S1

S1 ANABOLIC AGENTS

- 1. ANABOLIC ANDROGENIC STEROIDS (AAS)
- a. Exogenous* AAS
- b. Endogenous** AAS

2. OTHER ANABOLIC AGENTS

- For purposes of this section:
- An **androgen** is any natural or synthetic steroid hormone that regulates the development and maintenance of male characteristics in vertebrates by binding to androgen receptors.
- * " exogenous" refers to a substance which is not ordinarily produced by the body naturally.
- ** " endogenous" refers to a substance which is ordinarily produced by the body naturally.

Exogenous AAS

- 1-Androstenediol (5α -androst-1-ene- 3β ,17 β -diol);
- 1-Androstenedione (5α-androst-1-ene-3,17-dione);
- 1-Androsterone (3α-hydroxy-5αandrost-1-ene-17-one);
- 1-Testosterone (17β-hydroxy-5α-androst-1-en-3-one);
- 4-Hydroxytestosterone (4,17βdihydroxyandrost-4-en-3- one);
- Bolandiol (estr-4-ene-3β,17β-diol);
- Bolasterone;
- Calusterone;
- Clostebol;
- Danazol ([1,2]oxazolo[4',5':2,3]pregna-4-en-20-yn-17α-ol);

- Dehydrochlormethyltestosterone (4-chloro-17 β -hydroxy- 17 α -methylandrosta-1,4-dien-3-one);
- Desoxymethyltestosterone (17 α -methyl-5 α -androst-2-en-17 β -ol);
- Drostanolone;
- Ethylestrenol (19-norpregna-4-en-17αol);
- Fluoxymesterone;
- Formebolone;
- Furazabol (17 α -methyl [1,2,5] oxadiazolo [3',4':2,3]-5 α androstan-17 β -ol);
- Gestrinone;

Exogenous AAS

- Mestanolone;
- Mesterolone;
- Metandienone (17β-hydroxy-17αmethylandrosta-1,4-dien- 3-one);
- Metenolone;
- Methandriol;
- Methasterone (17 β -hydroxy-2 α ,17 α -dimethyl-5 α -androstan-3-one);
- Methyldienolone (17β-hydroxy-17α-methylestra-4,9-dien- 3-one);
- Methyl-1-testosterone (17 β -hydroxy-17 α -methyl-5 α androst-1-en-3-one);
- Methylnortestosterone (17 β -hydroxy-17 α -methylestr-4-en-3-one);

- Methyltestosterone;
- Metribolone (methyltrienolone, 17β -hydroxy- 17α methylestra-4,9,11-trien-3-one);
- Mibolerone;
- Norboletone;
- Norclostebol;
- Norethandrolone;
- Oxabolone;
- Oxandrolone;
- Oxymesterone;
- Oxymetholone;
- Prostanozol (17β-[(tetrahydropyran-2-yl)oxy]- 'Hpyrazolo[3,4:2,3]-5α-androstane);

Exogenous AAS

- Quinbolone;
- **S**tanozolol;
- Stenbolone;
- **T**etrahydrogestrinone (17-hydroxy-18a-homo-19-nor-17α- pregna-4,9,11trien-3-one);
- Trenbolone (17β-hydroxyestr-4,9,11-trien-3-one);

 and other substances with a similar chemical structure or similar biological effect(s).

Endogenous AAS when administered exogenously

- **19-N**orandrostenediol (estr-4-ene-3,17-diol);
- 19-Norandrostenedione (estr-4-ene-3,17-dione);
- Androstanolone (5α -dihydrotestosterone, 17β -hydroxy- 5α -androstan-3-one);
- Androstenediol (androst-5-ene- 3β ,17 β -diol);
- Androstenedione (androst-4-ene-3,17dione);
- **B**oldenone;
- Boldione (androsta-1,4-diene-3,17-dione);
- Nandrolone (19-nortestosterone);

- Prasterone (dehydroepiandrosterone, DHEA, 3β-hydroxyandrost-5-en-17-one);
- Testosterone;
- and their metabolites and isomers, including but not limited to:
- 3β -Hydroxy- 5α -androstan-17-one;
- 5α-Androst-2-ene-17-one;
- 5α -Androstane- 3α , 17α -diol;
- 5α -Androstane- 3α , 17β -diol;
- 5α -Androstane- 3β , 17α -diol;
- 5α -Androstane- 3β , 17β -diol;
- 5β -Androstane- 3α , 17β -diol;

