



Performance Enhancing Drugs, Nutritional Supplements and Sports Drug Testing

Jeffrey M. Anderson, MD

Director of Sports Medicine

UConn Division of Athletics

Independent Program Administrator

Major League Baseball's Joint Drug
Prevention and Treatment Program

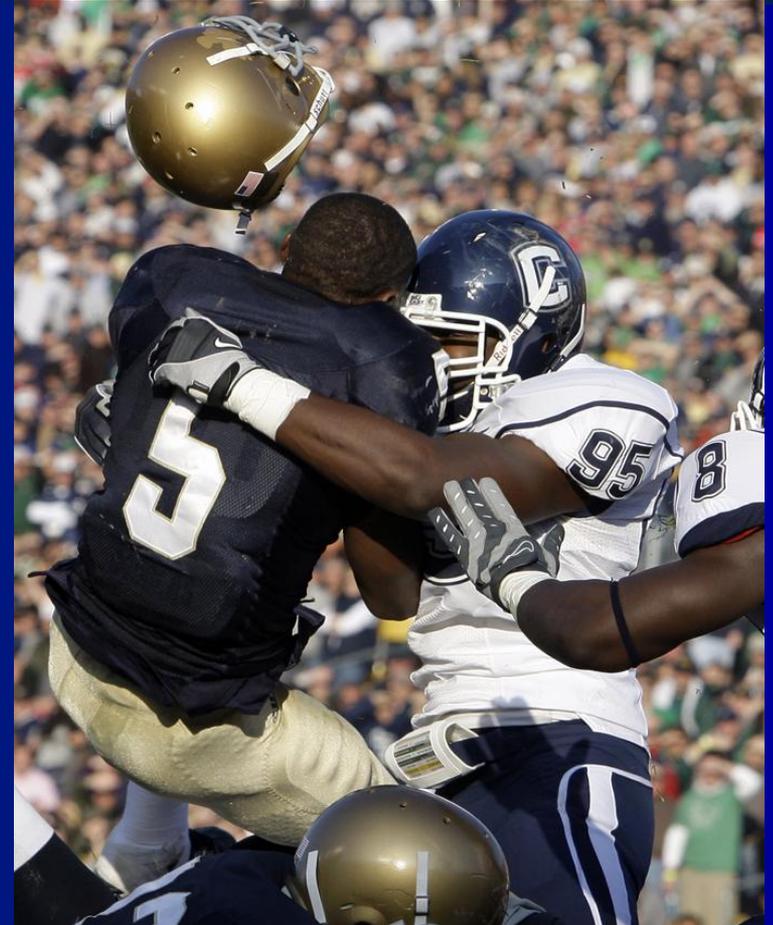
Objectives

- Review the physiology of performance enhancing drugs
- Discuss the history of their use
- Describe the area of nutritional supplements and discuss specific supplements
- Supplements and drug testing
- Identify important components of an ideal drug testing program



Background

- Intense motivation to win
- Athletes willing to risk personal health for athletic gain
- Societal pressure
- Parental/coaching pressure

