# 2024 Primary Care Hawaii Conference Performance Enhancing Drugs

April 1, 2024 Jason D. Brayley, MD





### **Performance Enhancing Drugs - Objectives**

- Review the general prevalence of performance enhancing drugs used in sports and athletic competition
- Understand how the most common categories of PEDs affect general health athletic performance
- Review strategies for office-based counseling of patients taking or considering using PEDs



### **Performance Enhancing Drugs - Disclosure**

I have nothing to disclose



### Why do athletes use supplements/PEDs?

- Aid in recovery
- Maintain health
- Improve performance
- Gain or neutralize advantage on competition
- Modulate body composition
- Compensate for poor diet





# What is Doping?

- Doping: Refers to the use of banned substances in sports
  - Definition developed by World Anti-Doping Agency (WADA) Code
  - Occurrence of one or more of the following:
    - Presence of a prohibited substance or its metabolites or markers in an athlete's body
    - Use or attempted use of a prohibited substance or prohibited method
    - Refusing, or failing without compelling justification, to submit sample collection after notification, as authorized in applicable antidoping rules, or otherwise evading sample collection
    - Violation of applicable requirements regarding athlete availability for out-of-competition testing, including failure to provide required information on whereabouts and missing tests that are declared based on reasonable rules
    - Tampering or attempting to tamper with any part of doping control
    - Possession or use of prohibited substances or methods
    - Trafficking of any prohibited substance or method
    - Administration (or attempted) of a prohibited substance or method to any athlete or assisting, encouraging, aiding, abetting, covering up, or any other type of complicity involving an antidoping rule violation or any attempted violation





# What is a Supplement?

1994 Dietary Supplements Health and Education Act (DSHEA):

"...a product, other than tobacco, which is used in conjunction with a healthy diet and contains one or more of the following dietary ingredients: a vitamin, mineral, herb or other botanical, an amino acid, a dietary substance for use by man to supplement the diet by increasing the total daily intake, or a concentrate, metabolite, constituent, extract or combinations of these ingredients"







### What is a supplement?

#### 2018 IOC Consensus Statement:

- (1) Functional foods: foods enriched with additional nutrients or components outside their typical nutrient composition (ie fortified/enriched foods)
- (2) Formulated foods and sport foods: products providing energy and nutrients in a more convenient form than normal foods for general nutrition support (e.g. liquid meal replacements) or for targeted use around exercise (e.g., sports drinks, gels, bars)
- (3) Single nutrients and other components of food or herbal supplements provided in **isolated or concentrated forms**
- (4) Multi-ingredient products containing various combinations of those products described above that target similar outcomes

# **Supplement Monitoring**

- World Anti-Doping Agency 1999
  - 1. Potential for enhanced performance
  - 2. Potential for being detrimental to health
  - 3. They violate the spirit of sport
- NSF International
  - Independently monitors supplement safety
  - Works with WADA, NFL, MLB, PGA
- Informed-Choice, Consumer Lab, USP, BSCG
  - Quality Assurance Programs for sports nutrition

ID No.	Prohibited Substance/Method	Type	When Prohibited
S0	Non-approved substances	Substance	At all times
S1	Anabolic agents	Substance	At all times
S2	Peptide hormones, growth factors, related substances, and mimetics	Substance	At all times
S3	Beta 2 agonists	Substance	At all times
\$4	Hormone and metabolic modulators	Substance	At all times
\$5	Diuretics and masking agents	Substance	At all times
\$6	Stimulants	Substance	In competition
S7	Narcotics	Substance	In competition
58	Cannabinoids	Substance	In competition
S9	Glucocarticoids	Substance	In competition
M1	Manipulation of blood and blood components	Method	At all times
M2	Chemical and physical manipulation	Method	At all times
M3	Gene doping	Method	At all times
PT	Aicohal	Substance	Particular sport
P2	Seta blockers	Substance	Particular sport





# **Collegiate Supplement Use**

 Nearly half of NCAA athletes reported habitual supplements use, with significant variation in patterns based on sex, sport-type, year in college, and weight status.