Endogenous AAS when administered exogenously

- 7α-Hydroxy-DHEA;
- 7β-Hydroxy-DHEA;
- 4-Androstenediol (androst-4-ene-3β, 17β-diol);
- 5-Androstenedione (androst-5-ene-3,17-dione);
- 7-Keto-DHEA;
- 19-Norandrosterone;
- 19-Noretiocholanolone;
- Androst-4-ene-3 α ,17 α -diol;
- Androst-4-ene-3α,17β-diol;
- Androst-4-ene-3β,17α-diol;
- Androst-5-ene- 3α , 17α -diol;

- Androst-5-ene-3α,17β-diol;
- Androst-5-ene-3β,17α-diol;
- Androsterone;
- Epi-dihydrotestosterone;
- Epitestosterone;
- Etiocholanolone.

Endogenous AAS when administered exogenously

- 7α-Hydroxy-DHEA;
- 7β-Hydroxy-DHEA;
- 4-Androstenediol (androst-4-ene-3β, 17β-diol);
- 5-Androstenedione (androst-5-ene-3,17-dione);
- 7-Keto-DHEA;
- 19-Norandrosterone;
- 19-Noretiocholanolone;
- Androst-4-ene-3 α ,17 α -diol;
- Androst-4-ene-3α,17β-diol;
- Androst-4-ene-3β,17α-diol;
- Androst-5-ene- 3α , 17α -diol;

- Androst-5-ene-3α,17β-diol;
- Androst-5-ene-3β,17α-diol;
- Androsterone;
- Epi-dihydrotestosterone;
- Epitestosterone;
- Etiocholanolone.

OTHER ANABOLIC AGENTS

Including, but not limited to:

- Clenbuterol
- selective androgen receptor modulators (SARMs, e.g. andarine, LGD-4033 ostarine and RAD140)
- tibolone
- zeranol and zilpaterol

كلنبوترول

- می تواند باعث افزایش سرعت متابولیسم و چربی سوزی، تنفس بهتر و تحریک سنتز پروتئین در عضلات شود.
- می تواند باعث افزایش ناگهانی فشار خون شود. همین امر می تواند باعث افزایش احتمال بروز هایپرتروفی بطن چپ شود.
 - باعث اختلال در خواب می شود.
 - بدن را از پتاسیم تهی می کند.

Selective Androgen Receptor Modulators (SARMs)

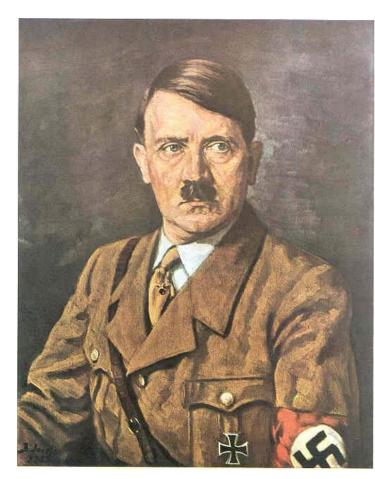
 a class of therapeutic compounds that have similar properties to anabolic agents, but with reduced androgenic properties. This property allows SARMs the advantage of androgen-receptor specificity, tissue selectivity, and the lack of steroid-related side effects.

Tibolone

• Tibolone is a synthetic steroid with weak estrogenic, progestogenic, and androgenic activity, and hence is an agonist of the estrogen, progesterone, and androgen receptors. It is a prodrug of several metabolites. The estrogenic effects of tibolone may show tissue selectivity in their distribution.

