

# **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**

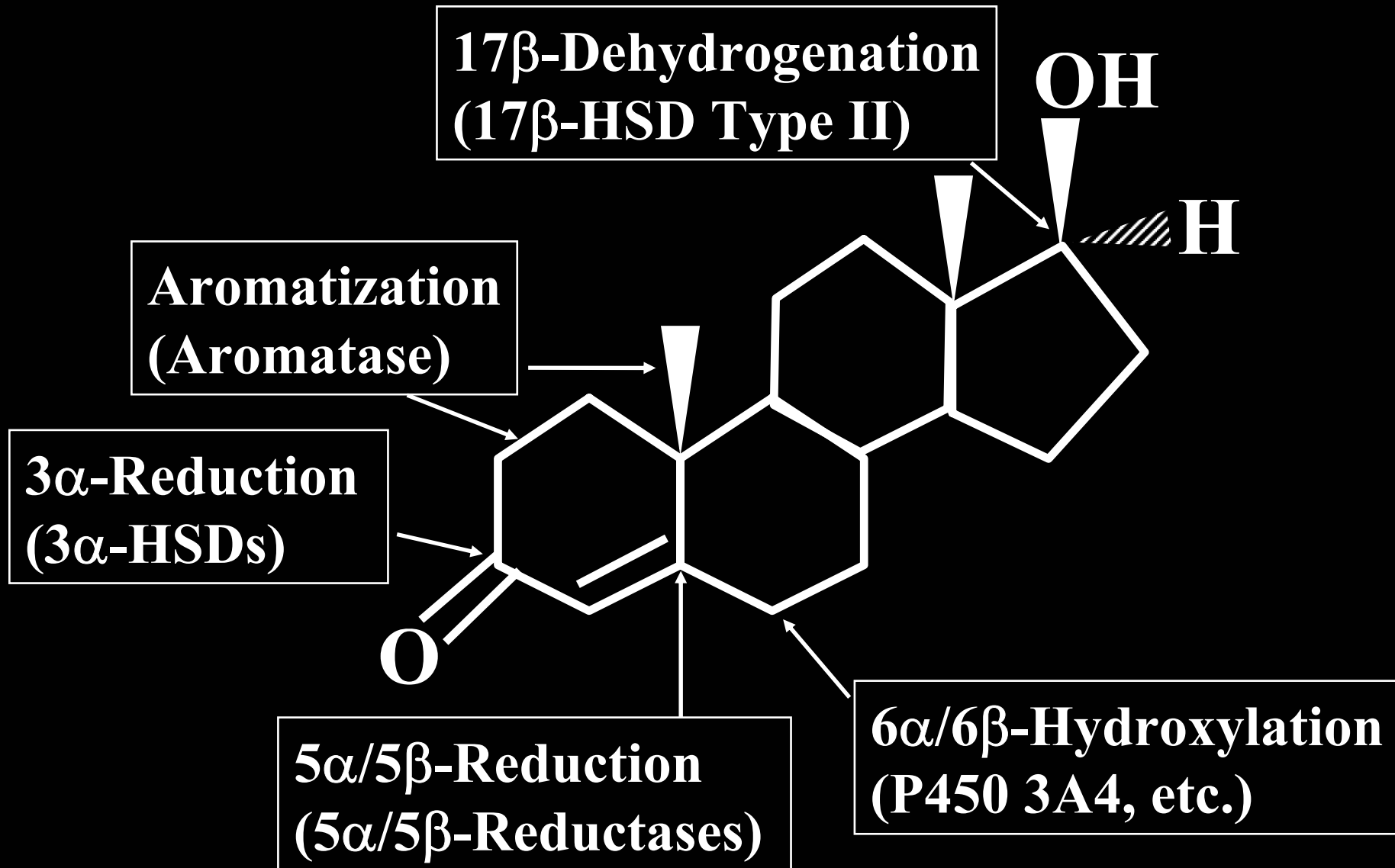
# **Anabolic Steroid Topics**

- **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**

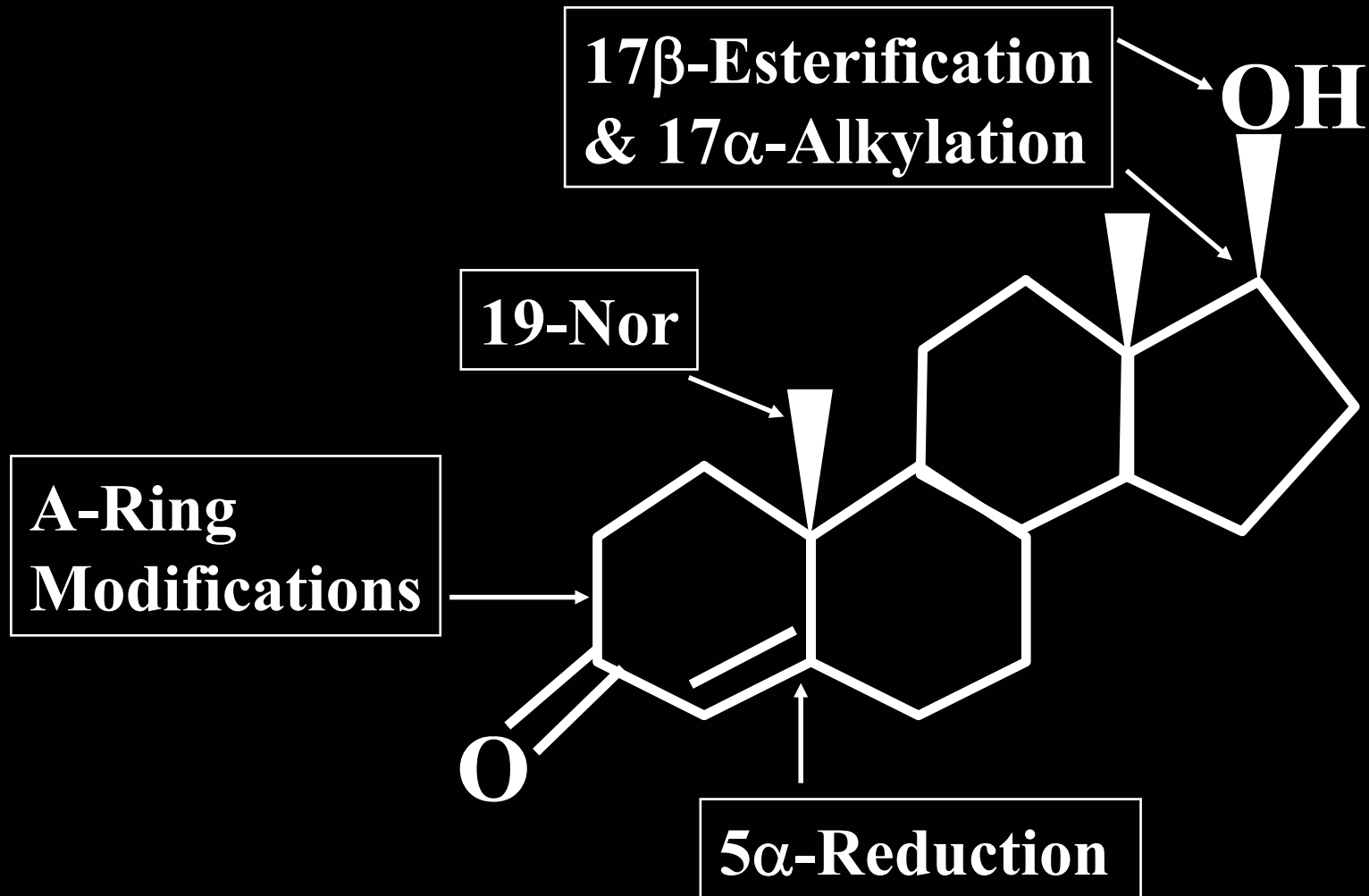
# **Anabolic vs. Androgenic**

- **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



# Testosterone & Derivatives



# 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 ( $E_2$  ↑ 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**







**Die Young**

**Die Strong**

**Dianabol®**

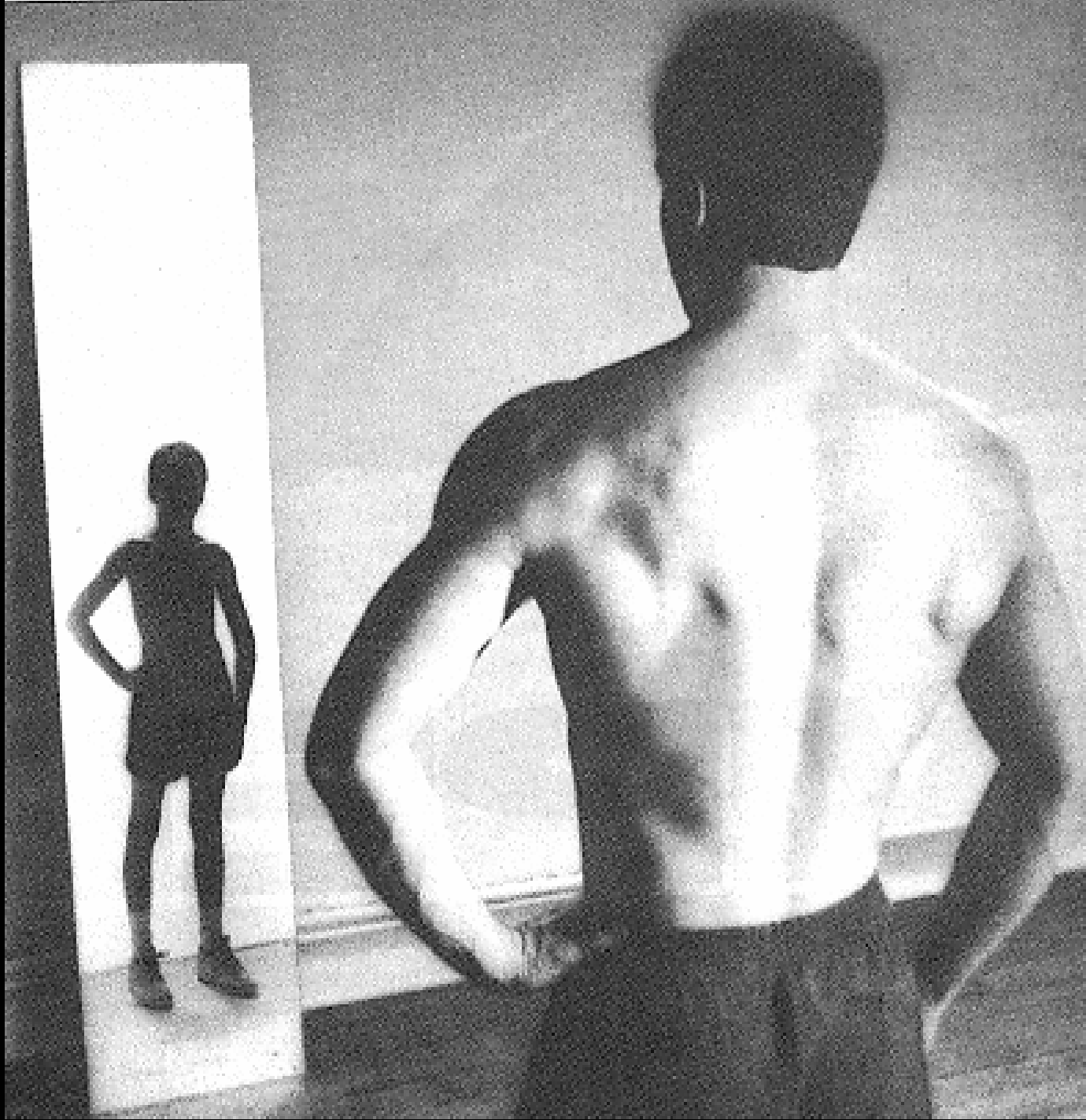


**“I started in high school weighing 140 pounds; I was Mr. Nobody. Sophomore year, I started taking steroids--my weight jumped 40 pounds and everybody suddenly wanted to be my friend. Since then I’ve had girls on one side, guys on the other. What more could I want?”**