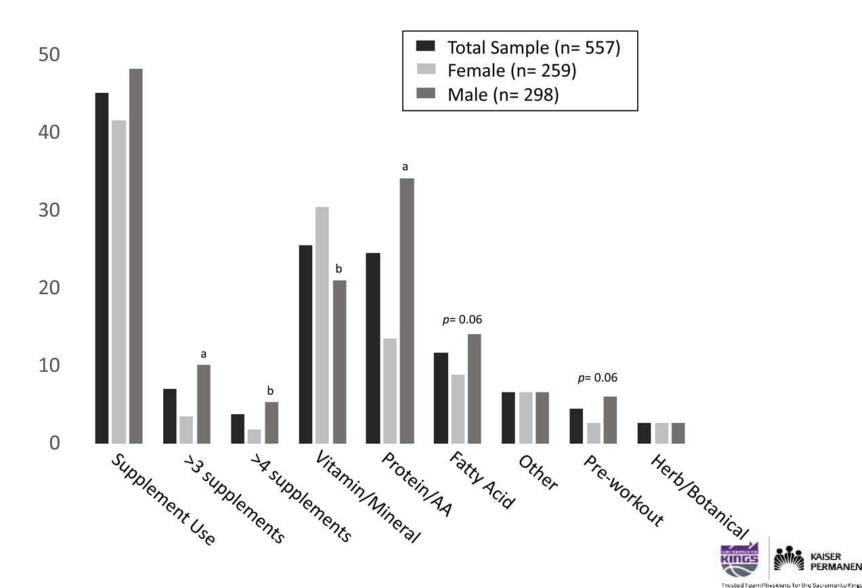




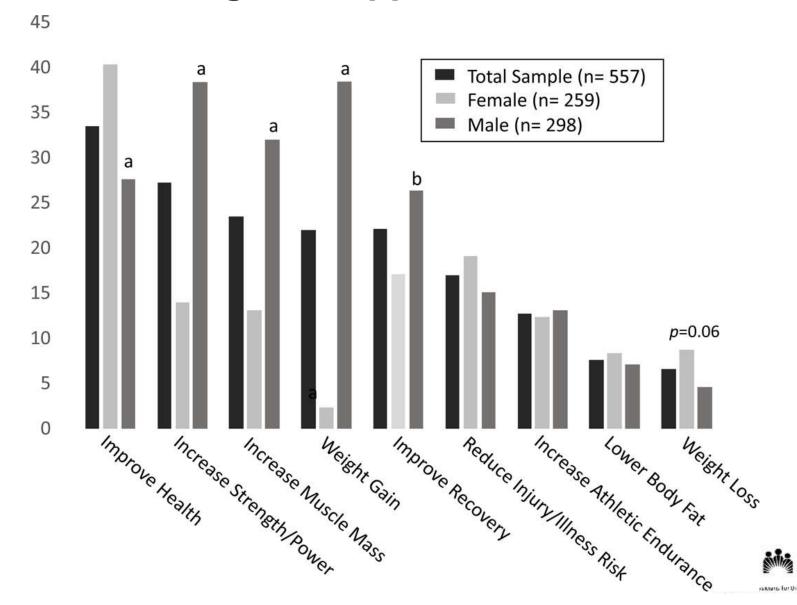
An investigation of habitual dietary supplement use among 557 NCAA Division I athletes, Barrack, et al. J Am Coll Nutr. 2020 Sep-Oct; 39(7): 619-627.



### **Collegiate Supplement Use**



### **Collegiate Supplement Use**



#### PED use in Adolescence

#### Anabolic-Androgenic Steroids:

- Increased muscle mass, speed, agility
- 1%-12% of HS Boys
- 0.5%-3% of HS Girls
- Football, wrestling, weight-lifting
- Acne, hepatic dysfunction, lipid changes, suppression of hypothal/pituitary axis, mania/aggression, premature closure of epiphyseal plates

#### Stimulants: amphetamine, d-methamphetamine, methylphenidate

- increase alertness and improve endurance, anaerobic performance, and reaction time
- Non-medical amphetamines (2015): 6.5%, 3-fold increase in collegiate athletes
- hypertension, tachycardia, heart attack, headaches, tremors, insomnia, anxiety/panic attacks, aggression, and psychosis

Performance-Enhancing Drug Use in Adolescence. White Pharm D, Nicole. Am J Lifestyle Med, 2017 Mar-Apr; 11(2): 122–124.



### PED use, continued...

#### Anabolic-Androgenic Steroids:

- Global lifetime prevalence rate 3.3 percent (6.4% men, 1.6% women)
- Higher among recreational vs professional athletes (18.4 vs 13.3%)
- Varied by region (highest in Middle East)

#### Growth Hormone:

5% US high school students report using GH

#### Patterns of use:

- Most users obtain androgens from the internet
- "Pyramiding" (escalating doses cycles of 6-12 weeks)
- "Stacking" (combining two or more steroids)
- "PCT" (post-cycle therapy)

Sagoe D, et al. The global epidemiology of anabolic-androgenic steroid use: a meta-analysis and meta-regression analysis. Ann Epidemiol 2014; 24:383.



### PED use, continued...

Users may attempt to counter side effects with other medications:

- Include both androgens and other drugs, such as:
  - Growth hormone additional anabolic effect
  - hCG to counteract reduction in testicular size resulting from high dose androgens
  - Aromatose inhibitor to counteract gynecomastia
  - 5-alpha reductase inhibitor to prevent balding and acne from androgens
  - Diuretics to promote water/fluid loss



### PED use, continued...

GCN > Racing > News

### 'It's a joke' – Anti-doping testers swoop Spanish amateur race, 130 riders abandon

'Anti-doping testing = punctures and abandons' says one rider amid suspicions around doping and test-evasion

( ) 06:53, Thursday 7th March 2024

Patrick Fletcher Deputy Editor

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### **Supplement Adverse Reactions/Contamination**

- Lack of knowledge:
  - 86% college-aged athletes unaware of ADRs
  - 62% unaware of active ingredient
  - 52% unaware of recommended dose
  - 36% aware of issues with contamination

Prohibited Contaminants in Dietary Supplements. Mathews MD, Nielson. Sports Health. 2018 Jan-Feb; 10(1): 19–30.



# My first professional team...









Dryden McKay, Hobey Baker Award winner as top NCAA men's hockey player, banned six months for an antidoping rule violation





Apr 18, 2022

- Tested positive for ostarine (SARM Selective Androgen Receptor Modulator) after being drug tested having been named an alternate player for the 2022 U.S. men's Olympic hockey team for the Beijing Games
  - "Trillionths of a gram"
- Sent supplements to third party tester
  - "found in an allegedly "all-natural" Vitamin D3 immune booster he had been taking for 10 days during the COVID-19 omicron variant surge"



# **Banned Substances (WADA)**

#### **■wada**



WORLD ANTI-DOPING CODE

INTERNATIONAL STANDARD

### PROHIBITED LIST

2024

This List shall come into effect on 1 January 2024.

