The Science Of Anabolic Steroid Abuse

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Androgens As Anabolic Agents

Myths

• Used Mostly By Professional Athletes
  – ....Well, Maybe Intense Bodybuilders....

• Users Die of Cancer, Liver Failure, Strokes
  – ....But Androgens Are Not Like Narcotics....

• It Is Not Germane To My Practice

• Have No Place In Good Medical Practice
Androgens As Anabolic Agents

Reality

• Common In General Population
  – Children To Businessmen; Entire Subculture
• Are Very Addicting In Specific Users
  – Pose Other Risks To Users And Contacts
• You Will Encounter Users In Your Practice
• Will Play A Prominent Role In Medicine
  – HIV, Cancer, Critical Illnesses, Elderly
Anabolic Steroid Topics

- What Are They
- Who Uses Them, Why, and How
- Evidence of Efficacy/Mechanism of Action
- Types and Severity of Side Effects
- Detection Technologies
- Precursors and Their Metabolism
Anabolic vs. Androgenic

- Anabolic: Ability to Aid Assimilation of Nutrients (Nitrogen) Into Tissue
- Androgenic: Masculinizing Properties
- “Weak Androgens” = Precursors of Strong
  - DHEA, Androstenedione
- Strong = Testosterone, Dihydrotestosterone
- Thus Far Inseparable
  - Presumed Same Mechanism of Action
Androgen Metabolism

- 17β-Dehydrogenation (17β-HSD Type II)
- Aromatization (Aromatase)
- 3α-Reduction (3α-HSDs)
- 5α/5β-Reduction (5α/5β-Reductases)
- 6α/6β-Hydroxylation (P450 3A4, etc.)
Testosterone & Derivatives

17β-Esterification & 17α-Alkylation

19-Nor

A-Ring Modifications

5α-Reduction
Target Organs and Physiological Effects of Testosterone and Metabolites

- CNS (↑ libido, well-being, aggression, spatial cognition)
- Hypothalamus/ Pituitary (↓ GnRH, LH, FSH; ↑ GH)
- Larynx (lowers voice)
- Breast (E₂ ↑ size)
- Liver (↓ SHBG, HDL)
- Kidney (↑ erythropoietin)
- Genitals (↑ development, spermatogenesis, erections)
- Prostate (↑ size, secretions)
- Skin (↑ facial/ body hair, sebum production)
- Bone (↑ BMD)
- Muscle (↑ lean mass, strength)
- Adipose Tissue (↑ lipolysis, ↓ abdominal fat)
- Blood (↑ hematocrit)
- Immune system (↓ auto-antibody production)
HOOKED ON STEROIDS

MUSCLE DRUGS

More than a million Americans, many of them teenagers, now use dangerous bodybuilding drugs

EXCLUSIVE:
Arnold Schwarzenegger speaks out against steroids
Anabolic Steroid Abuse

Prevalence

• High School
  – 3-12% M, 0-4% F; 30% Nonathletes

• College Athletes
  – 2-30% M, 2-10% F
  – Football, Track & Field

• Professional & Elite Athletes
  – Estimated 30-100%
  – Highest in Powerlifters, Bodybuilders
Anabolic Steroid Users
Two Major Dichotomies

• Professional Athletes vs. Recreational
  – Different Goals and Fear of Drug Testing
  – Escalation Greater With Non-professionals

• Male vs. Female Athletes
  – Men: All Sports, Greater in Power Sports
  – Women: More Restricted Use
    Bodybuilders, Track & Field, Sprint Swimmers
    Usage Gaining In Other Sports & Youths
“The root of steroid use is society's addiction to bigger, faster, stronger. The win-at-all-costs mentality leads to cheating and unethical behavior. I regret few things, but I do regret selling myself out by using drugs to compete.”