# **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

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

Olivardia et al Am J Psychiatry 157:1291-1296 (2000)

# 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 Responsive 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  $\beta$ -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**

<b><u>Side Effect</u></b>	<b><u>Agents</u></b>
<b>Gynecomastia</b>	<b>Tamoxifen</b> <b>Testolactone</b>
<b>Acne</b>	<b>Tretinoin</b>
<b>Testicular Atrophy</b>	<b><math>\beta</math>-hCG</b>

**This Gets Pretty Expensive...**

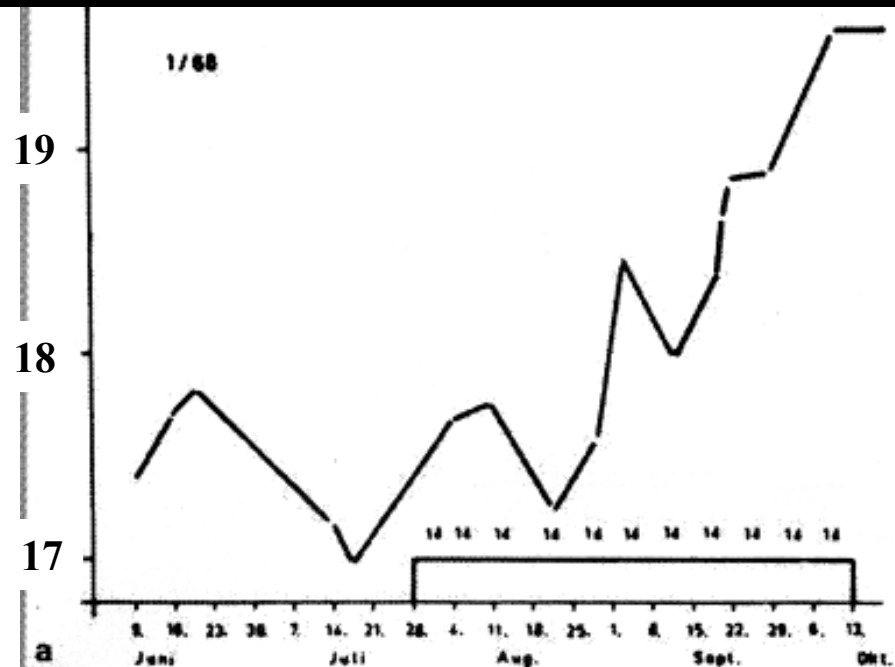
# **Androgens: Do They Work??**

## **Problems With Earlier Studies**

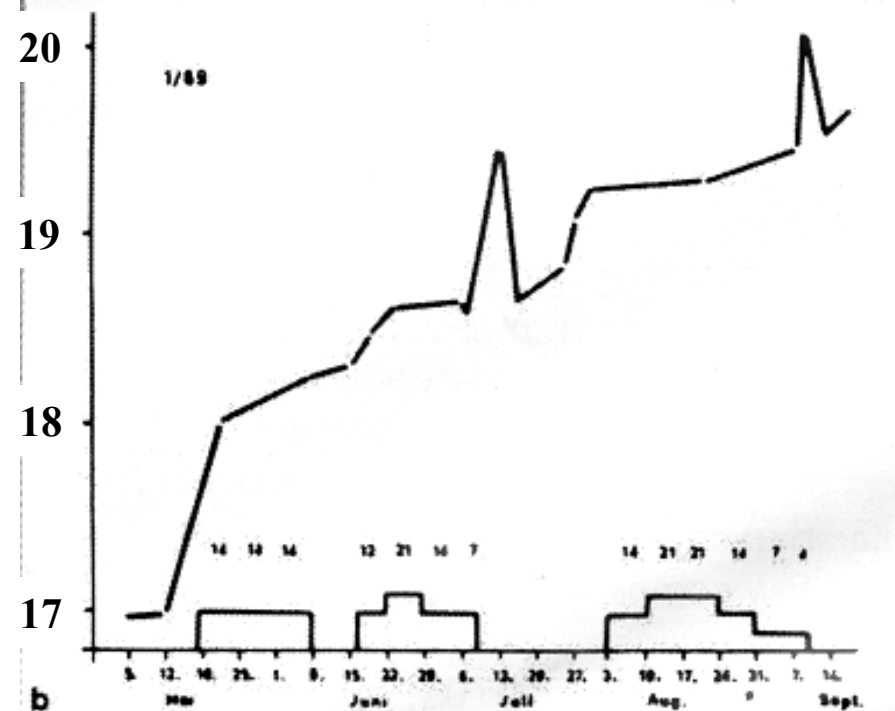
- **Largely Observational & Uncontrolled**
- **Selection Bias/Extrapolation of Results**
- **Blinding Impossible**
- **Informed Consent a Major Issue**
- **Duration of Studies**
- **Tendency to Increase Strength**
  - **Continuously Training Subjects**
  - **Methandrostenolone Rx, 1-RM Assessment**

# Oral-Turinabol Effect On Shot Put Distance, GDR Female Athlete

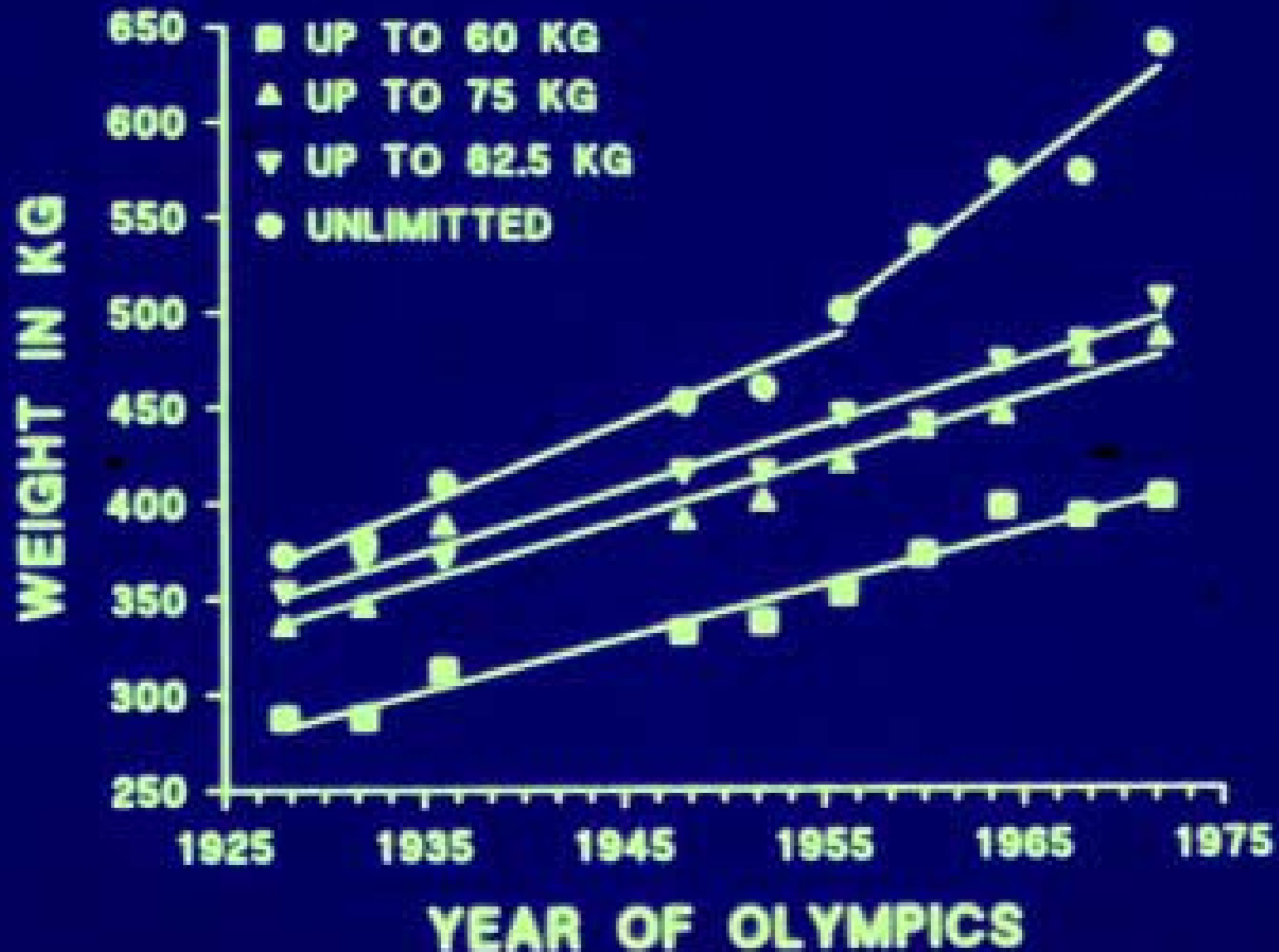
Distance (meters)



Distance (meters)



# IMPROVEMENT IN WEIGHT LIFTING





# Supraphysiologic Testosterone

Change	<u>No Exercise</u>		<u>+ Exercise</u>	
	<u>Plac.</u>	<u>Test.</u>	<u>Plac.</u>	<u>Test.</u>
Weight (Kg)	1.3	3.5	0.9	6.0
Quads (mm <sup>2</sup> )	0	600	530	1,200
Bench (Kg)	0	9	10	22
Squat (Kg)	3	13	25	38

**Bhasin et al NEJM 335:1-7 (1996)**

# “Inside the Numbers”

Bhasin et al

	<u>No Exercise</u>		<u>+ Exercise</u>	
	Placebo	Test.	Placebo	Test.
<u><math>\Delta</math>Bench</u>	0	2.2	8.4	2.8
$\Delta$ Wt				
<u><math>\Delta</math> Squat</u>	1.8	2.9	18	4.7
$\Delta$ Wt				

# 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

	Placebo		Testosterone		
	<u>Start</u>	<u>End</u>	<u>Start</u>	<u>End</u>	
YMRS	0.3	1.1	0.5	3.9**	
PSAP	208	222	208	362*	*p<0.05 **p<0.01
Manic Score	7.9	7.4	7.5	9.2**	
Liking Score	50	50	51	55**	

Pope et al Arch Gen Psychiatry 57:133-140 (2000)