#### S1 ANABOLIC AGENTS

#### PROHIBITED AT ALL TIMES (IN- AND OUT-OF-COMPETITION)

All prohibited substances in this class are non-Specified Substances.

Anabolic agents are prohibited.

#### S1.1. ANABOLIC ANDROGENIC STEROIDS (AAS)

When administered exogenously, including but not limited to:

- 1-Androstenediol (5a-androst-1-ene-3ß, 17ß-diol)
- 1-Androstenedione (5a-androst-1-ene-3, 17-dione)
- 1-Androsterone (3a-hydroxy-5a-androst-1ene-17-one)
- 1-Epiandrosterone (3ß-hydroxy-5g-androst-1-ene-17-one)
- 1-Testosterone (17ß-hydroxy-5a-androst-1en-3-one)
- 4-Androstenediol (androst-4-ene-3ß, 17ß-diol)
- 4-Hydroxytestosterone (4,17ß-dihydroxyandrost-4-en-3-one)
- 5-Androstenedione (androst-5-ene-3,17-dione)
- 7a-Hydroxy-DHEA
- 7ß-Hydroxy-DHEA
- 7-Keto-DHEA
- 11ß-Methyl-19-nortestosterone
- 17a-Methylepithiostanol (epistane)
- 19-Norandrostenediol (estr-4-ene-3,17-diol)
- 19-Norandrostenedione (estr-4-ene-3,17-dione)
- Androst-4-ene-3,11,17- trione (11-ketoandrostenedione, adrenosterone)
- Androstanolone (5a-dihydrotestosterone, 17ß-hydroxy-5a-androstan-3-one)
- Androstenediol (androst-5-ene-3ß,17ß-diol)

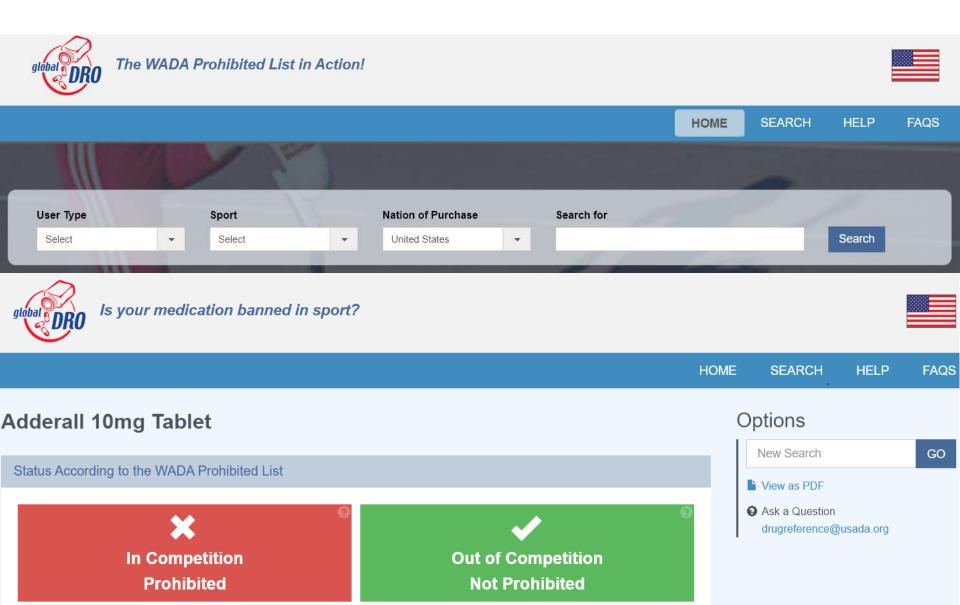
- Androstenedione (androst-4-ene-3,17-dione)
- Bolasterone
- Boldenone
- Boldione (androsta-1,4-diene-3,17-dione)
- Calusterone
- Clostebol
- Danazol ([1,2]oxazolo[4',5':2,3]pregna-4-en-20-yn-17a-ol)
- Dehydrochlormethyltestosterone (4-chloro-17ß-hydroxy-17a-methylandrosta-1,4-dien-3one)
- Desoxymethyltestosterone (17a-methyl-5a-androst-2-en-17ß-ol and 17a-methyl-5aandrost-3-en-17ß-ol)
- Dimethandrolone (7a,11ß-Dimethyl-19nortestosterone)
- Drostanolone
- Epiandrosterone (3ß-hydroxy-5g-androstan-17-one)
- Epi-dihydrotestosterone (17ß-hydroxy-5ßandrostan-3-one)
- · Epitestosterone
- Ethylestrenol (19-norpregna-4-en-17a-ol)
- Fluoxymesterone
- Formebolone
- Furazabol (17a-methyl [1,2,5] oxadiazolo[3',4':2,3]-5a-androstan-176-ol)

### **USADA**





### **Patient/Provider Resources**



- Definition: Testosterone or T-like synthetic drugs
  - Exogenous AAS synthetic analogs of testosterone
  - Endogenous AAS naturally occurring, involved in metabolic pathways of testosterone
- Medical indications: hypogonadism, severe osteoporosis, breast carcinoma
- Ergogenic claims:
  - Increase muscle bulk
  - Increased muscle strength
  - Possibly improving anti-catabolic effect, recovery