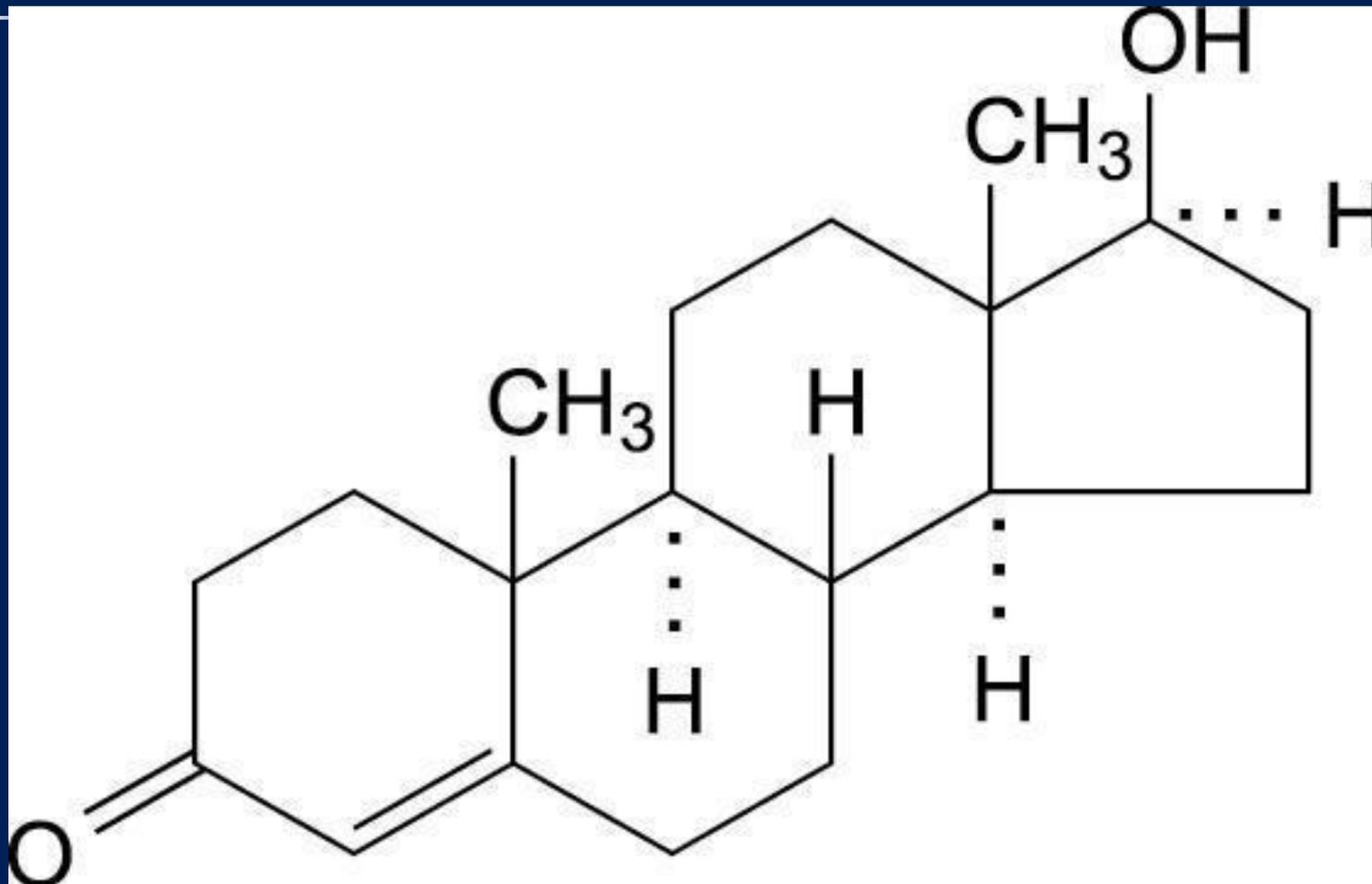


Anabolic Ergogenic Aids



© WENN

Testosterone

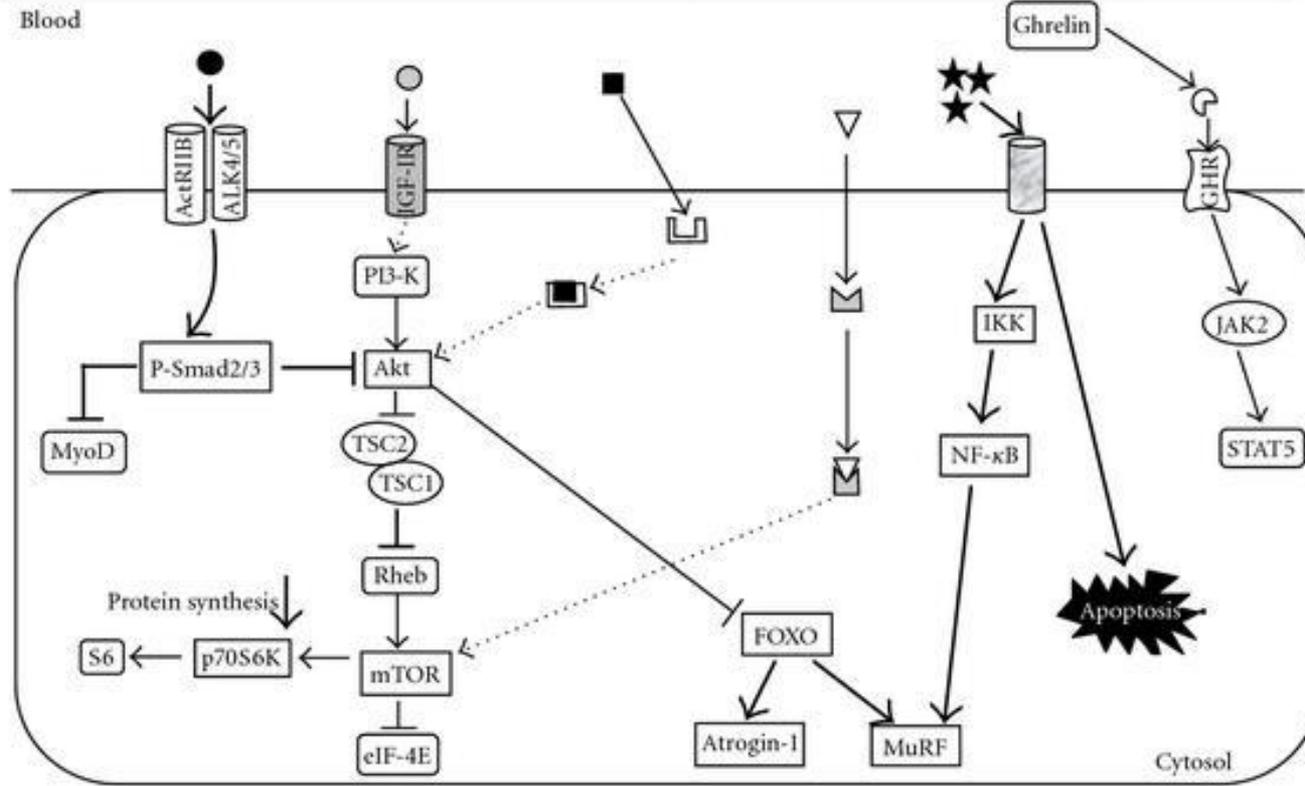




Cellular Signalling

- Akt/mTOR Signalling pathway vital to protein synthesis
- Can be stimulated by the mechanical effects of lifting, hormonal influences, and immunologic influences

Sarcopenic muscle



- IGF-I
- ⤵ GH
- ▽ Testosterone
- Myostatin
- ⊞ Androgen receptor
- ★ TNF-α
- Estrogen
- ⊞ Estrogen receptor

Endogenous vs. Exogenous AAS



■ Endogenous

- Testosterone
- Androstenedione
- Androstenediol
- DHEA
- 19-norandrosterone
- 19-noretiocholanolone

■ Exogenous

- Nandrolone
- Norandrostenedione
- Methandienone
- Methyltestosterone
- Stanozolol
- Boldenone
- Trenbolone

AAS Effects on muscle

- Most potent stimulators of protein synthesis at the cellular level
- Effects are noted with supraphysiologic doses (10x-100x)
- Clearly have a positive effect on muscle growth and hypertrophy



History of AAS

- Brown-Sequard 1889
- Zoth and Pregl 1920s
- Late 30s-testosterone synthesized by German scientists
- 1950s-Soviet use of testosterone in athletes
- 1960s-John Ziegler-Dianabol



