation has been shown to lower cholesterol and triglycerides in both diabetic and non-diabetic subjects. Many forms of chromium have demonstrated this effect, but the value appears to be only in those with low initial chromium nutritional status. The typical changes are a 10 percent reduction in total cholesterol and triglycerides and a two percent increase in HDL.9-14

- These are significant changes as every one percent decrease in total cholesterol corresponds to a 2-3 percent reduction in heart disease and stroke. Every one percent increase in HDL-cholesterol levels carries a 2-4 percent decrease in risk of cardiovascular disease.15

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Body Fat Reduction and Lean Mass Gains

- Chromium supplementation has been shown to facilitate reductions in body fat and increase lean muscle mass. Lean mass gains have been especially noteworthy in subjects taking chromium supplements in conjunction with resistance training, in both young males and females. However, even in older and elderly subjects chromium supplementation has produced significant reductions in body fat and moderate increases in muscle mass compared to placebo.

- Typical doses for weight loss and lean mass gains have used 200-400 mcg per day. Additional studies are underway to determine the degree to which chromium may be helpful as a weight loss and anabolic aid.2,16,17,18 Presumably chromium is effective in these applications due to its ability to increase insulin sensitivity, thereby lowering plasma insulin levels. Higher insulin levels tend to convert more carbohydrates into fat and insulin resistance decreases protein synthesis in muscles and amino acid uptake.2

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Dosage Ranges:

- Glucose Intolerance: 200-400 mcg per day
- Cholesterol and Triglyceride: 200-1,000 mcg per day
- Weight Loss and Lean Mass Gains: 200-400 mcg per day2
- Type-II Diabetics: 500 mcg of chromium, taken twice per day has been shown to decrease glycolated hemoglobin, glucose, insulin and cholesterol variables 19. Chromium supplementation has been shown to reverse corticosteroid–induced Diabetes (200-1000 mcg).20

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Side Effects and Toxicity

- Trivalent chromium (nutritional chromium) has a very large safety range and there have been no documented signs of chromium toxicity in any of the nutritional studies at levels up to 1 mg (1,000 mcg) per day.21

- Some patients have reported increased dream vividness and decreased sleep requirements with chromium supplementation taken at 7:30 p.m., daily (50 mcg).22

- At levels of intake between 1,200 mcg and 3,400 mcg of chromium picolinate a case of anemia, liver dysfunction and other problems appeared after four to five months.23

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Drug-Nutrient Interactions

- Chromium supplementation may enhance the effects of drugs for diabetes (e.g., insulin, blood-sugar lowering agents) and possibly lead to hypoglycemia. Therefore, diabetics taking these medications should supplement chromium only under the supervision of their attending physician.

- Doses of glyburide (a hypoglycemic sulfonylurea drug used to lower blood sugar in type II diabetics) will need to be lowered if chromium supplementation is initiated, in most cases.

- Insulin-dependent diabetics may also be required to lower their insulin dosage if chromium supplementation is implemented.24

- Corticosteroid drugs - may increase urinary loss of chromium.21

- Insulin (Type-I Diabetics) - chromium can potentiate the action of insulin, thus affecting insulin dose requirements (do not supplement with chromium without cooperation of attending diabetic physician).25

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Nutrient-Nutrient Interactions

- **Refined Sugars:** excess sugar intake has been shown to increase urinary loss of chromium.26

- **High Carbohydrate Diet:** high carbohydrate consumption has been shown to increase the urinary loss of chromium.27

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Reference 1: Chromium Update:

Chromium is shown to potentiate insulin function, thus improving glucose uptake and protein synthesis.

Chronic chromium deficiency increases blood cholesterol and decreases sensitivity to insulin, thus increasing risk of developing type 2 diabetes.

Some adult Americans consume less than 50-200 mcg per day (estimated safe and adequate level). This occurs because foods high in chromium:

Brewer's yeast, broccoli, wheat germ, nuts, liver, prunes, egg yolks, apples with skins, asparagus, mushrooms, wine, and cheese – do not usually form a significant part of diet.

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Food Processing removes considerable chromium.

Strenuous exercise and high-CHO diet promote urinary loss of chromium, thus increasing potential for chromium deficiency.

Studies in recent years have not shown increased lean mass gains with chromium supplementation in fit and unfit individuals, including young and older subjects.

Chromium competes with iron for binding to transferrin – a plasma protein that transports iron form ingested food and damaged RBC's and delivers it to tissues in need of iron. However, high-dose chromium studies (924ug per day) did not show any effects on hematologic measures or indices of iron status.

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Hydroxycitric acid

- HCA found in the Garcinia cambogia fruit from south-east Asia (used as a curry substance)
- HCA shown to inhibit ATP citrate lyase, which ultimately blocks the conversion of glucose to fat in the liver (by limiting the availability of Acetyl CoA units for fatty acid synthesis
- Thus, glucose is driven into glycogen stores in liver, and once saturated, stimulates Vagus nerve to convey message to suppress thalamus appetite center in brain
- Animal studies confirm weight reduction effect in animals
- Human studies show best results in combination with chromium, and also see decline in serum triglycerides and cholesterol
- Expansion of glycogen stores may help athletes (750-1,500 mg per day of HCA is usual supplemental daily dosage)

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HCA Inhibits CHO Conversion To Fat and Promotes Body Fat Reduction

Title: **Chemistry and biochemistry of (-)-hydroxycitric acid from Garcinia.**

Author(s) : Jena BS; Jayaprakasha GK; Singh RP; Sakariah KK

Author's Address : Human Resource Development, Central Food Technological Research Institute, Mysore 570 013, India.

Source : Journal of agricultural and food chemistry [J Agric Food Chem] 2002 Jan 2; 50 (1), pp. 10-22.

Pub. Type : Journal Article; Review; Review, Tutorial

Language : English

Journal Info : *Country of Publication:* United States *NLM ID:* 0374755 *ISSN:* 0021-8561 *Subsets:* IM

MeSH Terms :
Citrates/*chemistry
Citrates/*metabolism
Clusiaceae/*chemistry
Lipids/*metabolism
Animal; Anti-Obesity Agents/chemistry; Anti-Obesity Agents/metabolism; Anti-Obesity Agents/pharmacology; Citrates/pharmacology; Energy Intake/drug effects; Enzyme Inhibitors/chemistry; Enzyme Inhibitors/metabolism; Enzyme Inhibitors/pharmacology; Fruit/chemistry; Human; Weight Loss

Abstract : (-)-Hydroxycitric acid [(-)-HCA] is the principal acid of fruit rinds of Garcinia cambogia, Garcinia indica, and Garcinia atroviridis. (-)-HCA was shown to be a potent inhibitor of ATP citrate lyase (EC 4.1.3.8), which catalyzes the extramitochondrial cleavage of citrate to oxaloacetate and acetyl-CoA: citrate + ATP + CoA --> acetyl-CoA + ADP + P (i) + oxaloacetate. The inhibition of this reaction limits the availability of acetyl-CoA units required for fatty acid synthesis and lipogenesis during a lipogenic diet, that is, a diet high in carbohydrates. Extensive animal studies indicated that (-)-HCA suppresses the fatty acid synthesis, lipogenesis, food intake, and induced weight loss. In vitro studies revealed the inhibitions of fatty acid synthesis and lipogenesis from various precursors. However, a few clinical studies have shown controversial findings. This review explores the literature on a number of topics: the source of (-)-HCA; the discovery of (-)-HCA; the isolation, stereochemistry, properties, methods of estimation, and derivatives of (-)-HCA; and its biochemistry, which includes inhibition of the citrate cleavage enzyme, effects on fatty acid synthesis and lipogenesis, effects on ketogenesis, other biological effects, possible modes of action on the reduction of food intake, promotion of glycogenesis, gluconeogenesis, and lipid oxidation, (-)-HCA as weight-controlling agent, and some possible concerns about (-)-HCA, which provides a coherent presentation of scattered literature on (-)-HCA and its plausible mechanism of action and is provocative of further research.

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HCA Decreases Body Fat and Lipogenesis In Rats

Title: **Effect of hydroxycitrate on food intake and body weight regain after a period of restrictive feeding in male rats.**

Author(s) : Leonhardt M; Hrupka B; Langhans W

Author's Address : Institute of Animal Sciences, Swiss Federal Institute of Technology, CH-8603, Schwerzenbach, Switzerland. monika.leonhardt@inw.agrl.ethz.ch

Source : Physiology & behavior [Physiol Behav] 2001 Sep 1-15; 74 (1-2), pp. 191-6.

Pub. Type : Journal Article

Language : English

Journal Info : *Country of Publication:* United States *NLM ID:* 0151504 *ISSN:* 0031-9384 *Subsets:* IM

MeSH Terms : Body Weight/*drug effects
Citrates/*pharmacology
Eating/*drug effects
Food Deprivation/*physiology
Animal; Diet; Dietary Carbohydrates/pharmacology; Dietary Fats/pharmacology; Energy Metabolism/drug effects; Fatty Acids/biosynthesis; Male; Rats; Rats, Sprague-Dawley; Support, Non-U.S. Gov't; Weight Gain/drug effects

Abstract : We examined whether dietary supplementation of hydroxycitrate (HCA), a competitive inhibitor of the extramitochondrial enzyme ATP-citrate-lyase, which inhibits lipogenesis, reduces food intake and body weight regain in rats after 10-15% weight loss. In four experiments, 24 male rats were fed restrictively (10 g/day) for 10 days and then given ad lib access to one of four different diets (HI-Suc=high sucrose; HI-Glu=high glucose; Chow=grounded standard rat chow; HI-Glu+Fat=high glucose+fat) varying in the content of fat and low molecular carbohydrates for the following 10 days. For half of the rats (n=12), the ad lib diet was supplemented with 3% (w/w) HCA. HCA reduced body weight regain with all diets except Chow. HCA also reduced food intake temporarily with three of the four tested diets. The suppressive effect of HCA on food intake was particularly strong with the HI-Glu+Fat diet (fat=24% of energy). With Diet HI-Glu and HI-Glu+Fat HCA reduced the feed conversion efficiency (cumulative body weight regain (g)/cumulative food intake (MJ)) during the 10 ad lib days, suggesting that it also increased energy expenditure. This effect seemed to be positively related to the glucose content of the diet. All in all, HCA reduced body weight regain after substantial body weight loss, and the effects are presumably linked to its inhibiting effect on lipogenesis, but the exact mechanism still has to be determined.