Steve Courson, Former Pittsburgh Steeler
“I started in high school weighing 140 pounds; I was Mr. Nobody. Sophomore year, I started taking steroids--my weight jumped 40 pounds and everybody suddenly wanted to be my friend. Since then I’ve had girls on one side, guys on the other. What more could I want?”
Anabolic Steroid Abuse
Getting Started

- Estimated 1,000,000 Users in USA
  - Burgeoning Use of Androgen Precursors
- 50% Adolescent
- Peers, Coaches, Parents
- Sports Performance
- Social Acceptance
- Distorted Body Image
“I’m not sure if steroids will hurt my body in the long run--it’s a gamble--but I’m living in the ‘now.’ I keep striving to get bigger--it’s like a disease. I’m 19 and weigh 200 pounds but still feel too small.”

“Our role model is this older guy at the gym....290 pounds without an ounce of fat. That’s our goal.”
Muscle Dysmorphia
aka Reverse Anorexia Nervosa

- Fear “Looking Small” Despite Being Muscular
- Want To Gain Weight But Be Lean, Muscular
- Avoid Body Exposure
- Exercise (Bodybuilding) Compulsively
- Obsessive Eating Behavior
- High Incidence Androgen Use
# Muscle Dysmorphia Characteristics

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<thead>
<tr>
<th></th>
<th>M.D.</th>
<th>Ctrl.</th>
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<tbody>
<tr>
<td>Number of Times You Weigh Yourself/Week</td>
<td>5.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Number of Times You Check Mirrors/Day</td>
<td>9.2</td>
<td>3.4</td>
</tr>
<tr>
<td>Minutes/Day Preoccupied Being Small</td>
<td>325</td>
<td>41</td>
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<thead>
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<td>Have You Worn Heavy Sweatshirts In Summer Or Refused To Remove Shirt?</td>
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<td></td>
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<tr>
<td>Yes</td>
<td>21</td>
<td>0</td>
</tr>
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<td>No</td>
<td>3</td>
<td>30</td>
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<th>M.D.</th>
<th>Ctrl.</th>
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<tbody>
<tr>
<td>Have You Given Up Enjoyable Activities To Go To The Gym To Get Bigger?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>24</td>
<td>11</td>
</tr>
<tr>
<td>No</td>
<td>0</td>
<td>19</td>
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</table>

Addiction

“You always end up taking more than you planned. Since it worked so good the last time, you always want to try more. I’m definitely hooked.”
Anabolic Steroid Addiction

• Psychological Dependency Common
  – Feeling of Invincibility on Drugs
  – Loss of Vigor and Size During Withdrawal
  – Distorted “Too Small” Body Image
    Perpetuates and Escalates Usage

• Physical Dependence Controversial
  – Vasomotor Instability Responsiveness to Clonidine
Anabolic Steroid Withdrawal
Biphasic Model

• First Phase (1-2 Weeks)
  – Agitation, Vasomotor Instability
  – May Require Hospitalization
  – Rx: Sedatives, Clonidine

• Second Phase (Months)
  – Depression, Lassitude
  – Hypogonadal State Exacerbates Symptoms
  – Rx: SSRIs, Testosterone Replacement
Anabolic Steroid Abuse

Getting Someone Off

• Acknowledge Value of Fitness & Exercise
• Set Realistic Goals: Weight, Strength
• Psychological, Nutritional Counseling
• Importance of Good Sleep Hygiene
• Taper Androgens
  – Set Schedule For Reaching Replacement Dose
  – ?? Benefit of β-hCG For Testicular Atrophy
Anabolic Steroid Abuse

Sources

• Coaches, Sports Personnel
• Unscrupulous/Misguided Physicians
• Black Market, Mail Order, Internet
  – ~$ 1 billion/year Plus OTC Precursors
  – > 100,000 Suppliers
  – 30% “Blanks”
• Veterinary Preparations
  – Mibolerone, Boldenone, Injectable Stanozolol
Anabolic Steroid Abuse
Patterns of Usage

