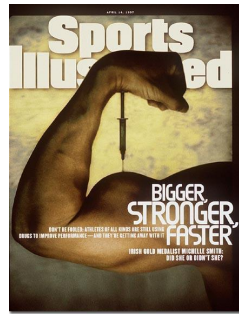
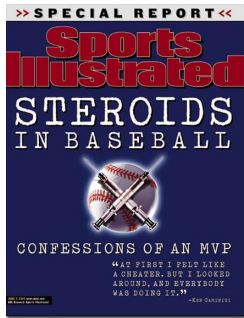


# The Safety and Efficacy of Dietary Supplements: An Evidence-Based Approach

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## Performance Drugs



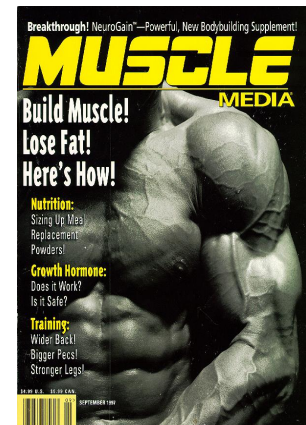
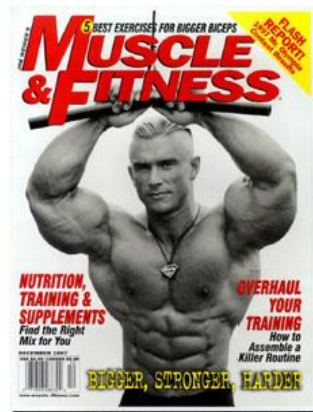
## Performance Supplements



## Confusion?

- Dietary Supplement Health and Education Act (DSHEA) of 1994
  - Places the burden of proof on the government if it wishes to take regulatory action against a supplement
  - The government must show that the supplement presents a "significant or unreasonable risk of illness or injury" under the conditions recommended or suggested in labeling
  - There is no requirement for manufacturers to provide evidence of product safety prior to marketing supplements
  - Drug regulation involves an extensive "premarket" evaluation of safety and effectiveness with explicit standards of evidence (including risk)

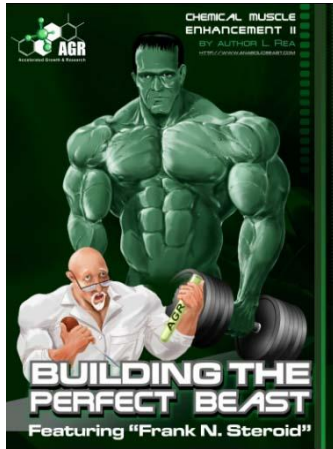
## Evidence Based?????



## Questions????

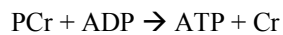
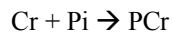
1. Is it safe?
2. Does it work?
3. Is it legal?

## Anabolic Agents vs Fat Burners



## CREATINE

- Proposed ergogenic mechanism



## Anabolic?

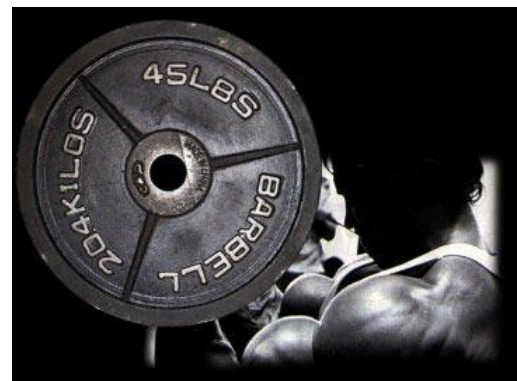
- Changes in Body Mass
  - Acute increase in body mass fairly consistent
    - Fluid retention - documented
    - Protein synthesis - ???

## Protein Synthesis

- Mechanism???
  - Enhanced phosphagen capacity
  - Increased cell volume
    - Haussinger et al.

