Evidence Based Approach to the Use of Dietary Supplements as Ergogenic Aids in Athletes.

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33rd Sports Medicine Symposium hosted by Central Connecticut State University

Declaration of Conflict of Interest:

- No Conflict: Elizabeth Tenison
  - The views presented in these slides and in today’s discussion are mine.
  - My views may not be the same as the views of my company’s clients or those of my colleagues.
  - Participants must use discretion when using the information contained in the presentation.

- No Conflict: Dr. Melissa Brown
  - The views presented in these slides and in today’s discussion are mine.
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Symposium Session Agenda:

- Fill the knowledge gap regarding efficacy of ergogenic dietary supplements with the goal of helping athletic trainers to remain current and up-to-date.
- Provide an evidence based review of the emerging ergogenic dietary supplements in comparison with a “food first” approach.
- Provide guidance on how to evaluate supplements in order to provide sound recommendations to athletes.
Learning Objectives:

1. Recognize emerging dietary supplements in the field of performance nutrition.
2. Demonstrate how to evaluate ergogenic dietary supplements for efficacy.
3. Select ergogenic dietary supplements with evidence-based efficacy regarding athletic performance and muscle soreness.

What is Sports Nutrition/Performance Nutrition?
Specialized branch of nutrition that studies food with relevance to athletic performance.

Signs An Athlete May Need to Improve Their Nutrition

- Training hard but not improving performance.
- Feeling tired or "run down" all the time.
- Early fatigue during games or intense practices.
- Excessive cramping and/or soreness of muscles.
- Frequent injuries.
- Lengthy recovery time from injury or simply from one game to the next.
- Frequent illnesses such as always seeming to have a cold.
- Frequent headaches.
- Legs feel heavy or weak during exercise.

CCSU Sports Medicine Symposium
Tuesday March 6, 2018
Healthy Eating Snapshot for Athletes

1. Follow a healthy eating pattern and appropriate distribution of calories from the macronutrients ("MACROS").
2. Aim for 3 balanced meals and 2-3 snacks per day. Don’t skip breakfast!!
3. Focus on whole grains, fruits, vegetables ["eat the rainbow"], lean protein, and healthy fats!
4. Limit processed foods and foods high in calories from added sugars, trans fats, and saturated fats.
5. Stay hydrated! Drink water throughout the day and leave the sports drinks to before, during and/or after training, events, and games.

Helpful Resources on Sports Nutrition To Provide Guidance to Athletes and Professionals Working with Athletes

Recommendations and Guidelines on Sports Nutrition Topics

- Academy of Nutrition and Dietetics’ Practice Group Sports, Cardiovascular and Wellness Nutrition (SCAN)
  - www.scandpg.org/
  - Resources and Fact Sheets
- Collegiate and Professional Sports Dietitians Association (CPSDA)
  - www.sportsrd.org/
  - Resources and Fact Sheets
- United States Olympic Committee (USOC)
  - www.teamusa.org
  - Resources and Fact Sheets
- National Athletic Trainers Association (NATA)
  - www.nata.org
  - Resources and Fact Sheets

Practice Application: Why Should Athletic Trainers Care About Sports Nutrition and Dietary Supplements?

- Value of optimal nutrition in sports performance has been acknowledged within the field of athletic training evidenced by the incorporation of a general nutrition content area to the Athletic Training Education Competencies.
- ATs are often the ones with the most frequent contact with the athletes.
- Athletes are susceptible to supplement marketing due to the desire to gain a competitive edge and most athletes are not well informed on this issue.
- Any nutrition information disseminated to the athletes must be accurate especially regarding questions about ergogenic dietary supplements.

Current Status of Dietary Supplement Intake Among Competitive Athletes

- According to a recent systematic review and meta-analysis by Knapik et al. (2016) which reviewed 159 studies internationally with sample sizes ranging from 12-2297:
  - Overall prevalence: 60% of any dietary supplement [range 4%-100%].
  - Vitamin and mineral: 42%.
  - Specific vitamin or mineral: 40%.
  - Amino acids or protein: 52%.
  - Creatine: 31%.
  - Herbal: 17%.
  - Sports drinks: 21%.
  - Sports bars: 11%.
  - Omega 3 fatty acids: 7%.
  - Caffeine: 5%.
  - Energy drink: 4%.
- In comparison to NHANES (U.S. general population):
  - Overall prevalence: 42-54%.
    - Mainly from vitamin and mineral supplements with only 1% attributed to amino acids.


