

Steroids & PEDs in Sports

THE DRUGS, THE MECHANISMS, THE PREVALENCE

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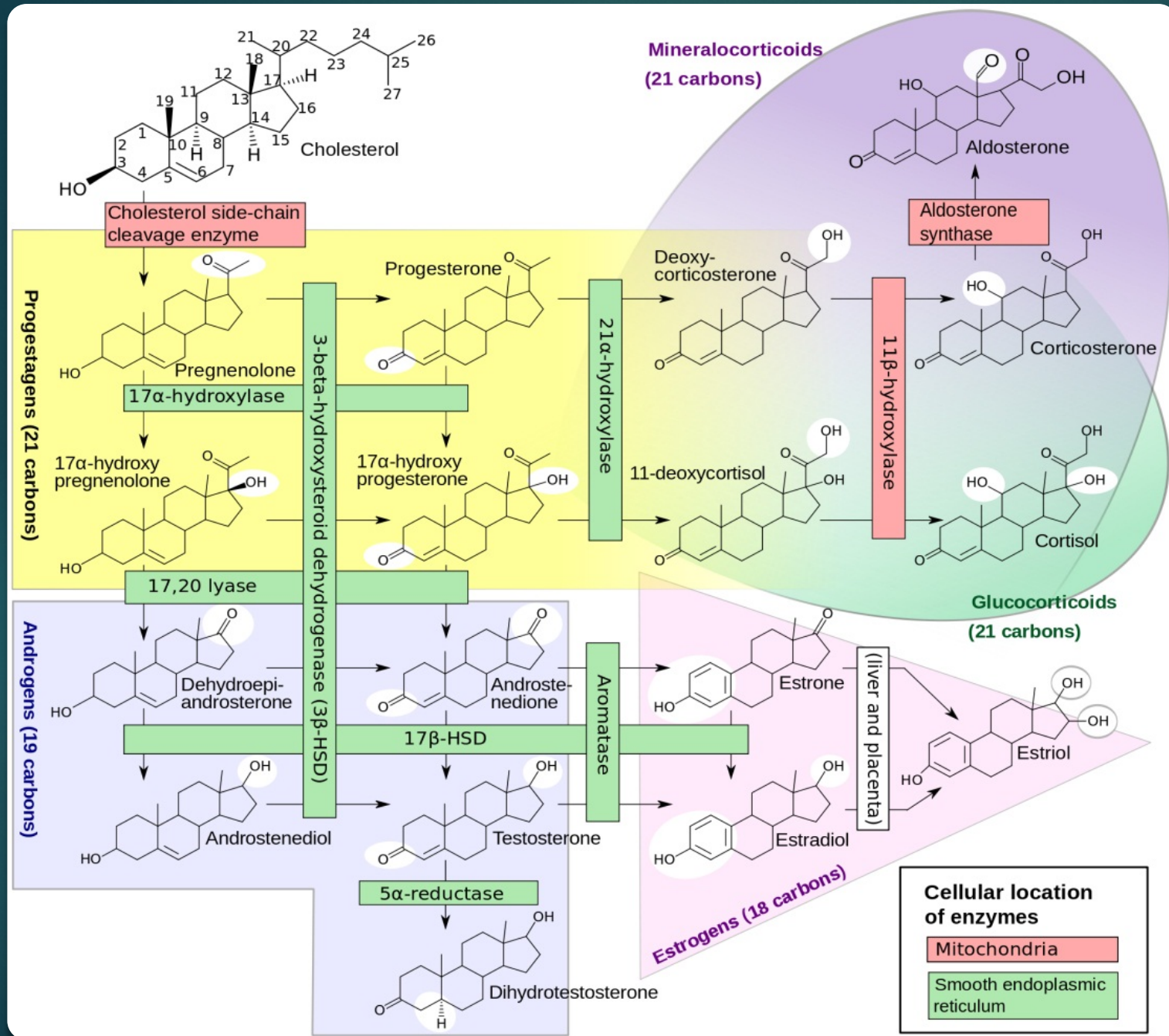
UHS SPORTS MEDICINE FOR THE AEC HEALTH & SAFETY SUMMIT



Disclosures : None

Overview of Presentation Topics

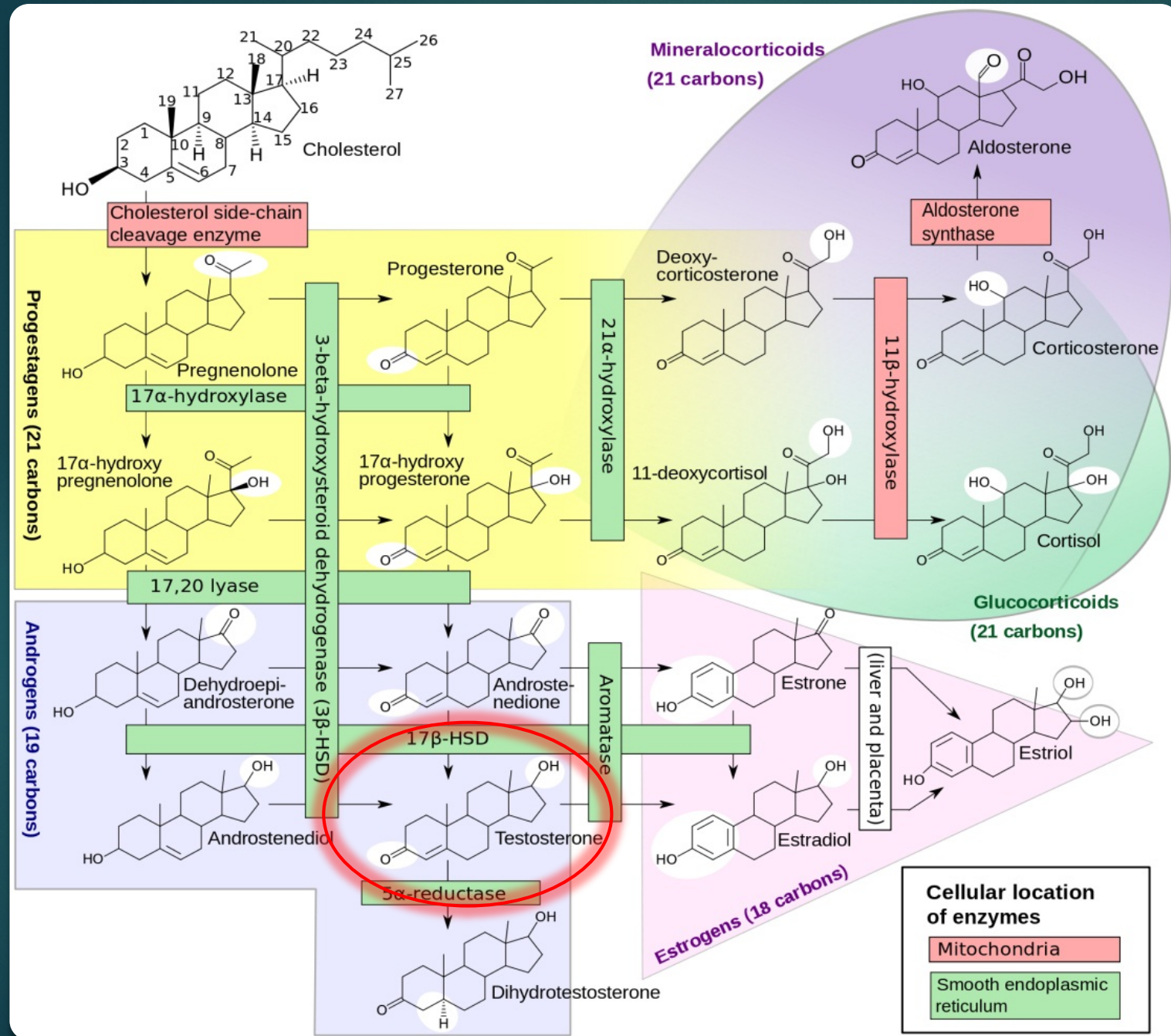
- ▶ Types of anabolic androgenic steroids (AAS)
- ▶ Side effects
- ▶ Detection
- ▶ Non-AAS hormonal PEDs and other PEDs
- ▶ Efficacy
- ▶ Therapeutic uses
- ▶ Incidence of use / abuse
- ▶ Why Care?