## CREATINE PHOSPHATE (CP)

for short term,  
high rates of  
energy production

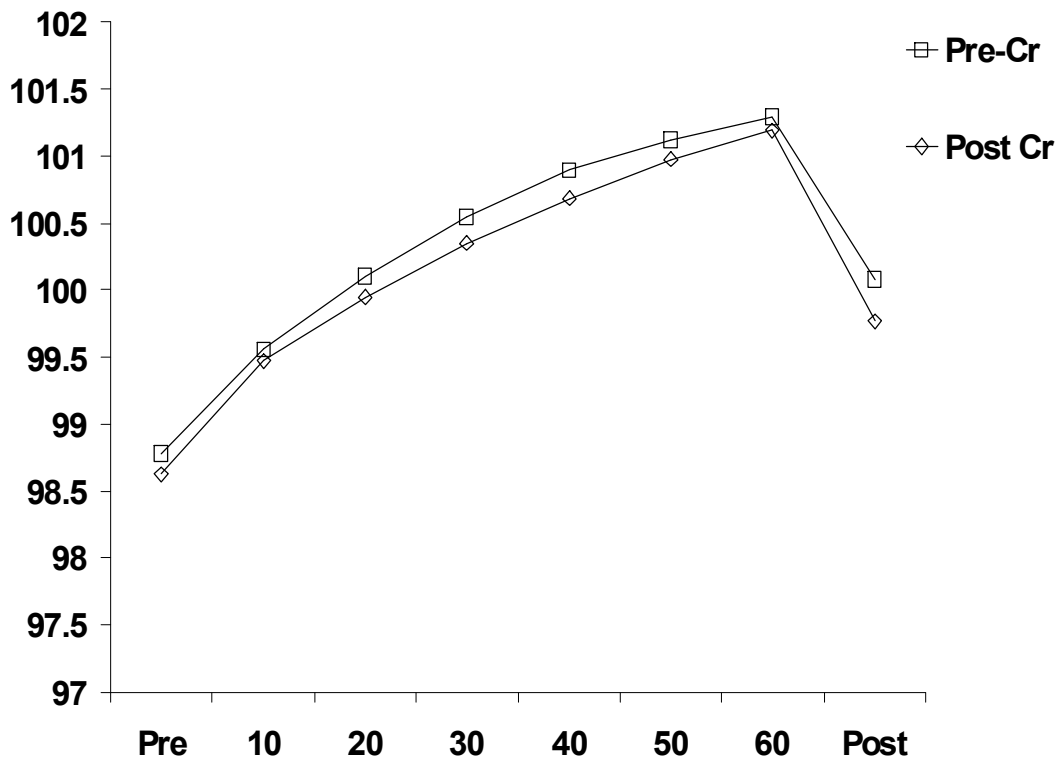


- Scientific evidence
  - Inhibition of CK inhibits protein synthesis (Carpenter et al.)
  - Increased satellite cell mitotic activity (Dangott et al.)
  - Increased muscle protein (Flisinska et al.)
  - Increased skeletal and cardiac muscle protein and increased myosin heavy chain synthesis (Ingwall et al.)
  - No effect on protein synthesis or breakdown (Louis et al. and Parise et al.)
  - Increased muscle CSA and strength following immobilization (Hespel et al.)
  - Increased myosin heavy chain and mRNA (Willoughby et al.)

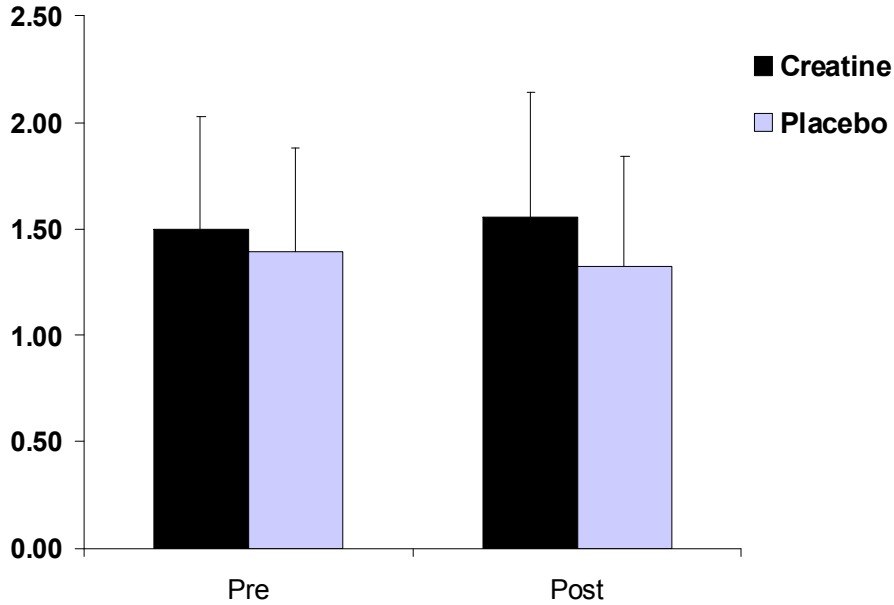
### Safety?