Definition of Dietary Supplement

- The law defines dietary supplements in part as products taken by mouth that contain a "dietary ingredient." Dietary ingredients include vitamins, minerals, amino acids, and herbs or botanicals, as well as other substances that can be used to supplement the diet.
- Dietary supplements come in many forms, including tablets, capsules, powders, energy bars, and liquids.
  - Note: an ergogenic aid refers to anything other than actual training that purports to enhance or improve athletic performance.

Regulation of Dietary Supplements

- Dietary Supplement Health and Education Act of 1994 [DSHEA].
- 1994 statute of United States Federal legislation which defines and regulates dietary supplements.
- Regulated by the Act under the FDA for Good Manufacturing Practices (21 CFR Part 111).
- Defines supplements as "food" and not "drugs"; different than other countries.

https://www.fda.gov
Regulation of Dietary Supplements

KEY POINTS

• No evaluations of effectiveness or safety prior to a product entering the market.
• Law does not include a requirement for a manufacturer to provide evidence of effectiveness or safety.
• Only way to remove a product from the market, is AFTER it is proven unsafe.
• The question of purity is of upmost importance to athletes in which contamination with regulated and/or banned substances can jeopardize their eligibility.
  • Can happen intentionally by a manufacturer or can happen inadvertently through the manufacturing process.
  • Common occurrence with supplements designed for weight loss and the building of muscle.

Need to Ask Specific Questions For Each Supplement

START HERE!

1. SAFE?
2. EFFECTIVE?
3. LEGAL WITHIN THE SPORT/ORGANIZATION?

Helpful Resources Provide Guidance to Athletes and Professionals Working with Athletes

Supplement Certification, Purity, Safety

• National Sanitation Foundation [NSF] Certified for Sport® – considered the “gold standard”
  • http://nsf.org
  • New Certified for Sport® App
  • Available on the website/Informed Choice App illustrating just how common it is for supplements to be contaminated with potentially harmful substances and the need for Good Manufacturing Practices.
• Informed Choice
  • http://www.informed-choice.org
• Consumer Lab
  • www.consumerlab.com
• US Pharmacopeia
  • www.usp.org
• FDA
  • www.fda.gov
  • Adverse events reporting, recalled products, regulatory after-market action against companies etc.
Helpful Resources Provide Guidance to Athletes and Professionals Working with Athletes

- National Collegiate Athletic Association (NCAA) [www.ncaa.com]
- Permissible and non-permissible lists
- Banned substances list
- International Olympic Committee (IOC) [https://www.olympic.org]
- World Anti-Doping Agency (WADA) and US Anti-Doping Agency (USADA) [www.wada.org, www.usada.org]
- Professional Sports
  - Each sport league will have its own list of banned/regulated substances.
- High School Sports
  - Information is more varied but a good starting point is each state’s interscholastic athletic website.

Examples Of Additional Questions To Ask Related to Safety and Effectiveness

- Is the claim physiologically/biologically plausible? What is the purported mechanism?
- Is there research/scientific evidence to support the claim? Quality & Quantity Matter!
- Was the research performed in the target population you are looking for?
- Where and when was it published (peer reviewed journal) and how was it funded (potential bias)?
- Has the study been replicated by other groups?
- Was the research hypothesis driven with clear objectives?
- What was the study design?
  - Gold standard: double blind, randomized, control trial!
- What was the number of subjects? [ie. Required power to detect statistical significance]
- Are the results significant not just statistically but with physiologic/biologic relevance?
- Dose response study with adequate length of time?
- Were the proper controls and valid variables/outcomes used?
- Were the proper controls and valid variables/outcomes used?
- Example of using a sport specific, intervene, “true world” performance test vs just post supplementation?
- Actual use of a sport specific, intervene, “true world” performance test vs just post supplementation?