# **“Inside the Numbers”**

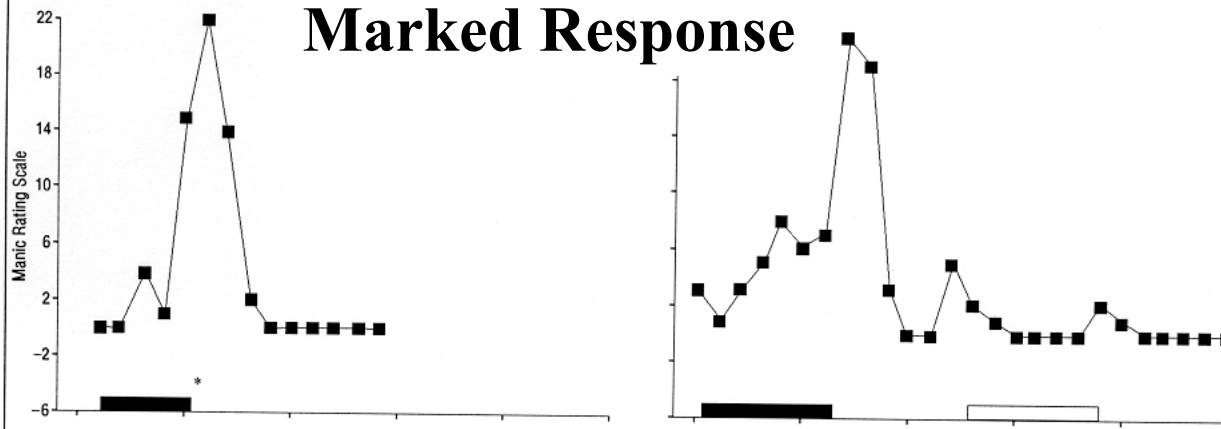
**Pope et al**

- **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**

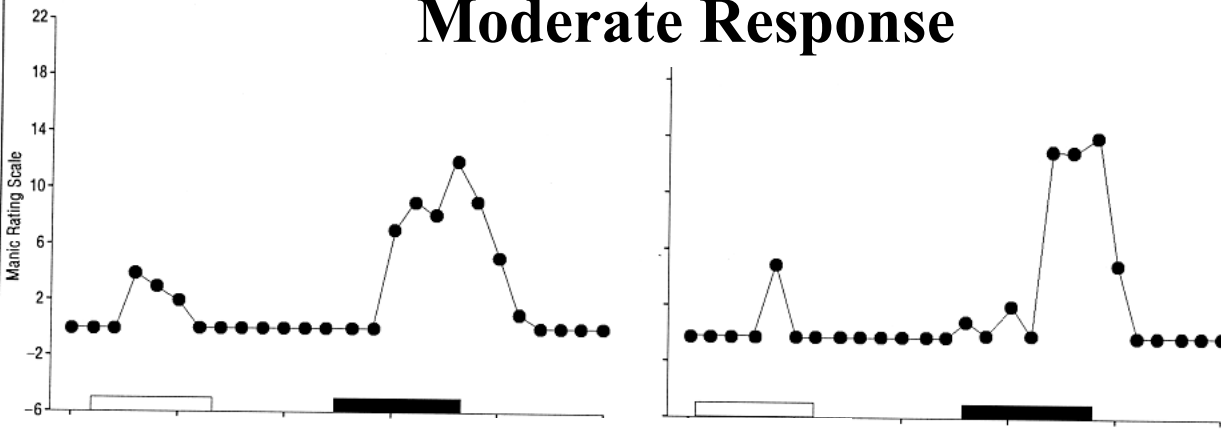
# Manic Response To Testosterone

Pope et al

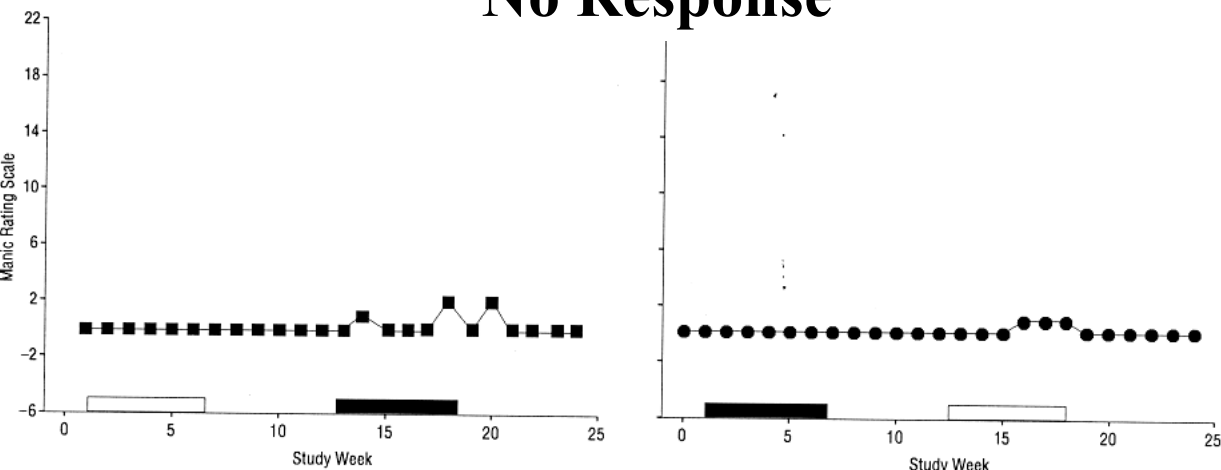
## Marked Response



## Moderate Response



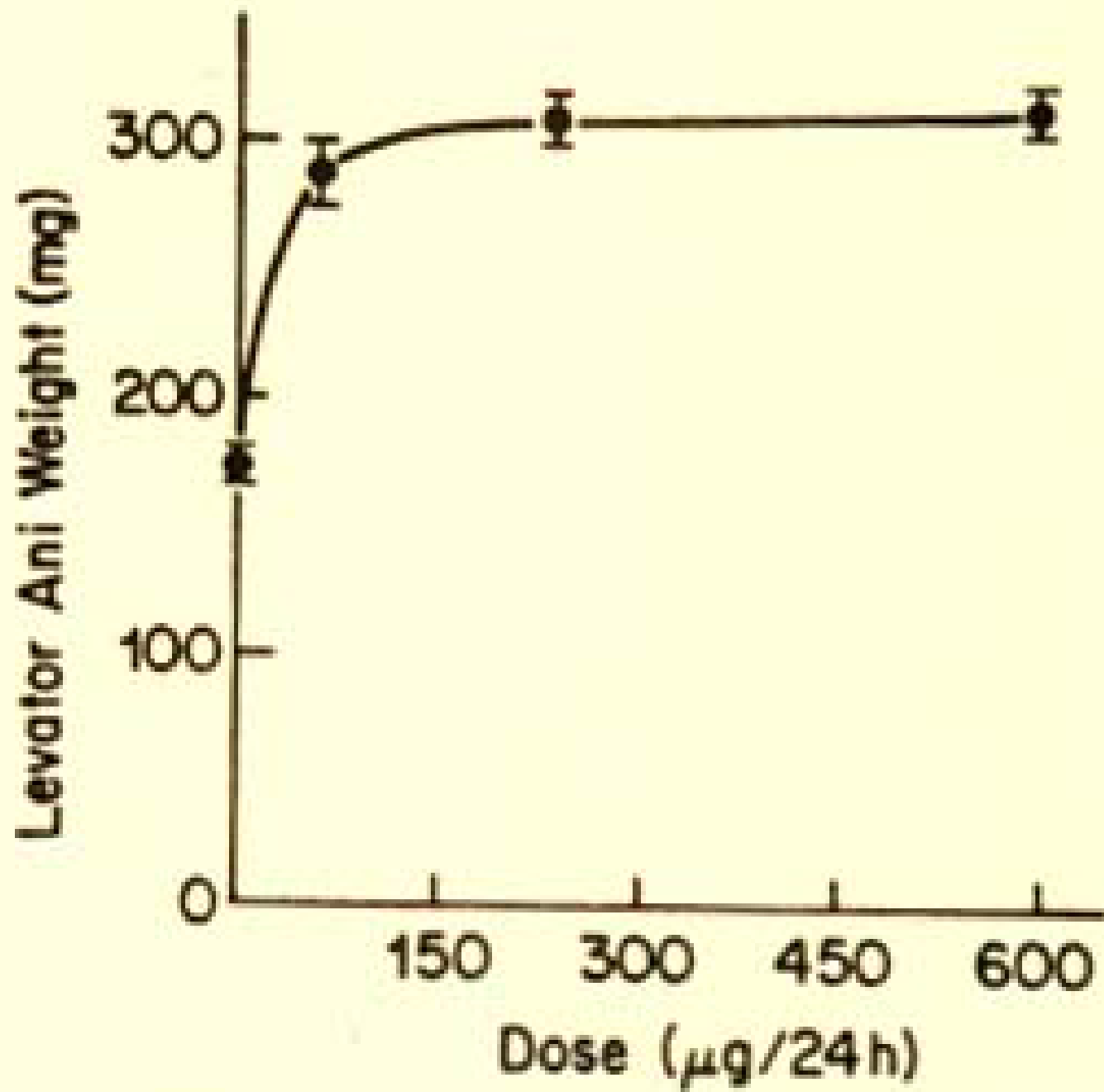
## No Response



# **Anabolic Action of Androgens**

## **Mechanistic Conundrums**

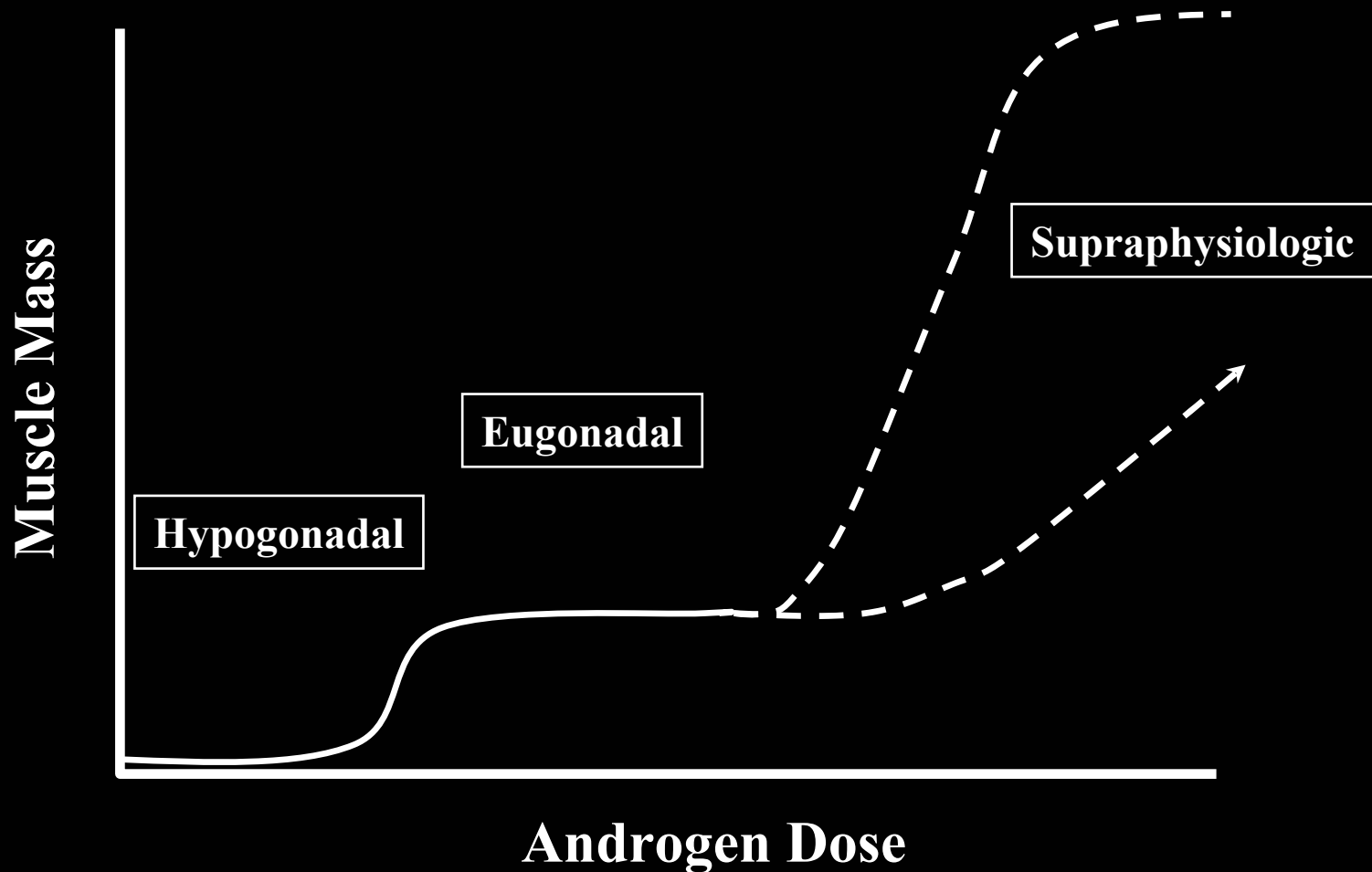
- **Cannot Extrapolate Data From Sexually Dimorphic Muscles in Lower Species**
- **Difficult to Demonstrate AR Protein, mRNA in Human Skeletal Muscle**
- **Classical Paradigm Fails to Explain Need for Supraphysiologic Concentrations**
- **Molecular Techniques Have Not Identified Target Genes (?IGF-1,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