History of AAS

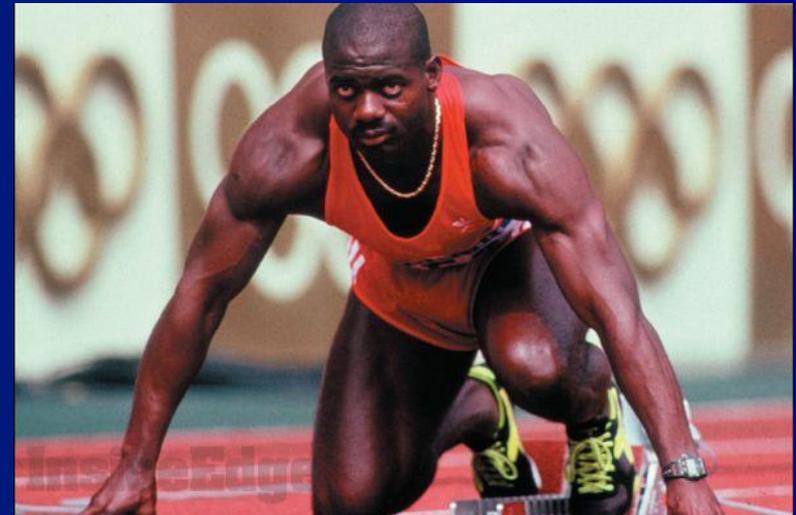


- 1960s and 1970s- rampant use-not illegal or banned
- 1970s-GDR swimmers
- Medical establishment still noted no benefit

History of AAS



- 1988-Ben Johnson +stanozolol test
- 1988-*Underground Steroid Handbook*-Duchaine
- 1991-Elashoff publishes review in *Annals of Internal Medicine* stating that no firm conclusion can be drawn on their effects



History of AAS



- 1996-Bhasin-first study documenting anabolic effects of steroids
- Late 90s-Early 2000s—baseball
- 2004-US Anabolic Steroid Control Act



Side Effects of AAS

■ Hepatic

- Liver injury (temporary vs. permanent)
- Hepatic tumors

■ Cardiac

- Lowered HDL, elevated LDL and triglycerides
- Increased thrombogenesis
- Cardiomyopathy

■ Genitourinary

– Males

- Impotence
- Oligospermia/azoospermia
- Gynecomastia

– Females

- Clitoromegally
- Menstrual disturbance
- Breast atrophy

Side Effects of AAS

- Dermatologic
 - Acne
 - Male-pattern baldness
 - Hirsutism
- Musculoskeletal
 - Tendon rupture



Figure: Severe acne conglobata induced by anabolic-androgenic steroids
The patient at the time of his ideal body image; the 21-year-old bodybuilder had a history of anabolic-androgenic steroid abuse (A). Severe acne conglobata (B); lesions include papules, pustules, abscesses, and deep ulcerations. Patient after 6 weeks of antiseptic-antibiotic therapy (C).

Side Effects of AAS

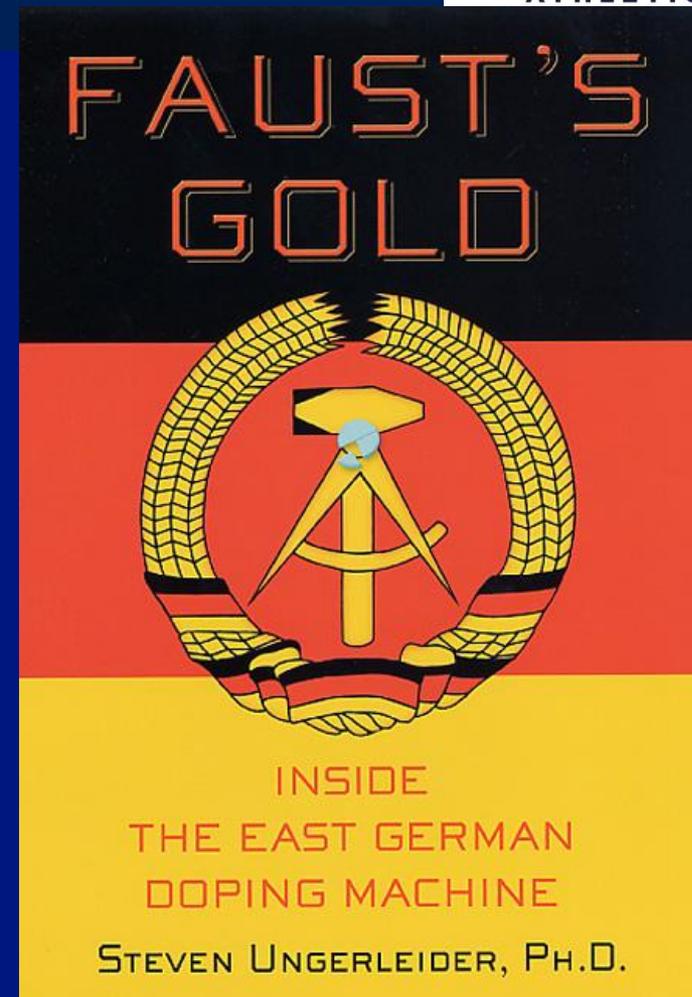


- Psychological
 - Aggressiveness
 - Rage
 - Delirium
 - Depression
 - Psychosis
 - Mania

How Common Are Side Effects?