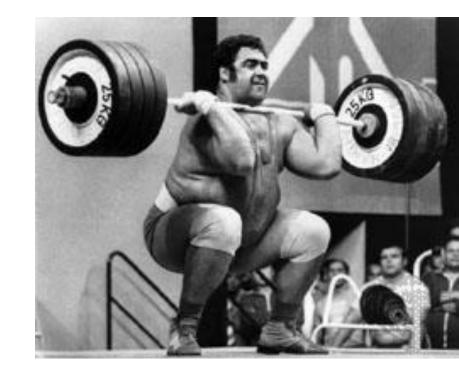
History

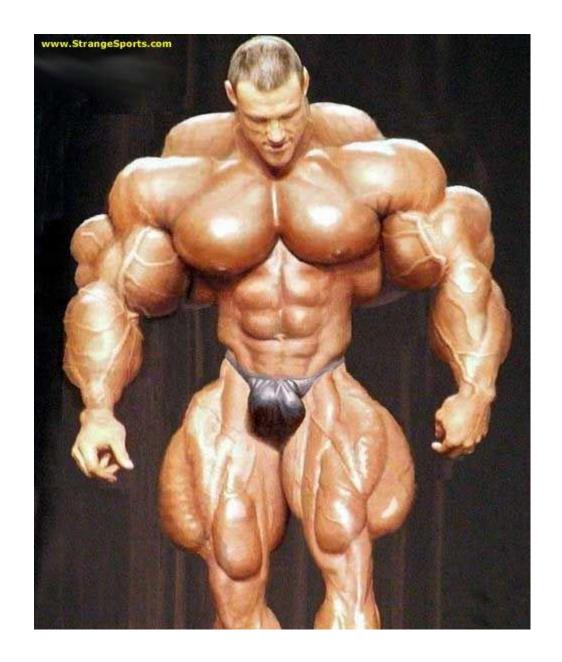
- WWII German scientists synthesized other anabolic steroids and experimented on concentration camp inmates to treat chronic wasting.
- Also given to German soldiers hoping to increase their aggression.
- Adolf Hitler rumored to take anabolic steroids.
- 1931 male hormone androstenone isolated
- 1934 androstenone synthesized
- 1935 testosterone identified and synthesized
- 1937 clinical trials on humans with testosterone began



History

- 1940s Soviet Union and Eastern Bloc Countries (East Germany) established steroid programs in Olympic and amateur weight lifters
- 1958 Dianabol (methandrostenolone) approved in U.S. by the FDA





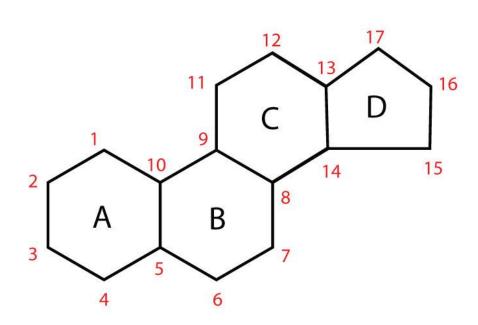


Definitions

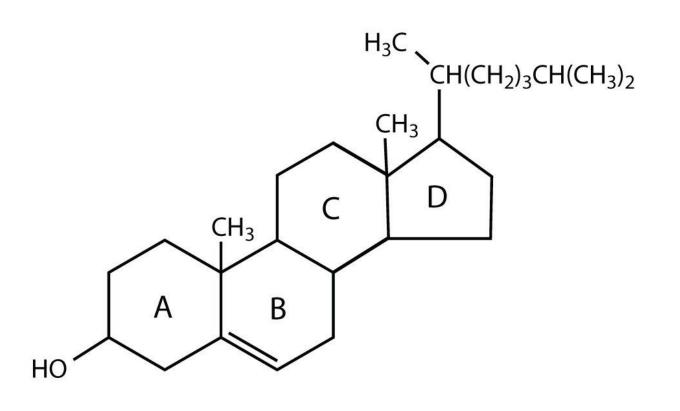
 Androgens: all male sex hormones, usually testosterone, but also testosterone derivatives

- Androgenic: refers to masculinizing properties such as libido, aggression, acne, hair growth and loss
- Anabolic: refers to assimilation of nitrogen into tissue (muscle growth)
- Cannot completely separate one from the other

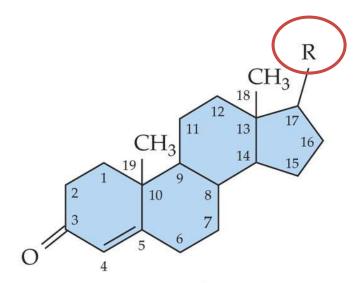
Anabolic steroid Anabolic/androgenic ratio Testosterone Methylandrostenediol Oxymetholone Oxandrolone 10 Nandrolone phenpropionate 10 Stanozolol 30