Steps in the Evidence Analysis Process

1. Formulate Formulate PICO question
2. Gather Gather research through a review of the literature
3. Appraise/Evaluate Critically Appraise/Evaluate the Studies
4. Summarize Summarize the evidence and provide conclusion.
5. Grade Grade the strength of evidence guides

[grading system adapted from the Academy of Nutrition and Dietetics’ Evidence Analysis Tools/2]
PICO question
Among competitive athletes (P), what is the effect of ergogenic dietary supplements (I) versus no ergogenic dietary supplements (C) on athletic performance and muscle soreness (O)?

Ergogenic Dietary Supplements that will be evaluated:
- Branched Chain Amino Acids
- Creatine
- Citrulline
- Anti-oxidants
- Collagen/ Vitamin C
- Omega-3 Fatty Acids
- Vitamin D

Outcomes:
- Athletic Performance
- Muscle Soreness
Methodology Used To Evaluate the Evidence

• National Library of Medicine’s PubMed database was searched using the terms from the PICO question with specific use of the terms related to the supplements of interest in this presentation and “human”, “English”, “athlete”, “trained”, “muscle*.”
• Also, consulted references of resulting articles.
• All study designs except for case reports.
• Critiquing the Studies to obtain a Strength of Evidence Grade: SOURCE FOR QUALITY CRITERIA CHECKLIST USED IN PRIMARY RESEARCH: Academy of Nutrition and Dietetics, Evidence Analysis Library.
• Individual study ratings have been combined to determine the overall strength of evidence.

Challenges We Faced In Reviewing Dietary Supplement Research

• Limited Human Studies.
• Most are not in a relevant population ie. Post-menopausal women, or “untrained” individuals or “recreational” athletes (not competitive athletes).
• Limited randomization, blinding, proper controls and small sample size.
• No placebo group. Did not controlled for current dietary intake.
• None compared the amount being provided in a supplement to an equivalent amount provided by a controlled diet.
• Very few dose response studies, highly variable doses among studies and very few measured supplement compliance.
• Many only looked at whether a supplement could correct a deficient/insufficient blood level rather than whether that correction led to any performance or recovery benefits.
• Some of the studies may have revealed a benefit but maybe they looked at the wrong period of time i.e. Training vs competition day.
• Few incorporated a pre-supplement baseline testing to compare to post-supplementation.
• In addition, few used a “real world”, sport specific performance indicator (many used lab engineered or lab controlled scenarios).
• The following slides are the summaries of studies done in competitive athletes only.
• Note: references for the individual supplements can be found grouped together at the end of the slide set.

Symbols used in the Academy’s Quality Checklist:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+), POSITIVE (GOOD)</td>
<td>AND/EAL Positive: indicates that the report has clearly addressed issues of inclusion/exclusion, bias, generalizability, and data collection and analysis.</td>
</tr>
<tr>
<td>(0), NEUTRAL (FAIR)</td>
<td>AND/EAL NEUTRAL: indicates that the report is neither exceptionally strong nor exceptionally weak.</td>
</tr>
<tr>
<td>(-), NEGATIVE (Weak)</td>
<td>AND/EAL NEGATIVE: indicates that these issues have not been adequately addressed.</td>
</tr>
</tbody>
</table>
What is the Evidence Regarding BCAA Supplements and effects on Athletic Performance and Muscle Soreness?

**WHOLE FOOD SOURCES**
- meat, chicken, fish, dairy products and eggs

**DOSAGE**
- ~2-3 g of leucine daily

**CLAIM**
- Increase muscle mass.
- Increase endurance and power.
- Attenuate muscle damage associated with exercise.

**Benzocaine**
- Topical anesthetic
- Used for minor pain relief

**BCAA Conclusion Statement**
- Muscle glycogen is depleted; BCAA are used as a fuel source leading to an increased level of serotonin as a byproduct of metabolism. Serotonin is associated with fatigue. BCAA supplements may mitigate serotonin formation [Fourre, 2017; Kreider, 2010; Williams, 2005].