- Side Effects
  - Only documented side effect is weight gain
- There have been anecdotal reports of side effects consisting of:
  - Muscle cramps
  - Heat illness
  - Muscle strains
  - Kidney dysfunction
  - Gastrointestinal distress

Core Temperature



## Fluid Loss



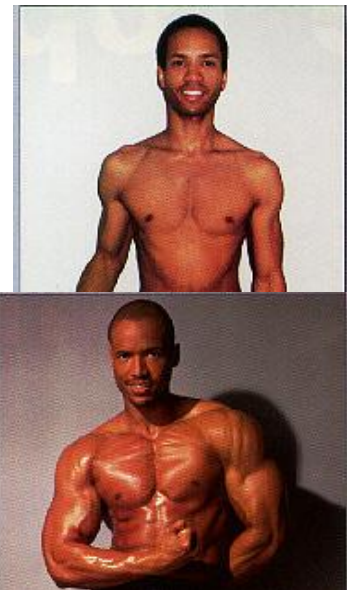
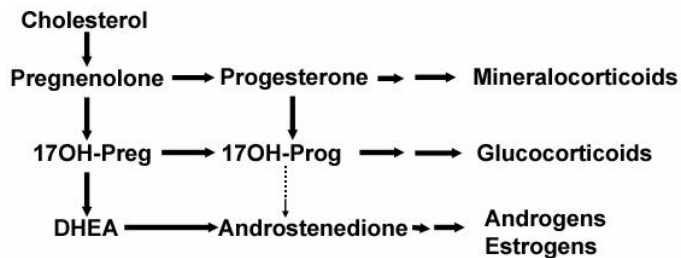
## Creatine Conclusions

- Studies suggest that creatine supplementation has an indirect effect on protein synthesis
- Creatine use has been widespread for over a decade and can be considered safe if used correctly
- At this time creatine is not banned by any organization

## TESTOSTERONE PRECURSORS (PRO-HORMONES)

- Dehydroepiandrosterone (DHEA)
- Androstenedione (Andro)
- Androstenediol
- Norandrostenedione (Norandro)
- Norandrostenediol

## Physiology of “Andro”



## Proposed Ergogenic Mechanism

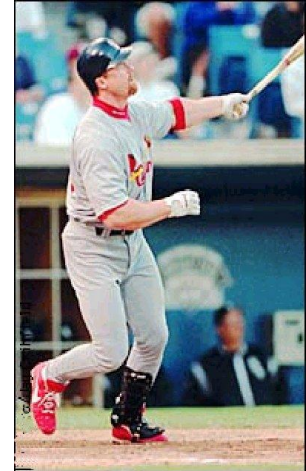
↑ Testosterone → ↑ Protein Synthesis → Muscle hypertrophy

## Efficacy?

- Increased testosterone in women for short period
- Increased andro and testosterone in post-menopausal women
- Increased andro and testosterone in older men and women

## Testosterone Levels

- 50-mg DHEA 3x/d x 8 weeks (Brown et al.)
  - Acute and chronic increase in A'dione
  - No change in acute or chronic testosterone
- 100-mg DHEA or 100-mg A'dione/d x 12 weeks (Wallace et al.)
  - No change in A'dione or testosterone
- 100-mg A'dione 3x/d x 8 weeks (King et al.)
  - Acute and chronic increase in A'dione
  - No change in acute or chronic testosterone
- 100-mg A'dione + 50-mg DHEA 3x/d x 8 weeks (Brown et al.)
  - Acute and chronic increase in A'dione
  - No change in acute or chronic testosterone
- 100-mg A'dione/d x 5 days (Rasmussen et al.)
  - No change in acute or chronic A'dione or testosterone
- 200-mg A'dione/d x 2 days (Ballantyne et al.)
  - Acute and chronic increase in A'dione
  - No change in acute or chronic testosterone
- 200-mg of A'dione or A'diol/d x 12 weeks (Broeder et al.)
  - Chronic increase in A'dione
  - No change in testosterone
- 200-mg of A'dione or A'diol (Earnest et al.)
  - Acute increase in A'dione
  - Acute increase in testosterone following A'dione only
- 100-mg A'dione/d x 7 days (Leder et al.)
  - Acute and chronic increase in A'dione
  - No change in testosterone
  - 42% increase in estradiol
- 300-mg A'dione/d x 7 days
  - Acute and chronic increase in A'dione
  - Only an acute increase in testosterone (34%)
  - 128% increase in estradiol



## Protein Synthesis

- No change in muscle protein synthesis or breakdown (Rasmussen et al.)
- No change in protein synthesis (Welle et al.)
- No change in muscle fiber cross sectional area (King et al.)