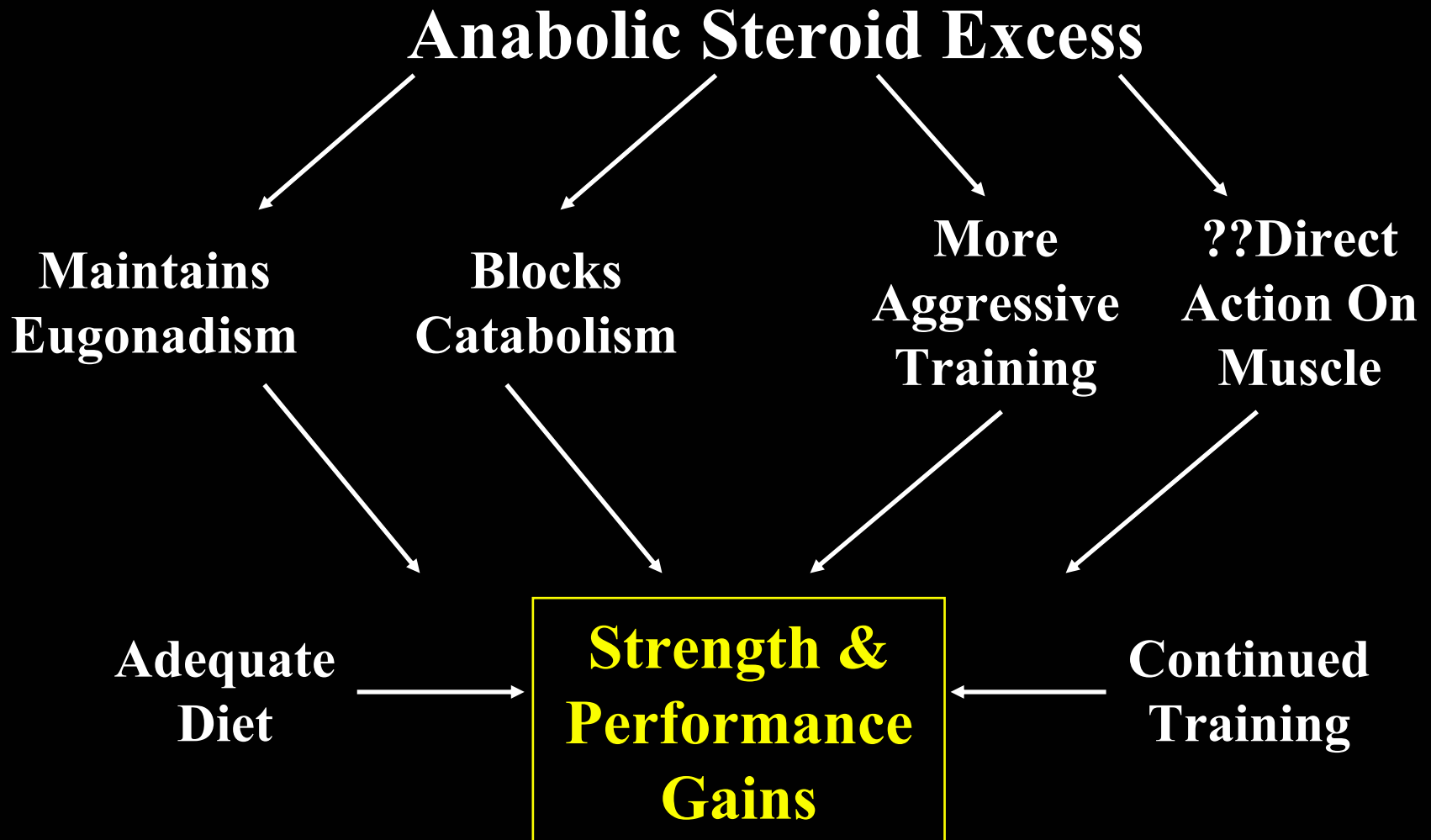


# Anabolic Action of Androgens

## Theoretical Dose-Response Curves



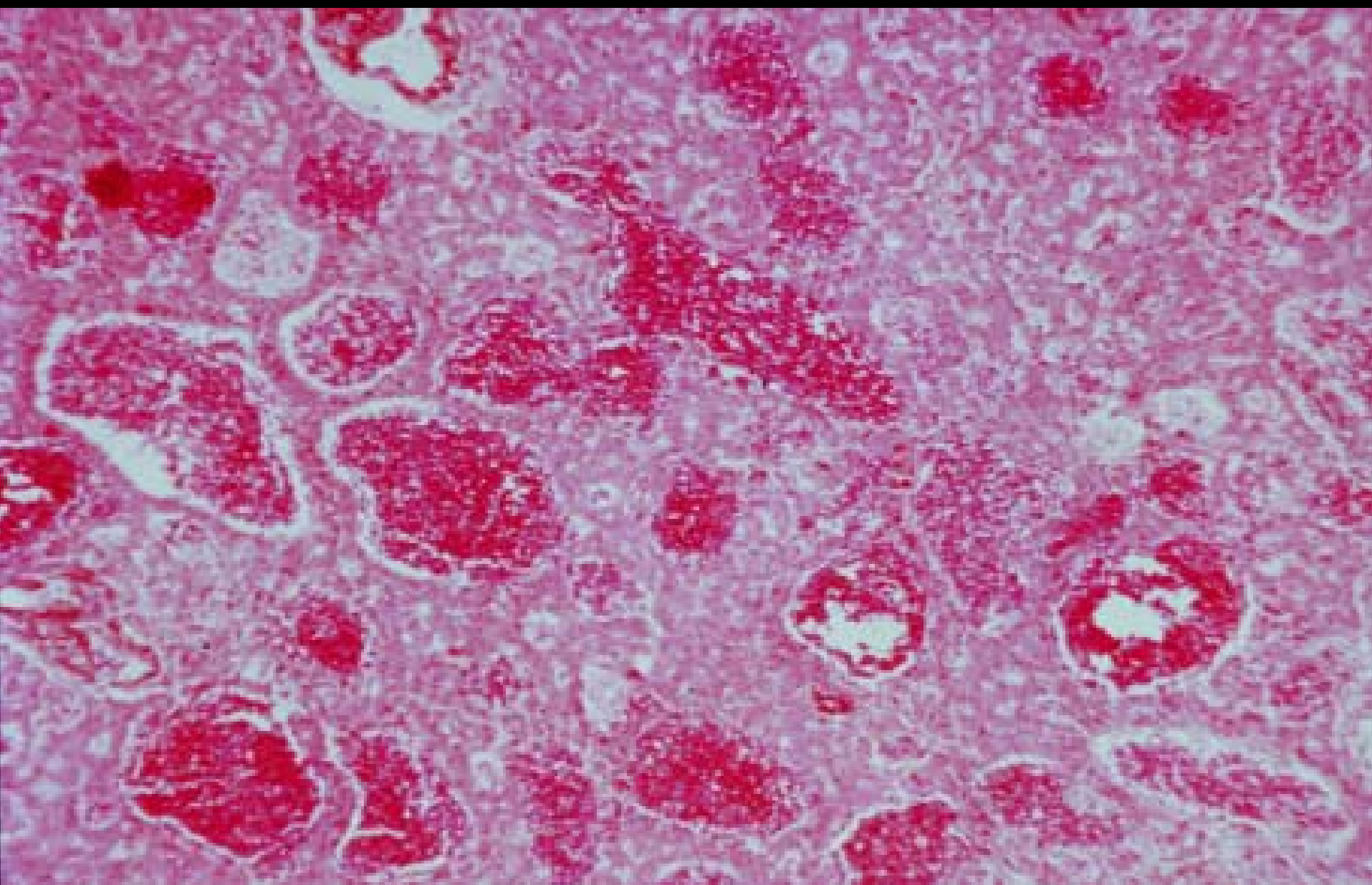
# Model For Androgen Action



# **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**





**TEAM**  
BETTER BODIES

# **Anabolic Steroid Abuse**

## **Side Effects: Female**

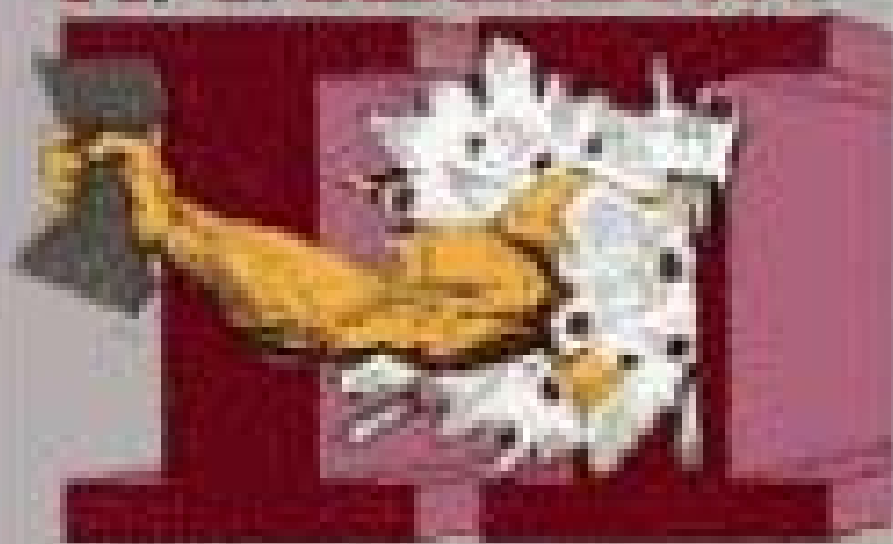
- **Amenorrhea**
- **Breast Atrophy**
- **Hirsutism**
- **Clitoromegaly**
- **Deepening of Voice**
- **Often Prominent and Irreversible**

**“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’**

UNDERGROUND  
**STEROID**  
HANDBOOK



DANIEL DELCHANE

**“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, 1<sup>st</sup> 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  $5\alpha$ :non- $5\alpha$  C<sub>19</sub> Steroids**
- **Isotope Ratio Mass Spectrometry**