(a) Steroid skeleton



(b) Cholesterol

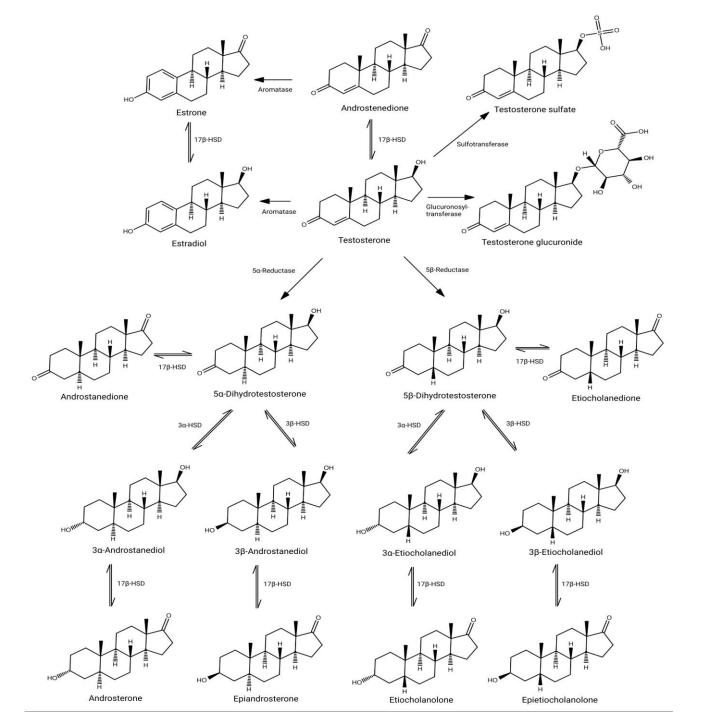


Core structure of testosterone-related steroids

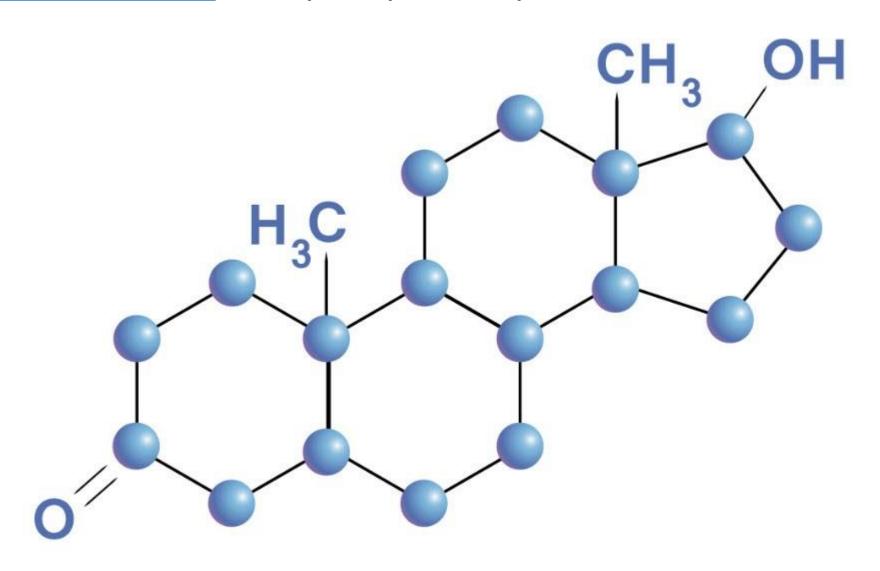
Chemical structures of some commonly abused anabolic steroids

