Trends in Performance Enhancing Drugs

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Session Objectives

After participation in the Trends in Performance Enhancing Drugs session, you will be able to:

1. Compare and contrast the common performance enhancing drugs.
2. Compare and contrast the mechanisms of action and adverse effects of common performance enhancing drugs.
3. Describe the associated risks of performance enhancing drugs and heat illness.
To gain a competitive advantage...

- **Hormonal PEDs**
  - Anabolic steroids, growth hormone, erythropoietin

- **Non-hormonal PEDs**
  - Stimulants, recreational drugs, nutritional supplements, energy beverages

- **Masking agents** - hide the use of hormonal and non-hormonal PEDs
Hormonal PEDs for strength

1976 - The International Olympic Committee (IOC) bans the use of steroids.

The use of androgens has spread from competitive sports to leisure and fitness sports.

Bodybuilders and non-athletes use androgens as a strategy to increase muscle mass, improve performance, and enhance physical attractiveness.

Meta-analysis of 187 studies, the overall global lifetime prevalence rate of anabolic steroid use was 3.3%: 6.4% in men, 1.6% in women.

In 2013, the CDC reported that 3.2% of high school students had taken an anabolic steroid without a doctor's prescription at least once.
Anabolic steroids

Anabolic Steroids – agonists at androgen receptors
• Stimulates protein synthesis, bone growth, adipose catabolism
• Increase lean muscle mass and strength
• Major mood disorders, aggressive behavior, hypogonadism, gynecomastia
• No effect on aerobic power, aerobic capacity, athleticism
Anabolic steroids

Most commonly used androgens are testosterone, stanozolol, nandrolone, trenbolone, and boldenone (a veterinary steroid)

Androgen precursors
  • Androstenedione and dehydroepiandrosterone (DHEA)

SARMs – selective androgen receptor modulators
  • None approved for human use in any country

human chorionic gonadotropin (hCG)
SERMs (tamoxifen, raloxifene)
Aromatase inhibitors (anastrozole)  } Increase serum testosterone concentrations
Growth hormone, IGF-1 and insulin

Human Growth Hormone (hGH)
- Clear effects on body composition (more muscle, less fat)
- Released from pituitary and activates release of IGF-1
- When combined with testosterone there is a greater performance enhancing effect than either alone
- Effects disappear 6 weeks after discontinuation
- Adverse effects include insulin resistance, hyperglycemia, diabetes, sodium retention, hypertension, cardiomegaly, premature epiphyseal closure
- Detected in blood because less than 0.1% is excreted in the urine
Growth hormone, IGF-1 and insulin

Insulin-Like Growth Factor (IGF-1)
- Effects similar to hGH; hypoglycemia
- Commercially available recombinant form
- Only detected through blood but no commercially available screening tests

Insulin
- Hypoglycemia
- Can be detected in urine but difficult to distinguish human insulin, insulin analogs, and porcine insulin

Rates of IGF--1 and insulin use for performance enhancement are lower than growth hormone
Hormonal PEDs for endurance

Why
• Maximal aerobic power
• Anaerobic capacity
• Aerobic/anaerobic metabolic efficiency

How
• Hemoglobin (RBC) volume expansion
Hormonal PEDs for endurance

Athletes have used methods to increase the oxygen--carrying capacity of the blood and thereby athletic performance for decades.

Training at high altitude

Transfusions

Erythropoietin to stimulate erythropoiesis
Oxygen-hemoglobin relationship

Oxygen transport system
• The main function is to transport oxygen
• Hemoglobin is a tetramer composed of 4 globin molecules
  • 2 alpha globins and 2 beta globins
• One hemoglobin molecule has the ability to transport up to 4 oxygen molecules bound to ferritin

Increase the blood’s maximum capacity to transport and utilize oxygen

Increase aerobic power and physical exercise tolerance
Erythropoietin use in blood doping

Erythropoietin (EPO)

- Protein hormone secreted by the kidneys
- Stimulates RBC production
- Increases both maximal aerobic power and capacity
- Indicated for use in anemia of chronic disease
- Major adverse effects of increased erythropoiesis include myocardial infarction, stroke, thromboembolic disease, and hypertension
- Numerous detection methods (direct and indirect)
Erythropoietin use in blood doping

CERA - Continuous Erythropoietin Receptor Agonist
• Approved for use in Europe and US but unavailable here due to legal issues
• As effective as erythropoietin at maintaining hemoglobin levels

Transfusion
• Whole blood
• Perfluorocarbons – liquid breathing
  • Synthetic or modified hemoglobin and liposome-encased hemoglobin
  • Developed for premature infants with respiratory deficits
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Stimulants

Amphetamine
D--methamphetamine
Ephedrine
Caffeine
Methylphenidate
Pseudoephedrine
Dimethylamylamine (DMAA)

Cocaine
Fenfluramine
Pemoline
Selegiline
Sibutramine
Strychnine
Modafinil

- Stimulants are known to be both physical and cognitive performance enhancers.
- Stimulants decrease appetite, increase energy, improve endurance, increase anaerobic performance, decrease feelings of fatigue, improve reaction time, increase concentration, improve working memory, increase alertness, and can lead to weight loss
Stimulants