- No controlled trials
- Variation in reports depending on perspective
- Temporary vs. permanent?
- GDR information is concerning





Growth Hormone

- Not just one hormone
- Several different isoforms—most common are the 20kD and 22kD isoforms
- Not completely clear which isoforms are most biologically active

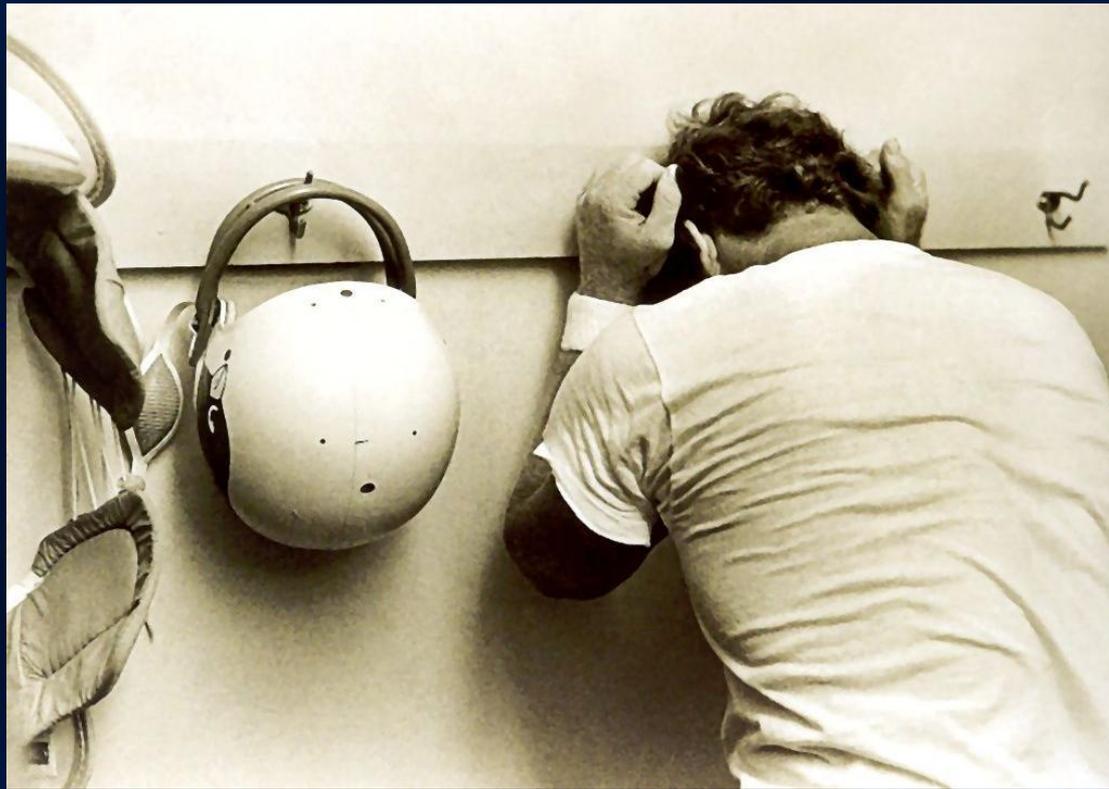
Bamberger M, Yaeger D: Over the edge.
Sports Illustrated April 14: 62-70, 1997



- 198 current or aspiring Olympians asked the following two questions:
 - Would you take a banned performance enhancer if it guaranteed you to win and not get caught? --98% “yes”
 - Would you take the same undetectable substance if it allowed you to win every competition for five years, then result in death? --more than 50% “yes”



UCONN
ATHLETICS



Jeff Summers Says...