**Urine Sample**

**C-18 or XAD  
Solid Phase Extraction**



**Enriched Pool of Steroids,  
Glucuronide and Sulfate Conjugates**

**$\beta$ -Glucuronidase  
Hydrolysis**



**Steroids & Steroid Sulfates**

**Organic Solvent  
Extraction**



**Steroids**

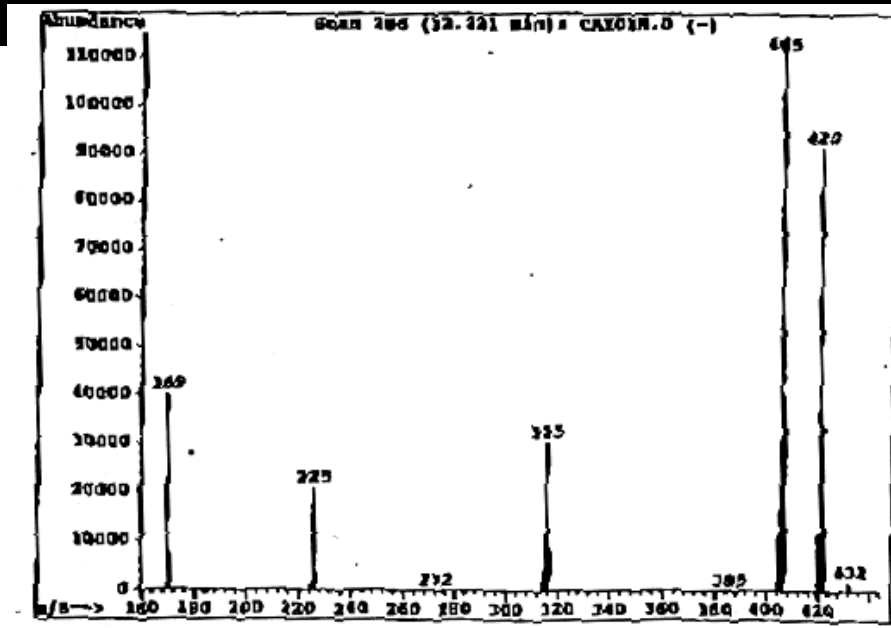
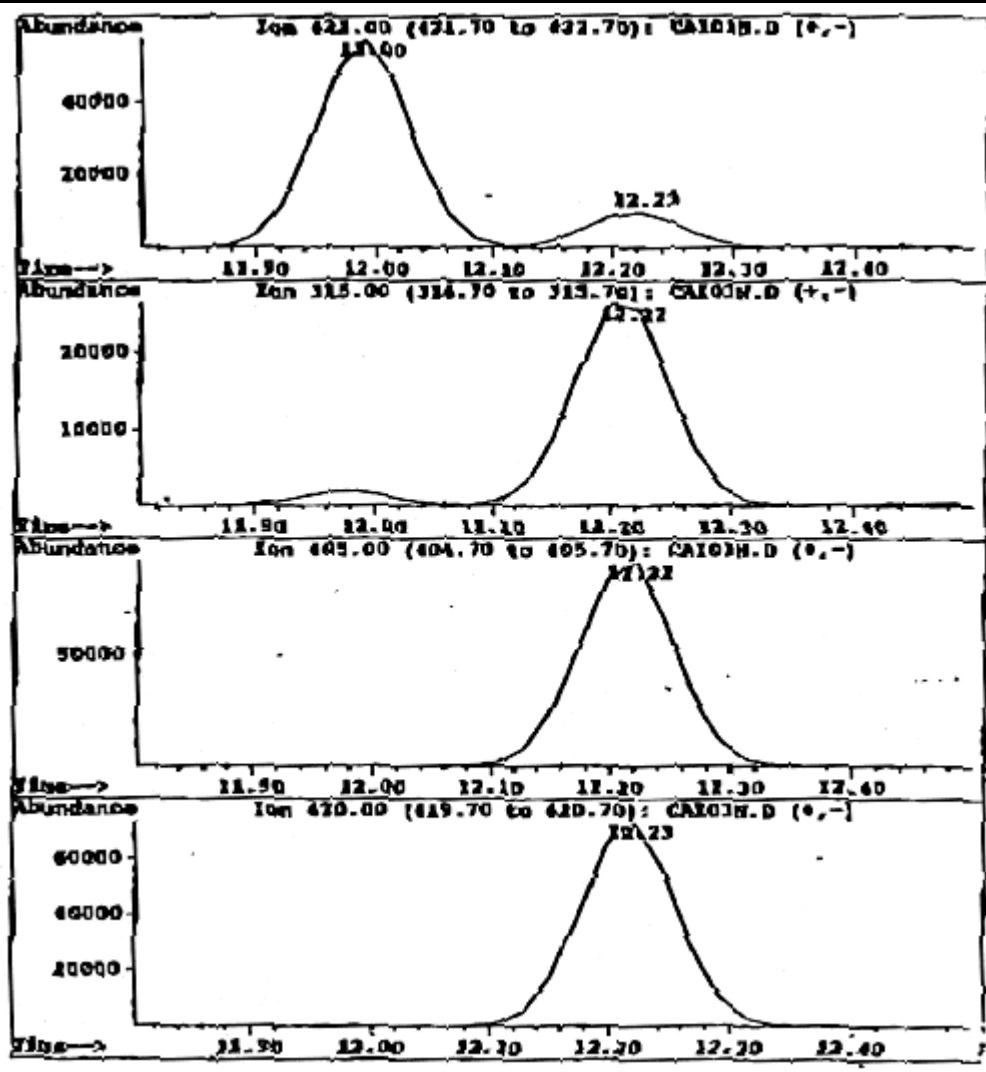
**MSTFA Derivitization  
+ Enol Catalyst**



**Steroid TMS-(enol)-  
Ether Derivatives**



# 19-Norandrosterone



<u>m/z</u>	<u>abundance</u>
169.10	35%
225.20	18%
315.30	26%
405.30	100%
420.30	80%

# Detecting Dihydrotestosterone

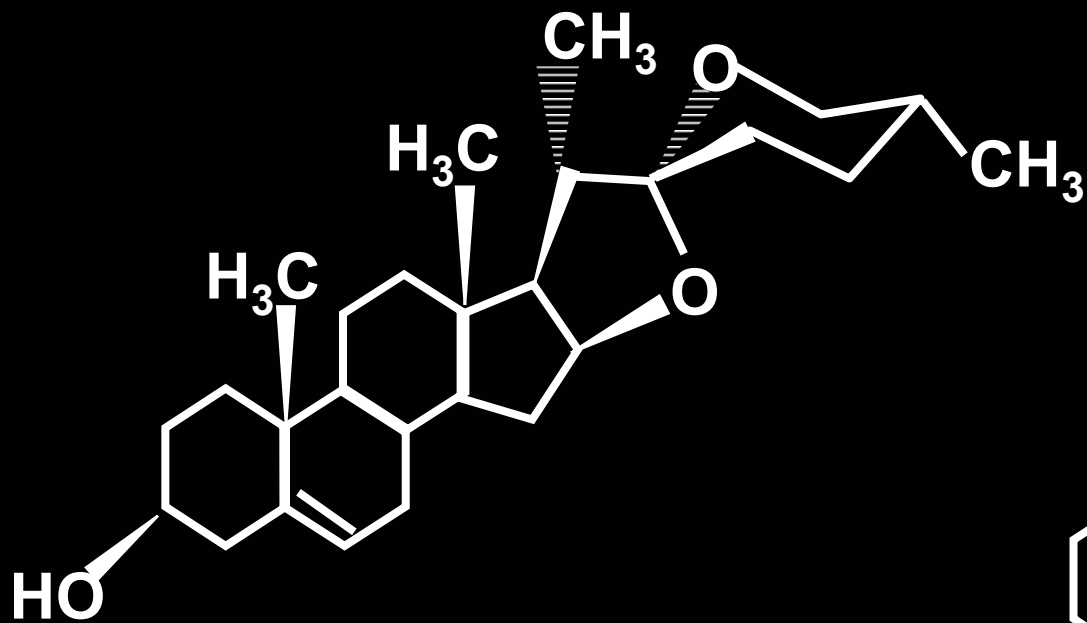
- **Problems: Short  $t_{1/2}$ , Endogenous DHT**
- **Isotope Ratio Mass Spectrometry**
  - **$^{13}\text{C}$  Content of Endogenous vs Exogenous DHT**
  - **$\delta^{13}\text{C}\text{‰} < -29$  Suggests Exogenous Source**
- **Ratios of  $5\alpha$ :non- $5\alpha$   $\text{C}_{19}$  Steroids**
  - **$5\alpha$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

# DHT: Chinese Women Swimmers

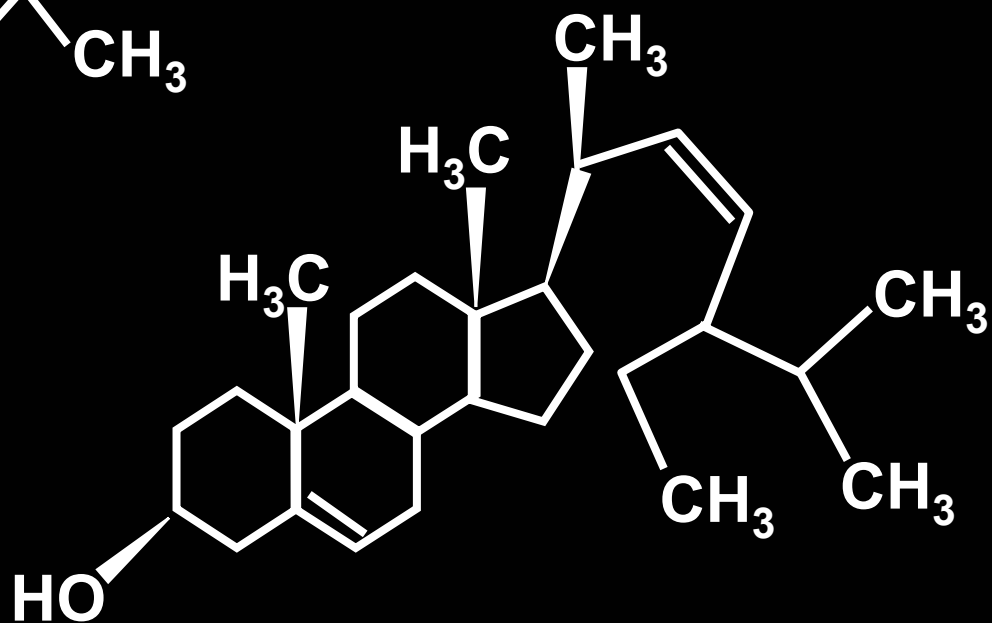
Athlete	DHT <sub>corr</sub>	5 $\alpha$ /5 $\beta$ -A	5 $\alpha$ A/Etio	DHT/EpiT
1	388.67	56.61	5.70	83.14
2	89.54	12.65	1.99	24.77
2	60.73	10.21	1.92	13.22
2	77.40	10.62	1.99	29.07
2	47.93	17.75	2.26	17.43
3	18.63	14.02	2.53	4.73
4	16.38	67.88	2.91	9.38
5	28.70	62.45	2.52	6.42
5	15.68	70.52	2.51	7.80

**Upper Limit:**            12.13            1.88            2.20            2.72

**Diosgenin**



**Stigmasterol**



# $\delta^{13}\text{C}$ Values For High T/EpiT Ratio

<b>Athlete</b>	<b>T/Epi-T</b>	<b>5<math>\beta</math>A</b>	<b>5<math>\alpha</math>A</b>	<b>5<math>\beta</math>P</b>	<b>5<math>\beta</math>P-5<math>\beta</math>A</b>	<b>5<math>\beta</math>P-5<math>\alpha</math>A</b>
<b>1</b>	<b>40</b>	<b>-30.42</b>	<b>-31.96</b>	<b>-25.67</b>	<b>4.8</b>	<b>6.3</b>
<b>2</b>	<b>29</b>	<b>-31.43</b>	<b>-34.57</b>	<b>-26.14</b>	<b>5.3</b>	<b>8.4</b>
<b>3</b>	<b>80</b>	<b>-28.76</b>	<b>-31.25</b>	<b>-23.06</b>	<b>5.7</b>	<b>8.2</b>
<b>4</b>	<b>10</b>	<b>-25.32</b>	<b>-25.76</b>	<b>-24.54</b>	<b>0.8</b>	<b>1.2</b>
<b>5</b>	<b>9</b>	<b>-24.82</b>	<b>-25.47</b>	<b>-23.49</b>	<b>1.3</b>	<b>2.0</b>
<b>6</b>	<b>8</b>	<b>-24.62</b>	<b>-26.04</b>	<b>-23.36</b>	<b>1.3</b>	<b>2.7</b>
<b>Control</b>		<b>-25.69</b>	<b>-26.35</b>	<b>-24.26</b>	<b>1.43</b>	<b>2.09</b>
<b>SD</b>		<b>0.92</b>	<b>0.68</b>	<b>0.70</b>	<b>0.68</b>	<b>0.63</b>

# **Drug Testing**

## **Strategies to Avoid Getting Caught**

- **Use Agents That Are Difficult to Detect**
- **Abstinence Periods**
  - **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**