- Bottom Line: Safe, possibly effective for minimizing skeletal muscle damage and offering ergogenic benefits and, in certain circumstances, BCAA may minimize skeletal muscle damage.

Strength of evidence =Grade 1; Good
Five Randomized Controlled Trials
What is the Evidence Regarding Creatine Supplements and effects on Athletic Performance and Muscle Soreness?

CLAIM
- Increased sprint performance.
- Increased work and exercise capacity.
- Enhanced recovery.

WHOLE FOOD SOURCES
- Red meat, white fish, and poultry.

DOSE
- 20 g/kg/day for 5 days.

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Author</th>
<th>Year</th>
<th>Region</th>
<th>Body Mass</th>
<th>Intervention</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parallel randomized double blinded trial</td>
<td>Silva et al</td>
<td>2015</td>
<td>Class A</td>
<td>31 Male elite wrestlers ranked in the top ten</td>
<td>Creatine supplementation vs placebo on SJ and BJ among highly trained university elite level volleyball players</td>
<td>SJ and BJ trained 5 days a week for 2 hours at time</td>
</tr>
<tr>
<td>Randomized Controlled Trial</td>
<td>Lamontagne</td>
<td>2011</td>
<td>Class A</td>
<td>20 elite female swimmers volunteered</td>
<td>Creatine supplementation on anaerobic performance and sprint performance</td>
<td>Creatine supplementation on anaerobic performance and sprint performance</td>
</tr>
</tbody>
</table>
| Randomized Controlled Trial | Butts | 2018 | Class A | 2015 | Rating + | Increased work and exercise capacity. 
Increased sprint performance. 
Enhanced recovery. |

Creatine Conclusion Statement

- Powerful antioxidants that work with glutathione to reduce oxidative stress. Aerobic exercise increases production of free radicals. Creatine is part of phosphocreatine which is needed to produce ATP. (Kreider, 2017 & Ilus, 2018).
- Bottom Line: Safe, effective for reducing oxidative stress, offering ergogenic benefits and, large doses are not beneficial.

Strength of evidence =Grade 1; Good 
Five Randomized Controlled Double Blinded Placebo Trial
What is the Evidence Regarding Citrulline Supplements and effects on Athletic Performance and Muscle Soreness?

**CLAIM**
- Improve athletic performance.
- Relieves muscle soreness.

**WHOLE FOOD SOURCES**
- Salmon, red meat, watermelon and leafy greens

**DOSE**
- 6-8 gms of L-Citrulline per day

<table>
<thead>
<tr>
<th>Study design</th>
<th>Author</th>
<th>Study Population</th>
<th>Intervention</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rating + Class A</td>
<td>Perez 2010 &amp; Wax 2015</td>
<td>12 advanced resistance trained males</td>
<td>Citrulline ingestion for 7 days</td>
<td>Performance of flat barbell bench presses in well trained males</td>
</tr>
<tr>
<td>Blinded Placebo Crossover Trial Randomized Controlled Double</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rating + Class A</td>
<td>Glenn 2016</td>
<td>41 males who trained &gt; 3 hours a week with a minimum of twice a week and competed in competitive tennis events for past 2 years</td>
<td>Citrulline ingestion for 7 days</td>
<td>Muscle soreness at 24 and 48 hours, grip strength, and vertical power in well trained male athletes</td>
</tr>
<tr>
<td>Blinded Placebo Crossover Trial Randomized Controlled Double</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rating + Class A</td>
<td>Suzuki 2016</td>
<td>10 well trained males (8 endurance athletes, 1 professional soccer player and 1 mixed martial arts competitor)</td>
<td>Citrulline ingestion for 7 days</td>
<td>Hand grip strength, vertical power and explosive power in well trained male athletes</td>
</tr>
<tr>
<td>Blinded Placebo Crossover Trial Randomized Controlled Double</td>
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**Citrulline Conclusion Statement**

- L-Citrulline is an amino acid that is a precursor for L-Arginine, which is a substrate for Nitric Oxide (NO). Nitric oxide enhances blood flow, muscle energy metabolism and mitochondrial respiration during physical activity. (Cunniffe, 2016 & Wax 2015)
- Bottom Line: Safe, possibly effective for reducing delayed onset muscle soreness and offering ergogenic benefits. Appropriate dose unknown.