Give Me Just
30
Seconds

**New & Improved
Super Muscle
Blasting Stack!**

**The 3 Most Potent
Muscle Builders Ever!!!**

**...And I'll Legitimately Prove To You *The*
Muscle-Building Gap Between Supplements
*And Sane Steroid Use Is Closing!***



Mandatory Initial Supplement Slide

- 1994—Dietary Supplement Health and Education Act (DSHEA) passed by congress
- Dietary supplements not subject to FDA oversight
 - No claims to treat specific medical conditions (but can make general health claims)
 - No premarket requirements for safety or efficacy testing
 - No establishment of good manufacturing practices (GMPs) until 2007

The Bottom Line

- When DHSEA passed, Congress noted that the \$4 billion industry was integral to the economy
- 2007 GAO report—the supplement industry worth \$23.7 billion



Nutritional Supplements



- Are neither inherently good nor inherently evil
- Contain metabolically and pharmacologically active substances – whether they're “natural” or not
- Need to be thought of in the same risk/benefit manner that we do other drugs
- Are generally produced in a setting with minimal to no oversight and variable quality control

Commonly Used Herbal Supplement On Campus



- Indigenous to Central and Southern Asia, but grown around the world
- Ameliorates nausea, stimulates hunger, lowers intraocular pressure, helps with pain control
- May trigger anxiety, psychosis, depression
- Long-term use carries the risk of carcinogenesis

Commonly Used Herbal Supplement On Campus



- Can be ingested orally—especially if incorporated into baked goods (brownies)
- Commonly ingested via inhalation-either in cigarette form, via a pipe, or via a large water-filled tube.
- Legal for medicinal purposes in 14 states



Specific Sports Supplements



Creatine

- The most studied of the various nutritional supplements
- Creatine phosphate is an anaerobic energy source in muscle
- Harris (1992) showed that muscle phosphocreatine stores could be increased approximately 20% with oral ingestion of creatine

Creatine



- Has been shown to be effective in improving brief bursts of exercise (<15sec)
- Used in training in an attempt to train harder
- Does not stimulate protein synthesis



Creatine side effects

- Fluid retention—but does not seem to alter fluid distribution (intracellular vs. extracellular)
- Documentation of increased compartment pressures (Potteiger 2001, 2002, Schroeder 2002, Hile 2006)
- Anecdotal reports of cramping—never replicated in controlled settings



Creatine side effects

- No negative effect on thermoregulation
- No documentation of hepatic, renal, or cardiac side effects

Creatine Summary



- Benefits short bursts of intense exercise
- Very limited side effects in 20 years of experience
- Risks
 - Contamination of product with other substances
 - Small risk of exertional compartment syndrome that is likely reversible with discontinuation



