Performance Enhancing Drugs in Sports

Mark D. Price, M.D., Ph.D
Assistant Professor, Department of Orthopedic Surgery
University of Massachusetts Medical School
Historical Perspective

- 1889 Brown-Sequard “reversed” aging process by injecting testicular extracts
- 1935 Testosterone first synthesized
- 1950’s Anabolic steroids used extensively in sports
- 1967 Banned by IOC
- 1972 first testing at Olympics

Silver, JAAOS 2001
The Problem

- 1-3 million Americans have tried steroids
- 6% of Indiana HS football players used steroids
  - 15% < 10y.o.
  - 14 y.o. mean start
- 5% of 10th graders have tried hGH

Stigler and Yesalis, J Comm Health 1999
Tokish et al, AJSM 2004
The Problem

- Scenario I:
  - Won’t get caught
  - Will Win
  - >98% yes

- Scenario II:
  - Won’t get caught
  - Win for next 5 years then die
  - > 50% yes

Bamberger and Yaeger, SI 1997
Overview

• Ergo = work; Genan = to produce

• Drugs and Supplements
• Biology
• Benefits and side effects
• Testing methods
Anabolic Steroids

• Modified analogs of testosterone
  – Maximize anabolic
  – Minimize androgenic

• Stimulate mRNA synthesis ➔ increased contractile proteins
Anabolic Steroids

- Bind androgen receptors → anabolic state
- Questionable effect?
Anabolic Steroids

- Anticatabolic effect
- Training ➤ glucocorticoids for glycogen breakdown
- Competitive inhibition of glucocorticoids for T receptors
Anabolic Steroids

- Increased aggression
  - Motivation \( \uparrow \) even with placebo

- Train harder, longer, more intensely

- Effect not uniform

Pope, H. G. et al. Arch Gen Psych 2000
Anabolic Steroids – The Good

- 43 Men, 10 weeks
  - 600 mg qwk

10 ↑ Fat-free muscle mass
10 ↑ Muscle size
10 ↑ Strength

Bhasin, et al, NEJM 1996
Anabolic Steroids – The Bad

• 30% with some side effect
  – Metabolic – electrolyte imbalances
  – Skin – acne, hirsuitism, alopecia, striae
  – Psychiatric
    • Aggressive, impulsive
    • Needle sharing
  – Decreased life span
    • 12.9% vs 3.1% mortality rate in 12 mo period for powerlifters

Anabolic Steroids – The Bad

- Cardiovascular
  - HDL, endothelial dysfunction
    - HTN, MI, sudden cardiac death
  - Reversible?

Ebenbichler et al, Atherosclerosis 2001
Anabolic Steroids – The Ugly
Anabolic Steroids - Testing

- Gas-chromatography
  - T:E ratio normally 1
  - Abnormal > 4

- Carbon Isotope Ratio testing
  - $^{12}C$: $^{13}C$ ratio
  - Delta < -30% abnormal

- 68 different isomers listed
- >$100 million black market sales
Human Growth Hormone

- Peptide secreted by pituitary
- Liver converts to IGF1
- Increased amino acid uptake and protein synthesis

LeRoith and Yakar, Nat Clin Pract Endocrinol Metab 2007
Human Growth Hormone

- 16 young men, 12 weeks
  - 40ug rhGH

Fat free mass and total body water

- No performance gains

**Table 2. Muscle strength improvement**

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Exercise + Placebo</th>
<th>Exercise + GH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Delta</td>
<td>% Change</td>
</tr>
<tr>
<td>Shoulder press</td>
<td>5.3±0.5</td>
<td>53±6</td>
</tr>
<tr>
<td>Bench press</td>
<td>6.1±0.7</td>
<td>43±6</td>
</tr>
<tr>
<td>Deltoids</td>
<td>4.4±0.5</td>
<td>47±7</td>
</tr>
<tr>
<td>Bicep curl</td>
<td>4.4±0.3</td>
<td>36±3</td>
</tr>
<tr>
<td>Latissimus</td>
<td>6.5±0.4</td>
<td>59±5</td>
</tr>
<tr>
<td>Flys</td>
<td>6.5±0.4</td>
<td>73±8</td>
</tr>
<tr>
<td>Knee extension</td>
<td>9.7±0.9</td>
<td>63±10</td>
</tr>
<tr>
<td>Leg press</td>
<td>4.9±0.7</td>
<td>26±4</td>
</tr>
<tr>
<td>Knee flexion</td>
<td>4.1±0.4</td>
<td>47±8</td>
</tr>
<tr>
<td>Average</td>
<td>5.8±0.6</td>
<td>50±4.8</td>
</tr>
</tbody>
</table>

Values are means ± SE. Final strength score greater (P < 0.01) than initial for all exercises in both groups. Delta scores represent absolute increase in no. of 4.5-kg wts lifted. Average and individual delta and % change scores were not different between groups.