#### Method of Action:

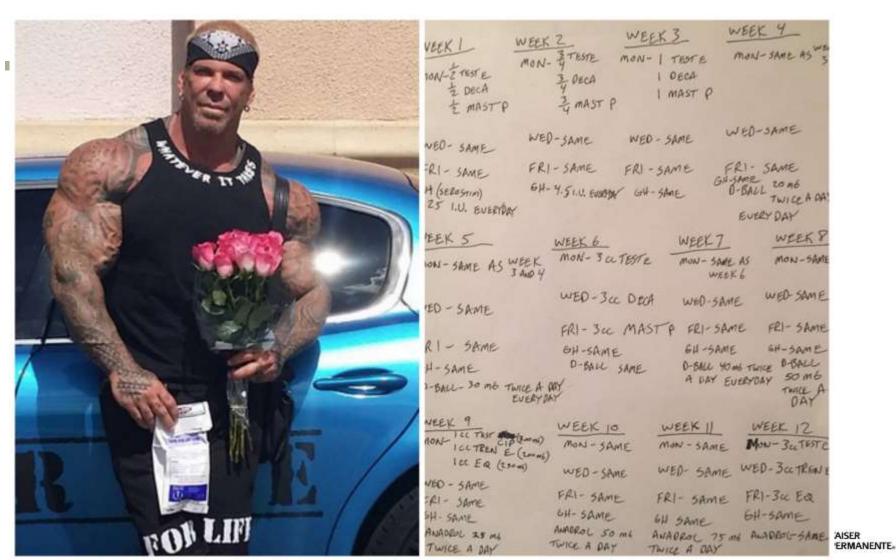
- Anabolic effects increase protein synthesis
  - Muscle fiber hypertrophy and formation of new fibers
  - Increased fat-free mass
- Anticatabolic effects
  - Reverse/limit catabolic effects of training → increased training load, improved utilization of ingested protein
- Androgenic effects enhance development of secondary male sex characteristics
  - Enhanced aggressive behavior → increased training intensity
- Manipulated to take advantage of or minimize effects



#### "Designer steroids":

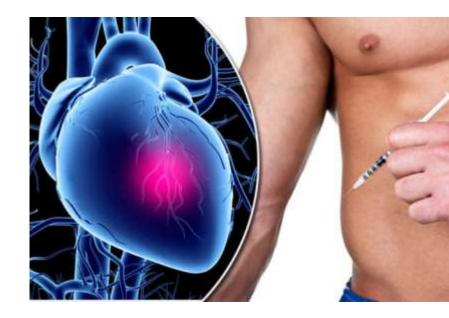
- Norbolethone
  - Anabolic activity possibly 20x higher
- <u>Tetrahydrogestrinone</u> (THG)
  - Closely related to gestrinone (progestin) and trenbolone (veterinary androgen)
  - Manipulated to break down in urine test preparation
  - Detected on anonymous syringe sent to USADA in 2003





#### Adverse reactions/side effects:

- GI liver toxicity (check LFTs)
- CV -
  - ↑ total & LDL, ↓ HDL
  - Hypertension (may be due to Na and H<sub>2</sub>O retention)
  - MI/CVA (may be due to cholesterol and HTN)
  - LV dysfunction with long-term use





#### Adverse reactions/side effects:

- Psych:
  - Increased aggressive behavior, irritability
  - Suicide ideation
- Immunity: reduced humoral immunity
- Skin: increased sebum → acne
- MSK:
  - Spontaneous tendon rupture
  - Premature closure of growth plates



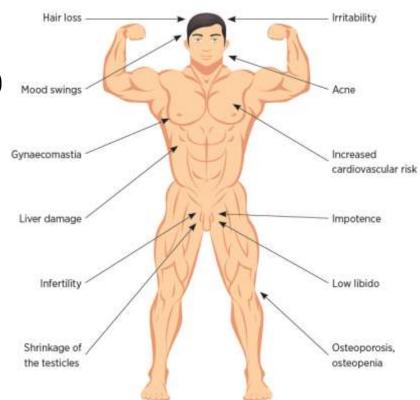


#### Adverse reactions/side effects:

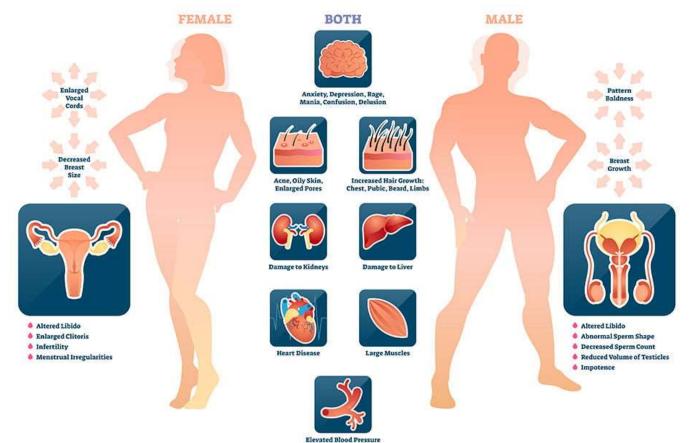
- Male
  - Decreased testicular size and sperm volume
    - Popular use of HCG to avoid testicular atrophy
  - Gynecomastia (T converted to estradiol)

#### Female

- LH, FSH, estrogen, progesterone
- Menstrual irregularities
- Male-pattern alopecia, hirsutism, deepened voice
- Most reversible on cessation of use\*









human reproduction ORIGINAL ARTICLE Andrology

# Disruption and recovery of testicular function during and after androgen abuse: the HAARLEM study

D.L. Smit<sup>1</sup>,\*, M.M. Buijs<sup>2</sup>, O. de Hon<sup>3</sup>, M. den Heijer<sup>4</sup>, and W. de Ronde<sup>1</sup>

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Submitted on September 27, 2020; resubmitted on December 4, 2020; editorial decision on December 7, 2020