Catecholamines
• Primary neurotransmitters of the sympathetic nervous system
• Epinephrine (adrenaline), norepinephrine (noradrenaline), dopamine
• Cause general physiological changes that prepare the body for physical activity (fight or flight response)
• Released by the adrenal gland during periods of stress, both psychological (chased by a bear) and physiological (e.g., low blood sugar levels)
Stimulants – catecholamines

Exogenous sources have the same effects as endogenous compounds (increased sympathetic tone)
• Increased heart rate and cardiac output
• Prolonged running time to exhaustion
• Decreased central fatigue
• Improved reaction time
• Cognitive function during sleep deprivation

No improvement in aerobic capacity or running speed
Amphetamine, methylphenidate, DMAA

- Commonly used for the treatment of ADHD

- DMAA (1,3-dimethylamylamine) is an amphetamine derivative that is widely used in sports supplements sold in the United States
Ephedrine, pseudoephedrine

Ephedrine is an agonist at both $\alpha$ and $\beta$ receptors; also enhances release of NE from sympathetic neurons

Marketed as a dietary supplement; banned by the FDA due to risk of heart attack and stroke
Cocaine

Blocks norepinephrine and dopamine transporters

Increases norepinephrine, dopamine, and serotonin in synapses

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Caffeine

• Nonspecific inhibitor of phosphodiesterase enzyme (PDE 1-5)
• Increases the concentration of cAMP
• cAMP increases strength of contraction in cardiac muscle and relaxes smooth muscle surrounding the vasculature
• Enhances prolonged and shorter, intense activity
• Caffeinated products are often used to improve athletic performance, as well as increase alertness in non-sporting events
• Caffeine has urinary thresholds set by the International Olympic Committee (IOC) and National Collegiate Athletic Association (NCAA)
Non-hormonal PEDs that impact strength

Creatine
• Provides an ATP source to muscle
• Increases intracellular volume
  • Results in “hypertrophy” of muscle tissue
• Variability with responders & nonresponders

Beta-2 Adrenergic Agonists
• When injected or taken orally can have anabolic effect and reduce body fat
• Prevents muscle loss after cessation of anabolic steroids (Clenbuterol, Terbutaline, Salbutamol, Fenoterol)
• NCAA and USOC only allow with prescription
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Masking Agents

Diuretics
• Quickly decreases body mass (sports with weight restrictions)
• Alters normal urinary excretion of performance-enhancing drugs

Probenecid
• Inhibits the reabsorption of uric acid at the proximal convoluted tubule
• Delays renal excretion of testosterone

Epitestosterone
• Co-administered with testosterone to normalize urine testosterone/epitestosterone ratio
Exercise related deaths

Demands of sport may place athletes in extreme weather conditions and tax temperature regulatory systems.

Medical condition could lower the threshold of temperature control.

Physiologic alterations enhance risk for potentially lethal arrhythmias:
- Blood volume
- Dehydration
- Electrolyte abnormalities

Medication could tip the balance.

100% preventable.
# Heat Illness - Symptoms

**First Stage**  
- Headache  
- Fatigue  
- Dizziness  
- Irritability  
- Anxiety  
- Chills  
- Nausea  
- Vomiting  
- Heat cramps

**Second Stage**  
- Confusion – altered mental status  
- Increased body temperature (may be asymptomatic in healthy athletes)  
- Rapid Pulse  
- Hyperventilation  
- Low Blood Pressure, syncope  
- Piloerection

**Late Stages**  
- Markedly increased body temperature  
- Greater than 41°C (106°F)  
- Lack of cooling despite stopping exercise  
- Profuse sweating that ceases despite high body temperature
Core temp. Dehydration

Effects

Heat dissipation
Blood volume
Cardiac output
Stroke volume

Heart rate
Muscle glycogen use
Lactic acid
Onset of fatigue

Results

Muscle Endurance
Aerobic Power
Work Capacity
Mental Acuity
## Risk for heat illness

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<thead>
<tr>
<th></th>
<th>Risk for heat illness</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Anabolic agents</td>
<td>Low risk</td>
<td>May cause HTN; drugs to treat may increase risk</td>
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<tr>
<td></td>
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<td>Creatine – dehydration and acute interstitial nephritis may increase risk</td>
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<tr>
<td>Hematopoietic agents</td>
<td>Low risk</td>
<td>Can lead to hypertension, heart disease, heat stroke, seizures, embolism</td>
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<tr>
<td>Sympathomimetics</td>
<td>High risk</td>
<td>Increased sympathetic tone</td>
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<tr>
<td></td>
<td></td>
<td>• Tachycardia</td>
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<td>• Hypertension</td>
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<td></td>
<td></td>
<td>• Decreases cutaneous blood flow and impaired heat dissipation</td>
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<tr>
<td>Masking agents</td>
<td>Moderate risk</td>
<td>Contribute to physiologic alterations (e.g., dehydration, electrolyte changes, decreased blood volume) placing at risk for lethal arrhythmias</td>
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References

2. www.uptodate.com