- ▶ Steroid synthesis starts with cholesterol
- ▶ Athletes benefit most from increasing testosterone and dihydrotestosterone
- ▶ Progestagens are intermediates
- ▶ Glucocorticoids and mineralocorticoids may have short-term benefits
- ▶ Estrogens cause many of the undesired side-effects

Steroidogenesis

Wikimedia Commons: steroidogenesis



Testosterone

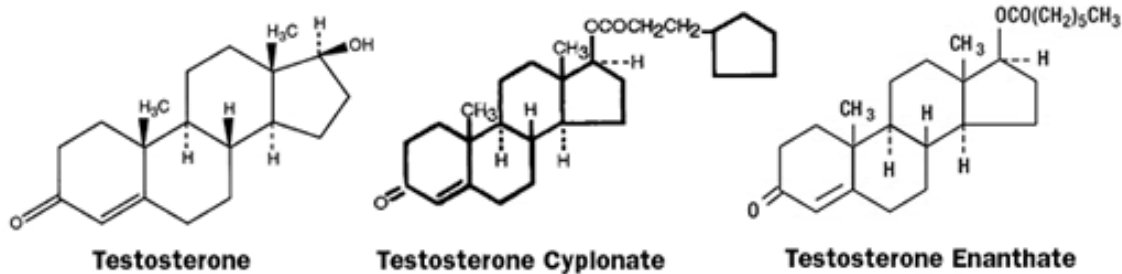
- All the same
- "Types" differ by attached ester

Testosterone analogs
Testosterone precursors
Pathway modifiers
Antiestrogens

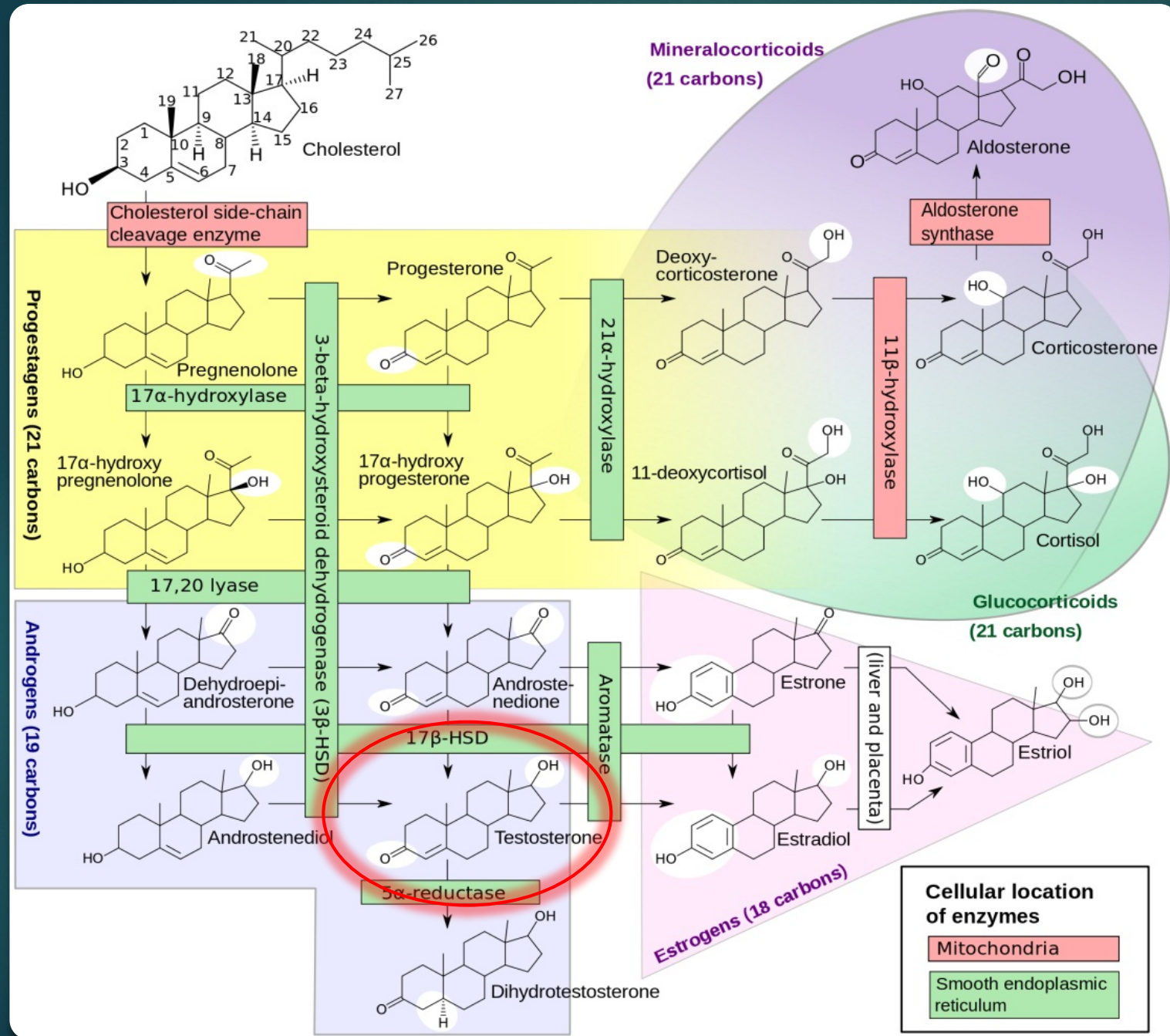
Steroidogenesis

Wikimedia Commons: steroidogenesis

Testosterone: Original and Best PED



- ▶ Effects
 - ▶ Increases strength & lean muscle mass
 - ▶ Reduces fat mass
 - ▶ Reduces recovery time
 - ▶ Increases RBC mass
- ▶ Testosterone is Testosterone: "Types" differ by the attached ester
 - ▶ Propionate, enanthate, cypionate, testosterone suspension, sustanon-250, omnadren
- ▶ Molecules with similar effects
 - ▶ Dihydrotestosterone
 - ▶ Testosterone analogs
 - ▶ Testosterone precursors
 - ▶ Steroidogenesis pathway modifiers / testosterone stimulants



Testosterone

Testosterone analogs

- stanozolol (Winstrol)
- nandrolone (Durabolin)
- tetrahydrogestrinone (the Clear)
- methandrostenolone (Dianabol)
- methasterone (Superdrol)