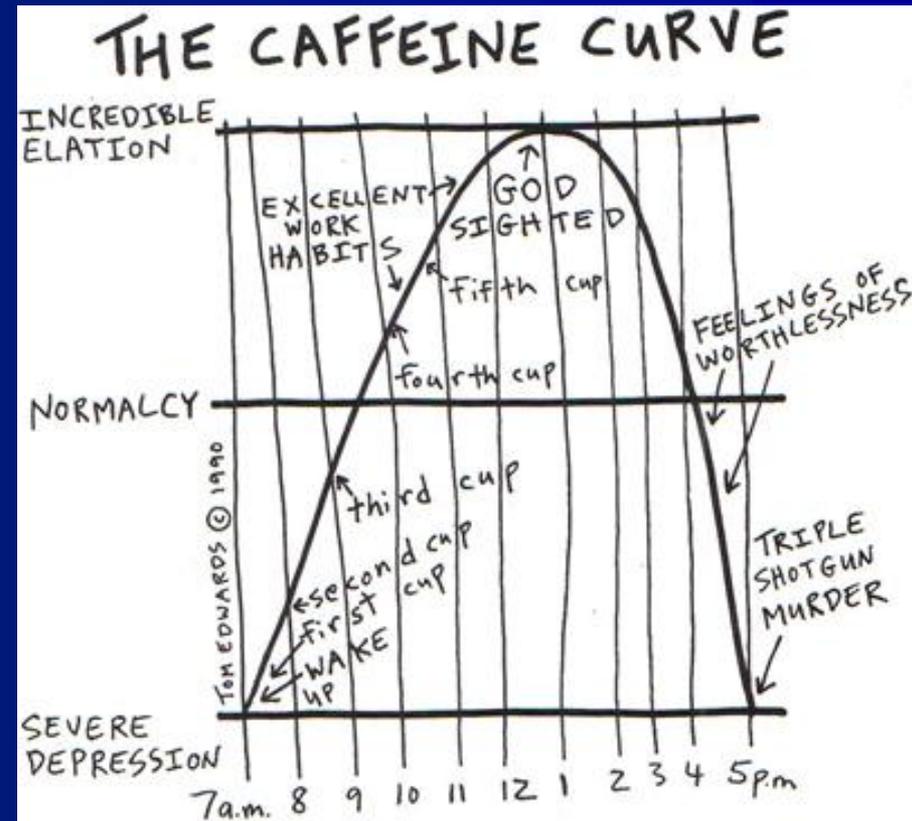
Protein Supplements

- US RDA of 0.8g/kg/d
- Probably underestimates athletes' needs
 - 1.2-1.4g/kg/d for endurance athletes
 - Up to 1.7g/kg/d for resistance athletes
- Intact, high quality protein sources, such as whey, casein, and soy are as good or better than amino acid supplements.

“Energy” Enhancers



- “Energy” drinks
- Caffeine
- Taurine
- Ginseng
- Guarana
- Bitter orange





Nitric Oxide Stimulators

- Arginine combined with alphaketo-glutarate
- Arginine stimulates nitric oxide release
- Nitric oxide is a vasodilator—allowing added blood flow to exercising muscle
- No documentation of increased NO levels in muscle
- No documentation of performance or muscle mass increase
- Costly—one popular product \$30 for 50 servings

“Fat Burners”



- Ephedra (now banned by the FDA)
- Bitter orange or synephrine
- L-carnitine
- Chromium picolinate

Anabolic Ergogenic Aids

- Testosterone and its analogues—both endogenous and exogenous
- Dramatic effect on muscle protein synthesis and muscle growth



Documented Steroid Contaminants of Supplements



- 19-nor-steroids
- Testosterone
- Metandienone
- Oxandrolone
- Stanozolol
- Methasterone

Drug Testing Risks

- Ingestion of a supplement with a listed banned substance
- Ingestion of a contaminated supplement
- Ingestion of a “fake” supplement





Ingestion of a Supplement with a Banned Substance on the Label

- Sophomore baseball pitcher positive for DHEA
- Appealed case based upon lack of knowledge that DHEA was banned
- Was told by salesperson at the store that the supplement was “legal”
- Acknowledged that DHEA was listed as an ingredient
- Never checked with his athletic trainer

Ingestion of a Contaminated Supplement



- Senior football student-athlete
- Tested positive for 19-norandrosterone and 19-noretiocholanolone
- Appealed the positive test because on the basis of a contaminated supplement
- None of the supplements the student-athlete admitted to using had a banned substance on their labels

Contamination of Supplements



- Geyer, et al. 2000
 - Norandrostenone contamination of supplements
- Geyer, et al. 2001
 - Seven different prohormones and testosterone detected in a creatine supplement
- Geyer, et al. 2002 and 2004
 - 15% of 634 nonhormonal supplements found to be contaminated with anabolic hormones



UConn
HUSKIES

Probable Deliberate Contamination of Supplements with High Amounts of Steroid

Table 2. Nutritional supplements faked with 'classic' anabolic androgenic steroids since 2002