• Cycles of 4-18 Weeks
• Drug Holidays of 1-12 Months
  – Pre-competition Diuretic “Washout”
• Multiple Agents (“Stacking”)
• Tendency to Escalate Dose Each Cycle
• Drugs to Counteract Side Effects
Anabolic Steroid Abuse
Polypharmacy To Negate Side Effects

<table>
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<th>Side Effect</th>
<th>Agents</th>
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<tbody>
<tr>
<td>Gynecomastia</td>
<td>Tamoxifen</td>
</tr>
<tr>
<td></td>
<td>Testolactone</td>
</tr>
<tr>
<td>Acne</td>
<td>Tretinoin</td>
</tr>
<tr>
<td>Testicular Atrophy</td>
<td>$\beta$-hCG</td>
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</table>

This Gets Pretty Expensive…
Androgens: Do They Work??

Problems With Earlier Studies

- Largely Observational & Uncontrolled
- Selection Bias/Extrapolation of Results
- Blinding Impossible
- Informed Consent a Major Issue
- Duration of Studies
- Tendency to Increase Strength
  - Continuously Training Subjects
  - Methandrostenolone Rx, 1-RM Assessment
Oral-Turinabol Effect On Shot Put Distance, GDR Female Athlete
IMPROVEMENT IN WEIGHT LIFTING

WEIGHT IN KG

YEAR OF OLYMPICS

- □ UP TO 60 KG
- ▲ UP TO 75 KG
- ▼ UP TO 82.5 KG
- ○ UNLIMITED

1925 1935 1945 1955 1965 1975
Supraphysiologic Testosterone

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<th>+ Exercise</th>
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<tr>
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<td>3.5</td>
</tr>
<tr>
<td>Quads (mm²)</td>
<td>0</td>
<td>600</td>
</tr>
<tr>
<td>Bench (Kg)</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Squat (Kg)</td>
<td>3</td>
<td>13</td>
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</table>

Bhasin et al NEJM 335:1-7 (1996)
“Inside the Numbers”
Bhasin et al

<table>
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<tr>
<th></th>
<th>No Exercise</th>
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<tr>
<td></td>
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<td>Test.</td>
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<tr>
<td>δ Bench</td>
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<td>2.2</td>
</tr>
<tr>
<td>δ Wt</td>
<td>1.8</td>
<td>2.9</td>
</tr>
<tr>
<td>δ Squat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>δ Wt</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Conclusions & Limitations

Bhasin et al

- Supraphysiologic Testosterone Doses (600 mg/wk) Increases FFBM, Strength
- Weight Gain Predominates
- “No” Change in Mood, Behavior --BUT
- 10 Week Study; No Post-Rx Follow-up
- Cannot Extrapolate to Elderly or Ill
- Cannot Extrapolate to Other Regimens
### Supraphysiologic Testosterone Effects On Mood & Aggression

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th></th>
<th>Testosterone</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>Start</td>
<td>End</td>
<td>Start</td>
<td>End</td>
</tr>
<tr>
<td>YMRS</td>
<td>0.3</td>
<td>1.1</td>
<td>0.5</td>
<td>3.9**</td>
</tr>
<tr>
<td>PSAP</td>
<td>208</td>
<td>222</td>
<td>208</td>
<td>362*</td>
</tr>
<tr>
<td>Manic Score</td>
<td>7.9</td>
<td>7.4</td>
<td>7.5</td>
<td>9.2**</td>
</tr>
<tr>
<td>Liking Score</td>
<td>50</td>
<td>50</td>
<td>51</td>
<td>55**</td>
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</table>

* *p<0.05
** *p<0.01

Pope et al Arch Gen Psychiatry 57:133-140 (2000)
“Inside the Numbers”

Pope et al

• Three Groups Of “Responses” To Testosterone
  – Marked (YRMS >20, Likely Manic Impairment): 2
  – Moderate (YRMS 10-19, Milder Hypomanic): 6
  – Minimal (YRMS<10): 42