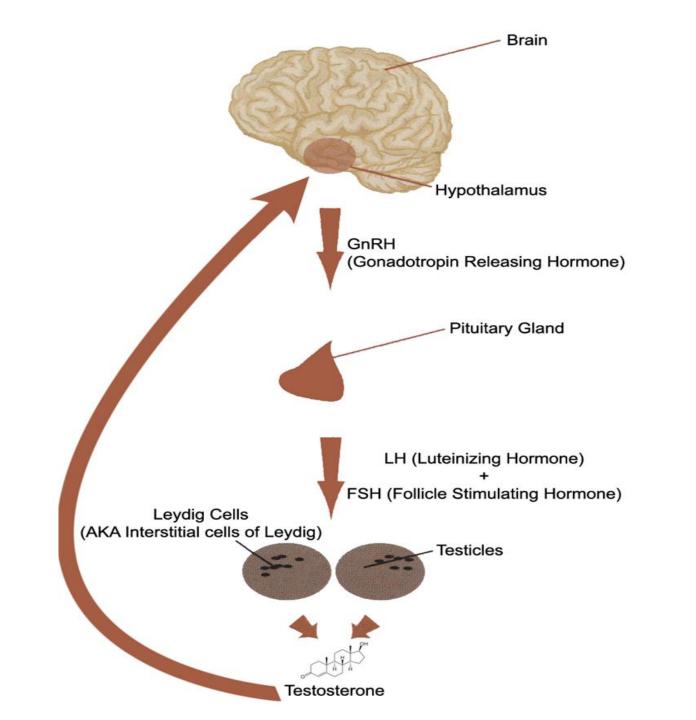
Compound	R	
Testosterone	— ОН	
Testosterone enanthate	— O — CO(CH ₂) ₅ CH ₃	
Testosterone undecanoate	— O — CO(CH ₂) ₉ CH ₃	
Testosterone cypionate	$-O-COCH_2CH_2$	
Nandrolone decanoate	— O — $CO(CH_2)_8CH_3$ (no methyl group at position 19)	
Nandrolone phenproprionate	$- O - CO(CH_2)_2$ (no methyl group at position 19)	

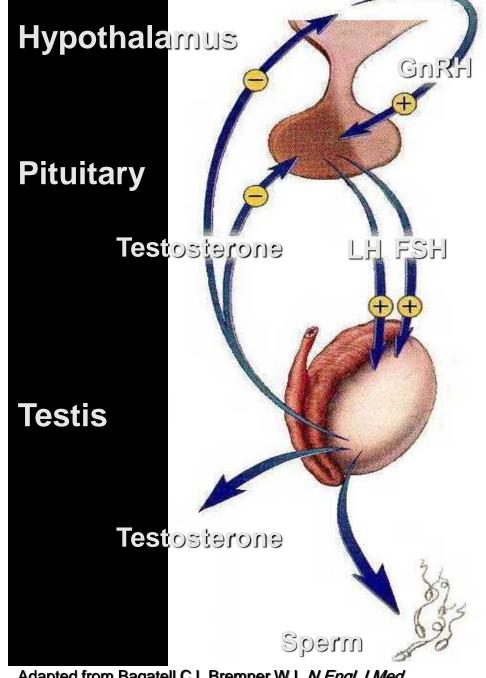
OCO(
$$CH_2$$
)₅ CH_3
 CH_3



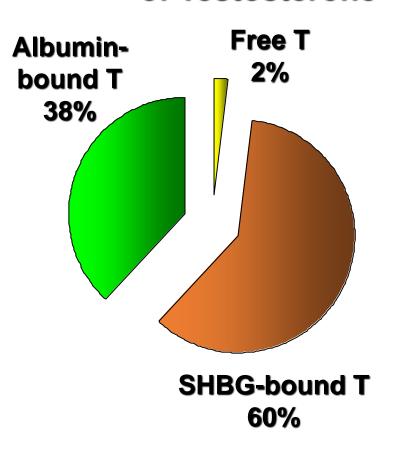
testosterone, 17β-hydroxy-4-androsten-3-one







Production and Regulation of Testosterone



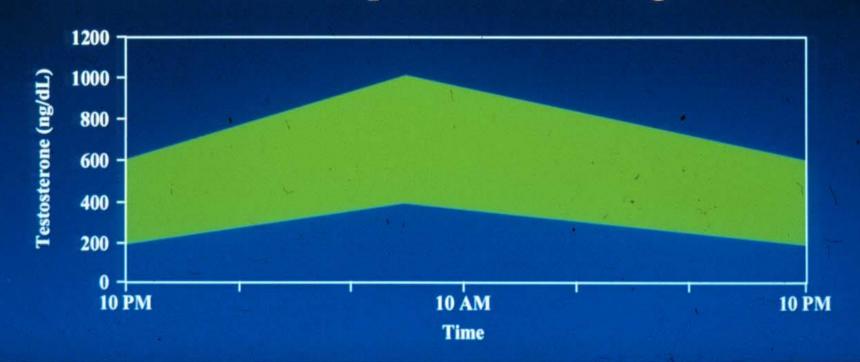
T = testosterone
Only 2% is free testosterone
and 98% is bound

Adapted from Bagatell CJ, Bremner WJ. *N Engl J Med.* 1996;334:707-715.