Product name (pharmaceutical form)	Company	Declared ingredients	Not declared 'classic' anabolic androgenic steroids and references
Stanozolol II (powder)	Pharmtec	AD-4-Complex nutrients, MetX synergistic blend, 1-T matrix, creatine monohydrate, thermogenic proprietary blend, ribose- 4 matrix	Metandienone 4 mg/ serving (10 g powder) ²⁸
Parabolon (powder)	Pharmtec	AD-4-Complex nutrients, MetX synergistic blend, 1-T matrix, creatine monohydrate, thermogenic proprietary blend, ribose-4 matrix	Metandienone 10 mg/ serving (10 g powder) ²⁹⁻³¹
Met-AD17-diol (capsules)	Pharmtec	Met-AD17-diol/1-T matrix	Metandienone <i>ca.</i> 9 mg/ capsule ²⁹⁻³¹
Stanozolol-S (fizzy tablets)	Senesco-Pharma	Several prohormones	Stanozolol <i>ca.</i> 15 mg/ tablet, Boldenone, DHT ³²
Parabolon-S (fizzy tablets)	Senesco-Pharma	Several prohormones	Metandienone <i>ca.</i> 17 mg/ tablet ³²
OXA 17-DION (capsules)	Muscle Inc. Ltd, Cyprus	5 alpha-androstan-2-oxa-17 alpha-methyl-17, beta-ol-3-one	Oxandrolone <i>ca.</i> 25 mg/ capsule ³³
TESTEXX (capsules)	Muscle Inc. Ltd, Cyprus	1,4-Androstadien-4-chloro-17 α -methyl-17 β -ol-3-one	Dehydrochloro-methyltestosterone <i>ca.</i> 25 mg/ capsule ³³
Primo 17-acetoxo (capsules)	Muscle Inc. Ltd, Cyprus	17 β -Acetoxo-1-methyl-5-alpha-androst-1-en-3-one	Metenolone acetate <i>ca.</i> 50 mg/ capsule ³³
Parabolon-B (blades)	Pharm-Tec	P-Blade 17Tren-1.4dien-3-one Beta-Compound	Metandienone <i>ca.</i> 10 mg/ blade ³³
Stanozolol-B (blades)	Pharm-Tec	S-Blade 5-Alpha Pyrazol-Compound	Stanozolol <i>ca.</i> 10 mg/ blade ³³

From Geyer, et al. J. Mass Spectrom. 2008



UCONN
ATHLETICS

Where Can I Turn For Help?

- www.nsf.com
- www.consumerlab.com
- www.usp.org
- www.drugfreesport.com



Drug Free Sport™



Be Sure It's CL Approved

ConsumerLab.com®

Celebrating 11 Years of Reporting 1999 – 2010

Our Mission: To identify the best quality health and nutritional products through independent testing.

Drug Testing



- Components of a strong testing program
- Methods
- Distinguishing endogenous and exogenous substances
- Growth hormone testing

Components of an Ideal Testing Program



- Frequent testing
- No notice testing
- Irregular, unpredictable scheduling
- Diligent collection procedures
- Impeccable chain of custody
- Appropriate penalties for violations
- Public announcement of penalties

Primary Purpose of Drug Testing



Deterrence

30 Percent Rule



- Larry Bowers-USADA
- If an athlete thinks there is a 30 percent chance of being caught, deterrence occurs

Drug Testing Lab Methods



- Gas chromatography/mass spectrometry
- Isotope-ratio mass spectrometry
- Growth Hormone Testing

How Do We Detect Exogenous Testosterone Use



- Testosterone:Epitestosterone ratio
- Normal under 4:1
- Many normal individuals above 4:1
- IRMS

GC/MS



- Has been the gold standard in testing
- Recognizes the unique spectrometric signature of individual chemicals after separation in a gas chromatography column

Growth Hormone Testing



- Synthetic hGH is the 22kD isoform
- Normal ratio of 22kD to other isoforms in human serum
- Elevated ratio indicative of exogenous use
- Some current problems with the statistical validity of the ratio

Final Question—Why????



- Anabolic steroids are banned and have potential side effects
- Nutritional Supplements have limited documented benefit
- Some nutritional supplements carry potential side effects
- Risk of contamination with banned substances
- Can be very expensive
- Yet—they net \$23.7 billion/yr—with about \$5 billion of that being from sports supplements

Here's Why



- “Easy results” in pill or powder form
- The pressure to have that little edge or to keep up with the opponent
- Hot-looking models use supplements
- “The establishment” is against it
- The newest thing is always best
- Manufactured in exotic lands with exotic names



Thank You