Testosterone precursors

Pathway modifiers

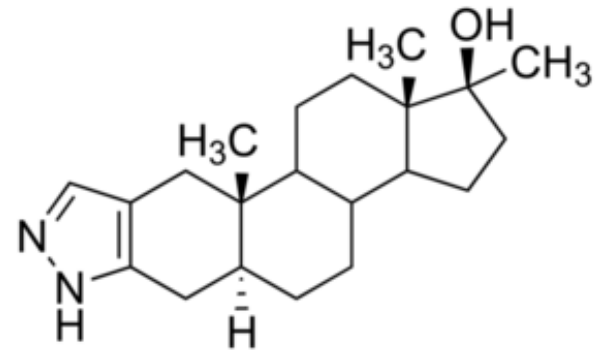
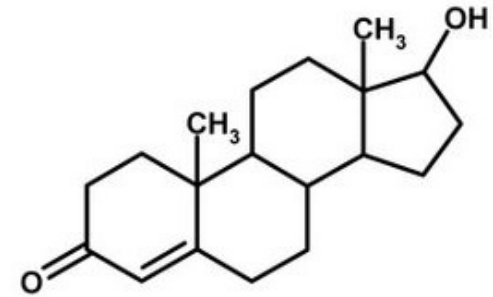
Antiestrogens

Steroidogenesis

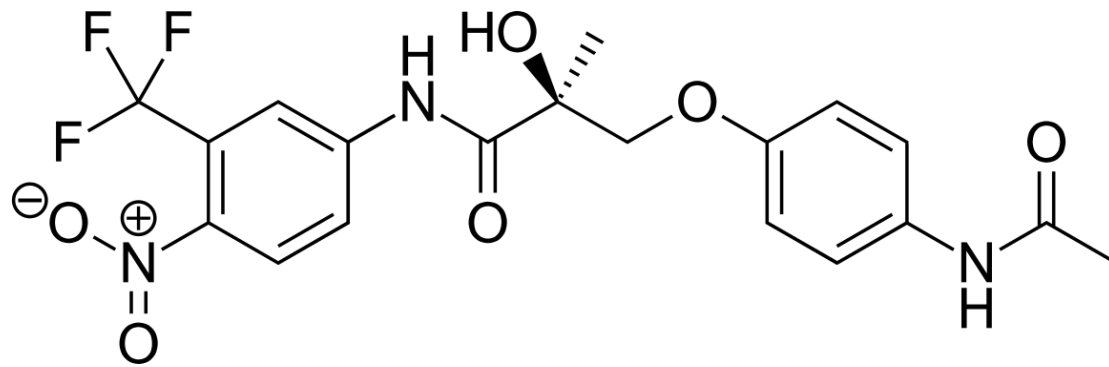
Wikimedia Commons: steroidogenesis

Testosterone Analogs 1

- ▶ Molecules with similar structure to testosterone
 - ▶ Testosterone esters are injected
 - ▶ Stanozolol (Winstrol) depot
 - ▶ Nandrolone (Durabolin, Deca-Durabolin, 19-nortestosterone)
 - ▶ Enanthate (Primobolan)
 - ▶ Cypionate
 - ▶ Trenbolone (Parabolan)
 - ▶ 17 α -alkylated androgens are usually taken orally
 - ▶ Methyltestosterone
 - ▶ Stanozolol (Winstrol)
 - ▶ Methandrostenolone (Danabol)
 - ▶ Methasterone (Superdrol)



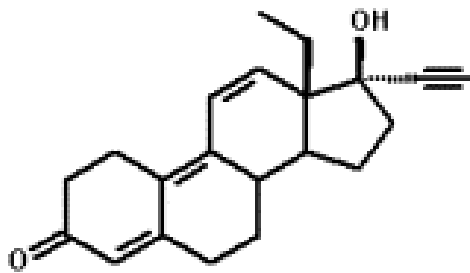
Testosterone Analogs 2



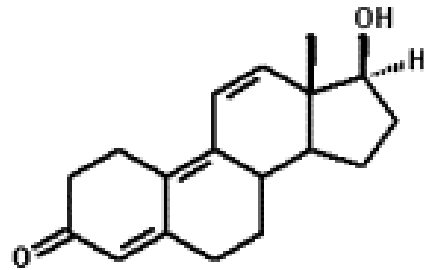
- ▶ Selective Androgen Receptor Molecules (SARMS)

- ▶ Andarine most well-known example
- ▶ Designed to have greater anabolic than androgenic effects
 - ▶ No clear evidence that any drug is anabolic without being androgenic
 - ▶ "Q-ratio" is the ratio of anabolic to androgenic effects

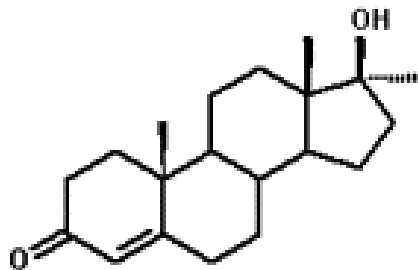
Testosterone Analogs 3



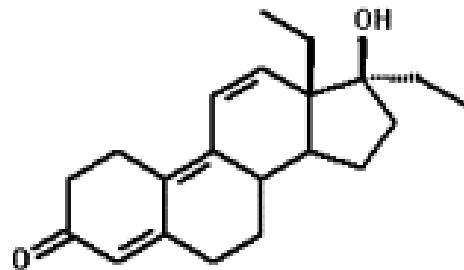
Gestrinone



Trenbolone



Methyltestosterone, ISTD



Tetrahydrogestrinone

- ▶ Designer steroids, designed to evade testing
 - ▶ No pharmacologic use, FDA regulation, or safety data
 - ▶ Poorly characterized, potentially dangerous
 - ▶ Tetrahydrogestrinone (The Clear) is best example
 - ▶ Highly potent per unit mass or volume
 - ▶ Acts on both testosterone and progesterone receptors
 - ▶ Based on the 1960's veterinary steroid trenbolone (Fina)
- ▶ Norboletone
 - ▶ In precursor to The Clear

Marion Jones, Jason Giambi, Barry Bonds



Implicated for transactions with Balco (Bay Area Laboratory Co-Operative), which supplied designer androgen tetrahydrogestrinone (the Clear)