• Placebo Period: 1 Moderate

• Conclusions—Supraphysiologic Testosterone:
  – ~5% Of Males Manic/Hypomanic; ~10% Partial
  – Lower Limit Of True Incidence (Dose, Duration)
  – Variable Responses Amongst Individuals
Manic Response To Testosterone
Pope et al
Anabolic Action of Androgens
Mechanistic Conundrums

• Cannot Extrapolate Data From Sexually Dimorphic Muscles in Lower Species
• Difficult to Demonstrate AR Protein, mRNA in Human Skeletal Muscle
• Classical Paradigm Fails to Explain Need for Supraphysiologic Concentrations
• Molecular Techniques Have Not Identified Target Genes (?IGF-1, Myostatin)
Anabolic Action of Androgens
Theoretical Dose-Response Curves

Muscle Mass

Hypogonadal
Eugonadal
Supraphysiologic

Androgen Dose
Model For Androgen Action

Anabolic Steroid Excess

- Maintains Eugonadism
- Blocks Catabolism
- More Aggressive Training
- ??Direct Action On Muscle

Strength & Performance Gains

- Adequate Diet
- Continued Training
Anabolic Steroid Abuse

Side Effects: CV, Liver

• Cardiovascular
  – Cardiomyopathy, HTN, Strokes, MIs

• Liver: Primarily Oral Agents
  – Hepatocellular Damage, Cholestasis
  – Peliosis Hepaticus, Tumors, CA

• Dyslipidemia
  – Raises LDL-C (Orals), Lowers HDL-C (All)
  – Activation of Hepatic Lipase
Anabolic Steroid Abuse
Side Effects: Brain

- Euphoria, Hypomania, Delusions, Paranoia
- Aggression, Rage, Murders, Sexual Abuse
  - Aggression “Beneficial” to Some Athletes
  - Gender Preference Same, Libido Increased
- Depression, Suicides During Withdrawal
- “Roided Out” Syndrome
  - Catastrophic Demise
Anabolic Steroid Abuse
Side Effects

• Children
  – Epiphyseal Plate Fusion
  – Disrupt or Initiate Puberty
• Infections
  – Abcess/Cellulitis in “Spot Shots”, HIV, Hepatitis
• Tendon Ruptures (? Overtraining)
• Acne, Pattern Baldness, Striae, Edema
• Polycythemia
Anabolic Steroid Abuse

Side Effects: Male

• Infertility
  – Incidence Increases With Duration of Use
  – Can Reverse With Discontinuation & $\beta$-hCG

• Gynecomastia
  – Aromatizable Testosterone Esters

• Prostatic Hyperplasia, ?CA
Anabolic Steroid Abuse

Side Effects: Female

- Amenorrhea
- Breast Atrophy
- Hirsutism
- Clitoromegaly
- Deepening of Voice
- Often Prominent and Irreversible
“Many of the athletes you now see pictured in this magazine will be dead within 10-15 years. Their deaths will not be painless. The abusive use of anabolic steroids will make their passing an ugly sight, as cancer rips through their bodies, unmercifully eating them up alive.”

-Bob Goldman

‘Death in the Locker Room’
“To say that steroids are dangerous is like saying that skydiving is dangerous, or skate boarding, or your bath tub.....

We have also not told you any horror stories of steroid abuse because we really don’t know any. We personally have not encountered athletes dying or becoming gravely ill from steroid usage. Sick people, we have, but not healthy athletes.”

-Underground Steroid Handbook, 1st Ed.
“I get side effects, like bloating, acne and a sore chest and nipples. But I don’t mind. It lets me know the stuff is working. Most guys say, ‘Cool, it’s real juice’.”