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Hydroxycitric Acid (HCA)

HCA is found in the Garcinia cambogia fruit from South-East Asia (used as a curry substance).

HCA has been shown to inhibit the enzyme ATP citrate lyase, which ultimately blocks the conversion of glucose to fat in the liver (by limiting the availability of Acetyl CoA units for fatty acid synthesis.

Thus, glucose is driven into glycogen stores in the liver, and once saturated, stimulates the Vagus nerve to transmit messages to suppress thalamus appetite center in brain.

Animal studies confirm weight reduction effect in animals.

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- Human studies show best results in combination with chromium, and also see a decline in serum triglycerides and cholesterol with this combined intervention. (1-11)

- Expansion of glycogen stores secondary to HCA supplementation may help athletes (750-1,500 mg per day of HCA is usual supplemental daily dosage) involved in endurance activities and in sports that demand repeated sprint intervals. (e.g. hockey, soccer, basketball etc.)

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Reference 1: HCA

Metabolically HCA acts as a competitive inhibitor of citrate lyase, inhibiting fatty acid synthesis (mostly from CHO intake). It also appears to increase glycogen synthesis as consequence of this effect. (Glycogen Replenishment – with less conversion of CHO to fat)

No ergogenic effects have been established in recent years, however.

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Catechins –from decaffeinated green tea:

Catechins are major component of polyphenolic compounds found in green and black tea.

Green tea has much higher quantities of polyphenolic compounds than black tea (including catechins like EGCG).

Clinical Studies:

Catechins proven to decrease body fat and overall body weight when provided to over weight subjects, compared to placebo – isocaloric diet and no exercise (5.3 lb weight loss in 3 months, compared to 2.9 lb weight loss placebo group) (Nagao T, 2005)

Catechin group also showed greater reduction in waist and hip circumference and greater decline in LDL- cholesterol (see review article)

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Another study by CK Maki et al (2008) showed that during a 12-week trial of overweight subjects, the catechin supplemented group experienced enhanced weight reduction effects of exercise (180 minutes per week) compared to the control group.

They also showed greater reduction in abdominal fat and more significant reduction in serum fasting triglycerides.

Mechanism(s) of Action:

1. Up-regulation of brown fat thermogenesis

2. Inhibitory activity of catechol-O-methyltransferase (COMT), which normally degrades catecholamines (epidephrine and norepidephrine), with net result of increased release of fat from fat cells and enhanced theromogensis

3. Inhibition of fatty acid synthesis (**Reference:** Int J Sport Nutr Exerc Metab. 2012 Apr;22(2):139-54. https://www.ncbi.nlm.nih.gov/pubmed/22465867)

In normal weight active men, green tea extract significantly increases fat oxidation by 17%, increasing fatty oxidation over 24-hr period in both sedentary and active lean individuals during exercise.

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Dosage: 625-690 mg catechin content used in clinical studies

Other Health Benefits of Catechins Using Similar Doses:

- Used successfully in breast cancer patients to induce apoptosis of tumor cells, while awaiting surgery (http://www.meschinohealth.com/blog/breast-cancer/2012/10/22/breast-cancer-patients-treated-green-tea-catechins-awaiting-surgery/)

- Blocks the progression of pre-malignant prostate disease into full blown prostate cancer in human studies (http://www.meschinohealth.com/blog/nutrition/mens-nutrition/2012/10/18/green-tea-catechin-supplement-prevents-prostate-cancer-men-pre-malignant-prostate-lesions/)

- Experimentally shown to increase nerve cell growth in hippocampus, improving memory. Green tea linked to improve memory in humans (http://www.meschinohealth.com/blog/alzheimers-disease-and-cognition/2012/09/06/egcg-green-tea-linked-memory/)

- Catechins also shown to reduce blood pressure and improve insulin sensitivity (reducing glucose levels) in human studies (http://www.meschinohealth.com/blog/heart-and-cardiovascular-health/2012/07/27/green-tea-catehins-shown-blood-pressure-blood-sugar-cholesterol-inflammation-mention-body-fat/)

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Example of Combination Supplement

Amount per 3 Capsules:

1. **Chromium** (chromium hvp/hap chelate) - 200 mcg – “inorganic chromium in not absorbed well, thus binging it to chelating agent greatly enhances absorption” (Reference 1)

2. **Garcinia cambogia** (50% Hydroxycitric Acid) -1500 mg

3. **Decaffeinated Green Tea Extract** (80% catechins, 50% EGCG) - 600 mg

Dosage:

- Weight loss and Diabetes Management - up to 3 caps per day (up to 6 caps in first 2-weeks)
- Optimizing Body Fat, Glycogen Replenishment (HCA) and Lean Mass Gains in Athletes – 2-3 caps per day

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Coleus Forskohlii (Forskolin)

General Features

- Coleus Forskohlii is a small perennial member of the mint family, which has been extensively used for many applications in Aryuredic medicine. Its unique active ingredient, the diterpene, forskolin, has been shown to activate the enzyme adenylate cyclase in various tissues, which in turn, increases cellular levels of cyclic AMP (Cyclic Adenosine Monophosphate).

- Cyclic AMP is nicknamed “the second messenger” as its synthesis triggers the action of various hormones, enzymes and other biological activities that have profound effects on local cells, as well as systemic effects, in some instances, on the entire body. It is primarily via the increased synthesis of cyclic AMP that Coleus Forskohlii may exert its medicinal influences on a significant number of common health conditions.1,11

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Principle Active Constituents

- The primary active constituent in coleus forkohlii is a diterpene compound (saponin) that is unique to this herb, known as Forskolin.1,11 Other diterpene compounds have also been isolated from coleus forskohlii, which may provide synergistic physiological effects. 12

Clinical Application and Mechanism of Action

Cardiovascular Conditions

- **Congestive Heart Failure** – as a therapeutic intervention in congestive heart failure forskolin has been shown to activate the enzyme adenylate cyclase, which increases production of cyclic adenosine monophosphate (cAMP) in heart muscle cells (cardiac muscle). Epinephrine has a similar effect on increasing cAMP. Increased levels of cAMP in turn, increases the ability of the heart muscle to produce ATP, which is the energy required for heart muscle contraction and optimal force of muscle contraction with each beat (increased stroke volume). Forskolin also relaxes the artery wall, decreasing blood pressure and thus, pre-load stress on the heart muscle. All of these effects appear to be mediated via increased cAMP synthesis, which acts as a secondary messenger on various cellular processes that manifest the stated outcomes.

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- **Hypertension -** as mentioned, forskolin relaxes blood vessel smooth muscles via increased cAMP synthesis, helping to reduce high blood pressure, by reducing resistance to blood flow.

- **Platelet Function** - forskolin antagonizes the action of platelet-activating factor (PAF) by interfering with the binding of PAF to receptor sites on cells. In turn, this reduces platelet stickiness as well as smooth muscle contraction of blood vessels and bronchiole air passageways. Once again, these effects are mediated through increased synthesis of cAMP.1,2,3,4,5

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Asthma and Skin Conditions

- **Asthma and Eczema –** both of these conditions are associated with a relative decrease in cAMP in bronchial smooth muscle and skin cells, respectively. In turn, this results in degranulation of mast cells and increased contraction of smooth muscle in the bronchiole passageways. Increased PAF also contributes to this problem. Pharmaceutical drugs for allergic conditions, asthma, and eczema are often aimed at increasing cAMP levels (corticosteroids, methylxanthines).6

- Corticosteroid drugs stimulate adenylate cyclase enzyme, increasing the synthesis of cAMP whereas, methylxanthine-containing drugs inhibit phosphodiesterase enzyme, which breaks down cAMP. Forskolin may be utilized alone or in conjunction with these drugs in the complementary management of these conditions.1,7,11

- **Psoriasis -** low levels of cAMP appears to disrupt the balance of cAMP with cGMP (Cyclic Guanine Monophosphate). In turn, this has been shown to cause rapid cellular proliferation (a rate that is 1,000 times faster than normal cells), which is a main feature of the psoriatic condition. In experimental studies Coleus Forskohliiadministration has been shown to slow the proliferation rate of skin cells by improving the relative balance of cAMP to cGMP.7

- Note: In general, the above noted physiological effects associated with Coleus Forskohlii explain its historical use for the treatment of cardiovascular conditions, asthma, skin conditions, and as an antispasmodic in the management of irritable bowel syndrome and uterine cramps. Unfortunately, no well-designed, large, clinical studies have been performed to establish its true therapeutic efficacy for any of these conditions and as such, recommending this herb for these conditions is primarily based upon historical use and animal experimental evidence supporting its role as an adenylate cyclase enzyme activator.11,13

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Lipolysis and Body Fat Reduction

- Recent evidence suggests that supplementation with Coleus Forskohlii may help to reduce body fat in overweight adults. As with other substances that increase cAMP (caffeine, adrenaline, ephedrine, epinephrine), forskolin enhances the breakdown and release of fat from fat cells.

- The synthesis of cAMP in fat cells initiates a chain events that results in hydrolysis of stored triglycerides by hormone sensitive lipase enzyme, with the subsequent release of free fatty acids and glycerol from fat cells.8,9,10 **Unlike ephedrine and other central nervous system stimulants, forskolin does not stimulate the nervous system**.

- Therefore, it does not produce the serious undesirable side effects associated with stimulant drugs and supplements (e.g. ephedrine) such as rapid heart rate, elevated blood pressure, seizures, sudden death heart attack, stroke, nervousness, anxiety, insomnia, atrial fibrillation of the heart etc.