Testosterone / Analogs Side Effects

In General

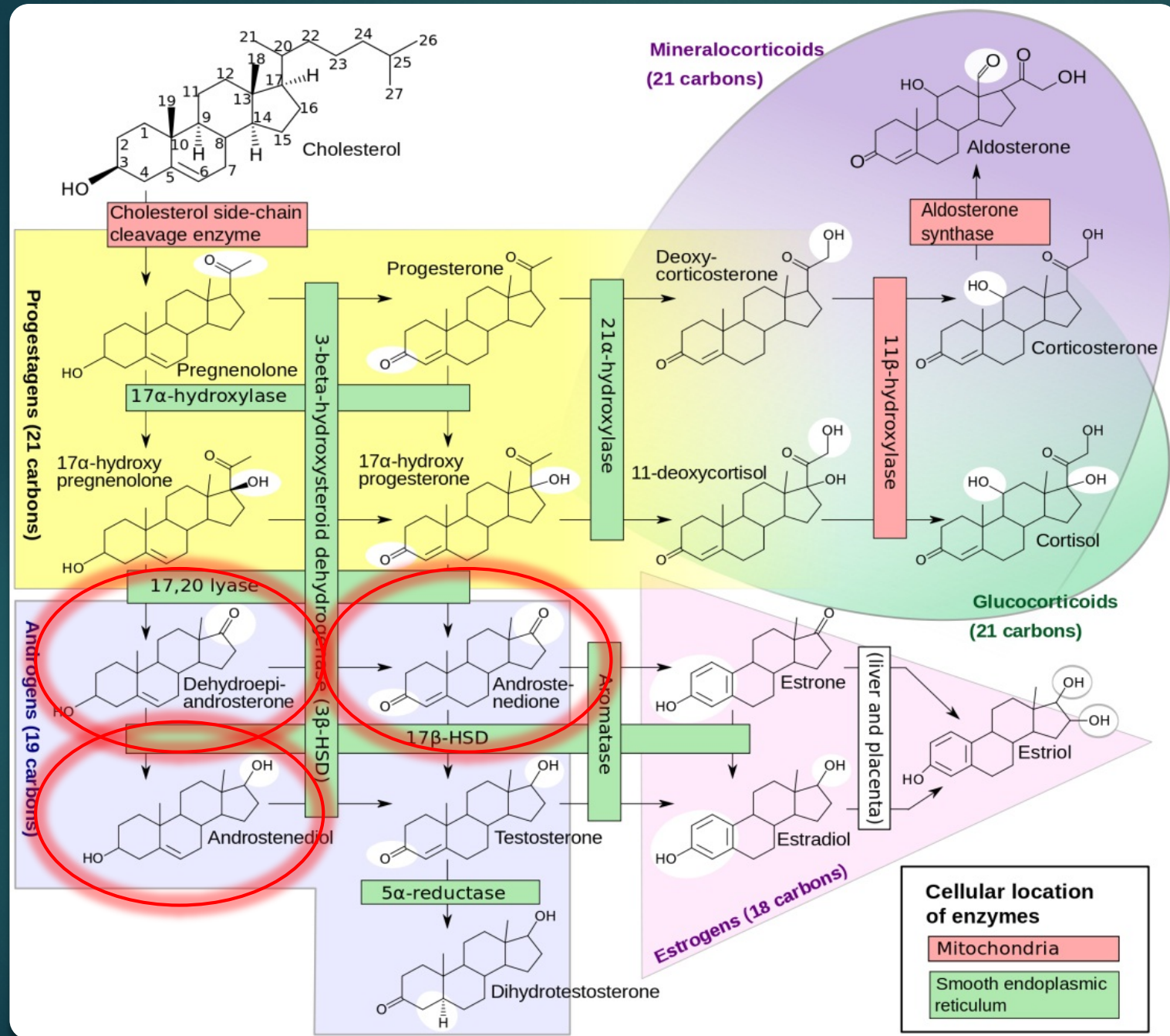
- ▶ Suppression of endogenous testosterone and gametogenesis, testicular atrophy
 - ▶ Usually recovers in 4 months
- ▶ Gynecomastia
- ▶ Premature physeal closure
- ▶ Left ventricular hypertrophy (data conflicting)
- ▶ Lower HDL, higher LDL (esp 17 α -alkylated)
- ▶ Hypertension
- ▶ Changes in concentrations of clotting factors, but unclear clinical import
- ▶roid rage in retrospective surveys, but not seen in controlled studies
- ▶ Erythrocytosis
- ▶ Hepatotoxicity
 - ▶ Abnormal LFTs, cholestasis, peliosis hepatis. Probably not hepatomas.
- ▶ Water retention
- ▶ Tendon rupture
 - ▶ Often biceps and triceps
- ▶ Infections from needle use
- ▶ ? Prostatic hypertrophy / cancer
 - ▶ Not seen at replacement doses but not studies at PED doses

Side Effects in Women

- ▶ Virilization
 - ▶ Hirsutism
 - ▶ Clitoromegaly
 - ▶ Male pattern baldness
 - ▶ Deepening of voice
- ▶ Acne
- ▶ Oligomenorrhea / amenorrhea
- ▶ Muscle dysmorphia

Detecting Testosterone & Analogs

- ▶ Analogs can be detected directly
- ▶ Testosterone
 - ▶ Testosterone glucuronide : epitestosterone glucuronide ratio (T/E ratio)
 - ▶ Ratio of ^{13}C to ^{12}C
 - ▶ Determined by gas chromatography
 - ▶ Exogenous testosterone made from plant sterols; have higher ^{12}C



Testosterone

Testosterone analogs

Testosterone precursors

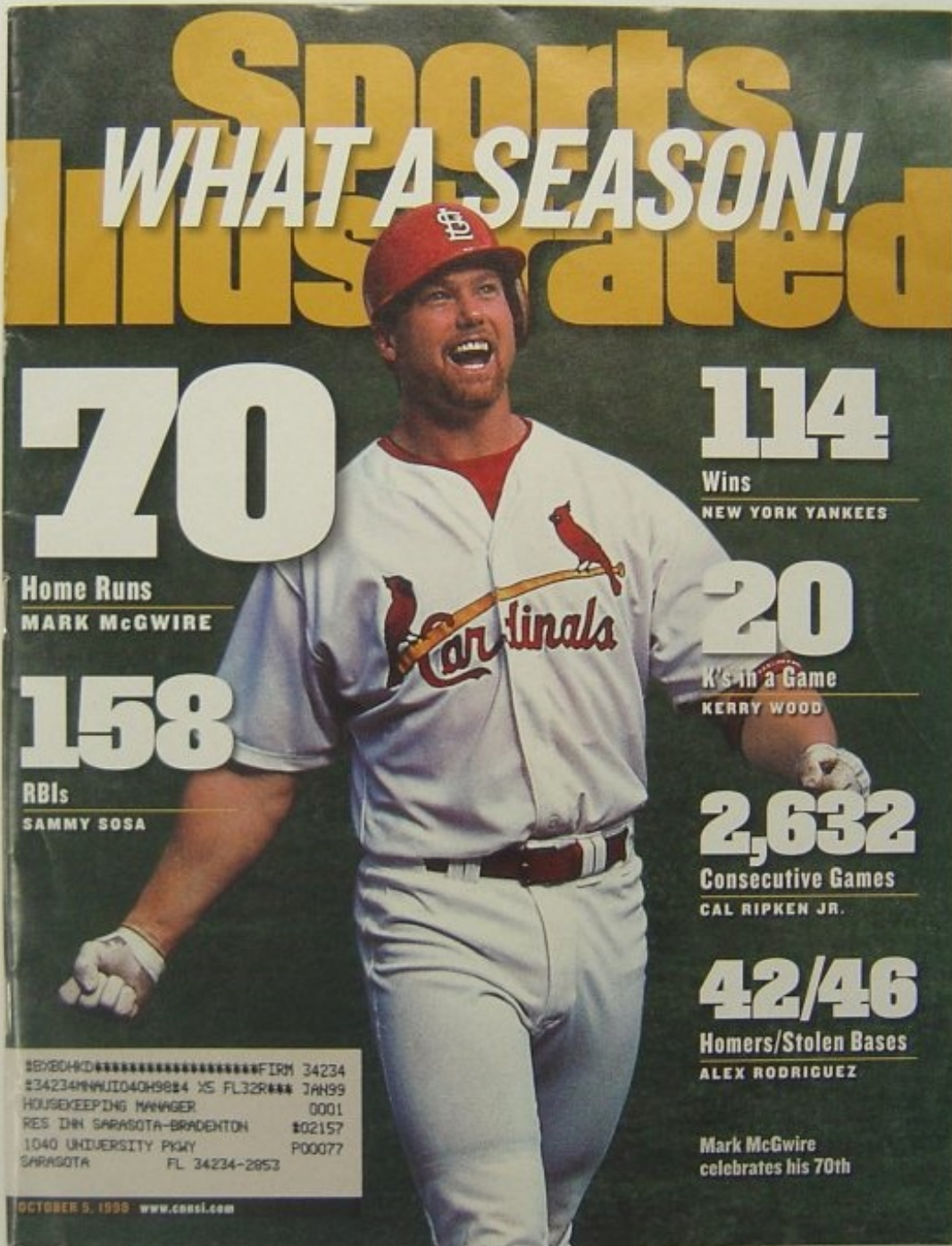
- Dehydroepiandrosterone (DHEA)
- Androstenedione
- Androstenediol

Pathway modifiers

Antiestrogens

Steroidogenesis

Wikimedia Commons: steroidogenesis



Mark McGwire

- ▶ Admitted to using androstenedione in 1998
- ▶ Same year he hit 70 home runs
- ▶ Androstenedione was legal in MLB until 2004

Going, going, gone.