Yarasheski et al, AJP Endocrinol Metab 1992
Human Growth Hormone

- 7 experienced weight lifters
  - 14 days rhGH

10 ↑ IGF1

- No change in protein synthesis or breakdown

Yarasheski et al. AJP 1993
Growth Hormone – Side Effects

• Acromegaly
• Water retention
• Insulin resistance
• Carpal tunnel syndrome
Growth Hormone - Testing

• Blood test ~ 24-48h
  – Measure % 20 kD hGH in rhGH
  – IGF1, procollagen III
  – May not be allowed

• Urine test ~ 2 wks
  – Nanoparticles concentrate

Green, AJSM 2006
Fredolini et al, Nano Res 2008
Erythropoietin

- Produced in kidney
- Stimulates increase in Hgb

↑ Oxygen-carrying capacity of blood

Spivak, Nat Rev Cancer 2005
Erythropoietin

- ↑ $O_2$ carrying capacity of blood
- ↑ Hct
- ↑ Hct 1 g/dL 8% → in VO$_2$ max

Ekhblom and Berglund, Scan J Med Sci Sports 1991
Erythropoietin

- 20 cyclists
- Double-blind, placebo
  - Hct 42 → 50
  - 7% ↑ VO₂ max
  - time to exhaustion


Figure 3—Mean (±SD) level of maximal oxygen uptake (bars) and time to exhaustion (circles) for the rhEPO-treated subjects (hatched/filled symbols, N = 10) and control subjects (open symbols, N = 10) before treatment (day 0) and in the posttreatment period (days P1–P28).
Erythropoietin – Side Effects

- ↑ blood viscosity
- ↑ thrombogenic potential
- ↑ MI risk

- 1997-2000: 18 cyclists dead of MI, CVA and PE.

Tokish et al, AJSM 2004
Erythropoietin – Testing

- **Blood** = indirect
  - Hct, reticulocytes, Fe, markers

- **Urine** = direct
  - Extra sugars
  - Isoform patterns

Caitlin et al, Clin Chem 2002

r-HuEPO
darbepoetin

Caitlin et al, Clin Chem 2002
Stimulants

- Amphetamines, Ephedrine

- Catecholamines ~ stimulate NE from sympathetic nerves

10 Strength, lung function, time to exhaustion

Bell et al, Med Sci Sport Exerc, 2002
Stimulants

• Side effects:
  – Anxiety, ventricular dysrhythmias, HTN, hallucinations, addiction

• Many OTC forms
  – 2004: Ephedrine removed
Creatine

• Introduced 1992

• Most widely used nutritional supplement
  – >$300 million/yr
  – 41-48% NCAA men
Creatine

- Important in synthesis of ATP

- 95% stored in skeletal muscle

- Naturally occurring, excreted by kidneys
Creatine

- ↑20-30% max lift
- ↑Power output in cyclists
- ↓1-2% mean sprint times
- ↑1-2kg weight, lean mass
- Good for short duration, anaerobic, max effort

Creatine – Side Effects

• Possible renal
  – Nephritis, Elevated Cre
  – dehydration

• Downregulation of transporter
  – Resistance?
  – Other Organs?

• Short-term probably safe
Androstenedione

- Popularized in 1998 home-run race
- Immediate testosterone precursor
- Degraded into free testosterone (?)
Androstenedione

- Most studies show no increase in T, strength, or body composition

King et al, JAMA 1999
Androstenedione – Side Effects

- All studies show increased estrogen
- HDL
- Down-regulation of T synthesis

Broeder et al, Arch Int Med 2000
Some of the rest...

- **Caffeine**
  - 15ug/ml legal limit (17mg/kg)
  - ~ 6-8 cups
  - Endurance events

- **Hydroxycut, Xenadrine** – oolong/green tea

Nagao et al, Am J Clin Nut 2005
What lies ahead?

Azzazy et al, Clin Biochem 2009
Summary

• Myriad of compounds for improving performance

• Testing lags development

• Should we test and ban or monitor and supervise?