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- Forskolin appears to facilitate an increase in cAMP within fat cells in a manner that by-passes stimulation of beta-adrenergic receptors on the fat cell membrane. By comparison, stimulant drugs, hormones, and supplements, such as ephedrine stimulate beta-adrenergic receptors on fat cells, heart muscle and on the sympathetic nervous system, which results in increased cAMP levels and induces a direct stimulatory effect on the heart, cardiovascular and nervous system.

- Several small clinical trials have shown that Coleus Forskohlii supplementation may help reduce body fat in overweight adults. In one study, subjects showed an average of 10 lbs of weight loss within an eight-week period. Subjects also showed an increase in their lean mass in this study. Experimental evidence indicates that forskolin also mildly stimulates thyroid cells, which may explain its reported thermogenic properties. This may further account for its ability to facilitate reductions in body fat in overweight subjects.14,15,16,17,18

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Dosage and Standardized Grade

- For all of the above conditions – the usual dose of Coleus Forskohliiis 250 mg, twice per day (standardized grade of 1% forskolin content) or 50 mg, twice per day (standardized grade of 18% forskolin, or 9 mg of forskolin per 50 mg tablet).11,19

Adverse Side Effects, Toxicity and Contraindications

- Coleus Forskohlii has been shown to be very non-toxic and is not associated with any significant side effects. It should be avoided in patients with peptic ulcers as it may increase stomach acidity, although no adverse events of this nature have been published.11,20

Drug-Nutrient Interactions

- Use with caution with patients on anti-asmathic and antihypertensive drugs, as forskolin may potentiate the effects of these drugs. As such, appropriate patient monitoring under these conditions is recommended.11,19

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L-Carnitine

Overview

- L-carnitine is a conditionally-essential amino acid in that we make less with age
- The liver makes L-carnitine, but for some individuals L-carnitine supplementation is beneficial
- L-carnitine transports long-chain fatty acids across the mitochondrial membrane for beta-oxidation to occur
- An L-carnitine deficiency leads to impaired fat burning
- Patients with congestive heart failure, angina, and other cardiomyopathies show benefit from L-carnitine supplementation
- Alzheimer's patients (mod. to advanced) show improvement with L-carnitine suppl (Acetyl L-carnitine) to improve energy synthesis for neurotransmitter synthesis and to increase mitochondrial membrane level of cardiolipin (an important phospholipid for energy transfer)

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- L-carnitine studies in weight loss patients and endurance athletes suggest improved fatty acid oxidation in skeletal muscle at a dose of 2,000 mg, 2-3 times per day.

- Some obese patients have been shown to have impaired L-carnitine synthesis, which limits fat burning capability

- L-carnitine also increases sperm counts and motility in infertile and possibly normal men

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Carnitine

General Features

- Carnitine is an amino acid made in the body that helps to facilitate the burning of fat. It primarily functions to transport long-chain fatty acids into the mitochondria of the cell, where these fats are metabolized to produce the ATP energy required to power biological activities of the cell. As muscle contraction of the heart is an ATP-dependent activity, the heart muscle, in particular, requires adequate concentrations of L-carnitine due to the heart muscle's high reliance upon fat as an energy source.

- Carnitine is produced in the liver, kidney and brain. Its precursor is the amino acid lysine. Carnitine deficiency in humans was first described in 1973. Until then it had been assumed that individuals could synthesize adequate amounts of carnitine, ingest adequate amounts of carnitine from food, or meet needs by a combination of both.

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- The discovery that some individuals require carnitine supplementation to maintain normal energy metabolism has prompted its use in clinical trials involving patients with cardiovascular diseases, Alzheimer’s disease and dementia, obesity, alcohol-induced fatty liver disease, low sperm counts and decreased sperm motility and as an ergogenic aid to enhance performance in endurance athletes.

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Supplementation Studies and Clinical Application

- Only L-carnitine should be used for supplementation purposes. D-carnitine has been shown to interfere with carnitine metabolism and reduce fatty acid metabolism and energy production.

- Also note, that when using L-carnitine to prevent or treat dementia or Alzheimer's disease, the only form that crosses the blood-brain barrier is Acetyl-L-carnitine.

- Cardiovascular Disease - In cases of angina, congestive heart failure and other cardiomyopathies , daily supplementation with 1,500-4,000 mg of L-carnitine has produced significant improvement in cardiac function in many clinical trials. This effect appears to be due to improved fat burning capability by cardiac muscle with resulting increased production of ATP energy, which is the energy substrate required for heart muscle contraction.

- Alzheimer's Disease and Age-Related Dementia - Acetyl-L-carnitine has been shown to improve cognitive function in patients with mild to moderate Alzheimer's disease and dementia. The usual daily dosage was 1,000-2,000 mg per day. This effect appears to involve better fat burning by brain cells to produce more ATP energy, and the fact that Acetyl-L Carnitine can induce synthesis of the memory chemical, acetylcholine and increase concentrations of the mitochondrial phospholipids known as cardiolipin, which is important for the transfer of electrons in the synthesis of ATP energy in brain cells.9

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- Male Fertility - Carnitine concentrations are critical to sperm energy metabolism, affecting sperm count and sperm motility. Studies with infertile men have demonstrated that supplementation with 3,000 mg per day of L-carnitine can significantly increase sperm counts and sperm motility. This effect is related to enhance ATP energy production as well.

- **Endurance Performance and Fat Burning** - Some preliminary trials reveal that L-carnitine supplementation can enhance fatty acid oxidation in skeletal muscle during endurance exercise in healthy subjects and athletes. The dosage for endurance athletes is usually 2,000 mg, two to three times per day. This evidence requires much more substantiation, however, certain obese patients have been shown to have a relative deficiency in L-carnitine that may impair their fat-burning ability, and they may thus, benefit from L-carnitine supplementation.

One study showed that supplementation with 2,000 mg of L-carnitine resulted in a 5.68% improvement in peak treadmill running speed, when given to marathon runners for a 6 week supplementation period (Nutrition Research, Vol 17, Issue 3, 1997).

- Protection Against Drug Toxicity - L-carnitine can protect the heart against the damaging effects of the chemotherapy drug adriamycin.

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Dosage Range

For most applications, 1,500 mg to 4,000 mg is the daily dosage. For brain function, only Acetyl-L-carnitine has been shown to be effective.

Toxicity and Contraindications

L-carnitine is extremely safe with no significant side effects reported in any human clinical studies.

Drug-Nutrient Interactions

- There are no reported drug-nutrient interactions of concern with L-carnitine. Note that the anti-seizure drug, Valproic acid and the HIV drug, AZT (zidovudine) have been shown to deplete L-carnitine levels in the body, and thus, supplementation with L-carnitine may be warranted under these circumstances

Synergistic Interactions

- L-carnitine and co-enzyme Q10 appear to work synergistically, enhancing the bioenergetics of mitochondrial oxidative phosphorylation in muscle, nerve and other tissues.
- Choline supplementation appears to spare L-carnitine and may increase intracellular carnitine levels. (20mg of choline per kg of body weight).

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Reference 1: Carnitine Update

In food, L-carnitine is found mostly in meat and dairy products. The liver and kidney synthesize L-carnitine from methionine and lysine with about 95% of the total 20 gm of carnitine located within muscle cells.

Transports long-chain fatty acids across mitochondrial membrane for beta-oxidation, as part of carnitine-acyl-coenzyme A transferase system and thus, represents a rate limiting step in fat burning (oxidative phosphorylation).

Recent studies show that ingesting 2,000 mg L-carnitine in healthy subjects does not affect fuel mixture catabolized or endurance performance aerobic capacity, or exercise level for the onset blood lactate accumulation

It also has not shown benefit on repetitive short-term anaerobic exercise

It may act as a vasodilator to enhance oxygen supply to muscles and reduce muscle soreness from exercise. A daily dosage of 3,000 mg has shown some promise in this area, but there are more impressive vasodilators (beet root juice, L-arginine, Coenzyme Q10)

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Panax Ginseng

- Some studies show ginsenosides increase fat-burning and oxygen utilization within skeletal muscle during exercise

- However, well-designed trial do not show performance-enhancing effects in endurance, aerobic capacity or other parameters of athletic performance

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Reference 1 Ginseng Update

"No compelling scientific evidence exists that ginseng supplementation offers any ergogenic benefit for physiological function or exercise performance".

Clinically, 1-3 gm of ginseng administered 40 minutes before an oral glucose challenge reduced postprandial glycemia in non-diabetic subjects.

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Coenzyme Q10

Overview

- CoQ10 acts as a electron acceptor and donor at various points within the electron transfer cytochrome chain within the mitochondria. Thus, it is essential for ATP synthesis

- Strenuous exercise lowers blood levels of CoQ10

- Some, but not all CoQ10 supplementation studies show improved work capacity of 3-29% in sedentary subjects and 4-32% in trained athletes

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- Several well-designed studies showed no change in time to exhaustion and total performance with CoQ10 suppl.

- Individual results may vary based upon genetic potential to synthesize optimal levels of CoQ10

- **Note:** CoQ10 levels decline with age, due to decreased synthesis, beginning around age 25. Thus, as athletes age, takin CoQ10 to optimize CoQ10 nutritional strategy and aerobic capacity is a prudent consideration, according to many anti-aging expertes

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CoQ10 and Exercise Performance

Title: **Effect of ubidecarenone oral treatment on aerobic power in middle-aged trained subjects.**

Author(s) : Bonetti A; Solito F; Carmosino G; Bargossi AM; Fiorella PL

thor's Address : Chair of Sport Medicine, University of Parma, Italy.

Source : Journal of sports medicine and physical fitness [J Sports Med Phys Fitness] 2000 Mar; 40 (1), pp. 51-7.