## Performance

- No changes in lean body mass or strength  
(King et al., Brown et al.)

## Others

- Boron
- Tribulus Terrestris
- Numerous others

## Safety?

### Known Side Effects

- Acne
  - Hair Loss
  - Oily Skin
  - Heart disease
  - Prostatitis
  - Growth plate closure
  - Gynecomastia
  - Increased cholesterol
  - Testicular atrophy
  - Kidney dysfunction
  - Liver cancer
  - Dependency
- Side Effects (females)
    - Lowered voice pitch
    - Hirsutism (changes in hair growth patterns, including facial hair)
    - Increased abdominal fat accumulation
    - General virilization

## Legal?

- These are Steroids!
- Banned substances by the:
  - NCAA
  - WADA
  - Pro Football
  - NBA
  - MLB
- Anabolic Steroid Act of 2004



## DHEA and Andro Conclusions

- Research supports increased testosterone in special populations
- Most research has failed to show increased testosterone in young healthy subjects
- At this time there is no data to support claims of improved performance
- There are known documented side effects side effects

## GAMMA-AMINOBUTYRIC ACID (GABA)

### Proposed Ergogenic Mechanism

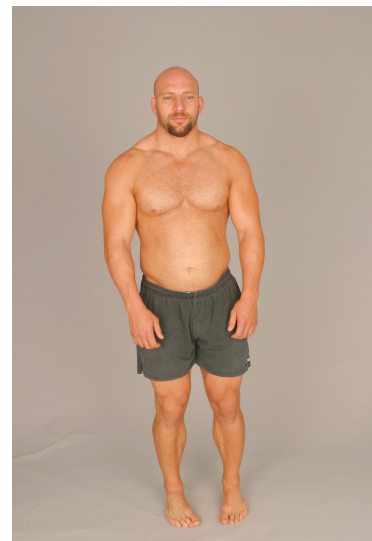
- Amino acid that functions as an inhibitory neurotransmitter in the brain
- Plays a significant role in hypothalamic-pituitary function
- Suggested to promote growth hormone secretion
- Exact mechanism unknown
  - Direct effect on hypothalamic and/or pituitary neurons?
  - Dopamine release?
  - GH releasing hormone?
  - Somatostatin?
  - Catecholamine release?

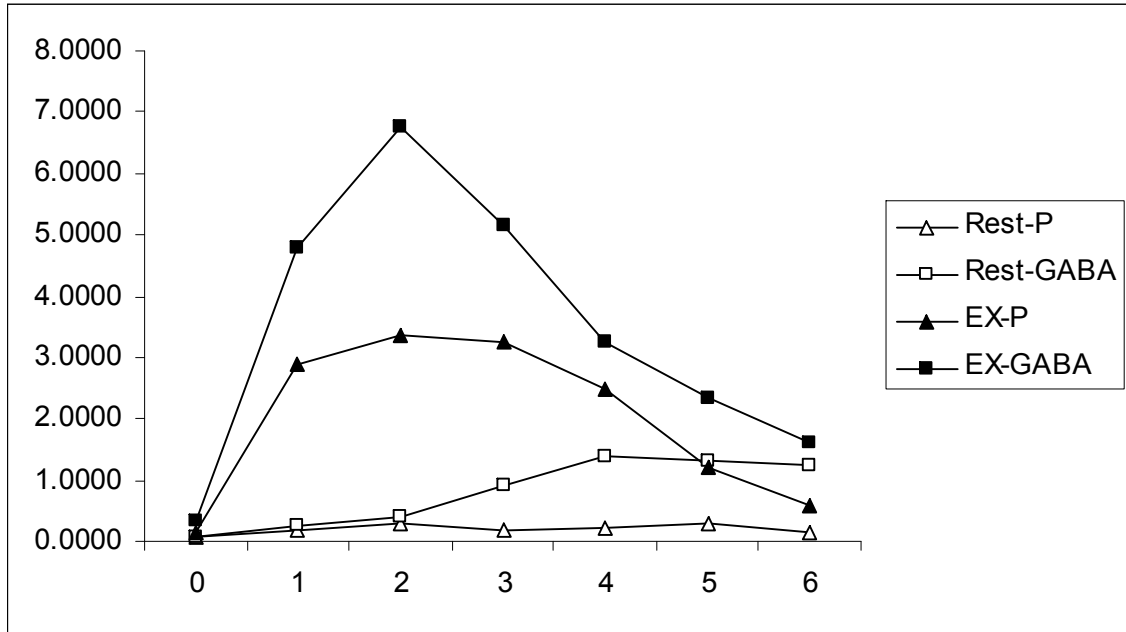
↑ GH → ↑ Protein Synthesis → Muscle hypertrophy