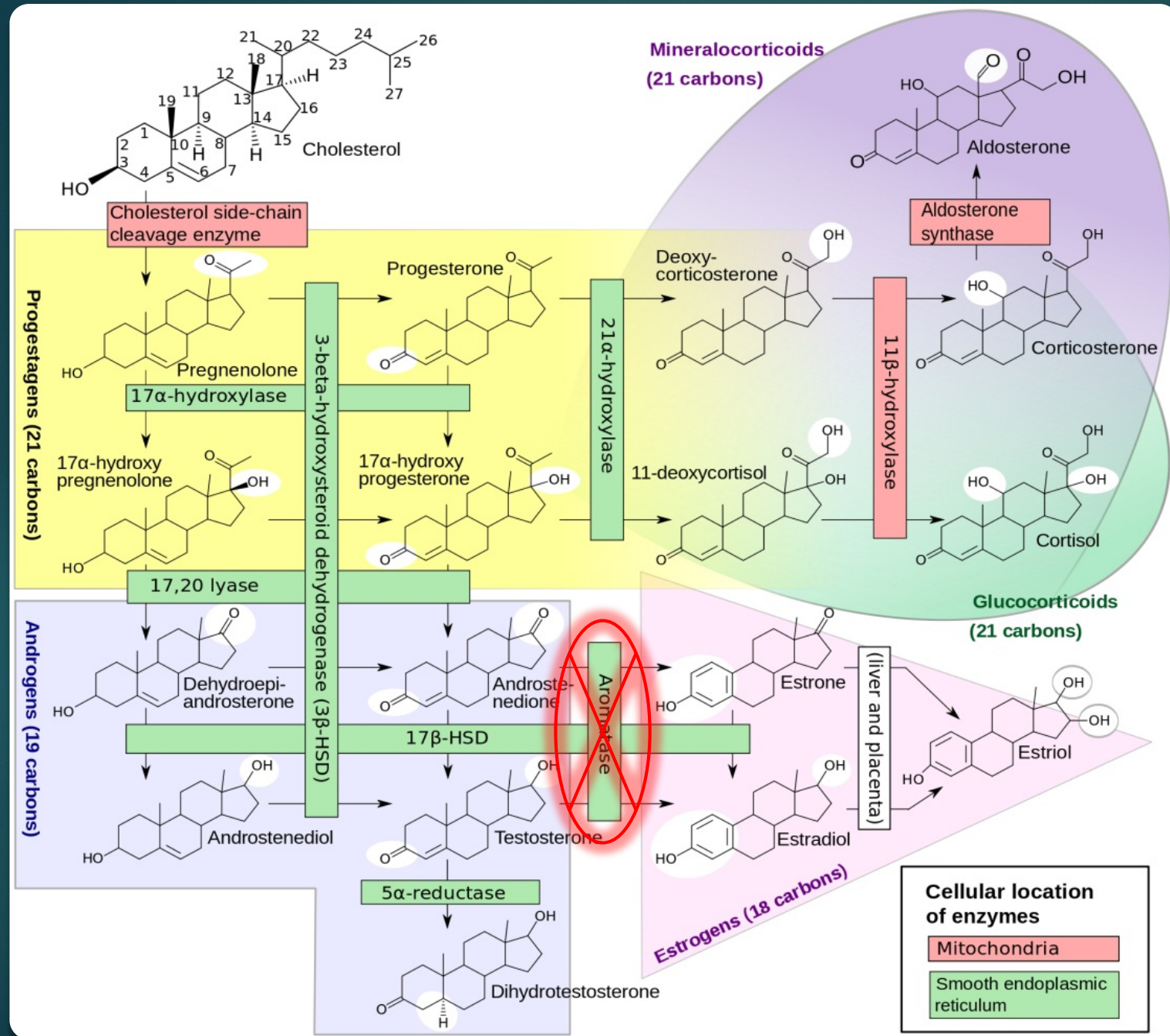
Time for more milk. It's got stuff leading sports drinks don't—like protein, potassium and calcium. That's why I always have an ice-cold glass... as soon as I get home.

got milk?

MARK MCGWIRE IS THE FIFTH MOST USED NAME IN AMERICAN FOOTBALL. MCGWIRE'S NAME IS USED IN 100% OF ALL FOOTBALL PLAYERS' NAMES. MCGWIRE IS THE MOST USED NAME IN FOOTBALL. MCGWIRE IS THE MOST USED NAME IN FOOTBALL.

Mark McGwire

- ▶ Admitted to using androstenedione in 1998
- ▶ In 2010 admitted to using steroids throughout his career



Testosterone
Testosterone analogs
Testosterone precursors

Pathway modifiers

Aromatase inhibitors

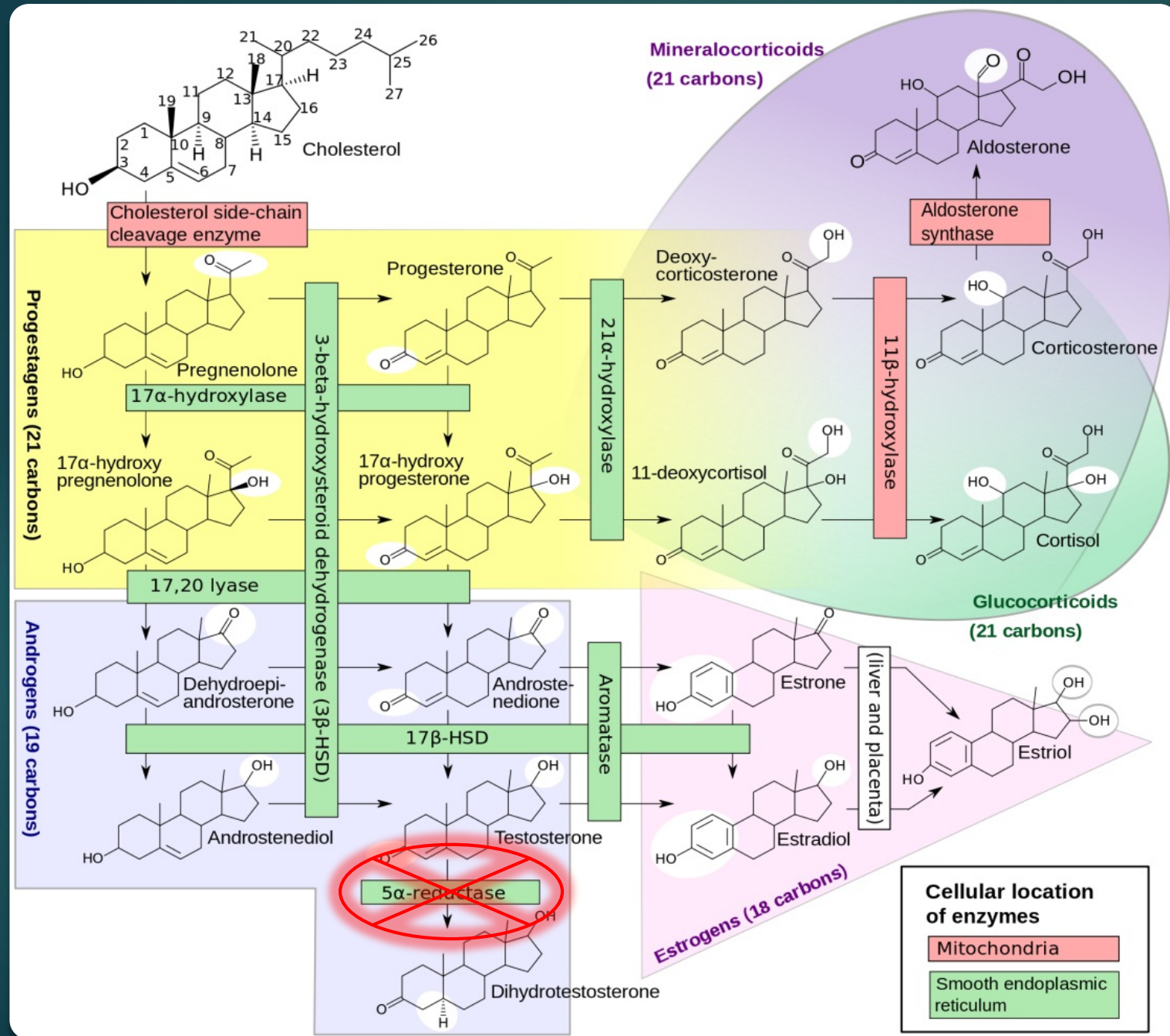
- exemestane
- anastrozole
- letrozole
- testolactone