Pub. Type : Clinical Trial; Journal Article; Randomized Controlled Trial

Language : English

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MeSH Terms :
Exercise*/physiology
Physical Fitness*/physiology
Antioxidants/*pharmacology
Exercise Tolerance/*drug effects
Ubiquinone/*analogs & derivatives
Adult; Bicycling/physiology; Human; Male; Middle Age; Single-Blind Method; Ubiquinone/pharmacology

Abstract : BACKGROUND: Coenzyme Q10 (CoQ10) plays an important role in oxidative mithocondrial phosphorylation and prevents lipid peroxidation in biological membranes. During sustained physical exercise, reactive oxygen species (ROS) production increase through several mechanism; one of them is the purine nucleotide cycle activation by shifting xanthine-dehydrogenase to xanthine-oxidase during AMP breakdown. The aim of this study was to evaluate the effect of CoQ10 treatment on aerobic power. METHODS: Experimental design: according to a single blind study design, 28 health male cyclists were randomized into two groups (CoQ10 or placebo) and remained on treatments for eight weeks; there were 5 drop-outs and only 23 subjects were completely evaluated. Before and at the end of the eight weeks, cyclists underwent cardiopulmonary exercise testing. Measures: a software system performed the necessary calculations to obtain the following parameters: oxygen uptake, CO2 production, minute ventilation, oxygen ventilatory equivalent, carbon dioxide ventilatory equivalent, oxygen pulse. Finally oxygen peak and anaerobic threshold were determined. Moreover blood inosine, hypoxanthine, xanthine, lactate and CoQ10 levels were measured before and immediately after each test. RESULTS: The results of this study showed that at the end of the eight weeks there was no difference between the two groups concerning physiological and metabolic parameters, but muscular exhaustion was reached at higher workloads in the CoQ10 group. CONCLUSIONS: In our experience ubidecarenone oral treatment does not improve aerobic power. The little improvement of tolerance to higher workloads may be due to the antioxidant activity of CoQ10.

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Coenzyme Q10 Referenced Studies

- Strenuous exercise lowers blood levels of coenzyme Q10 (CoQ10). Some, but not all, studies using supplementation with CoQ10 at 60 to 100 mg per day, have reported improvements in work capacity ranging from 3 to 29% in sedentary individuals and from 4 to 32% in trained athletes. (1)

- However, several well-designed studies involving trained athletes have failed to show improvement in time to exhaustion and total performance in CoQ10 supplementation trials. (2,3,4)

- CoQ10 is a key agent in the production of ATP, as it acts as an electron shuttle in the transfer of hydrogen electrons between cytochromes in the mitochondria of the cell. (1,2)

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B-Vitamins

- B-Vitamins required for many reactions involved in energy production (e.g. NAD, FAD, decarboxylation, CO_2 fixation, pyruvate conversion to acetyl-Co A, RBC formation etc.)

- Studies reveal that athletes have a higher requirement for many B-Vitamins

- But, Mega-doses of B-Vitamins not shown to enhance performance

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B-Vitamins Referenced Studies

- B-Vitamins are important to athletes because many of them are required for energy production and studies indicate that exercising individuals have an increased need for many B-Vitamins.

- If the need is not met then it may impair performance to some degree.

- Supplementation with mega-doses of B-Vitamins have failed to show any significant improvement with performance parameters and thus, a moderate level of B-Vitamin supplementation may be a more prudent strategy.(1,2,3,4,5,6,7)

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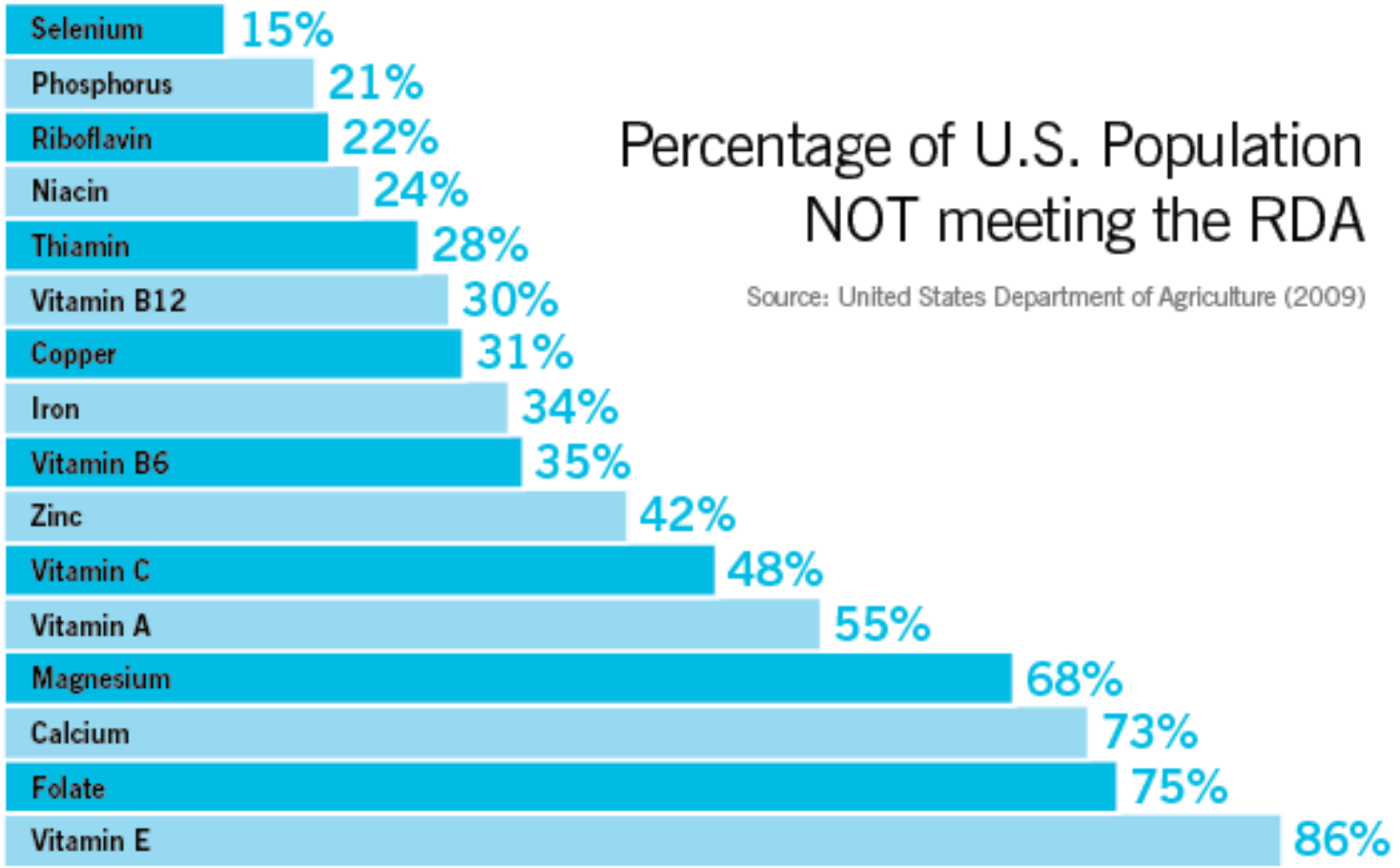
Note % of people not meeting RDA for various B-vitamins daily:
B2, B3, B1, B12, B6, Folic acid



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2. van der Beek EJ, van Dokkum W, Wedel M, Schrijver J, van den Berg H. Thiamin, riboflavin, and vitamin B6: impact of restricted intake on physical performance in man. J Am Coll Nutr 1994; 13: 629-640.
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7. Manore MM. Vitamin B6 and exercise. Int J Sport Nutr 1994; 4: 89-103.
8. Williams M. Dietary supplements and sports performance. J Int Soc Sports Nutrition, vol 1, number 2. 2004. Pages 1-6.

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Iron

- Iron requirements are often increased in athletes due the increased loss of iron that occurs from red blood cell hemolysis and gastrointestinal loss and the increased demand for iron, which results from the increased synthesis of myoglobin, mitochondrial cytochromes, and hemoglobin associated with athletic training.

- Iron deficiency anemia is the end stage of iron deficiency and is defined as a hemoglobin level below 120 gm/L in women and 140 gm/L in men. However, signs of iron deficiency, including weakness, compromised performance and/or compromised immune function can occur before frank anemia is present. Thus, early indicators of iron deficiency should be recognized and is reported to require the presence of any two of the following biomarkers:
- Serum ferritin levels below 12 –20 mcg/L
- RBCP (protoporphyrin) level above 1.8 mmol/L RBC
- Transferrin saturation less than 18% (1) (Weight L, Sports Anemia. Sports Medicine. July, 1993)

- Iron is also lost in sweat, which adds to the loss of iron in athletes, and women lose iron during normal menstruation. As such, endurance athletes frequently are found to have low body-iron levels, in the absence of anemia. (2,3,4)

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1. Weight LM. “Sports anaemia”. Does it exist? Sports Med 1993; 16(1): 1-4.
2. Mechrefe A, wexler B, feller E. Sports anemia and gastrointestinal bleeding in endurance athletes. Med Health R I 1997; 80: 216-218.
3. Clarkson PM. Micronutrients and exercise: antioxidants and minerals. J Sports Sci 1995; 13: S11-24 [review].
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- With serum ferritin levels between 12-29 ug/L, a chelated iron supplement is often helpful in raising iron nutritional status, reducing URTIs and improving energy, immune system function and exercise performance. Chelated iron is absorbed better than inorganic iron and is not constipating.

- With serum ferritin levels below 12 ug/L a prescription iron is usually necessary – often 300 mg ferrous sulfate, 3x daily. Recall that iron absorption is only 5-10% from inorganic iron of this type and tends to be constipating.

Example of Chelated Iron Supplement with Red Blood Cell-Promoting Factors:

One Capsule Contains:

- Iron-bisglycinate – 45 mg
- Vitamin C – 50 mg
- Vitamin B12 (methylcobalamin) – 50 mcg Folic Acid – 50 mcg
- Vitamin B6 – 10 mg
- Vitamin B2 – 5 mg
- Copper- 500 mcg

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Minor Iron Deficiency Impairs Athletic Performance

Title: [Iron deficiency in female athletes]

Transliterated Title: Deficiência de ferro em atletas femininas.

Author(s): Faintuch JJ; Lima FR; Carazzato JG

Author's Address: Grupo de Medicina Esportiva e pela Clínica Geral do Hospital das Clínicas da Faculdade de Medicina da USP.