- 98 Men who hadn't used AAS in 3 months prior to study
- Gave no advice regarding cycles (participants did own programs of 6 weeks minimum, 2 forms of AAS)
- 37 had low testosterone at start of study
- Almost all had normal testosterone by 3 months after end of cycle, 100% by 12 months (if normal at baseline)
- Sperm production normal by 47-56 weeks, up to 69 weeks in some



#### **Testosterone Precursors**

#### Androstenedione:

- Widely used/promoted
- OTC until 2004
- Does not appear to have anabolic effect like testosterone (little, if any effect on serum testosterone)

#### Dehydroepiandrosterone (DHEA):

- Available as nutritional supplement
- Reported to increase muscle strength
- Not androgenic itself, but is converted to testosterone and raises serum concentrations in women (but not men)



#### **SARMs**

- Definition: Selective Androgen Receptor Modulator
  - Non-steroidal, orally active molecules developed to bind more efficiently with androgen receptors in certain tissues (muscle/bone) vs genital tissue
  - Ostarine
  - Similar to AAS but with less androgenic effects (less prostate disease in men, virilization in women)

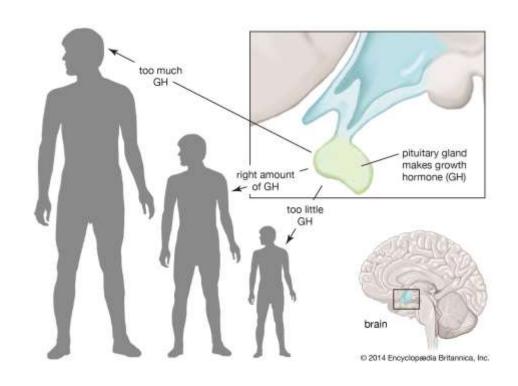
#### MOA:

- Selectively binds androgen receptors high anabolic activity in skeletal muscle
- Medical indications: Muscle wasting caused by chronic disease (cancer, HF, COPD, ESRD, HIV)
  - Investigational drugs
- Ergogenic claims: increased lean muscle mass



#### Definition:

- Polypeptide hormone produced by pituitary
- Species-specific
  - Bovine and porcine hormones have no effect in humans
- Medical indications: dwarfism, short stature





#### MOA: anabolic

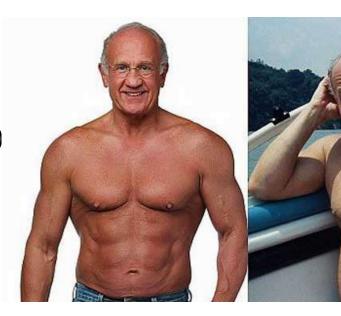
- — ↓ glucose and protein metabolism, ↑ fat metabolism
- → protein synthesis
- Stimulates IGF-1 (↑ muscle growth)

#### Ergogenic claims:

- Increase lean body mass
- Decrease fat mass

#### Dosing/administration:

Subcutaneous





#### Adverse reactions/ side effects:

- Acromegaly/gigantism
  - Narrow window 2x recommended dose
- Hypothyroidism
- Hypercholesterolemia,
   MI, CHF, cardiomyopathies,
   myopathies
- Diabetes mellitus
- Osteoporosis





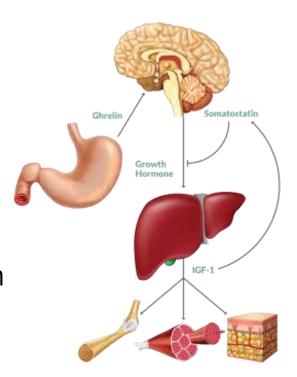






### **Insulin-Like Growth Factor-1**

- Definition: somatomedin (growth factor)
  - Somatomedins are a group of proteins that promote cell growth and division in response to stimulation by growth hormone
- MOA:
  - Stimulated by hGH
  - ↑ glucose & amino acid uptake, inhibits apoptosis
  - — ↑ lipolysis indirectly by suppressing insulin
- Medical indications: dwarfism, DM2
- Ergogenic claims: increased fat metabolism, lean body mass
- Adverse reactions/side effects:
  - Hypoglycemia
  - − ↓ hGH secretion
  - Disruption in insulin-glucagon axis

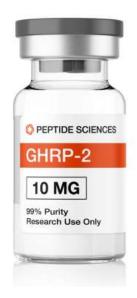




# **Growth Hormone-Releasing Peptides**

#### Definition:

- constitute a group of small synthetic peptides that stimulate growth hormone secretion and downstream axis activity.
- MOA: stimulates hGH secretion
- Ergogenic claims: increase lean body mass
- Dosing/administration: PO, IV, nasal
- Adverse reactions/side effects: similar to growth hormone





# **Human Chorionic Gonadotrophin (HCG)**

- Definition: glycoprotein hormone produced by the placenta (small amounts in liver, colon, pituitary)
- MOA: stimulate sex steroid hormone biosynthesis in the gonads
- Ergogenic claims:
  - Increases endogenous production of testosterone
  - Maintains testicular volume in male athletes using AAS
- Adverse effects: gynecomastia; headaches, depression, edema
- Only prohibited in male athletes (variable levels in females)





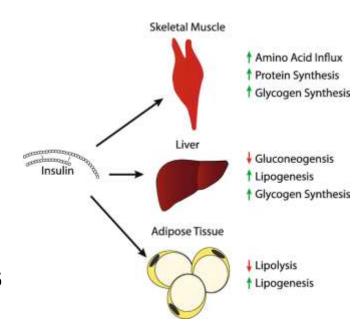
### Insulin

#### MOA:

- May be used along with AAS
- Deters lipolysis, glycolysis, gluconeogenesis, proteolysis, ketogenesis
- Ergogenic claims: enhance anabolic effects of AAS → increase lean body mass