↑ GH → Increased lipid metabolism

### Efficacy?

- 5-g GABA increased resting GH levels
  - Cavagnini et al., 1980
- GABA dose response increase in GH (rats)
  - Acs et al., 1990
- GABA increased GH in young but not older rats
  - Mergl et al., 1995
- Suggested to inhibit GH response to exercise
  - Lovino et al., 1985, Steardo et al., 1986





### Safety?

- Tingling sensation in the skin
- Shortness of breath
- Drowsiness

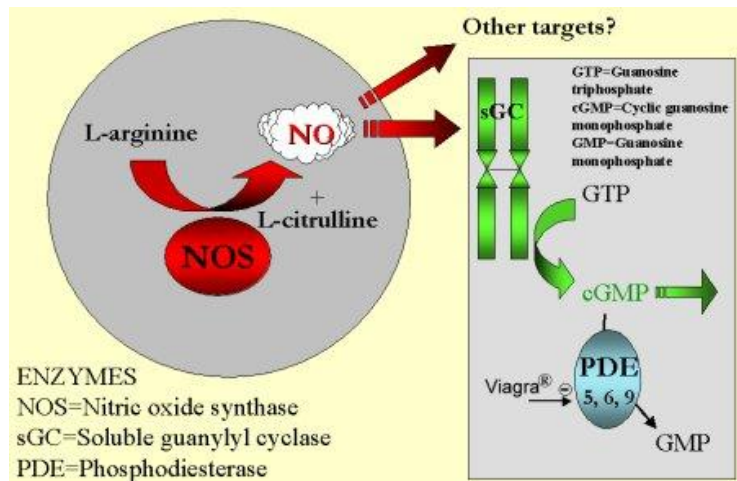
### GABA Conclusions

- No performance studies have been published
- Conclusions regarding GH response and safety cannot be made at this time
- GABA is not banned

### NO<sub>2</sub> (ARGININE AKG)

#### Proposed Ergogenic Mechanism

- Nitric oxide is produced from arginine and oxygen (nitric oxide synthase)
- Enhanced nitric oxide (NO<sub>2</sub>) production
- Vasodilation
- Enhanced blood flow to skeletal muscle (muscle pump)



## **Efficacy?**

- L-arginine enhanced nitric oxide production and aerobic exercise capacity in rats (Maxwell et al., 2001)
- L-arginine improved endothelium-dependent vasodilation in CHF patients (Hambrecht et al., 2000)
- L-arginine increased blood flow and distance on a 6-min walk test in CHF patients (Rector et al., 1996)

## **Safety?**

- Do not take if;
  - Pregnant
  - Erectile dysfunction
  - Hypertension
  - Cold sores
  - Psychosis

## **NO2 Conclusions**

- No performance studies have been published
- Appears to be safe
- NO2 is not banned

## **Others**

- HMB
- Chromium Picolinate
- Vanadyl Sulfate
- GAKIC
- Anator P70

## **CAFFEINE**

- Found in coffee, tea, cocoa, chocolate, some soft drinks, and numerous medications
- Crosses the membranes of all tissues in the body, including the blood-brain barrier
- Can exert its effects on both the CNS and the peripheral tissues resulting in a number of physiological effects

## **Proposed Ergogenic Mechanism**

- Increased Lypolysis / Glycogen Sparing
  - Blockage of Adenosine Receptors
  - Increased Epinephrine Levels
  - Inhibition of Phosphodiesterase
- Increased Muscular Contraction
  - Increased Intracellular Calcium
- Reduced Perception of Fatigue
  - CNS Stimulant