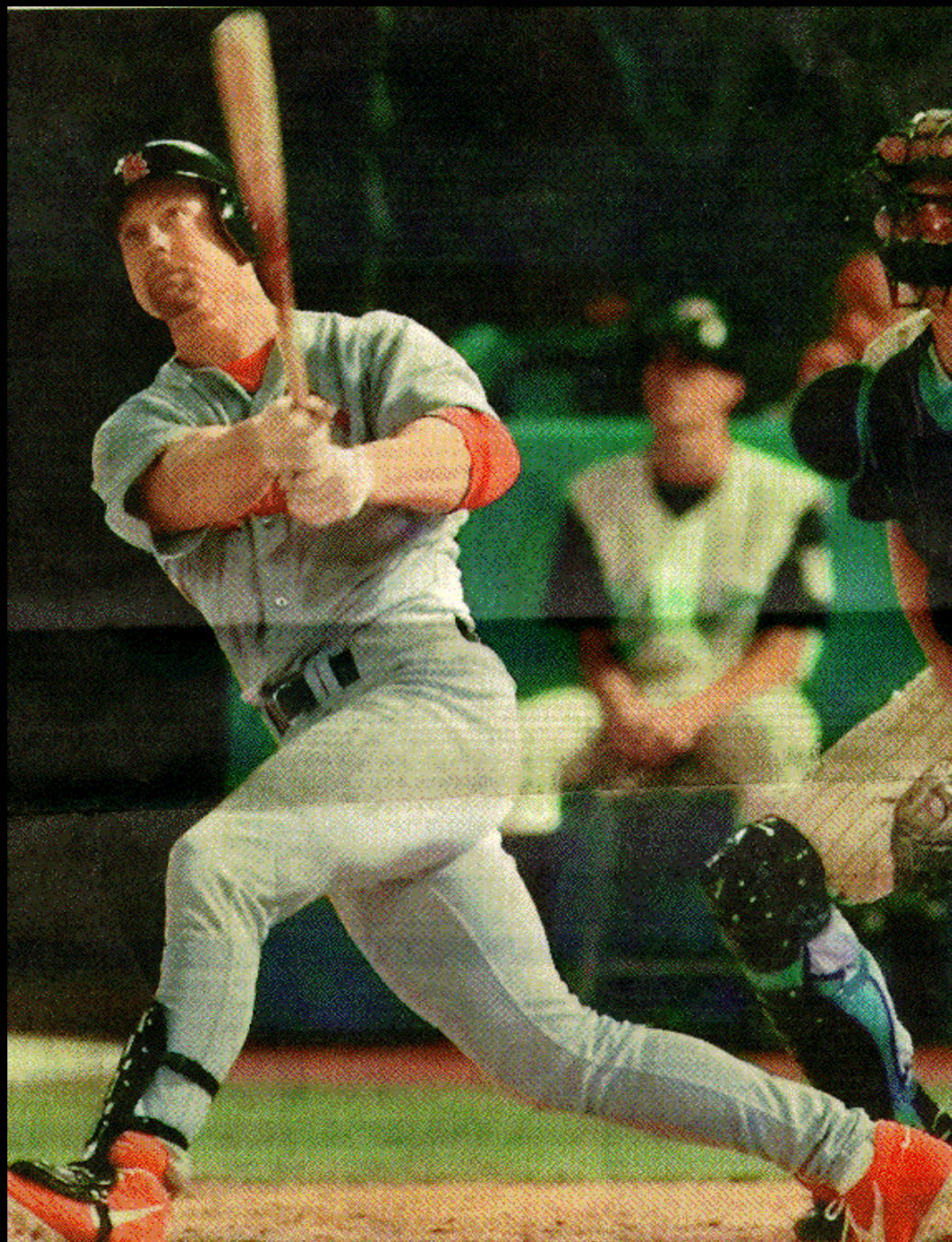
**Tribulus Terrestris ----- 500 mg**

**Chrysin ----- 100 mg**

**Phosphatidyl Serine ----- 200 mg**

**Saw Palmetto ----- 250 mg**

**Zinc (Glycinate) ----- 8 mg**

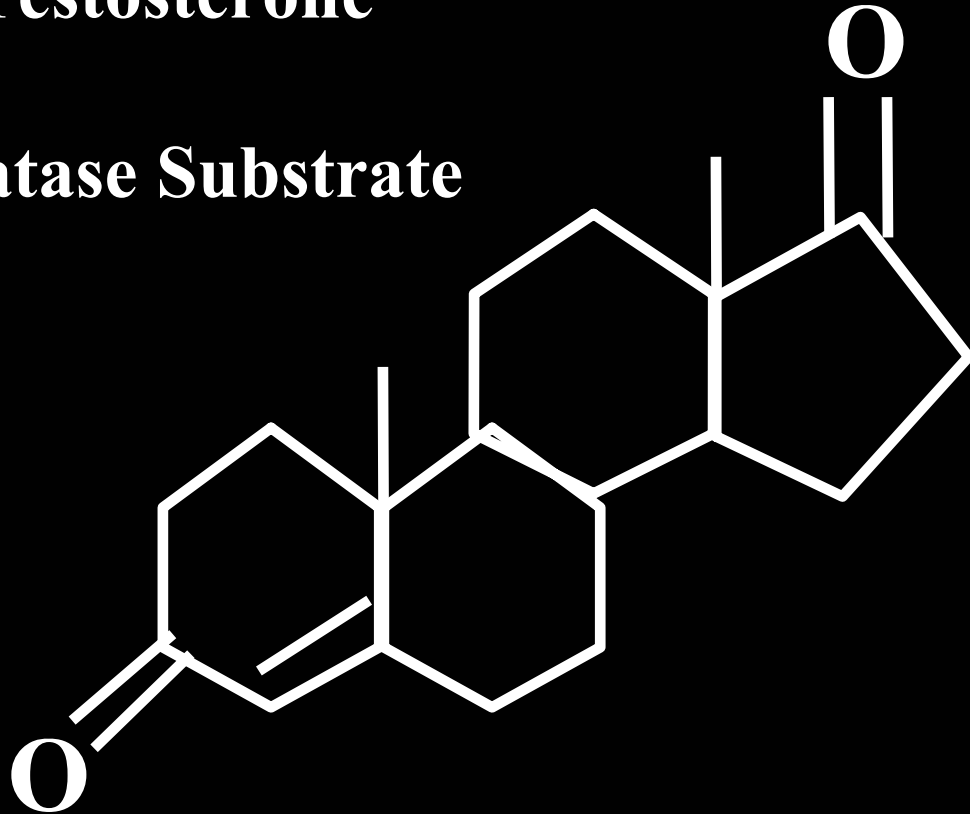


# Androstenedione

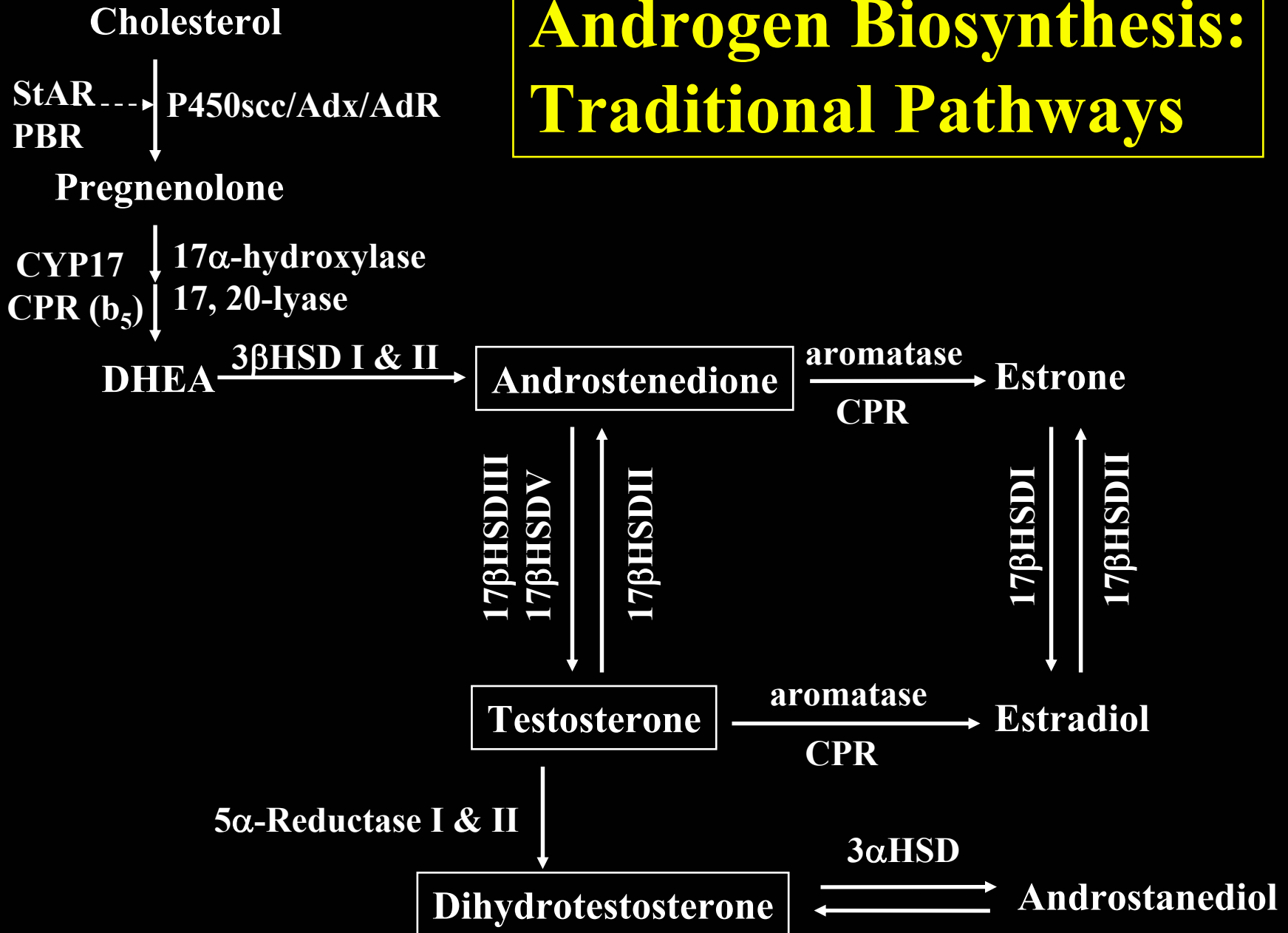
-One Step From Testosterone

17 $\beta$ -HSD III & V

-Preferred Aromatase Substrate



# Androgen Biosynthesis: Traditional Pathways



# **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**

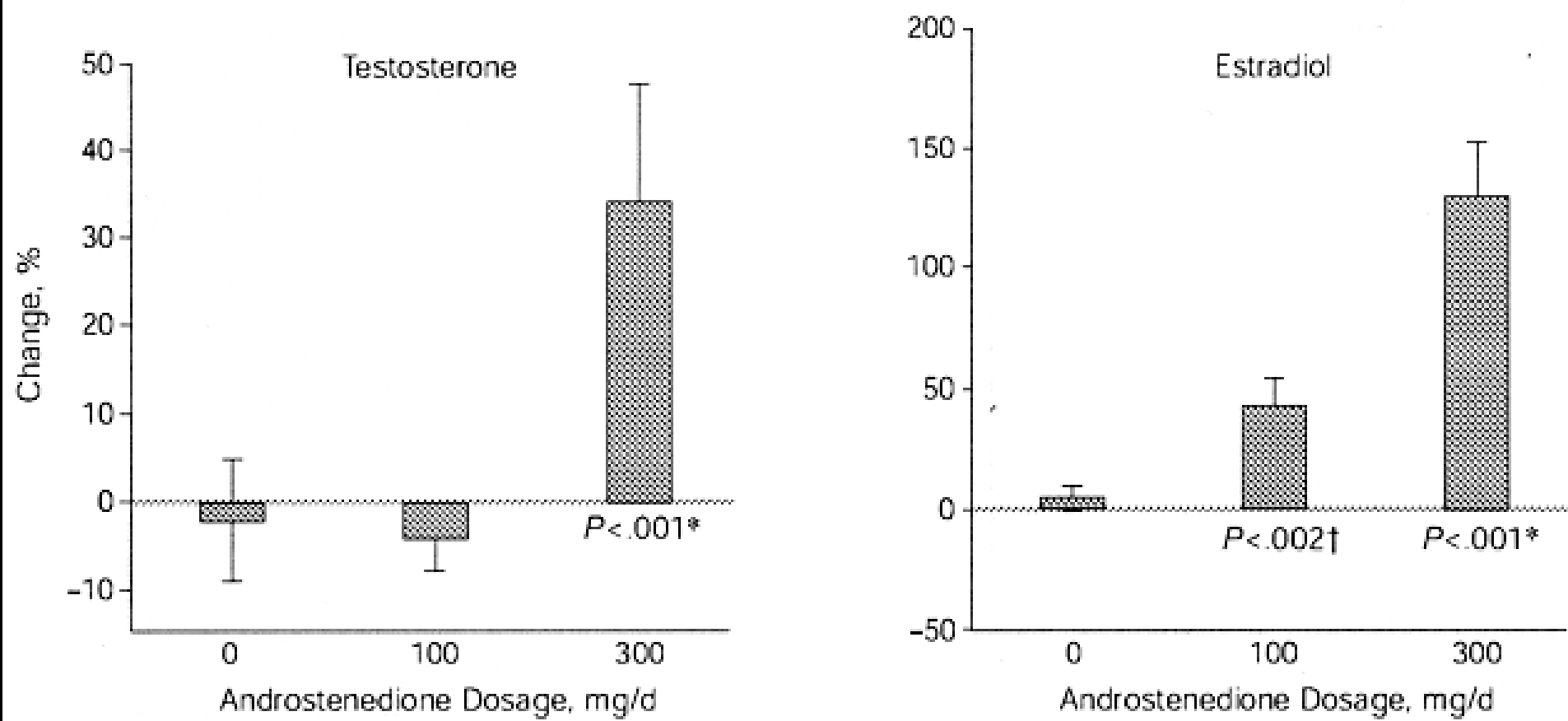
**King et al JAMA 281:2020-2028 (1999)**

**Brown et al Int J Sport Nutr Exerc Metab 10:340-59 (2000)**

**Leder et al JAMA 283: 779-782 (2000)**

**Broeder et al Arch Intern Med 160:3093-3104 (2000)**

**Figure 2.