5 α -reductase inhibitors

Antiestrogens

Steroidogenesis

Wikimedia Commons: steroidogenesis



Testosterone
 Testosterone analogs
 Testosterone precursors
Pathway modifiers
 Aromatase inhibitors
 5 α -reductase inhibitors
 • dutasteride
 • finasteride
 Antiestrogens

Steroidogenesis

Wikimedia Commons: steroidogenesis

How AAS Are Taken

- ▶ Route:
 - ▶ Injected or orally depending on type of drug
 - ▶ Testosterone esters injected
 - ▶ Alpha alkylated testosterone orally
- ▶ Timing:
 - ▶ Cycling
 - ▶ Changing the AAS regimen periodically to prevent acclimation, stagnation
 - ▶ Pyramiding
 - ▶ Gradually increasing the dose over time until peak effect is achieved
 - ▶ Then gradually tapering dose as competition approaches
- ▶ Combinations:
 - ▶ Stacking
 - ▶ Taking drugs in combination to increase effect
 - ▶ Average number of AAS stacked by athletes is 3.1

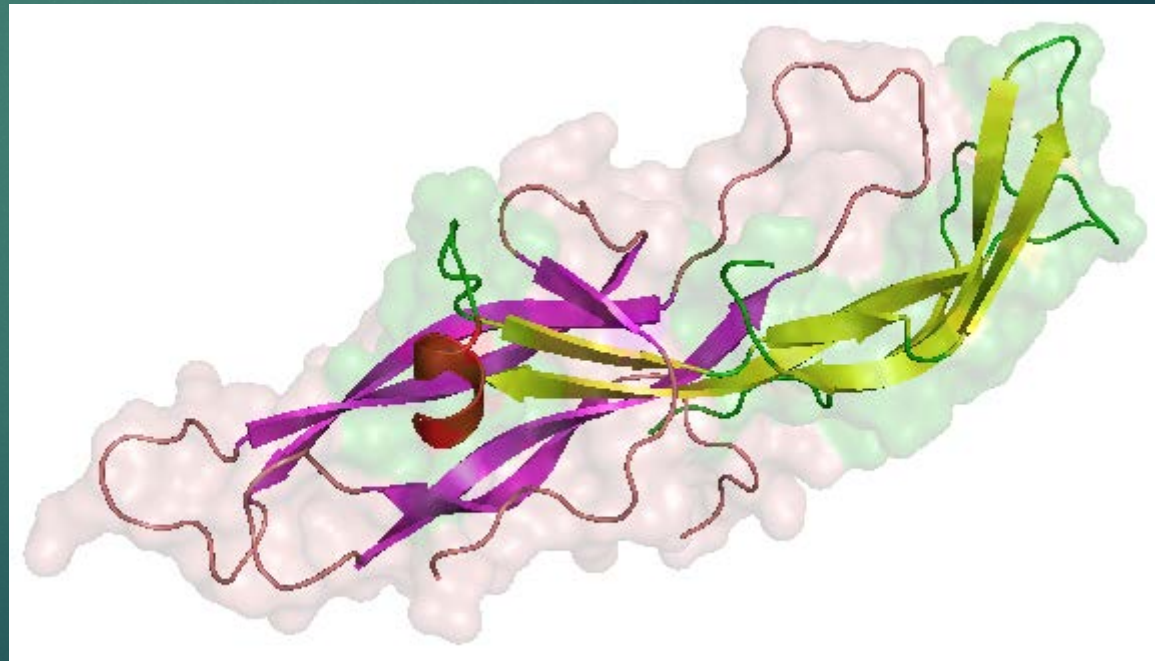
Human Chorionic Gonadotropin (HCG)

Function

- ▶ Agonizes luteinizing hormone receptors of Leydig cells
- ▶ Stimulates testosterone production
- ▶ Often used in testosterone supplementation off-cycle to prevent rapid muscle loss
- ▶ May kick-start endogenous testosterone production
 - ▶ Recommended not to prescribe for that purpose, since a banned substance in itself

Detection

- ▶ Urine test can quantify HCG
 - ▶ In females also detects pregnancy
 - ▶ In males also detects certain types of cancers