-Teenage User
Drug Testing Technology

- Synthetic Steroids: GC/MS of Metabolites
  - HPLC-MS of Conjugated Metabolites
- Testosterone: T/Epi-T Ratio > 6 (nl < 2)
  - T/LH > 30; Ketoconazole Suppression Test
- Ratios of 5α:non-5α C₁₉ Steroids
- Isotope Ratio Mass Spectrometry
Urine Sample

C-18 or XAD Solid Phase Extraction

Enriched Pool of Steroids, Glucuronide and Sulfate Conjugates

β-Glucuronidase Hydrolysis

Steroids & Steroid Sulfates

Organic Solvent Extraction

Steroids

MSTFA Derivitization + Enol Catalyst

Steroid TMS-(enol)-Ether Derivatives
19-Norandrosterone

<table>
<thead>
<tr>
<th>m/z</th>
<th>abundance</th>
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<tbody>
<tr>
<td>169.10</td>
<td>35%</td>
</tr>
<tr>
<td>225.20</td>
<td>18%</td>
</tr>
<tr>
<td>315.30</td>
<td>26%</td>
</tr>
<tr>
<td>405.30</td>
<td>100%</td>
</tr>
<tr>
<td>420.30</td>
<td>80%</td>
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</table>
Detecting Dihydrotestosterone

- Problems: Short $t_{1/2}$, Endogenous DHT
- Isotope Ratio Mass Spectrometry
  - $^{13}$C Content of Endogenous vs Exogenous DHT
  - $\delta^{13}$C‰ < -29 Suggests Exogenous Source
- Ratios of $5\alpha$:non-$5\alpha$ C$_{19}$ Steroids
  - $5\alpha$-/5$\beta$- Androsterone-3$\alpha$,17$\beta$-diols
  - Developed by Mitsubishi Chemical Co.
  - Busted Chinese Swim Team ‘94 Asian Games
## DHT: Chinese Women Swimmers

<table>
<thead>
<tr>
<th>Athlete</th>
<th>DHT&lt;sub&gt;corr&lt;/sub&gt;</th>
<th>5α/5β-A</th>
<th>5αA/Etio</th>
<th>DHT/EpiT</th>
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<tbody>
<tr>
<td>1</td>
<td>388.67</td>
<td>56.61</td>
<td>5.70</td>
<td>83.14</td>
</tr>
<tr>
<td>2</td>
<td>89.54</td>
<td>12.65</td>
<td>1.99</td>
<td>24.77</td>
</tr>
<tr>
<td>2</td>
<td>60.73</td>
<td>10.21</td>
<td>1.92</td>
<td>13.22</td>
</tr>
<tr>
<td>2</td>
<td>77.40</td>
<td>10.62</td>
<td>1.99</td>
<td>29.07</td>
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<tr>
<td>2</td>
<td>47.93</td>
<td>17.75</td>
<td>2.26</td>
<td>17.43</td>
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<tr>
<td>3</td>
<td>18.63</td>
<td>14.02</td>
<td>2.53</td>
<td>4.73</td>
</tr>
<tr>
<td>4</td>
<td>16.38</td>
<td>67.88</td>
<td>2.91</td>
<td>9.38</td>
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<tr>
<td>5</td>
<td>28.70</td>
<td>62.45</td>
<td>2.52</td>
<td>6.42</td>
</tr>
<tr>
<td>5</td>
<td>15.68</td>
<td>70.52</td>
<td>2.51</td>
<td>7.80</td>
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</table>