** Mean Percentage Change in Area Under the Curve for Serum Testosterone and Estradiol Concentrations, Days 1 and 7

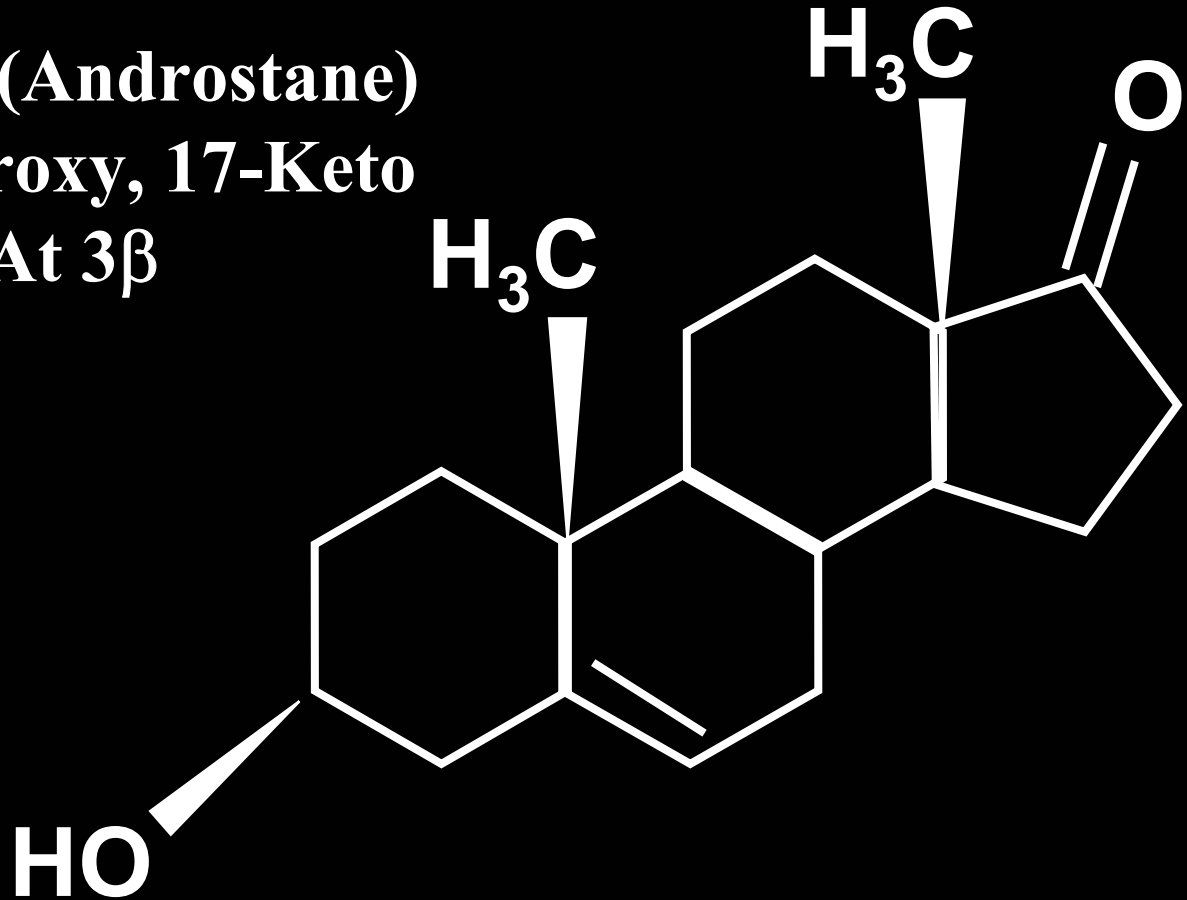


**Table 3.** Mean Concentrations of 19-Norandrosterone and 19-Noretiocholanolone After Oral Administration of 10 µg of 19-Norandrostenedione to 4 Subjects

Time, h	Concentration, Mean (Range), ng/mL	
	19-Norandrosterone	19-Noretiocholanolone
0-2	17.2 (2.8-48.9)	5.2 (1.1-16.7)
3-4	5.6 (4.4-7.6)	1.3 (0.6-1.9)
5-6	1.2 (0.6-1.7)	0.3 (0.1-0.3)
7-8	0.5 (0.1-0.8)	0.2 (0.1-0.3)

# DHEA

- 19-Carbon (Androstane)
- $-\Delta^5$ ,  $3\beta$ -Hydroxy, 17-Keto
- $-\text{SO}_4$ , 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 & 3 $\alpha$ ,5 $\alpha$ -Pathways