## Efficacy?

- 20% greater time to exhaustion compared to a control group
- Increased plasma fatty acids
  - Costill, 1978
- 20% increase in work rate during 2 hours of cycling
  - Ivy, 1979
- Conflicting results throughout the 80s
- Well controlled studies in the 90s showed endurance improvements ranging from 20-50%
- Some report increased epinephrine, fatty acids, and glycogen sparing while most suggest the central fatigue theory as the primary mechanism

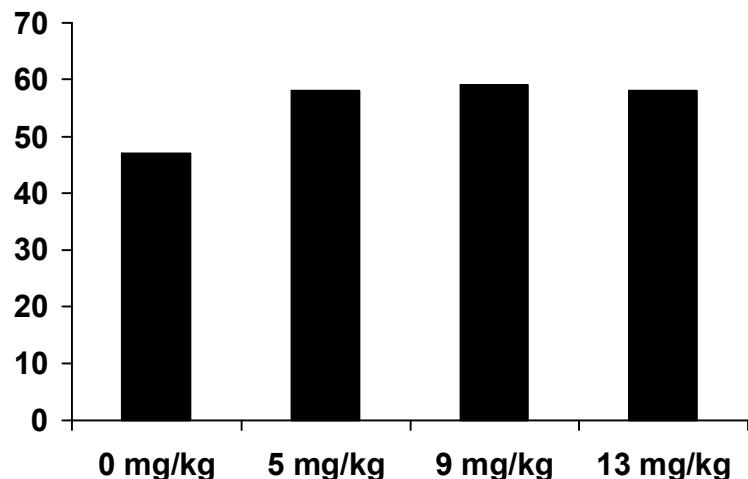
## Safety?

- Anxiety
  - Jitters
  - Dizziness
  - Headache
  - Inability to focus
  - Irritability
  - Insomnia
  - Frequent urination
  - Gastrointestinal distress
- Side effects associated with higher doses
    - Cardiac arrhythmias
    - Hallucinations
  - In massive doses, caffeine is lethal
    - A fatal dose of caffeine can range from 3- to 10-gm (about 170 mg/kg body mass) resulting in seizures, tachycardia, or ventricular dysrhythmias

## Legal?

- Caffeine is a restricted substance!
- NCAA
  - > 15mg / L (urine)

In one study, only a group receiving 13-mg/kg had an average urinary caffeine level that exceeded the banned limit. Groups ingesting 5- and 9-mg/kg did not, however they experienced similar increases in performance (time until exhaustion cycling at 80%  $\text{VO}_2$  max).



## **Caffeine Conclusions**

- Research supports thermogenic and fat burning potential
- At this time there is conflicting data regarding claims of improved performance
- Side effects are minor unless taken in large doses
- Caffeine is a restricted substance

## **EPHEDRA**

- Ma Huang herb containing ephedrine (drug)
- Mimics sympathetic nervous system stimulation
- Creates an adrenalin-like rush
- Stimulates alpha and beta receptors sensitive to epinephrine and norepinephrine
- Thermogenic / Lipolytic

## **Efficacy?**

- Studies have shown that ephedrine has thermogenic and fat burning properties
- The effects have been observed in a clinically obese population (Astrup, 1992, Astrup, 1992, Pasquali, 1987, Toubro, 1993)
- 24 mg had no effect on (Sidney & Lefcoe, 1977);
  - muscle strength or endurance
  - cardiorespiratory endurance
  - vertical jump
  - reaction time
  - anaerobic capacity
  - hand-eye coordination
  - speed
- No effect on performance (Bright, 1981, Clemons, 1993, Gillies, 1996, Sidney, 1997)
- 38% improvement in time to exhaustion
- 64% improvement in time to exhaustion
- Improved running time (3.2 Km)
  - 75-mg of ephedrine with 375-mg of caffeine (Bell et al.)

## Safety?

- Tremors
- Restlessness
- Irritability
- Anxiety
- Insomnia
- Headaches
- Hypertension
- Heart Palpitations
- Hypoglycemia
- Breathlessness
- Arrhythmias
- Psychosis

## Legal?

- Ephedrine was banned by IOC in 1972 because of its cardiac stimulating and mood altering effects
- Ephedrine is banned by the NCAA, WADA, MLB, and NFL
- FDA ban on ephedra April 1, 2004
  - Overturned by a federal judge in Utah in April, 2005 (Nutraceutical Corp vs FDA)

## Ephedra Conclusions

- Research supports thermogenic and fat burning potential in special populations only
- At this time there is no data to support claims of improved performance from ephedra ingestion
- There are known documented side effects side effects
- Banned by various states and sport organizations

**Thank You**