Source: Revista do Hospital das Clinicas [Rev Hosp Clin Fac Med Sao Paulo] 1998 Jul-Aug; 53 (4), pp. 181-3.

Pub. Type: Journal Article

Language: Portuguese

Journal Info: *Country of Publication:* BRAZIL *NLM ID:* 0415246 *ISSN:* 0041-8781 *Subsets:* IM

MeSH Terms: Sports*
Anemia, Iron-Deficiency/*diagnosis
Iron/*metabolism
Adolescence; English
Abstract; Female; Ferritin/blood; Hemoglobins/analysis; Human; Iron/blood

Abstract: Iron deficiency and anemia have been reported frequently in athletes. In São Paulo-Brazil among elite athletes overt anemia is uncommon, but our studies showed that they were in a borderline anemic state. Sports anemia is used to describe both pseudodilutional anemia and the true anemia of athletes. We studied 12 female young athletes, all with normal hemoglobin. Four athletes had laboratory features (serum ferritin, red cell volume, and/or transferrin saturation) suggestive of iron deficiency. There are association of high iron body stores with cardiac arrhythmia, carotid atherosclerosis, myocardial infarction, liver and colorectal cancer but minor iron deficiency may impair the physical fitness.

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Magnesium

- Magnesium deficiency can reduce exercise performance and contribute to muscle cramps. (1)

- One double-blind study showed that magnesium supplementation at 390 mg per day in tri-athletes improved swimming, cycling, and running times. (2)

- Approximately 28% of magnesium is found in muscle tissue, where it contributes to energy production, protein synthesis, muscle contraction, and nerve conduction.

- It is required by more than 400 enzymes in human physiology and is excreted more rapidly during periods of stress. (3,4,5,6)

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References: Magnesium

1. McDonald L, Keen CL. Iron, zinc and magnesium nutrition and athletic performance. Sports Med 1988; 5: 171-184 [review].
2. Golf SW, Bender S, Gruttner J. On the significance of magnesium in extreme physical stress. Cardiovasc Drugs Ther 1998; 12(suppl 2): 197-202.
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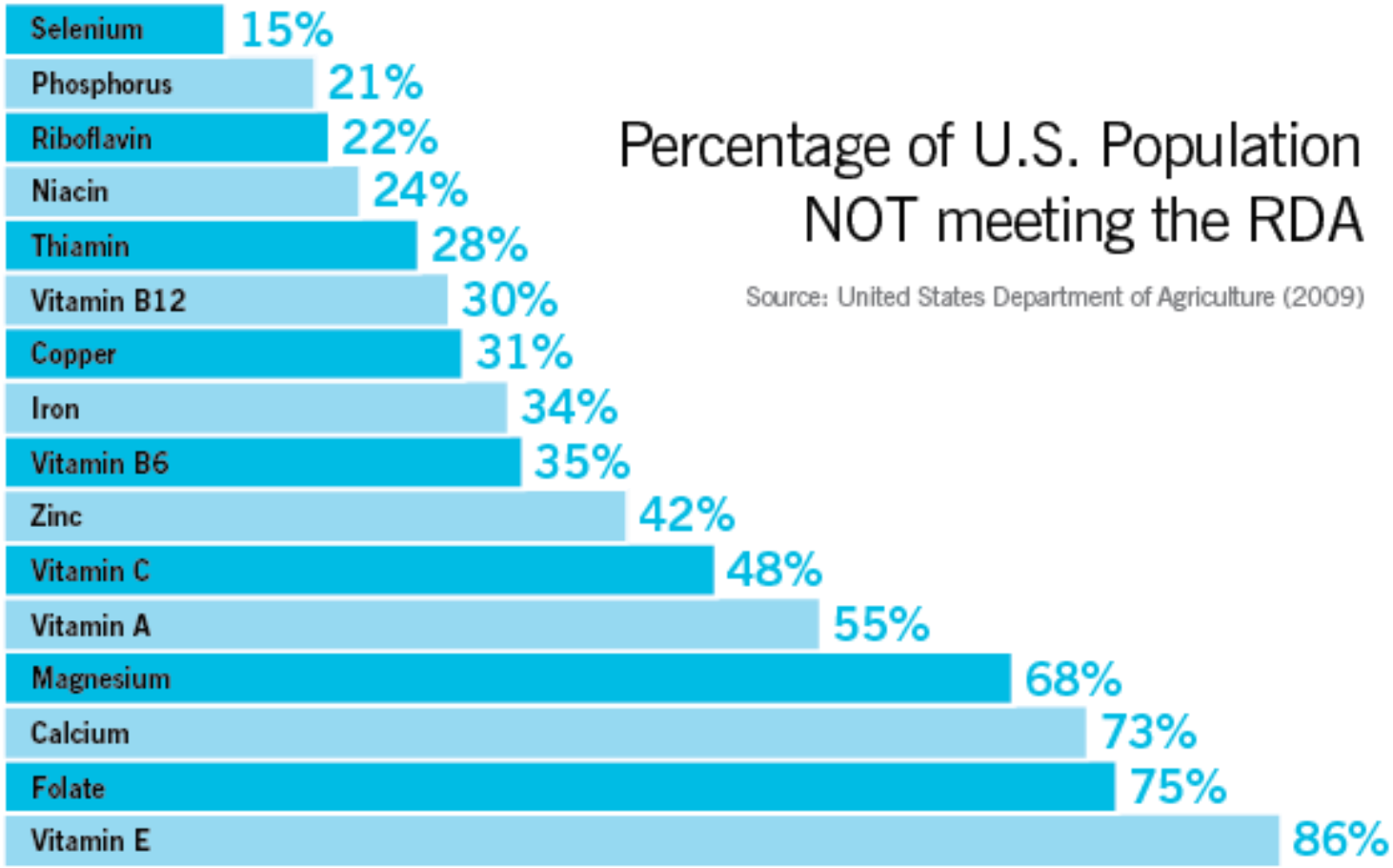
68% of Americans Don`t Meet RDA for Magnesium



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Magnesium Improves Performance In Sleep-Deprived Athletes

Title: **Efficacy of oral magnesium administration on decreased exercise tolerance in a state of chronic sleep deprivation.**

Author(s) : Tanabe K; Yamamoto A; Suzuki N; Osada N; Yokoyama Y; Samejima H; Seki A; Oya M; Murabayashi T; Nakayama M; Yamamoto M; Omiya K; Itoh H; Murayama M

Author's Address : Second Department of Internal Medicine, St Marianna University School of Medicine, Kawasaki, Kanagawa, Japan.

Source : Japanese circulation journal [Jpn Circ J] 1998 May; 62 (5), pp. 341-6.

Pub. Type : Clinical Trial; Journal Article; Randomized Controlled Trial

Language : English

Journal Info : *Country of Publication:* AUSTRALIA *NLM ID:* 7806868 *ISSN:* 0047-1828 *Subsets:* IM

MeSH Terms : Exercise Tolerance/*drug effects
Exercise Tolerance/*physiology
Magnesium/*pharmacology
Sleep Deprivation/*physiology
Administration, Oral; Adult; Blood Pressure/drug effects; Blood Pressure/physiology; Calcium/blood; Chronic Disease; Erythrocytes/chemistry; Erythrocytes/drug effects; Erythrocytes/metabolism; Exercise/physiology; Fatigue/blood; Fatigue/drug therapy; Fatigue/physiopathology; Heart Rate/drug effects; Heart Rate/physiology; Human; Magnesium/administration & dosage; Magnesium/blood; Male; Norepinephrine/blood; Support, Non-U.S. Gov't; Time Factors; Treatment Outcome

Abstract : We have previously reported that chronic sleep deprivation causes a deficiency of intracellular magnesium (Mg) and decreased exercise tolerance. The aim of this study was to clarify whether oral administration of Mg could be effective in restoring the exercise tolerance that is decreased by chronic sleep deprivation. A bicycle ergometer cardiopulmonary exercise test was performed by 16 healthy volunteers (mean age 21.9 years). They were divided into 2 groups: 8 received doses of 100 mg of Mg orally per day for 1 month (Mg group) and the remaining 8 received no Mg and served as the control group. The study conditions were designed as follows: (1) the usual state (good sleep); and (2) the sleep-deprived state (sleeping time up to 60% less than the usual state for 1 month). The ratio of intracellular Mg content of the sleep-deprived state to the usual sleep state was significantly higher in the Mg group ($p<0.05$) than the untreated control group. There was no difference between the sleep-deprived state and the usual state with regard to anaerobic threshold and peak oxygen uptake in the Mg group, whereas both of these decreased in the sleep-deprived state in the control group. These results indicate that decreased exercise tolerance observed in the sleep-deprived state could be improved by oral Mg administration.

CAS Registry No.: 51-41-2 (Norepinephrine)

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Reference 1 Magnesium Update

- Magnesium plays a vital role in muscle and liver glycogen synthesis from blood-borne glucose.

- The 20-30 gm of magnesium in the body also potentiates cofactors to degrade glucose, fatty acids and amino acids during energy metabolism (ATP synthesis in glycolysis and oxidative phosphorylation).

- Magnesium also required for protein synthesis and lipid synthesis and proper functioning of neurotransmitter system.

- With potassium and sodium helps to stabilize blood pressure in normal range

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- Magnesium also regulates RNA and DNA synthesis, thus regulating cell growth, reproduction and the structure of cell membranes.

- **Has inherent role as a calcium-channel blocker,** a magnesium deficiency can cause high blood pressure and cardiac arrhythmias to develop by allowing too much calcium into cardiac muscle cells.

- Intense sweating causes small magnesium loss

- Some, but not all studies, show that magnesium supplementation (about 200 mg per day) increased muscle strength in resistance training vs placebo.

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Journal Magnesium Research (2006)

- This research has shown that exercise induces a redistribution of magnesium in the body to accommodate metabolic needs.

- There is evidence that marginal magnesium deficiency impairs exercise performance and amplifies the negative consequences of strenuous exercise (e.g., oxidative stress).