## Precursors

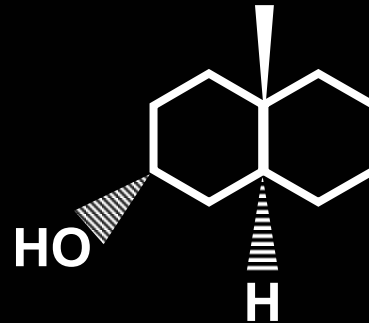
- Pregnenolone
- Progesterone

CYP17  
17 $\beta$ HSDIII  
5 $\alpha$ -Red-II

5 $\alpha$ -Red-I  
3 $\alpha$ HSDs  
CYP17/SLTase

## Androgens

- Testosterone
- Dihydrotestosterone



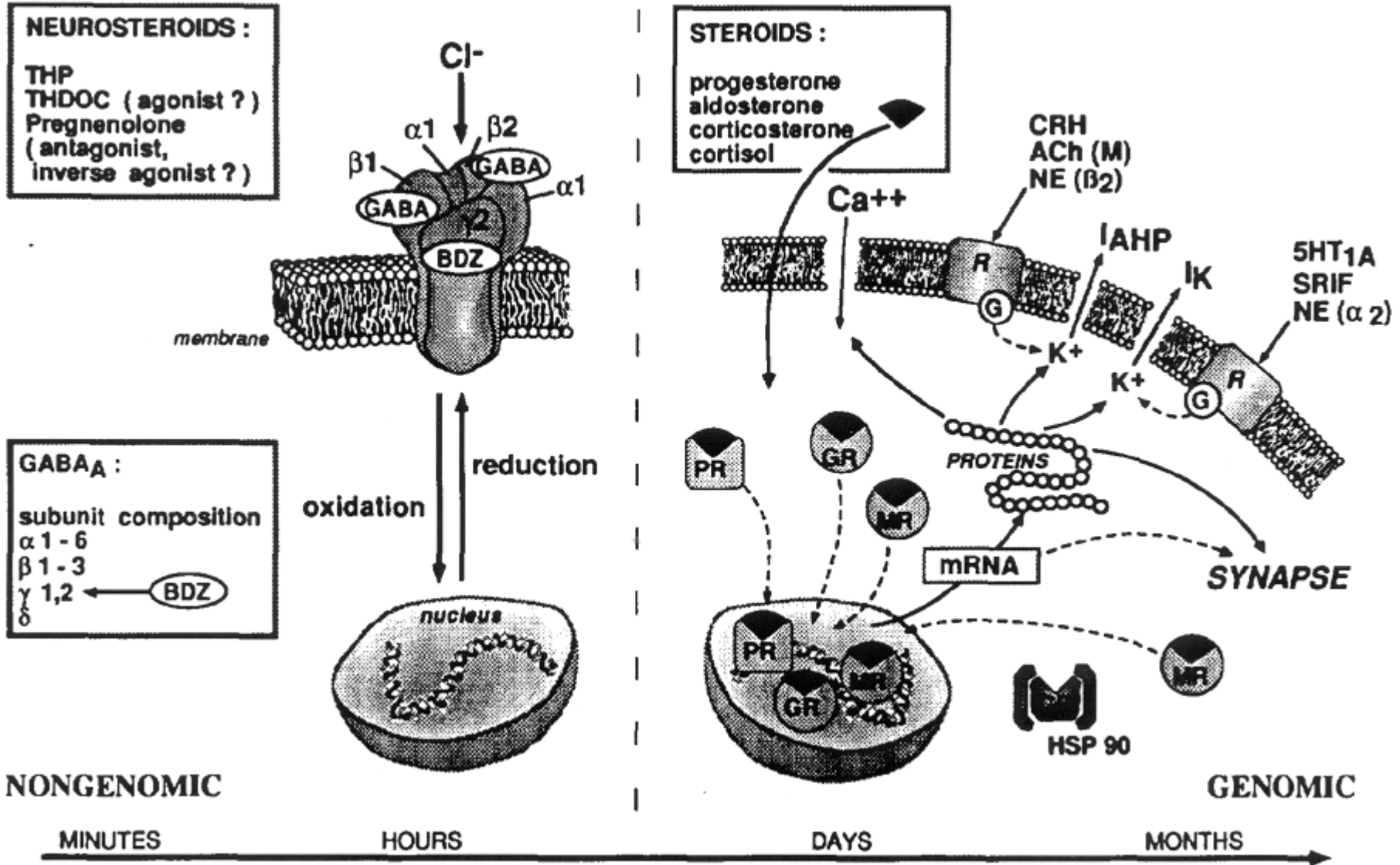
## Neurosteroids

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

Nuclear Hormone Receptor  
Genomic Actions

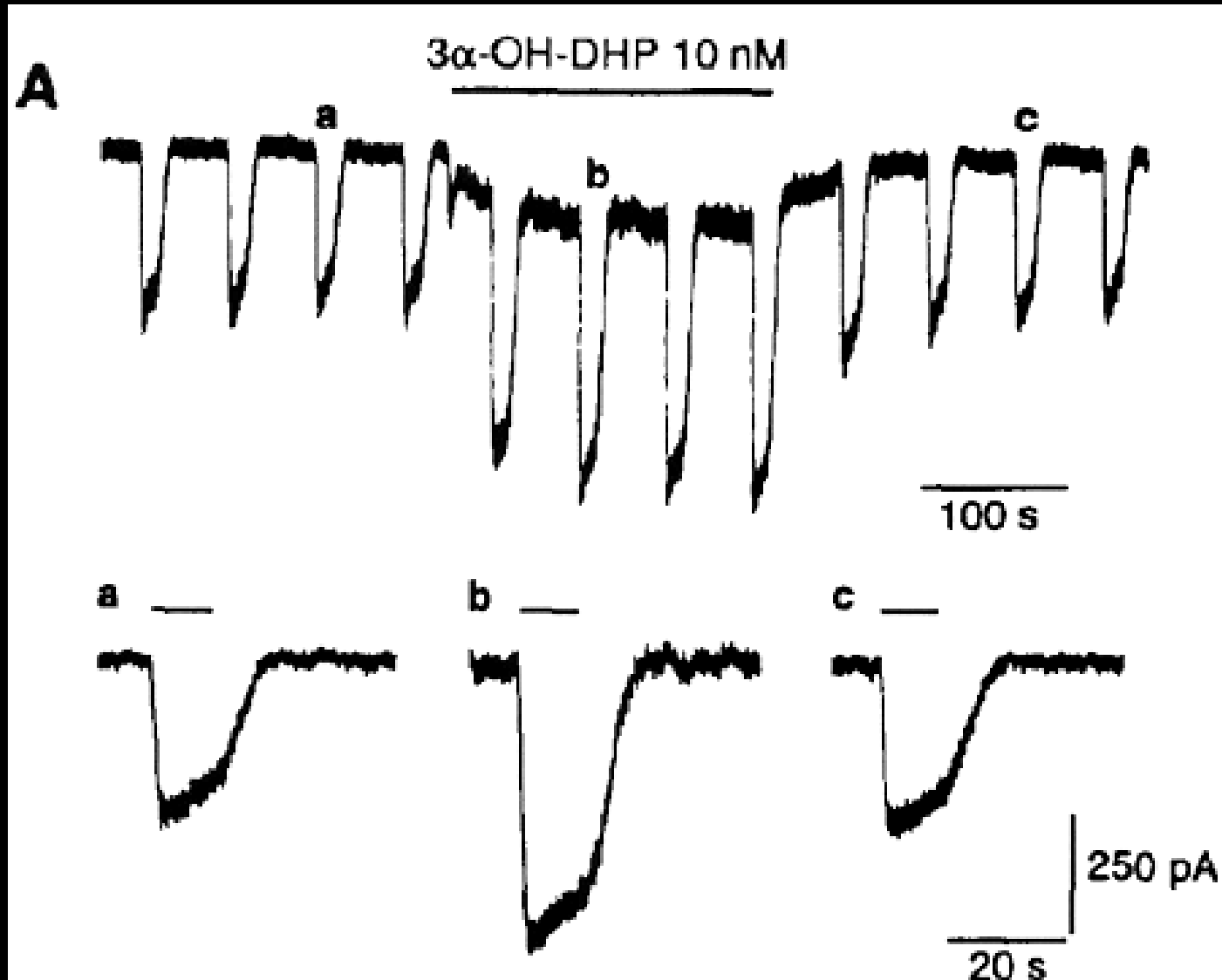
Ion Channels  
Non-Genomic Actions

# Steroid Hormone Action: Dichotomy?



# Allopregnanolone

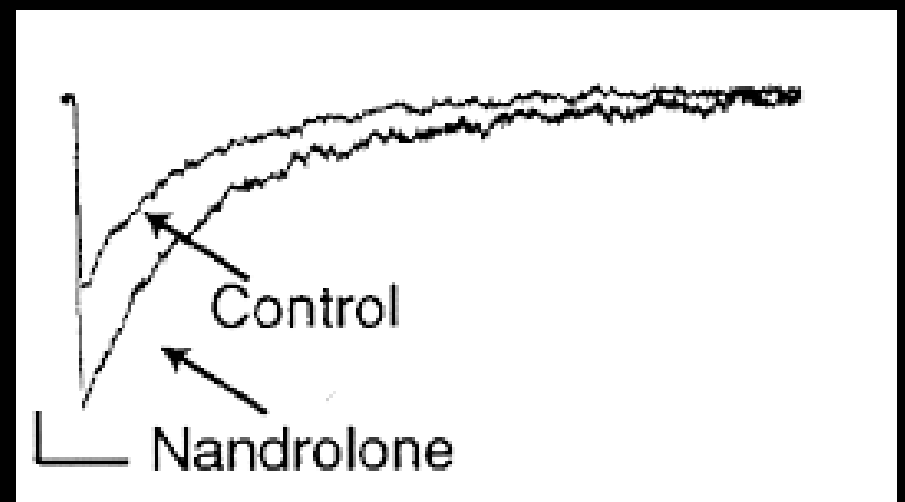
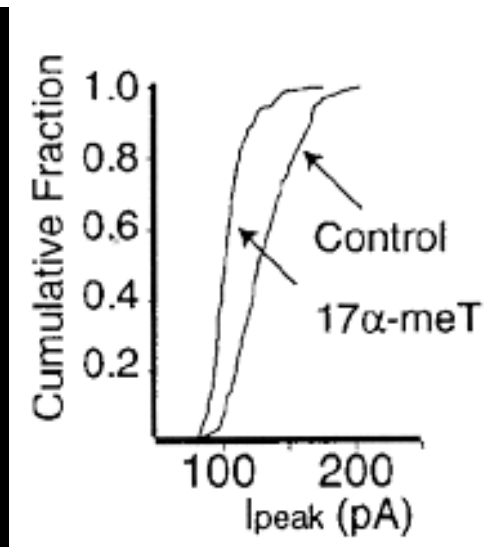
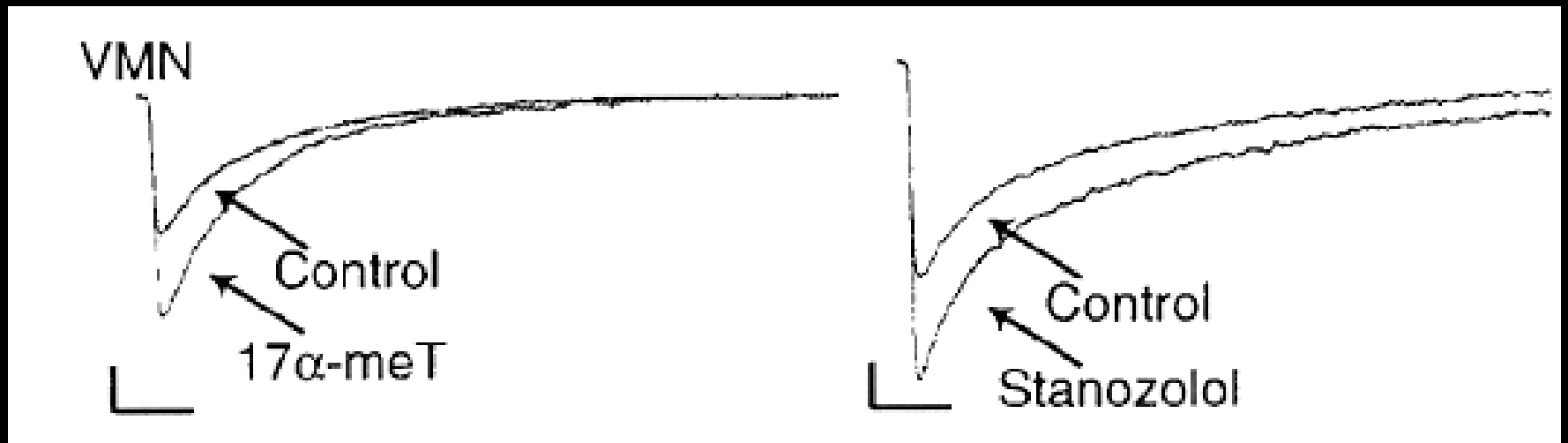
## Potentiation of GABA/Cl<sup>-</sup> Currents



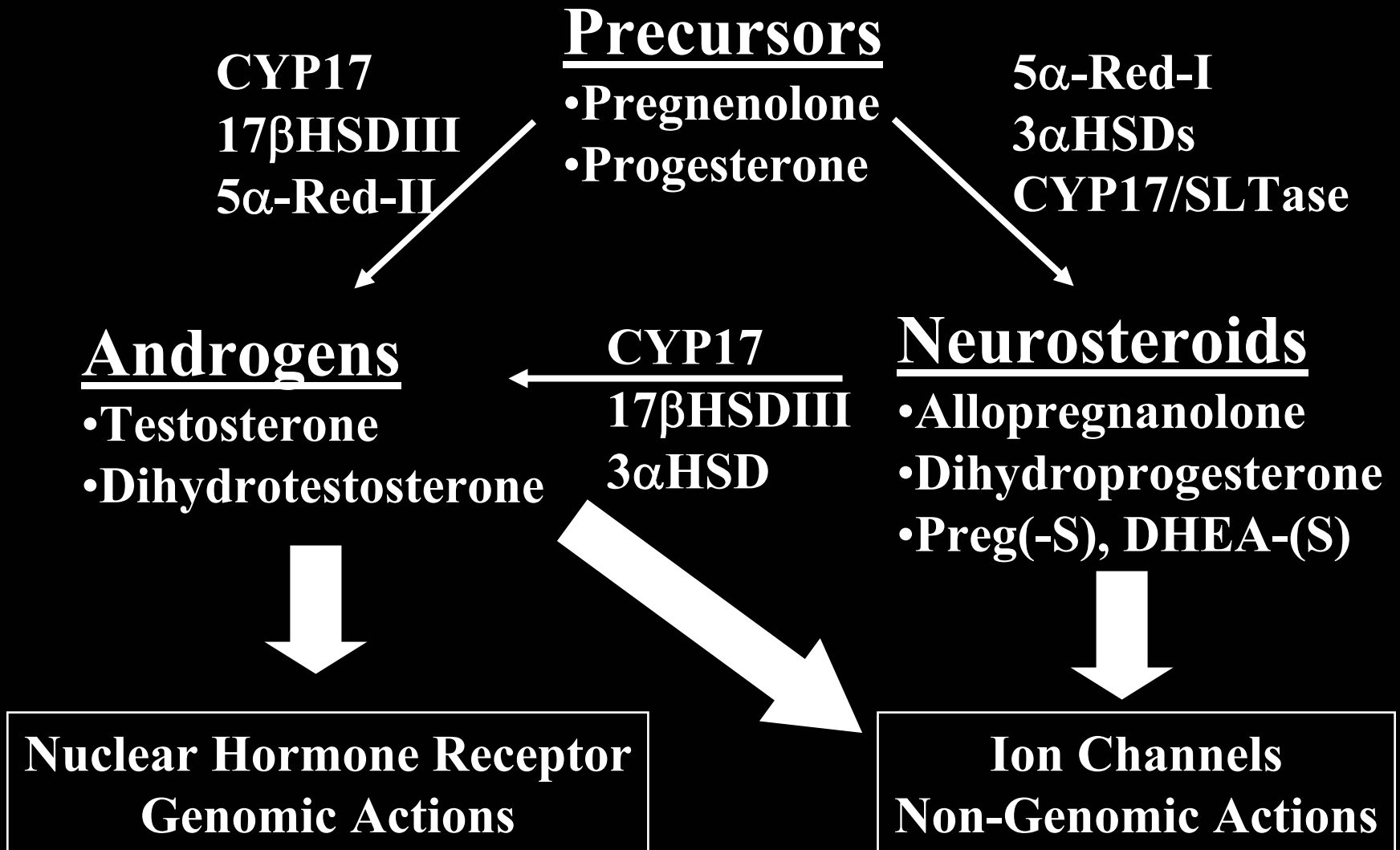


# Synthetic Androgens

## Potentialiation of GABA/Cl<sup>-</sup> Currents



# Neurosteroids & Androgens



# **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.”**