Strength of evidence = Grade 1; Good
Five Randomized Controlled Double Blinded Placebo Trial
What is the Evidence Regarding Omega-3 Fatty Acid Supplements and effects on Athletic Performance and Muscle Soreness?

**CLAIM**
- Reduce inflammation.
- Support Immune Function.
- Support Muscle Repair and Remodeling.

**WHOLE FOOD SOURCES**
- Cold water fatty fish (tuna, salmon), fish oils, krill oil

**DOSAGE**
- 0.2-2.4 g/day EPA/DHA (DRI/AI=1.1-1.6g/day)

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**Omega-3 FA Conclusion Statement**

- N-3 fatty acids are essential fatty acids that serve as precursors to eicosanoids with anti-inflammatory properties. Supplementation of n-3FA has been purported to be beneficial to athletes by decreasing inflammation, supporting immune function and supporting muscle repair and remodeling.

- Bottom Line: Limited human studies in competitive athletes; evidence does not support the hypothesis that omega 3 PUFA supplementation is effective in enhancing athletic performance.

  - Not all used proper dietary controls, did not select an appropriate placebo (needs to be one that will not alter the n-6:n-3 ratio) and most did not measure supplement compliance during the study.

- Strength of evidence=fair/weak
- Number of relevant human studies in competitive athletes=5  RCTs
What is the Evidence Regarding Vitamin C Supplements and effects on Athletic Performance and Muscle Soreness?

**CLAIM**
- Act in an antioxidant capacity to reduce inflammation (see antioxidant section).
- In combination with collagen/gelatin, promote collagen synthesis.

**WHOLE FOOD SOURCES**
- Gelatin, vitamin C rich foods such as oranges, berries, grapefruit

**DOSE**
- ≥15g collagen hydrolysate with ≥50mg Vit C 1 hr before training
- [RDA=75-90mg/day]

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Class:</th>
<th>Rating</th>
<th>Purpose</th>
<th>Study Population</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shaw et al, 2017</td>
<td>A, RCT</td>
<td></td>
<td>To determine whether gelatin+vit C supplementation combined with exercise could increase collagen synthesis.</td>
<td>8 healthy male subjects</td>
<td>5g or 15g of vitamin C-enriched gelatin or placebo.</td>
<td>Blood sample taken every 30 minutes post consumption of gelatin or placebo for amino acid content. Blood samples also obtained before and 1 hour after 5x use with engineered ligaments. Blood was added to engineered collagen for 4 days to measure effect on collagen content and mechanics. 1 hour after total supplement, subjects completed 4 sets of jumping rope in order to stimulate collagen synthesis.</td>
</tr>
</tbody>
</table>

**Vitamin C + Gelatin Conclusion Statement**

- Vitamin C is required for collagen synthesis and in combination with gelatin, is purported to be beneficial in reducing injuries and enhancing tissue repair during intermittent exercise.
- Bottom Line: Encouraging and interesting results yet too preliminary to provide conclusive and overwhelming evidence. Future larger scale, well-designed RCTs in competitive athletes are needed.

Strength of evidence=fair-weak
Number of relevant human studies in competitive athletes=1
What is the Evidence Regarding Vitamin E/Antioxidant Supplements and effects on Athletic Performance and Muscle Soreness?

Vitamin E/Antioxidant Conclusion Statement

- Due to the effects of vitamin C on oxidative stress, the research on vitamin C supplements for athletic performance is extensive. However, the Evidence is mostly weak, purported benefits are minimal, and there is no evidence for beneficial effects at high altitude.
- Vitamin D's role in athletic performance is still unclear. More research is necessary to determine the optimal dosage and duration of supplementation.
- Vitamin E is another antioxidant that has shown promise in reducing muscle damage and improving recovery in athletes. However, evidence is mixed and more research is needed to confirm these findings.
- Beta-carotene is the precursor to vitamin A and has shown promise in reducing inflammation and improving recovery. However, more research is needed to determine the optimal dosage and duration of supplementation.