Manny Ramirez

SUSPENDED FOR 100 GAMES IN APRIL
2011 WHILE ON THE LA DODGERS FOR
HCG USAGE

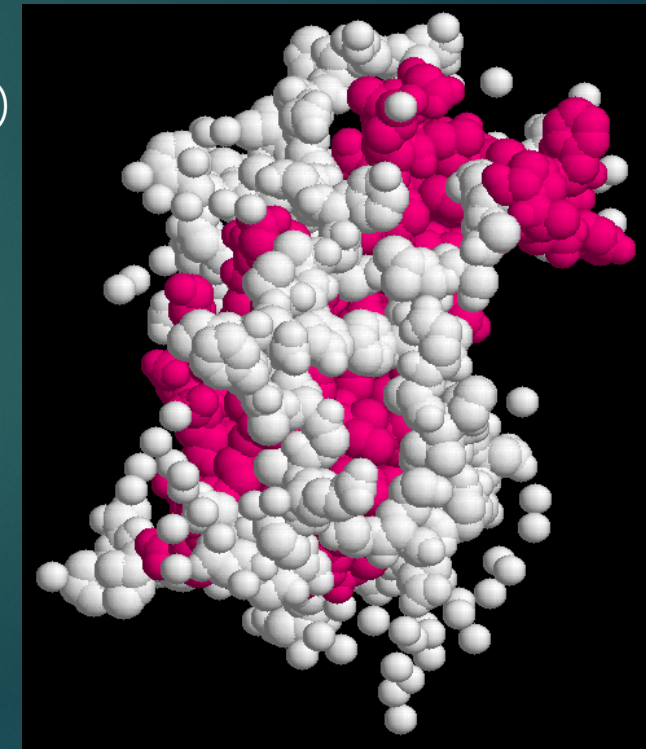
Growth Hormone

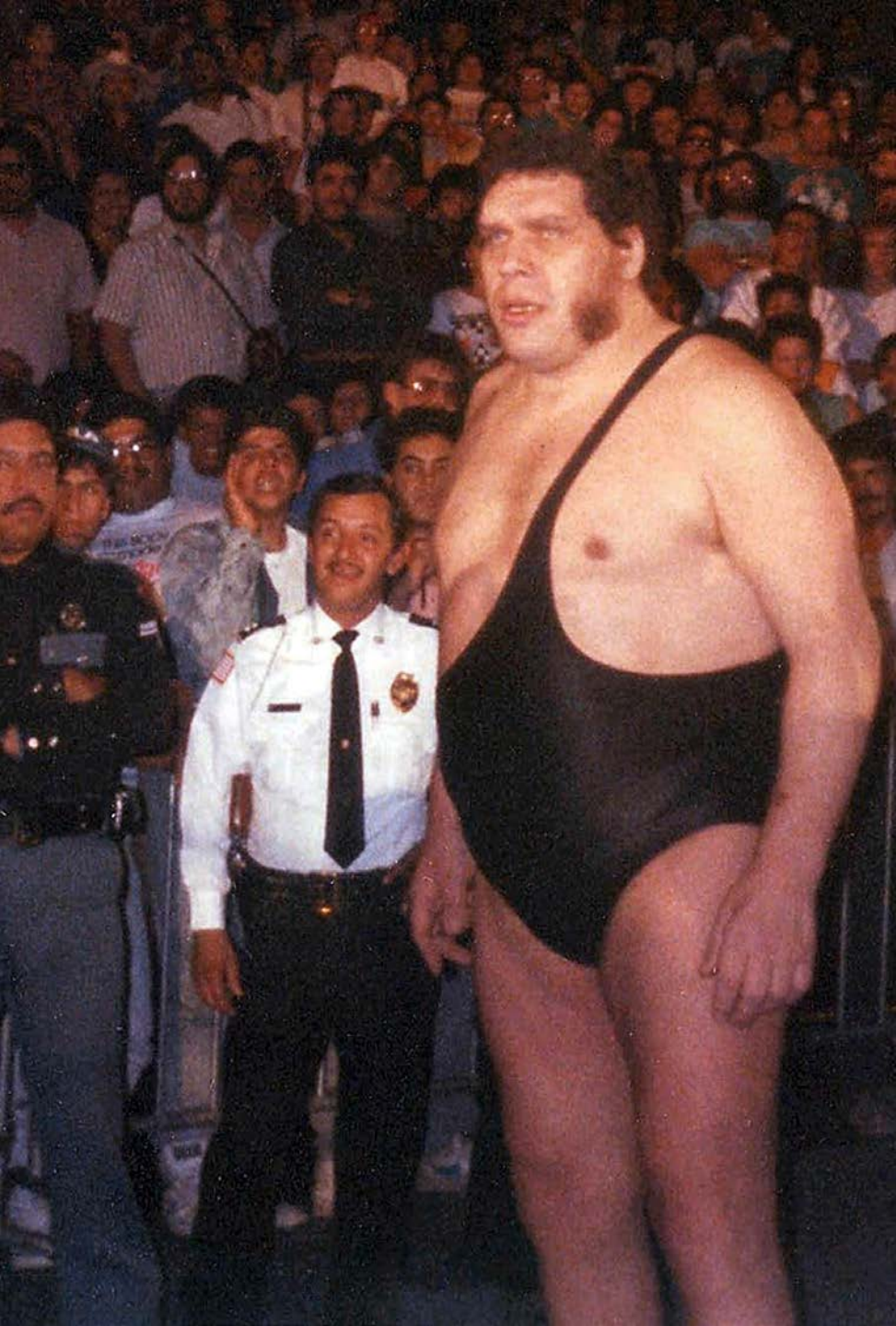
Use

- ▶ Benefits
 - ▶ Increases muscle mass
 - ▶ Decreases fat mass
 - ▶ Increases fat metabolism
 - ▶ To reduce atrophy in testosterone off-cycle
 - ▶ Liked for difficulty of detection
 - ▶ Thought to promote cartilage
- ▶ Insignificant benefit for strength
- ▶ Usually taken every other day in ~6 month cycles with 3-6 months off
- ▶ Usually taken in cocktails
- ▶ Increases IGF-1 production

Side-Effects

- ▶ Insulin resistance, hyperglycemia, diabetes
- ▶ Sodium retention, hypertension, cardiomegaly
- ▶ Physeal closure (in pediatrics)
- ▶ Myopathy
- ▶ Carpal tunnel syndrome
- ▶ Theoretical risk of
 - ▶ Acromegaly
 - ▶ Cancers including prostate





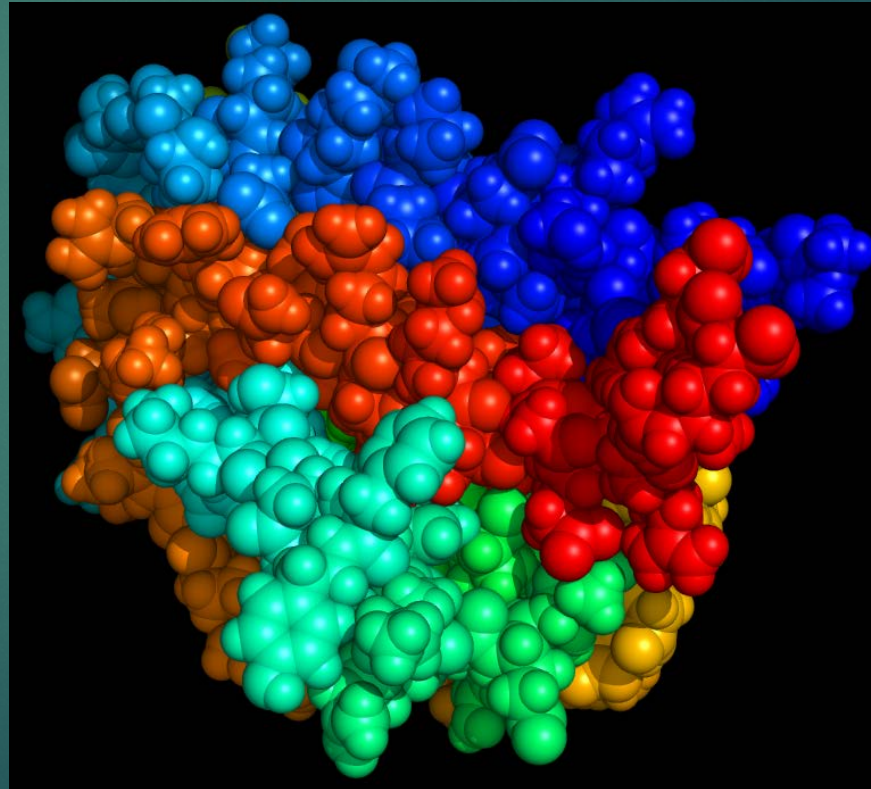
Erythropoietin

About

- ▶ AKA EPO, epoietin, darbepoietin, Procrit
- ▶ Stimulates hematopoiesis
- ▶ Increases hematocrit
 - ▶ Thus increases $\dot{V}O_2\text{max}$

Side-Effects

- ▶ Increases blood viscosity
- ▶ Associated with stroke





Team US Postal Service

- ▶ George Hincapie, Lance Armstrong (front)
- ▶ Implicated in EPO use by testimony of cyclists, not failed tests
- ▶ Armstrong stripped of 7 Tour de France titles
- ▶ From 1996-2010 only one Tour de France winner kept his medal (Carlos Sastre, 2008)



Fausto Coppi

Won Tour de France in 1949 and 1952

- ▶ Question: Do cyclists take la bomba (amphetamine)?
- ▶ Answer: Yes, and those who claim otherwise, it's not worth talking to them about cycling.
- ▶ Question: And you, did you take la bomba?
- ▶ Answer: Yes. Whenever it was necessary.
- ▶ Question: And when was it necessary?
- ▶ Answer: Almost all the time.