**Upper Limit:** 12.13  1.88  2.20  2.72
### δ¹³C Values For High T/EpiT Ratio

<table>
<thead>
<tr>
<th>Athlete</th>
<th>T/Epi-T</th>
<th>5βA</th>
<th>5αA</th>
<th>5βP</th>
<th>5βP-5βA</th>
<th>5βP-5αA</th>
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<td>1</td>
<td>40</td>
<td>-30.42</td>
<td>-31.96</td>
<td>-25.67</td>
<td>4.8</td>
<td>6.3</td>
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<td>2</td>
<td>29</td>
<td>-31.43</td>
<td>-34.57</td>
<td>-26.14</td>
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<td>3</td>
<td>80</td>
<td>-28.76</td>
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<td>-23.06</td>
<td>5.7</td>
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<td>4</td>
<td>10</td>
<td>-25.32</td>
<td>-25.76</td>
<td>-24.54</td>
<td>0.8</td>
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<td>5</td>
<td>9</td>
<td>-24.82</td>
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<td>-23.49</td>
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<td>6</td>
<td>8</td>
<td>-24.62</td>
<td>-26.04</td>
<td>-23.36</td>
<td>1.3</td>
<td>2.7</td>
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<tr>
<td>Control</td>
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<td>-26.35</td>
<td>-24.26</td>
<td>1.43</td>
<td>2.09</td>
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<tr>
<td>SD</td>
<td></td>
<td>0.92</td>
<td>0.68</td>
<td>0.70</td>
<td>0.68</td>
<td>0.63</td>
</tr>
</tbody>
</table>
Drug Testing
Strategies to Avoid Getting Caught

• Use Agents That Are Difficult to Detect
• Abstention Peroids
  – Synthetic Injectables Can Last > 6 Months
• Diuretics to Dilute Urine
• Bacterial Contamination
• Tampering With Samples
Recent Developments

The Good News

- DEA: Androgens Labeled CIII Drugs
- Ciba: Discontinued Dianabol Production
- Transdermal Testosterone Preparations
- Medical Community Recognition
  - Scope of Problem and Motivation of Users
  - Interest In Studying Issue Scientifically
- Sports: Random Testing, Better Methods
  - Decline In Women’s Strength Events
Recent Developments

The Bad News

- Evidence of Increased Use in Females
- Professional Strategies To Subvert Testing
  - Shift To T, DHT & Derivatives
  - Boutique Labs Synthesize Custom Androgens
  - Usage Infiltrating All Sports
- Precursors as “Nutritional Supplements”
Dietary Supplements Health and Education Act of 1994 (DSHEA)

- “Dietary Supplements” Exempt From Premarket Safety Evaluations
- Defined As Any Product Containing a “Dietary Substance” Labeled As “Dietary Supplement”
- Adulteration With Untested Ingredients Allowed If Inadequate Data To Exclude Risk
- Truth, Safety Is Manufacturer’s Responsibility
DHSEA: The Bottom Line

• You Can Sell Practically Anything You Want As A “Dietary Supplement”
• You Do Not Need To Prove That It Is Safe Before You Start Selling It
• You Can Interpret Any Data However You Want To Claim Benefit For “Structure or Function”
• The Onus Is On The FDA To Prove Guilt/Harm
  – The FDA Has Never Successfully Prosecuted a Case
Dyma-Bol

DSS Price $46.32/Caps 60ct
DSS Price $27.49/Spray

Dyma-Bol is the strongest prohormone anabolic steroid alternative available on the market today. Look at the ingredients below.

2 capsules contain:

Nor Androstendiol ---------- 25 mg
19 Norandrostendione ------ 50 mg
4 Androstendiol ---------- 75 mg
5 Androstendiol ---------- 75 mg
4 Androstene 3, 17 Dione --- 75 mg
Tribulus Terrestis --------- 500 mg
Chrysin ------------------- 100 mg
Phosphatidyl Serine ------- 200 mg
Saw Palmetto ------------- 250 mg
Zinc (Glycinate) --------- 8 mg
Androstenedione

-One Step From Testosterone

17β-HSD III & V

-Preferred Aromatase Substrate
Androgen Biosynthesis: Traditional Pathways

- **Cholesterol**
  - StAR
  - P450scc/Adx/AdR
  - PBR

- **Pregnenolone**
  - CYP17
  - CPR (β)
  - 17α-hydroxylase
  - 17, 20-lyase

- **DHEA**
  - 3βHSD I & II

- **Androstenedione**
  - aromatase
  - CPR

- **Androstanediol**
  - 3αHSD

- **Testosterone**
  - 17βHSDII
  - 17βHSDI
  - aromatase
  - CPR

- **Dihydrotestosterone**
  - 5α-Reductase I & II

- **Estrone**
  - 17βHSDI
  - 17βHSDII

- **Estradiol**
  - 17βHSDI
  - 17βHSDII

- **Androstanediol**
  - 3αHSD
Androstenedione

- Sparse Data About Oral Use Before 1998
- Robust Metabolism By Hepatic P450s
- Banned By Most Sports Authorities
- Safe?? Efficacy?? Placebo??
- Dietary Supplement????
Oral Androstenedione
Strength, Testosterone, Estrogens