- **Strenuous exercise apparently increases urinary and sweat losses that may increase magnesium requirements by 10-20%.**

- Based on dietary surveys and recent human experiments, a magnesium intake less than 260 mg/day for male and 220 mg/day for female athletes may result in a magnesium-deficient status.

- Recent surveys also indicate that a significant number of individuals routinely have magnesium intakes that may result in a deficient status. Athletes participating in sports requiring weight control (e.g., wrestling, gymnastics) are apparently especially vulnerable to an inadequate magnesium status.

Reference: https://www.ncbi.nlm.nih.gov/pubmed/17172008

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Vitamin D

- Impaired muscle function has been coupled to vitamin D deficiency in young women and elderly men and women.

- A study of male and female swimmers (16-24 years) showed that 45% of swimmers have blood vitamin D levels below 50nmol/L.

- Among male swimmers those with higher vitamin D blood levels had higher hand grip strength than those with insufficient vitamin D status (below 50.6 plus or minus 6.4 nmol/L vs 41.1 plus or minus 1.78 nmol/L)

Reference:

- Int J Sport Nutr Exerc Metab. 2017 Oct;27(5):399-407. doi: 10.1123/ijsnem.2016-0248. Epub 2017 May 30: https://www.ncbi.nlm.nih.gov/pubmed/28556690

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Docosahexaenoic Acid (omega-3 fat)

DHA Supplementation Improves O2 Uptake in Muscle Cells

- Animal studies have suggested improved oxygen uptake by skeletal muscles upon exercise with DHA (omega-3 fat enriched diet)

- 26 trained males enrolled in study showed that DHA supplementation (560 mg DHA/ 140 mg EPA) for 8-weeks improved DHA incorporation into muscle cell phospholipids with subsequent improved uptake of oxygen by exercising skeletal muscle, modulating oxygen consumption during intense exercise-lowering the oxygen cost of physiologically stressful cycling (6-min time trial) in trained male athletes.

- Int J Sport Nutr Exerc Metab. 2017 Aug;27(4):335-343. doi: 10.1123/ijsnem.2016-0150. Epub 2017 Mar 24. https://www.ncbi.nlm.nih.gov/pubmed/28338369

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Medium-chain Triglycerides (MCT)

Consuming MCT does not inhibit gastric emptying as does consuming common fat, but conflicting evidence exists about their use in exercise

Can MCT supplementation provide an instant source of fat for muscles, thereby slowing muscle glycogen depletion?

Ingesting CHO with MCT has shown a small improvement (2.5%) in cycling speed over 40-km, with a slight slowing of glycogen depletion. Beverage containing 10% glucose, or 4.3% MCT emulsion, or 10% glucose plus 4.3% MCT emulsion.

MCT may cause cramping and diarrhea when ingested prior to and during exercise, as do not stimulate bile secretion

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Some athletes use 380 mg MCT oil/kg body weight per hour before exercising 1-hour at 60-70% of aerobic capacity – metabolic mixture did not change and blood ketones rose

Some athletes have tried 30 gm MCT before exercise, with minimal effect on slowing glycogen depletion and increasing fatty acid oxidation

In general, relatively small alterations in the substrate oxidation occurs by increasing the availability of FFA during exercise at 65-90% of aerobic capacity: this likely accounts for its small effect on exercise capacity.

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Pyruvate Supplementation

Some studies have shown that pyruvate supplementation improves aerobic performance:

100 gm mixture of 25 gm pyruvate plus 75 mg dihydroxyacetone (DHA) – both are 3-carbon compounds of glycolysis - increased upper and lower body aerobic endurance by 20%, compared to subject ingesting isocaloric glucose polymer

The pyruvate-DHA mixture increased cycle ergometer time to exhaustion of the legs by 13 mins and arm-cranking exercise time by 27 mins

Supplement Manufacturers Recommend – 600 mg capsules – 2-4 capsules per day to enhance athletic performance

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Proponents of pyruvate supplementation suggest:

Pyruvate elevates extracellular pyruvate augmenting glucose transport into active muscles, increasing glucose substrate as energy source for ATP production and conserving skeletal muscle glycogen.

Also, In conjunction with CHO diet of 55%, pyruvate supplementation shown to further enhance pre-exercise glycogen levels.

Both of these effects enhance aerobic exercise performance.

Pyruvate added to calorie-restriction also shown to enhance weight loss effect (loss of body fat in obese humans) without increasing lean mass catabolism. Mechanism unknown, but several studies show success with dosage 20 gm sodium pyruvate plus 16 gm sodium pyruvate to 1,000 calorie liquid meal diet. Supplemented group lost more weight than group using only the liquid meal diet (1,000 calories). – 13 lbs lost vs 9 lbs lost in 3 weeks.

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Glycerol Supplementation – May Help Maintain Hydration

Glycerol- the 2-carbon molecule increase osmotic diuresis.

During exercise glycerol levels rise from triglyceride hydrolysis (adipose tissue). The glycerol filtration in the kidney is reabsorbed dragging water with it back into the bloodstream.

Ingesting water with glycerol increases body's fluid volume and plasma glycerol concentration. This results in increased renal filtration, but the proximal and distal tubules reabsorb much of the glycerol and its osmotic forces help reabsorb water from the tubules back into the bloodstream – exerting an true osmotic diuresis that helps maintain body fluid levels. This is beneficial during exercise

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When consumed with 1-2 liters of water, glycerol facilitates water absorption from the intestine and causes extracellular fluid retention mainly in the plasma fluid compartment. This helps guard against heat stress during exercise and enhances athletic performance (and reduces risk of dehydration and heat injury)

Dose= 1 gm glycerol/kg body wt mixed into 1-2 liters of water consumed is pre-exercise glycerol dose, which lasts up to 6 hours (increased osmotic effect)

Not all studies have shown this effect but consensus is that glycerol aids hydration in this manner. But more research is required

Side Effects: nausea, dizziness, bloating, light-headedness

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Glucosamine Sulfate and MSM

- Glucosamine sulfate is used to make N-acetyl galactosamine sulfate by chondrocytes: an essential monosaccharide for the production of the proteoglycan, chondroitin sulfate, which lies between collagen fibers (ground substance) within joint cartilage

- Glucosamine sulfate supplementation also increases collagen formation by fibroblasts, as does exercise.

- OA patients have been shown to improve with glucosamine sulfate suppl (1,500 mg/day)

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- In one study 51 athletic males and 17 females with cartilage damage, took a dose of 1,500 mg of glucosamine sulfate per day for 40 days (then 750 mg for another 100 days). Of the 68 participants, 52 showed complete cure of their injury and resumed training. A 12 month follow-up showed no regression of symptoms (Colgan Chronicles, Aug. 29, Vol.2, issue5:8,1)

- Chondroitin Sulfate is too large to get absorbed, only 9-12% absorption possible and still too large to enter chondrocyte (molecular weight of 50,000, glucosamine is 211) Possibly the sulfur component is used to stimulate synthesis of glycosaminoglycans, and used to support proteoglycan structure within cartilage
- Many arthritic patients claim to benefit from sulfur springs

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MSM (methylsulfonylmethane)

- Joint cartilage requires sulfur to maintain structural integrity and is a naturally-occurring substance in food chain
- Sulfate is required for glycosaminoglycan synthesis
- MSM studies suggest it is useful in conjunction with glucosamine sulfate in the treatment of various sports injuries involving joint cartilage (Jacob S.W., Lawrence R.M., Zucker M. 1999)
- MSM also has mild anti-inflammatory effects as well as supporting joint cartilage integrity
- Doses as low as 250 mg per day can be effective, but often a daily dosage of 1,000-2,000 mg is employed

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Example of Glucosamine Formula With MSM

Amt per 3 capsules:

1. Glucosamine Sulfate - 1500 mg
2. MSM (Methyl Sulfonyl Methane) - 400 mg
3. Quercetin - 300 mg
4. Bromelain Enzymes (2,400 GDU) - 300 mg

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Natural Anti-Inflammatory Agents

- Various anti-inflammatory bioactive agents derived from herbs and accessory nutrients can be used to suppress joint, tendon, bursa, and muscle inflammation arising from sports injuries

- As these agents do not cause erosion or ulceration to the gastrointestinal tract, or are known to produce liver or kidney toxicity and do not hasten the erosion of joint cartilage, they may be considered in place of NSAIDs or as a means to lower the requirement for NSAIDs, and other anti-inflammatory drugs that carry a higher risk of toxicity and other undesirable side effects.

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Some effective natural anti-inflammatory agents include:

1. **Curcumin** - (90% std grade from turmeric, up to 400 mg, 3X daily) – inhibits cyclooxygenase and lipoxygenase
2. **Boswellia** - (std to 70% boswellic acids, up to 150 mg, 3X daily) – inhibits lipoxygenase
3. **White willow extract** (std to 15% salicin, 100 mg, up to 3X daily) – inhibits cyclooxygenase and mild analgesic
4. **Ginger** - (std to 5% gingerols, 500 mg, up to 3X daily) – inhibits cyclooxygenase and lipoxygenase
5. **Bromelain enzymes** - (400 mg, up to 3X daily) – inhibits cyclooxygenase and lipoxygenase; also is fibrinolytic dissolving clots and reducing swelling from physical trauma (e.g. boxing)
6. **Devil's Claw** – (100-400 mg, up to 3X daily) – Unknown action
7. **Quercetin** – (300 mg, up to 5X daily) – anti-histamine and blocks release of other pro-inflammatory agents
8. **MSM** – (250-2,000 mg per day) – experimental evidence suggests anti-inflammatory action

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Example of Natural Anti-Inflammatory

Amt per 3 caps:

1. Turmeric extract (95% Curcumin) - 632 mg
2. Boswellia (std. 70% Boswellic acid) - 600 mg
3. White Willow Extract (std. 15% salacin) - 100 mg
4. Ginger Root Extract (std. 5% gingerol) - 150 mg

Dosage:

- Acute Inflammation: 3-4 caps/3x daily
- Sub-acute Inflammation: 3-4 caps/2x daily
- Low-grade Inflammation: 3 caps/day
- Cancer Prevention: 2 caps/day

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Alcohol

Stomach absorbs 15-25% of alcohol ingested. The small intestine absorbs the remainder

The liver detoxifies alcohol at rate of 10gm per hour = one alcoholic beverage

Consuming 2 alcoholic drinks within one hour produces a blood alcohol concentration between 0.04-0.05 g/dL. But, factors such as age, body mass, body fat and gender influence alcohol blood levels

A blood alcohol concentration above 0.40 g/dL (at or above 19 drinks in 2-hrs) leads to coma, respiratory depression, and eventual death

Research has not shown an ergogenic effect of alcohol on exercise performance

Moreover, it acts as a CNS depressant (regarding memory, visual perception, speech, motor coordination), which hinder exercise performance and skill

But can produce anti-tremor effect to help pistol shooting and archery (beta-blockers have also been used by these athletes)

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Even small amounts of alcohol (social drinking) impair cardiac functioning – depressed myocardial contractility and **blunts liver's capacity to synthesize glucose from non-carbohydrate sources via gluconeogenesis.** Each of these impairs performance in high intensity aerobic activities that rely on gluconeogenesis to some degree.