#### Dosing/administration:

- Fast-acting insulin immediately after workout along with glucose and protein drink
- Goal: replenish glycogen and ATP quickly, promote protein synthesis and muscle growth
- Adverse reactions/side effects: hypoglycemia (lethal), lipodystrophy, insulin resistance/autoantibodies
- Detection/regulations: no approved testing





### Caffeine

- Caffeine: Most common ergogenic aid
- MOA: Increased endorphin release, improved neuromuscular function (may enhance Ca2+ release from the sarcoplasmic reticulum and improve motor unit recruitment by inhibiting the action of adenosine on the central nervous system)
  - 3-6 mg/kg: increased endurance/running pace/sprint velocity, 60 min before exercise
  - Increase aerobic effort/duration/tolerance, mild anaerobic improvement
  - Increased mood/reaction time
  - Less perceived fatigue/lower RPE

Guest NS, et al. International society of sports nutrition position stand: caffeine and exercise performance. J Int Soc Sports Nutr. 2021 Jan 2;18(1):1.

Del Coso, J, et al. Caffeine containing energy drink improves physical performance of elite rugby players during a simulated match. Appl. Physiol. Nutr. Metab. 2013, 38, 368–374



### **Creatine**

- Creatine: Commonly used in HS/Collegiate Athletes
- MOA: Supplementation increases muscle creatine stores, augmenting the rate of PCr resynthesis
  - enhances repetitive short-term, high-intensity sports or resistance training
  - Greater gains in lean muscle mass, strength, power

#### Dietary sources:

Fish, beef (1lb is ~ 1g)

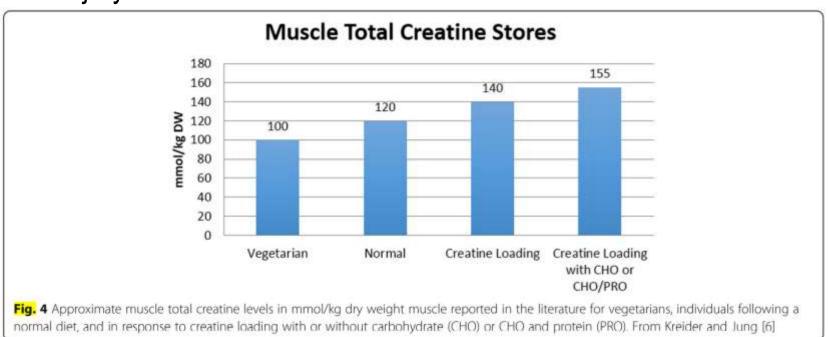
#### Dosing:

- Loading phase: ~20 g/day, 5-7 days, divided QID
- Maintenance: 5g daily
- Consumption with carbs/protein may facilitate uptake via insulin stimulation.



### **Creatine Safety**

- Long term studies of 4+ years had no adverse health effects
- Side effects: 1-2kg weight gain
- Does not impair kidney/GI function, dehydration/cramping
- Weak evidence to support injury prevention heat illness, MSK injury

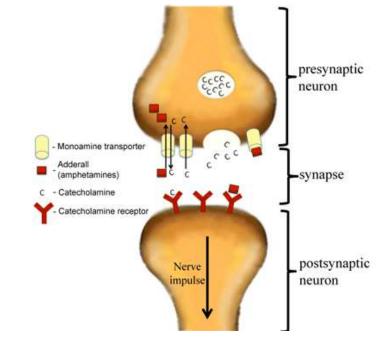


Kreider RB, et al. International Society of Sports Nutrition position stand: safety and efficacy of creatine supplementation in exercise, sport, and medicine. J Int Soc Sports Nutr. 2017 Jun 13;14:18.



# Amphetamines: "Caffeine on caffeine"

- Definition: indirectly acting sympathomimetic amine
- Epidemiology:
  - 2012 NCAA study 16% athletes have used ADHD medications (9% without prescription)



- MOA: increased release of endogenous catecholamines → ↑ HR and BP, bronchodilation, ↑ metabolic rate, ↑ FFA production
- Medical indications: narcolepsy, ADHD



# **Amphetamines**

#### Ergogenic claims:

- Delayed fatigue
- Increased alertness
- Enhance speed, power, endurance, concentration

#### Dosing/administration:

- PO
  - Effect within 30 minutes
  - Duration 12-24 hours

#### Studies:

- Mixed evidence
  - Better support for simple repetitive tasks
  - Less support for complicated tasks
- Improved performance in trained swimmers, weight throwers, runners





### **Amphetamines**

#### Adverse reactions/side effects:

- CNS excitation
  - Behavioral anxiety, euphoria, psychosis
  - Insomnia, dizziness, restlessness, tremor
  - Confusion, paranoia, delirium
  - Cerebral hemorrhage
- Systemic hypertension, angina, nausea/vomiting, abdominal pain
- Addiction
  - Withdrawal fatigue, lethargy, depression





- Definition: synthetic congeners of naturally occurring catecholemines
  - Ephedrine, pseudoephedrine, phenylephrine
- MOA: depends on specificity of drug
  - Alpha effects: smooth muscle contraction (vasoconstriction)
  - Beta₁ effects: ↑ intracellular cAMP
     (↑ HR and strength of contraction)
  - Beta<sub>2</sub> effects: smooth muscle relaxation, bronchodilation
- Medical indications:
  - Nasal congestion, allergic reactions, asthma
  - AV block
  - Weight loss supplements