Strength of evidence: Fair-Weak
Number of relevant human studies in competitive athletes: 5-10 is needed to confirm the benefits of vitamin C, vitamin E, and beta-carotene supplementation on athletic performance and muscle recovery.
What is the Evidence Regarding Vitamin D Supplements and effects on Athletic Performance and Muscle Soreness?

### Vitamin D Conclusion Statement

- Vitamin D is a fat soluble vitamin that may have beneficial effects on athletic performance and muscle soreness through a reduction in inflammation, supporting the immune system and muscle repair and remodeling. Further, there is believed to be a high prevalence of Vitamin D deficiency among athletes (Owens, 2018).

- Studies included measured an effect on performance or muscle; not just whether supplementation could increase (correct) vitamin D blood levels.

- Bottom Line: Inconclusive evidence to support a recommendation to supplement vitamin D in competitive athletes. All but one study showed an increase in serum 25(OH)D levels but no statistically significant differences in the performance measures. If athletes undergo screening of their D levels, supplementation should be based on the need for overall health and not as an attempt to enhance athletic performance until supported by evidence.

- Most lacked proper dietary controls and did not measure supplement compliance during the study.

Strength of evidence=fair
Number of relevant human studies in competitive athletes=5 RCTs
Conclusion

• Since so few human studies in competitive athletes exist, our focus shifted from simply compiling this presentation to more of a "call to action". MORE WELL-DESIGNED, RELEVANT, AND VALID RESEARCH IS NEEDED!
• Until well-designed studies are done in the human athletic population clearly showing a dietary supplement to be superior to an adequate, well-balanced, whole-food diet, optimized for performance, then we must continue to recommend "food first".
• Consider that "whole food" contains many different nutrients and compounds in more physiological amounts that provide less risk of harmful effects and toxicity.
• One particular nutrient in isolation may not be beneficial and may in fact, have detrimental effects.
• Synergy amongst these nutrients and compounds may be the key factor.
• A compound that has not yet been identified may actually be the critical factor.

Clinical Bottom Line:

• Evidence does not support supplementation of omega-3 PUFA, vitamin C, or antioxidant combinations for enhanced athletic performance and muscle soreness, with some possible benefits for citrulline.
• Evidence to show that supplementation with branched chain amino acids and creatine has positive benefits on athletic performance and muscle recovery. Of importance, is that the same benefits can be found with sufficient intake of high protein food sources such as meat, dairy, nuts and legumes1. A food first approach with a well-balanced diet that includes high protein food sources and antioxidant-rich foods provide the benefit of a more balanced profile of the nutrients and is less costly compared with supplemental form.
• Athletic Trainers should recommend a food first approach to nutrition to promote highest athletic performance. Avoiding commercialized supplements is best because the contents are not FDA approved, products are not regulated, may be contaminated or contain banned substances2. In the absence of strong scientific evidence of efficacy and safety regarding a supplement, the recommendation for a food first approach is best practice.


Case Study

YOUR ATHLETE

20 year old collegiate football player with the goal of increasing explosive power and speed; asking about Supplement X4 recommended by a friend from the gym back home.

Supplement X4
Claim: Explosive energy, increased focus and speed during workouts and quicker recovery.
WHAT ARE THE STEPS YOU SHOULD TAKE?
• START HERE! Is the athlete's diet currently adequate, well balanced and optimized for performance within their sport and training regimen?
• Let's assume the diet is already optimized for health and performance. What's next?

SAFE? EFFECTIVE? LEGAL WITHIN THE SPORT?

RECOMMENDATION TO ATHLETE: SKIP THIS SUPPLEMENT!

QUESTIONS?

“Some nutritional supplements help some athletes in some sports some of the time, but no supplement helps all athletes all of the time, causing recommendations for nutritional supplement use to be difficult to make on a team or program basis.”

References: Branched-Chain Amino Acid Supplementation

Reference: Creatine Supplementation


References: L-Citrulline Supplementation


References: Omega 3 Supplementation

References: Vitamin C/gelatin Supplementation


References: Vitamin E/Antioxidant Supplementation