Alcohol is not a good energy substrate for exercise as it does not alter the metabolic mixture to enhance exercise and **substituting alcohol in place of a CHO-containing sports drink post-exercise decreases optimal glycogen replenishment**

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Alcohol exaggerates dehydration effect of exercise in a warm environment by acting as **potent diuretic** (depresses release of ADH-vasopressin)

This impairs thermoregulation during heat stress, thus placing athlete at greater risk for heat injury during exercise

After exercise alcohol consumption shown to increase urine output to greater degree than and lower plasma volume at 6-hrs post exercise compared to subjects drinking non-alcoholic beverages. **As such, alcoholic beverages impede rehydration after exercise, and during exercise**

As well, alcohol acts as peripheral dilator **allowing excess heat loss during cold exposure**, increasing risk of hypothermia. “A good stiff drink does not warm you up”.

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Androstenedione and DHEA Supplements as Anabolic Enhancement Agents

- In recent years, many athletes have initiated the practice of ingesting testosterone precursors in an attempt to increase their blood levels of testosterone into a supra-physiological range.

- Higher testosterone levels increase protein synthesis by directly up-regulating the genes within the nuclear DNA of the cell that increase protein synthesis activity, and thus lay down a greater number of myofibrils within the cytoplasm of the muscle cell; increasing its strength and cross-sectional density.

- Higher testosterone levels (from use of anabolic drugs) also shortens the recovery time between heavy work outs, enabling an athlete to work out harder on a day to day basis, eliminating the need for long recovery periods. This also gives the athlete an advantage with respect to the speed at which positive training adaptations can occur.

- Testosterone precursors include dehydroepiandrosterone (DHEA) and androstenedione. In testosterone synthesis, cholesterol is first converted to pregnenolone in the testes, and adrenal glands (and in the female ovaries), then pregnenolone is converted to DHEA, then DHEA is converted to androstenedione, then androstenedione is converted to testosterone. However, testosterone can be further converted to estrogen (17-B-estradiol) in these body organs and released to the circulation.

- Fat cells and skeletal muscle cells can also extract androstenedione from the blood stream and convert it into estrone (a form of estrogen). Some androstenedione is released from the adrenal glands during steroidogenesis, and this is the usual way that fat cells and muscle cells gain access to androstenedione for estrone production. However, when taking androstenedione as a supplement an athlete increases their potential to synthesize both testosterone and estrogen (both 17-B-estradiol and estrone), and there appears to be wide variation between individuals as to which pathway will be the dominate one. (1,2,3,4, 12,13,14)

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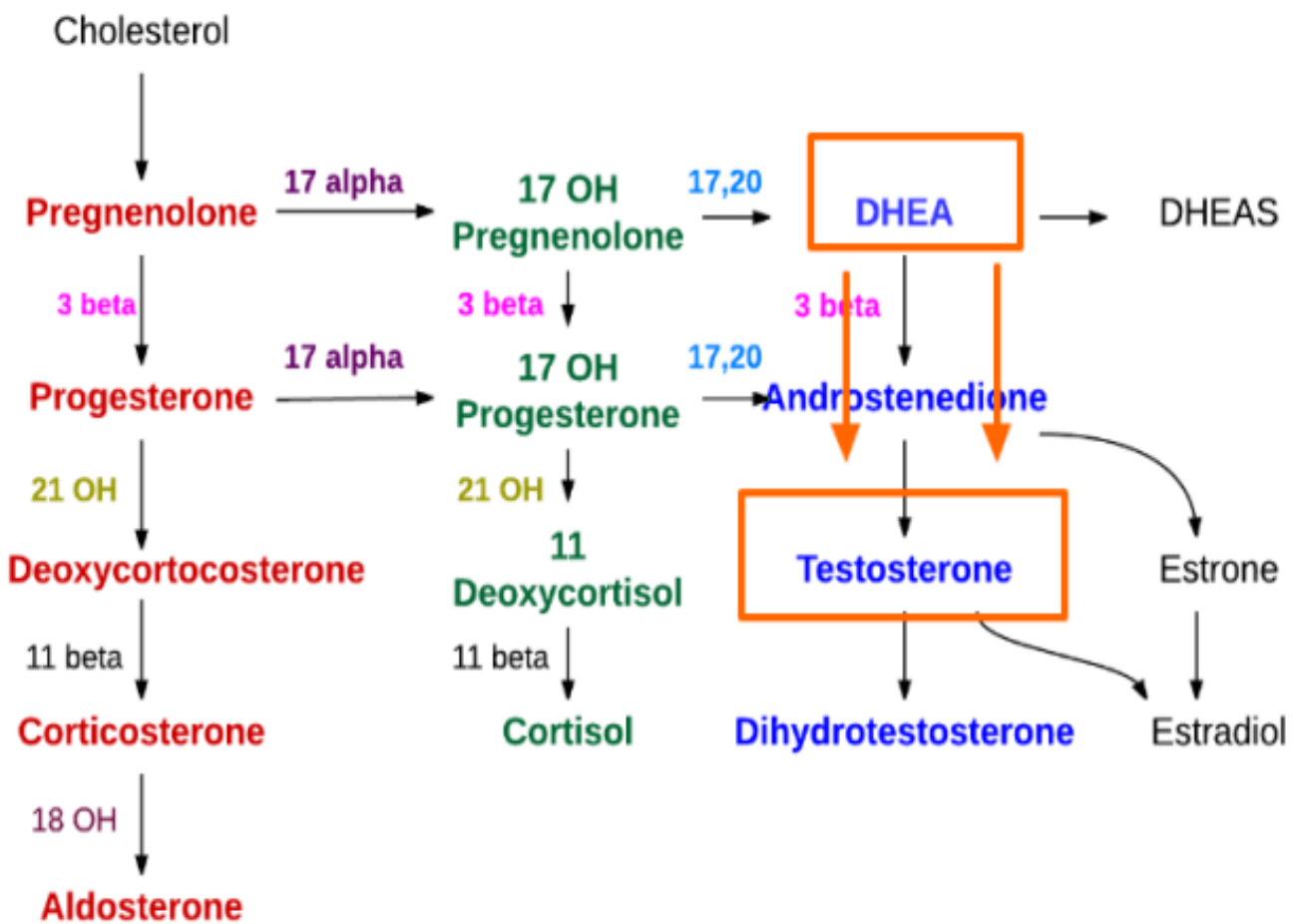

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- One study showed that 100 mg of androstenedione supplementation raised testosterone to six-times the normal blood levels in women, and was much more effective at raising serum testosterone levels than was supplementation with DHEA. (2)

- Men supplementing with androstenedione have shown an initial elevation in testosterone, followed by a gradual decline (even though androstenedione supplementation was maintained), suggesting that the body adapts to the ingestion of androstenedione by slowing down its own internal synthesis of this androgens. (4)

- Various controlled studies indicate that in some men 300 mg of androstenedione raises blood levels of both estrogen and testosterone, while in other men only their estrogen levels become elevated. Lower doses of androstenedione (100 mg per day) have been shown to only increase estrogen levels in men. (5,6) Studies also suggest no discernible increase in strength, muscle mass or performance enhancement in subjects employing strength training and other training methods, compared with those not taking the androstenendione. Further, androstenendione has been shown to reduce HDL-cholesterol levels (the good cholesterol), which is a risk factor for coronary heart disease. (7,8)

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- Androstenedione (19-norandrostenendione and 19-norandrostenediol) are potential metabolic precursors of other steroid hormones in the body, and are considered by U.S. law as prohormones without proven therapeutic, curative or diagnostic properties, and therefore available as over-the-counter drugs. (9)

- A survey of 511 anonymous clients entering five different gymnasiums revealed that 18% of men and 3% of women had used androstenedione or other adrenal hormones (e.g. DHEA) within the last three years.

- Extrapolation of this data suggests that 1.5 million gymnasium clients have used these prohormone supplements (drugs) within the last three years in the U.S. (10) Certain sports organizations have banned the use of DHEA and androstenedione based upon their known adverse side effects, their steroid structure, and potential to enhance androgen levels in the body (International Olympic Committee (IOC) had banned DHEA, and the IOC, the National Collegiate Athletic Association (NCAA) and the National Football League (NFL) have banned androstenedione). (11)

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- In general, the research shows that the use of androstenedione and DHEA do not provide a significant anabolic effect on the body, and appear to raise estrogen levels in men much more than testosterone, and the elevation in testosterone that may result, is transient and not sustained, making it unlikely to have an effect of lean mass and strength gains.

- Androstenedione and DHEA have been around for over 50 years. If they truly had a remarkable anabolic effect it would have surfaced by now as East German athletes began experimenting with them back in the 1960's. A review of the East German steroid bible (State Plan 14-25), after the fall of the Berlin Wall, did not suggest any significant benefits from the use of these prohormones, no matter how they were taken (orally, nasal spray etc.)