#### Ergogenic claims:

- Improved endurance (esp cycling)
- Additive effect to caffeine

#### Adverse reactions/side effects:

- Worse with increased dosing
- Anxiety, insomnia, drowsiness
- Stroke, tremors, seizures
- GI distress, palpitations, arrythmias, hypertension





- High profile cases ephedra (?)
  - Korey Stringer (Minnesota Vikings)
  - Rashidi Wheeler (Northwestern)
  - Steve Bechler (Baltimore Orioles)









#### Clenbuterol

- Beta<sub>2</sub> agonist used for bronchodilation with anabolic potential
  - Not legally available in US for asthma
- Used in livestock to increase muscle mass and decreased fat mass

- What about other Beta<sub>2</sub> agonists?
  - Dose-dependent



### **Aromatase Inhibitors & SERMs**

- Definition: Substances that oppose estrogen
  - Aromatase inhibitors (anastrazole, letrazole)
  - Selective estrogen receptor modifiers (tamoxifen, raloxifene)
  - Clomiphene
- MOA:
  - Used to counteract estrogenic effects of AAS
  - May help resume testosterone production
- Medical indications: breast cancer, ovulation induction
- Ergogenic claims: no inherent benefits



### **Aromatase Inhibitors & SERMs**

#### Adverse reactions/side effects:

- Aromatase inhibitors joint aches, stiffness
- SERMs masculinization (females), DVT
- Clomiphene GI, blurred vision, headaches



### **Blood Doping**

Definition: Infusion of blood into a non-anemic athlete for increasing

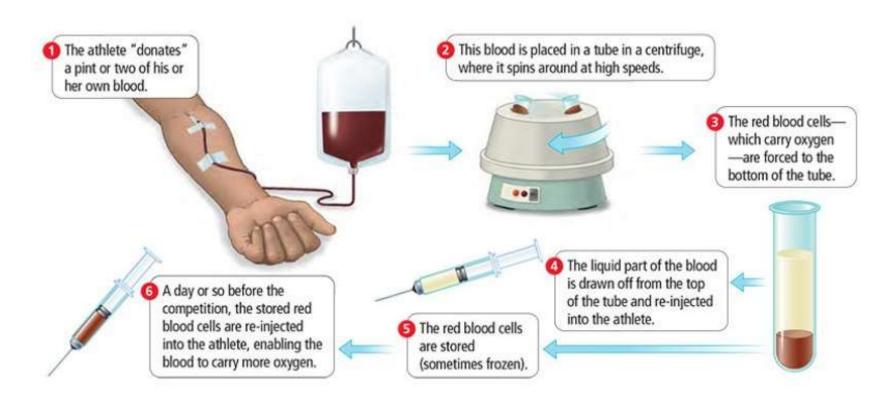
RBC mass

Autologous (from same person)

- Heterologous (donated from another person)
- MOA: increased O₂ delivery and hemoglobin
- Ergogenic claims:
  - Improved endurance
  - Increased VO<sub>2</sub>max
  - Improved maximal O<sub>2</sub> consumption, increased total exercise time
- Risks: rapid BP changes, atherosclerosis, oxidative damage to organs, blood-borne infections, iron deposition



# **Blood Doping**



900-1800mLcryopreservedautologous blood

- Infusion reactions (esp heterologous)
- Increased blood viscosity



# The Day My Sporting Dreams Died...

https://www.youtube.com/watch?v=oW9npI3Z-1A



# The Day My Sporting Dreams Died...



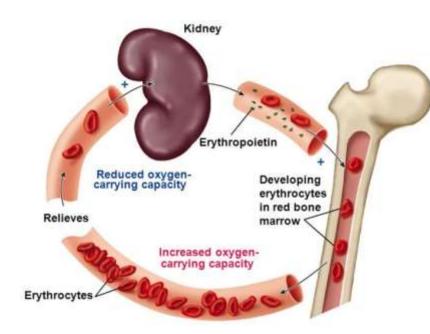


#### Definition:

- <u>EPO</u> = sialic acid-containing hormone that enhances erythropoiesis
- Recombinant EPO (r-HuEPO)
  - Discovered in response to increased attention/risk of blood doping

#### MOA:

- Secreted by kidneys, stimulates bone marrow
  - Stimulates formation of proerythrobalsts
  - Stimulates release of recticulocytes
- Increased RBC production
  - EPO inversely related to circulating RBCs
- Increased O<sub>2</sub> carrying capacity





#### Medical indications:

- ESRD, renal anemia
- Anemia secondary to prematurity, MM, cancer, AIDS

#### Ergogenic claims:

- Increased VO<sub>2</sub>max by 10%
- Increased aerobic oxidation, limits anaerobic production → endurance



Asbel Kiprop (Kenya) – 1500m Olympic Gold Medal in Beijing 2008; banned 4 years in 2019



#### Dosing/administration:

- Subcutaneous
- 15-500 U/kg r-HuEPO 3x/week
- Onset ↑ RBC production within days
- Duration 3-4 weeks



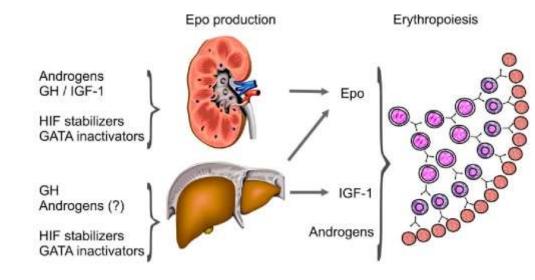


- Adverse reactions/side effects:
  - In anemic patients:
    - Hypertension, esp in hypertensive patients
  - In normal hemoglobin:
    - Increased blood viscosity
      - Attenuated by dehydration
      - May lead to CVA/MI, vascular thrombosis
    - Hypotension, hyperkalemia, Fe deficiency
    - Risk of IV medications/bloodborne infections
  - Recombinant batch variability, contamination with bacterial endotoxins