Other Drugs

- Stimulants / Thermogenics

- Caffeine
- Herbals
 - Red Bull, 5 Hour Energy, other drinks
- Amphetamines
 - ADHD drugs
 - Decongestants
 - Methylhexanamine (DMAA)
 - Ephedra (ma huang)
 - Dimethylamylamine / methylhexanamine
- Old fashioned
 - Strychnine
 - Nicotiny alcohol

- Catecholamine modifiers

- β -blockers/agonists
- α -blockers/agonists

- Diuretics & laxatives

- Weight loss, test evasion

- Analgesics

- All types
- Ketorolac big in NFL
- Superman effect

- Thermogenics

- Ephedrine
- 2,4-dinitrophenol (no antidote)

- Herbals

- Tongkat ali

- Masking drugs

Dangerous Drugs at Vitamin Stores

USA Today, 7/25/2013, "Sports supplement designer has history of risky products"

- **Craze sold at GNC, Walmart, Amazon, Bodybuilding.com among others**
 - USADA tests revealed it contains several amphetamines not on the label
 - 2012 Bodybuilding.com "Supplement of the Year"
- **Founder, Matt Cahill, investigated & jailed for previous supplements containing dinitrophenol (1990s) and 2 designer steroids (2000s)**
 - Dinitrophenol supplement
 - Caused blindness, deaths
 - Banned for human use in 1930s for causing blindness
 - Designer steroids
 - Posed as landscaping company to purchase pesticide from China
 - Never tested on humans
 - Sold as sports supplement
 - Caused hepatic failure, death
- **Amy Eichner of USADA: "players like Matt Cahill are ubiquitous in supplement industry"**

Signs of Use

Physical

- Rapid performance gains
- Rapid size / muscularity increases
- Hypermuscularity
- Tendinopathies, ruptures
- Virilization (more females)
- Acne
- Gaining >20 lbs/year lean bodyweight

Behavioral

- Secretive actions
- High dietary supplement interest / use
- Physique or diet obsession
- Other high-risk behaviors
- Cavalier attitude about supplements
- Using the lingo: "stacks," "cycles," names of PEDs



Elite Natural Bodybuilder:
Rob Riches: 5'10, 180 lbs

Would not counsel
that you can get
the same results
with hard work.

Natural bodybuilding
restricts certain PEDs

Professional
bodybuilding does not
restrict PED use



Elite Professional Bodybuilder:
Jay Cutler: 5'9, 310 lbs

Incidence of Doping, NCAA Report

- ▶ NCAA 2005, 2009, 2013, (2017) Substance Use Reports
 - ▶ “Anonymous” survey of 20,474 athletes (2009 version) from stratified random sample of all NCAA schools
 - ▶ All schools asked to participate (2013)
 - ▶ Results have consistently indicated
 - ▶ Very low incidence of PED use
 - ▶ Declining rates of PED use
- ▶ Validity?

NCAA Report (2013)

- ▶ Overall doping reported as rare, decreasing
- ▶ Similar across divisions I, II, III

PATTERNS OF ERGOGENIC DRUG USE OVERALL AND BY DIVISION

OVERALL PERCENTAGE OF USE WITHIN LAST 12 MONTHS												
Division	Division I			Division II			Division III			Overall		
Year	2005	2009	2013	2005	2009	2013	2005	2009	2013	2005	2009	2013
Amphetamines	4.0%	3.7%	4.2%	3.7%	3.2%	3.9%	4.6%	4.1%	5.7%	4.2%	3.7%	4.7%
Anabolic Steroids	1.1%	0.4%	0.3%	1.3%	0.4%	0.7%	1.0%	0.5%	0.5%	1.1%	0.4%	0.5%
Ephedrine	NA	1.1%	0.4%	NA	0.9%	0.4%	NA	0.9%	0.6%	NA	0.9%	0.5%

NCAA Report (2013)

- Steroid use several times more common in males

PATTERNS OF ERGOGENIC DRUG USE BY SEX

OVERALL PERCENTAGE OF USE WITHIN LAST 12 MONTHS						
Sex	Female			Male		
Year	2005	2009	2013	2005	2009	2013
Amphetamines	3.7%	3.3%	3.7%	4.5%	4.0%	5.3%
Anabolic Steroids	0.3%	0.2%	0.1%	1.7%	0.5%	0.7%
Ephedrine	NA	0.9%	0.4%	NA	0.9%	0.5%

NCAA Report (2013)

- Comparison across different sports

PATTERNS OF ERGOGENIC DRUG USE BY MEN'S SPORTS

OVERALL PERCENTAGE OF USE WITHIN LAST 12 MONTHS												
Substance	Year	Baseball	Basketball	Football	Golf	Ice Hockey	Lacrosse	Soccer	Swimming	Tennis	Track	Wrestling
Amphetamines	2005	4.0%	1.9%	4.0%	4.5%	NA	14.4%	5.3%	3.6%	3.8%	2.6%	7.3%
	2009	4.2%	1.8%	3.9%	3.2%	NA	12.2%	4.3%	3.9%	3.5%	1.4%	7.6%
	2013	7.7%	2.2%	3.9%	5.3%	7.3%	11.9%	6.1%	6.9%	2.9%	2.4%	12.6%
Anabolic Steroids	2005	2.1%	1.6%	2.4%	1.1%	NA	1.5%	0.9%	0.8%	0.0%	0.8%	2.1%
	2009	0.6%	0.2%	0.8%	0.9%	NA	1.1%	0.2%	0.0%	0.6%	0.4%	0.0%
	2013	0.8%	0.4%	0.9%	0.2%	1.1%	0.7%	1.2%	0.1%	0.0%	0.3%	0.3%
Ephedrine	2005	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	2009	1.0%	0.6%	1.2%	0.6%	NA	2.3%	0.2%	0.9%	0.2%	0.8%	0.8%
	2013	0.2%	0.4%	0.6%	0.4%	2.2%	1.2%	0.9%	0.6%	0.4%	0.3%	0.1%

Different Results with a Different Survey Method

- ▶ NY Times reported unpublished study of >2000 track & field athletes
 - ▶ Anonymously asked: "Have you knowingly violated anti-doping regulations by using a prohibited substance or method in the past 12 months?"
 - ▶ Used "randomized response" so athletes knew response was anonymous
 - ▶ Yes from 29% of athletes at 2011 world championships
 - ▶ Yes from 45% of athletes at Pan-Arab Games
 - ▶ <2% of WADA drug tests in 2010 were positive
 - ▶ WADA told researchers not to publish their data
- ▶ Sport governing bodies, national organizations, teams often have no incentive or disincentive to catch dopers


Why Care At All?

- ▶ To protect the safety of the participants in sport
- ▶ To prevent coercive environment in which athletes must dope to compete at all
- ▶ To support good role models

Turning a blind eye to doping does not level the playing field – it just allows different people to win.

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Thank you
Questions?