- Only one review suggests that a rise in testosterone levels of 140-180% and 211-237% is possible in male subjects after ingestion of 50 and 100 mg of androstenedione, respectively. However, no one knows how long these levels lasted. One other publicized study indicated a 34% rise in the 480 minutes (eight hours) following the ingestion of a single dose of 300 mg of androstenedione. Therefore, the possibility exists that for some athletes a testosterone spike, and in theory a training benefit, may occur.

- Research indicates that the risk to benefit ratio for androstenendione favors the risk. Androstenedione supplementation is associated with increased body fat, likely due to its propensity to raise estrogen levels, which makes it anti-ergogenic. Androstenedione is associated with a 12% (5 mg/dL) drop in HDL-cholesterol levels, and an increased risk of benign prostatic hyperplasia, according to one case report and a primate model of the disease. Acne may also be a side effect of taking this supplement.

- Thus, unlike the well established muscle and strength gains, and other ergogenic effects associated with taking anabolic drugs (illegal), the use of androstenedione and DHEA are not proven to have these benefits, particularly in young male subjects.

- There is some evidence that androstenedione in males over 50 can increase serum levels of testosterone, and that females taking DHEA can significantly increase their serum testosterone levels as well.

- In women, the use of androstenedione has been suggested to deepen the voice, cause hypertrophy of the thyroid cartilage, produce hirsutism, decrease breast size, and promote clitoromegaly, in a similar manner as do anabolic steroid drugs. (12,13,14,)

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Reference 1 DHEA and Androstenedione

One study showed a small increase in lean mass and strength gain in middle-aged men and women using DHEA supplementation (100 mg per day for 3 months) combined with resistance training compared to the period of performing resistance training with no DHEA supplementation.

Elderly men and women also saw improvements in lean mass strength with DHEA and intensive resistance training, more so than without DHEA.

DHEA groups also increased immune function in middle-age and elderly men and women.

But DHEA may disrupt menstrual cycles in women, produce hirsutism in women, and lower HDL-cholesterol.

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DHEA may stimulate growth or otherwise dormant prostate cancer cells or cause benign prostatic hyperplasia. If cancer is present DHEA may accelerate its growth.

However, DHEA may help counter Metabolic Syndrome by reducing abdominal fat and improving body's use of insulin in elderly men and women.

DHEA may reduce the required dose of corticosteroid medication required by patients with autoimmune disease Lupus, which would reduce side effects such as accelerated osteoporosis that accompany corticosteroid therapy.

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Androstenedione dosages as high as 300 mg/day have elevated testosterone levels by 34%, but chronic administration also elevated serum estradiol and estrone in men and women – this response could offset any potential anabolic effect.

Overall, studies suggest no long-term significant effect on testosterone and training response- muscle size and body composition.

Androstenedione appears to also lower HDL-cholesterol and increase risk of gynecomastia due to higher estrogen synthesis, as well as increased risk of pancreatic and other cancers.

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Summary Of Accepted Ergogenic Aids and Antioxidant Support

Title: Effective nutritional ergogenic aids.

Author(s) : Applegate E

Author's Address : Nutrition Department, University of California - Davis, 1 Shields Avenue, Davis, CA 95616, USA.

Source : International journal of sport nutrition [Int J Sport Nutr] 1999 Jun; 9 (2), pp. 229-39.

Pub. Type : Journal Article; Review; Review, Tutorial

Language : English

Journal Info : *Country of Publication:* UNITED STATES *NLM ID:* 9307702 *ISSN:* 1050-1606 *Subsets:* IM

MeSH Terms : Dietary Supplements*
Energy Metabolism*
Exercise/*physiology
Amino Acids/administration & dosage; Antioxidants/administration & dosage; Caffeine/administration & dosage; Creatine/administration & dosage; Dietary Carbohydrates/administration & dosage; Dietary Proteins/administration & dosage; Human; Sodium Bicarbonate/administration & dosage

Abstract : Athletes use a variety of nutritional ergogenic aids to enhance performance. Most nutritional aids can be categorized as a potential energy source, an anabolic enhancer, a cellular component, or a recovery aid. Studies have consistently shown that carbohydrates consumed immediately before or after exercise enhance performance by increasing glycogen stores and delaying fatigue. Protein and amino acid supplementation may serve an anabolic role by optimizing body composition crucial in strength-related sports. Dietary antioxidants, such as vitamins C and E and carotenes, may prevent oxidative stress that occurs with intense exercise. Performance during high-intensity exercise, such as sprinting, may be improved with short-term creatine loading, and high effort exercise lasting 1-7 min may be improved through bicarbonate loading immediately prior to activity. Caffeine dosing before exercise delays fatigue and may enhance performance of high-intensity exercise.

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Putting It All Together

Dietary Composition for Various Athletes

1. **Body Builders** – High protein diet-40%; 40%-CHO; 20%-Fat (minimal aerobic activity as fear lean mass catabolism)

2. **Interval Athletes** (hockey, soccer, basketball etc.) – Protein 20-25%; CHO-55-60%; Fat-15-20% **(and people who train like me with resistance training and cardio training for anti-aging and overall health benefits)**

3. **Endurance Athletes** – Protein-15-20%; CHO-60-70%; Fat -5-20%

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3-4 hours before competition/training:

- High CHO diet, with moderate protein (20-40 gm) and low in fat (but include good fats – olive oil, fish, avocado etc.
- Pre-hydration should be considered (water or water with glycerol – I-2 liters of water with 1 gm glycerol)
- Beetroot Juice – for endurance events and time trial-based sports where increased oxygen deliver enhances power output

1-hour before competition/training:

- Small CHO snack if necessary:
- For Sprint Events – sodium bicarbonate or sodium citrate
- For Sprint/Explosive Sports, Interval Sports or Endurance Events – 250 mg caffeine
- Some additional fluids (water)

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20-30 minutes Prior to Competition/Training:

13-20 oz water – possibly add 20 gm of fructose for endurance or interval sports, and/or BCAA powder for all types of competition and training

During Endurance Events and Interval Sports:

- First 30-60 minutes consume water only (5-8 oz/10-15 mins)
- After 30-60 minutes consume CHO-containing sports drink (5-8% CHO concentration) – 5-8% oz/every 10-15 mins
- If event is lasting more than 90 minutes ensure that sports drink contains sodium, as well as CHO (5-8% concentration)
- Some sports drinks also contain small amount of protein or amino acids in addition to CHO and sodium (also worth considering)

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1st Two-Four Hours Post Competition/Training:

- Fluid intake of 125-150% of fluid requirement based on body weight lost (1lb=16 oz fluid loss) – drink beyond thirst mechanism and include sports drink to initiate immediate glycogen synthesis right after exercise ends
- Consume a high-CHO meal within 2-hours of competition/training
- Ingest 2-5 gm of L-glutamine to prevent weakening of immune system, help with glycogen re-synthesis, re-establish glutamine blood and muscle levels, and reduce on-going muscle catabolism
- Within 4 hours consume at least 20-40 gm of high quality protein

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During Ensuing 20-22 Hours:

- Continue to rehydrate (water, and possibly pinch of salt)
- Ingest daily protein requirement (1.25-2.0 gm/kg body weight, possibly up to 3.0 gm per kg) – depending on type of athlete and program
- Continue to replenish glycogen stores with optimal CHO intake- based on type of athlete and program (40-65% of total daily calories) – if gaining body fat then CHO intake is likely too high
- Keep bad fats out of the diet, and include small amount of good fats with meals and snacks (fish, avocado, olive oil, nuts)

- **Pre-Sleep Protein with small amount of CHO** – 30 minutes before sleep it's helpful to consume 20-40 gm of protein with small amount of CHO, in order to prevent catabolism during sleep (fasting state) and elevate morning metabolism

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Protein Considerations:

- Most athletes count protein grams through the day (125-200 grams)
- Best to get protein from **low-fat** food sources (other than fish)
- Animal protein is higher in EAA's and BCAA's, providing superior quality, and easier to attain 20-40 grams per meal - chicken, turkey, fish, Cornish hen, egg whites, low fat yogurt (Greek Yogurt), non-fat or 1% milk, cheese under 4% MF – but also soy foods are consideration
- Whey protein is a strong consideration (EAA's, BCAA's, with highest Leucine concentration – up-regulating mTOR pathway for MPS)
- Vegetarians can get ample protein. Egg whites are a strong consideration, along with Low Fat Dairy products (Greek Yogurt), Soy and Rice Protein, and of course, Whey Protein
- Vegans can use Soy and Rice Protein as key sources, along with beans, peas, lentils and higher-protein grains (quinoa), and are likely to greatly benefit from Creatine supplementation.

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Primary Supplement Considerations

Creatine Monohydrate – loading dose, followed by maintenance dose for explosive sports, interval sports, rehabilitation, anti-aging (preserving lean mass and MPS)

High Potency Multiple Vitamin and Mineral – antioxidant enriched, B-50 complex, magnesium, chromium, zinc, iron, vitamin D (1,000 IU), etc.

Essential Oils Supplement – high in DHA (500-600 mg DHA yield per day) – especially for aerobic athletes and interval athletes

Fat Metabolizers-Lean Mass Enhancers: Chromium; HCA; Catechins from decaffeinated green tea

Growth Hormone Secretagogues – for those over 35yrs, once IGF-1 baseline level is established at or below 225 ng per ml (Ornithine, Arginine, L-Glutamine etc. or Meditropin: https://www.supplementcritique.com/meditropin-review/

Coenzyme Q10 – for those over 40 yrs – aerobic capacity

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Secondary Supplement Considerations

Pyruvate – shows great promise to enhance glucose utilization and glycogen replenishment

L-Carnitine – stubborn weight loss patients or athletes

Coleus Forskolin – stubborn weight loss patients or athletes

HMB – shows promise for enhanced lean mass gains and/or anti-catabolic but expensive and uncertain efficacy at this point

Medium-chain Triglycerides – may enhance aerobic performance by sparing muscle glycogen depletion (keep an eye on this research)