# Other Artificial O<sub>2</sub> Carriers

- Continuous EPO receptor activator (CERA)
  - Administrated once monthly
- EPO mimetic peptides (Hematide)
- HIF-stabilizers
  - Hypoxia-inducible factors
  - Transcription factors
  - Respond to decreased O2





# **Masking Agents**

#### Diuretics

- Ergogenic claims:
  - Rapidly lose weight prior to competition
  - Aid in the excretion of or to dilute the presence of illegal substances in the urine
- Adverse effects: dehydration, hypotension, muscle crams, electrolyte abnormalities





# **Masking Agents**

- Probenecid
  - Accelerate the excretion of prohibited substances
  - Reduces the urinary excretion of AAS from the body
- Plasma volume expanders (mannitol, dextran, hydroxyethyl starch/HES)
  - Dilutes concentration of hemoglobin and erythrocytes (disguise use of EPO)



# **Gene Therapy/Gene Doping**

- Goal: artificially alter gene expression in an otherwise healthy individual
- Typically using biologic vector (eg viral)
- Targeted genes:
  - Endurance
    - EPO
    - Peroxisome proliferator-activated receptor delta (PPAR)
    - PEPCK
    - Vascular endothelial growth factor
  - Strength
    - IGF-1
    - Myostatin
  - Tissue repair
    - Bone morphogenic protein
    - Endorphins





### What do we do as clinicians?

#### Be aware of:

- Inquire about supplement use/motivations
- patients that may participate in competitive sports
- Compete in sport where excess androgens are perceived to improve performance
- USADA/WADA (updates published every January)
- Some banned drugs may be taken for medical purposes
- Physical characteristics suggesting possible PEDS
  - Men: small testes, low sperm count, high Hgb/Hct, undetectable LH, excessively muscular
  - Women: hirsuitism, balding, acne, excessively muscular, irregular menses, breast atrophy
- Non-judgemental approach
- Remember many of these individuals struggle with body image disorders ("muscle dysmorphia")



#### REVIEWS



#### Harm Reduction in Male Patients Actively Using Anabolic Androgenic Steroids (AAS) and Performance-Enhancing Drugs (PEDs): a Review

Alex K. Bonnecaze, MD<sup>1</sup>, Thomas O'Connor, MD<sup>2</sup>, and Cynthia A. Burns, MD<sup>1</sup>

<sup>1</sup>Dept of Internal Medicine, Section on Endocrinology and Metabolism, Wake Forest University School of Medicine, Winston-Salem, NC, USA; <sup>2</sup>Dept of Internal Medicine, University of Connecticut School of Medicine, Farmington, CT, USA.

- Focus on harm reduction as primary goal
- Develop relationship, inquire about underlying concerns
- Many patients coming off AAS have anhedonia/depression/sexual side effects
- Use as opportunity to assess full personal/family health history
- Do not preach to stop AAS on first visit (less likely to follow up, seek advice from "bro science")
- Consider screening/treatment of AAS-related cardiovascular conditions, behavioral disorders, and hematologic disorders to further reduce self-harm during AAS use
- Do not prescribe medications that may have anabolic effects during AAS use <a href="#"><a href="#">



### PEDs – cessation

Table 1 Proposed Methods for Transitioning Off AAS

Author	Proposed methods
Anawalt 2019 <sup>2</sup> Rahnema et al.	Method 1: "Immediate discontinuation of AAS with no medical therapy"
	<ul> <li>Method 2: "Discontinuation of AAS and initiation of a limited course of clomiphene</li> </ul>
	therapy"  • Method 3: "Discontinuation of AAS and
	initiation of a limited course of hCG therapy"
	Method 4: "Conversion of nonprescription AAS to prescription testosterone" The author
	additionally notes "For these patients, the author
	has prescribed intramuscular dosages of up to
	twice the typical replacement dosage with a taper
	to physiologic dosage over several months"
2014 <sup>23</sup>	<ul> <li>4-week testosterone taper with SERM (Clomi- phene 25 mg every other day), followed by</li> </ul>
	rechecking testosterone and gonadotrophs. After
	4 weeks, the author suggested ending testosterone therapy and continuing SERM use, also adding hCG 1000–3000 IU SQ 3 times weekly if labs
	suggested a poor response.
	After 8 weeks, the authors recommend
	rechecking testosterone and gonadotrophs. At
	week 10, SERM dose should be reduced to 50%
	of starting dosage and continued until the target testosterone level is achieved.
	<ul> <li>Also mentioned is that some men using chronic high doses of AAS may have direct testicular</li> </ul>
	damage-thus not responding to agents other than testosterone.

Anawalt BD. Diagnosis and management of anabolic androgenic steroid use. J Clin Endocrinol Metab. 2019

Rahnema CD, et al. Anabolic steroid-induced hypogonadism: diagnosis and treatment. Fertil Steril. 2014;101(5):1271–9



### Patient/Provider Resources

- Drug Free Sport
- NCAA Banned Substances Website
- Independent Quality Assurance:
  - www.usp.org/USPVerified
  - www.consumerlab.com
- WADA/USADA Website
- Global DRO (Drug Reference Online)



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# Thank you!