Adapted from Braunstein GD. In: *Basic & Clinical Endocrinology*. 5th ed. Stamford, Conn. Appleton & Lange; 1997:403-433.

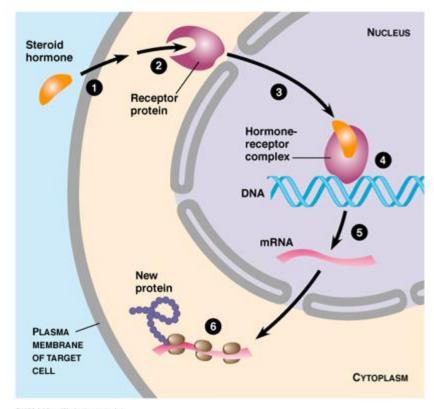
Normal Testosterone Secretion

- 3 to 10 mg/day
- Serum concentration ~300 to 1000 ng/dL
- Diurnal Variation peak in AM, trough in PM

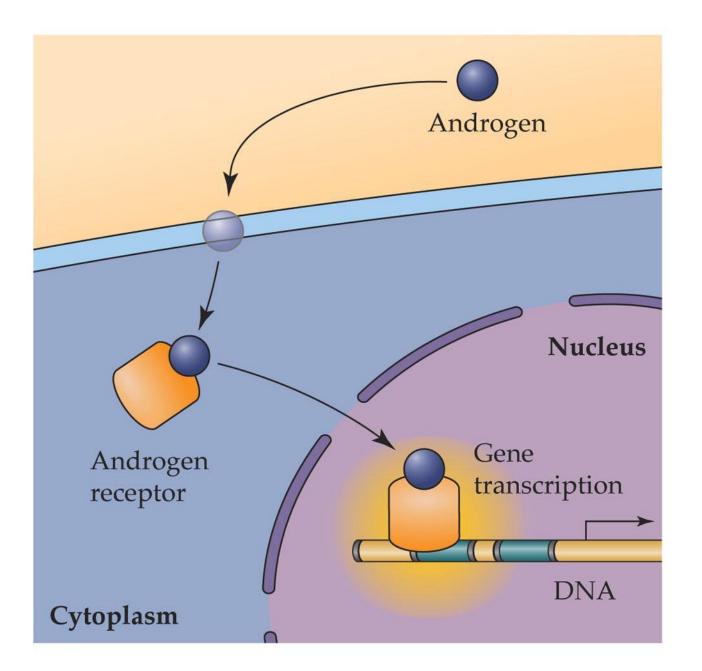


Anabolic Steroids Biochemical Mechanisms

- Steroid hormones mainly interact with cells by binding to proteins called steroid receptors
- After binding, proteins move into the cell nucleus and can alter the expression of genes or activate processes in other parts of the cell



C1999 Addison Wesley Longman, Inc.



Testosterone Deficiency with Aging

- Decline in Testosterone with age
 - Decrease in testosterone production
 - Decrease in testosterone clearance
 - Increase in SHBG
 - may be due to higher serum estradiol levels from increased adipose tissue
 - Therefore, bioavailable T decreases more than total T
 - Circadian rhythm (higher T values in AM) lost with aging

The Effects Of Testosterone

Skin:

Hair Growth Collagen growth



Brain:

Increased Sex Drive Improved Mood Confidence Memory function

Sex Organs:

Sperm Production Erektile Function Prostate Growth





Bone Marrow:

Red Blood Cell Production



Muscle Growth Increased Strength Increased Endurance





Bones:

Maintenance Of Bone Mass Density

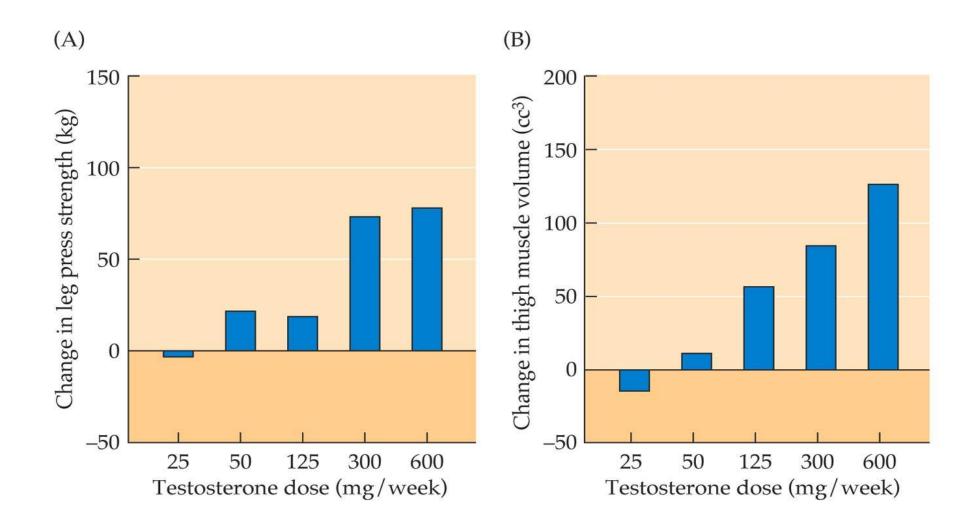
Target Organs and Physiological Effects of Testosterone and Metabolites

- CNS (↑ libido, well-being, aggression, spatial cognition)
- Hypothalamus/ Pituitary (↓ GnRH, LH, FSH; ↑ GH)
- Larynx (lowers voice)
- Breast ($E_2 \uparrow size$)
- 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)

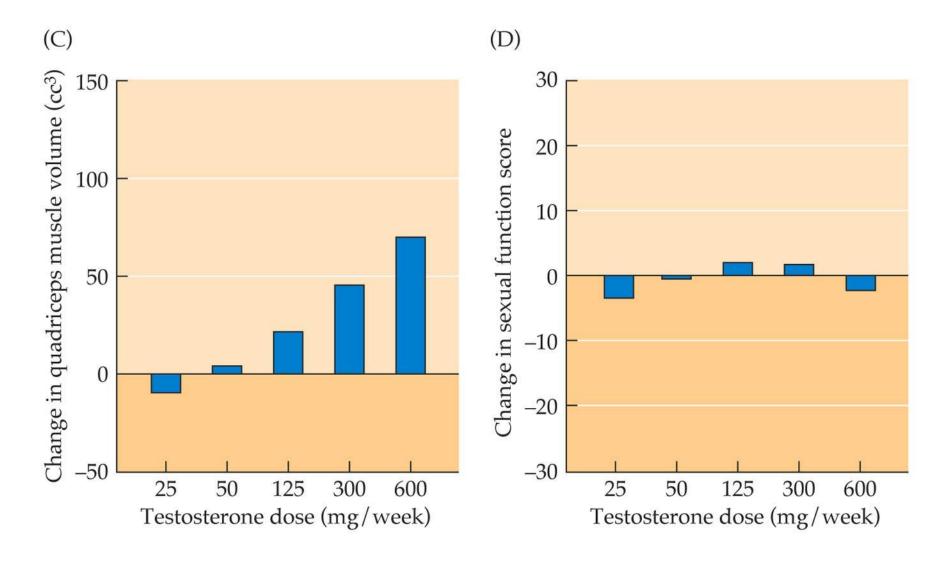
Anabolic Steroids Medical Uses

- Bone marrow stimulation aplastic anemia
- Growth stimulation use GH now
- Appetite stimulate AIDS, cancer
- Induction of male puberty extreme delay
- Reversible male contraceptive future
- Hormone replacement therapy (men)
- Gender dysmorphia psyciatric