• Circulating Testosterone Concentrations
  – No Effect At 100 mg/d (King)
  – Variable Small Rise At 300 mg/d (Brown, Leder)
• Strength: No Effect Shown (King, Broeder)
• Estrogens: Consistent, Marked Elevations

Figure 2. Mean Percentage Change in Area Under the Curve for Serum Testosterone and Estradiol Concentrations, Days 1 and 7.
Table 3. Mean Concentrations of 19-Norandrosterone and 19-Noretiocholanolone After Oral Administration of 10 μg of 19-Norandrostenedione to 4 Subjects

<table>
<thead>
<tr>
<th>Time, h</th>
<th>19-Norandrosterone</th>
<th>19-Noretiocholanolone</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>17.2 (2.8-48.9)</td>
<td>5.2 (1.1-16.7)</td>
</tr>
<tr>
<td>3-4</td>
<td>5.6 (4.4-7.6)</td>
<td>1.3 (0.6-1.9)</td>
</tr>
<tr>
<td>5-6</td>
<td>1.2 (0.6-1.7)</td>
<td>0.3 (0.1-0.3)</td>
</tr>
<tr>
<td>7-8</td>
<td>0.5 (0.1-0.8)</td>
<td>0.2 (0.1-0.3)</td>
</tr>
</tbody>
</table>
DHEA

-19-Carbon (Androstane)
-\Delta^5, 3\beta-Hydroxy, 17-Keto
-SO_4, Ester At 3\beta
DHEA: How Does It Work?

- **Conversion To Androgens**
  - 50 mg/d Raises Testosterone In Women
- **Intrinsic Activity Of DHEA(S) In Brain**
  - Trophic Effects On Cultured Neurons
  - GABA, NMDA, Sigma Receptor-Channels
- **Actions Of Weird Metabolites:** The “Neurosteroids” Concept
Neurosteroids & 3α,5α-Pathways

Androgens
- Testosterone
- Dihydrotestosterone

Precursors
- Pregnenolone
- Progesterone

Neurosteroids
- Allopregnanolone
- Dihydroprogesterone
- Preg(-S), DHEA-(S)

Nuclear Hormone Receptor
Genomic Actions

5α-Red-I
3αHSDs
CYP17/SLTase

17βHSDIII
5α-Red-II
CYP17

Ion Channels
Non-Genomic Actions
Steroid Hormone Action: Dichotomy?
Allopregnanolone
Potentiation of GABA/Cl\(-\) Currents
Synthetic Androgens
Potentiation of GABA/Cl⁻ Currents
Neurosteroids & Androgens

CYP17
17βHSDIII
5α-Red-II

Precursors
• Pregnenolone
• Progesterone

5α-Red-I
3αHSDs
CYP17/SLTase

Androgens
• Testosterone
• Dihydrotestosterone

Neurosteroids
• Allopregnanolone
• Dihydroprogesterone
• Preg(-S), DHEA-(S)

Nuclear Hormone Receptor
Genomic Actions

CYP17
17βHSDIII
3αHSD

Ion Channels
Non-Genomic Actions
Anabolic Steroid Abuse

Conclusions

• Prevalence High
  – Athletes, Adolescents, Increasing in Girls
• Psyche Predisposes to Escalating Use
• Aids in Weight > Strength, Not Endurance
• Mechanism Complex
• Side Effects Numerous Albeit Mostly Rare
• Precursor Use Out of Control
• Sparse Data, Careful Studies Needed
“We’re not freaks or addicts. We’re using modern science to reach our goals.”