Muscle strength & volume following chronic testosterone administration to men



Muscle strength & volume following chronic testosterone administration to men



Performance enhancement of a former East German female shot-putter

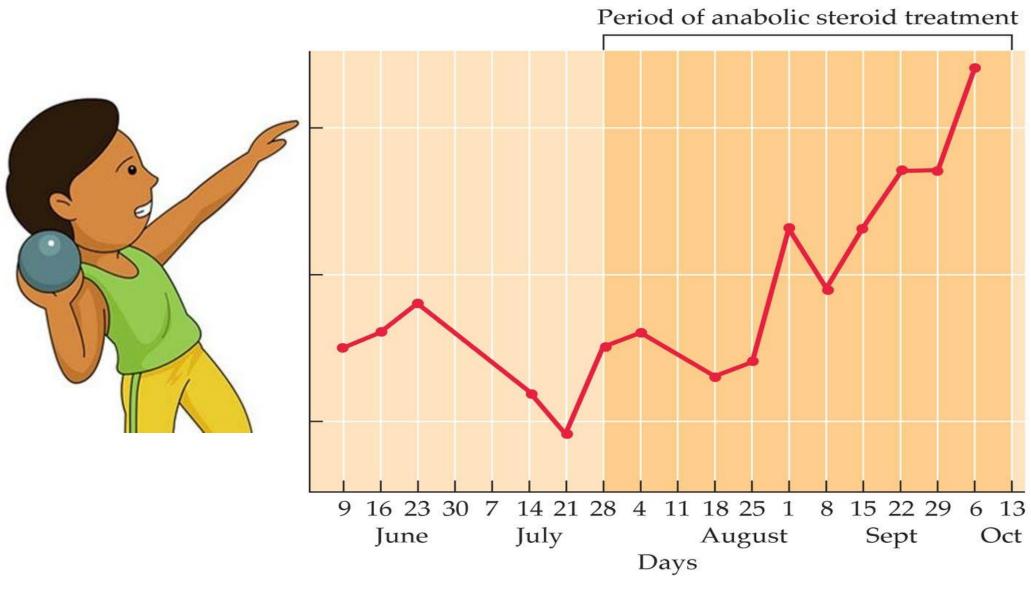


TABLE 15.2 Some Common Anabolic Steroids

Generic name	Trade name	Route of administration
Methandrostenolone	Dianabol	Oral
Testosterone undecanoate	Andriol	Oral
Oxandrolone	Oxandrin	Oral
Oxymetholone	Anadrol	Oral
Stanozolol	Winstrol	Oral or injection
Testosterone cypionate	Depot-Testosterone	Injection
Testosterone enanthate	Primotetson	Injection
Nandrolone phenylpropionate	Durabolin	Injection
Nandrolone decanoate	Deca-Durabolin	Injection
Methenolone enanthate	Primobolan Depot	Injection

Anabolic Steroids Administration







3 common forms of AS administration:

Oral – most convenient (dangerous - liver)

 Injectable – intramusclar not intravenous (HIV and Hepatitis)

Transdermal – self adhesive skin patches

شكل مصرف











شيوه مصرف

ROUTES



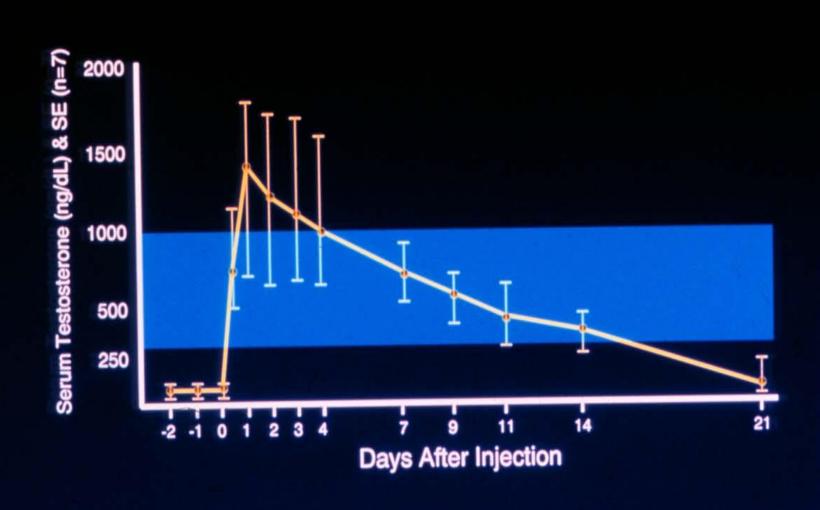




- توده ای: مصرف چند نوع استروئید آنابولیک همزمان به منظور در گیر شدن همه گیرنده ها و اثر بخشی بیشتر
 - چرخشی: یک دوره چند هفته ای مصرف و یک دوره چند هفته قطع مصرف. آثار سوء دارو را کم می کند.
 - هرمی: به تدریج به اوج می رسد و بعد به تدریج کم می شود. اثر ترک داروی کمتری دارد.

نیمه عمر و زمان تشخیص

Testosterone Serum Levels After Injection



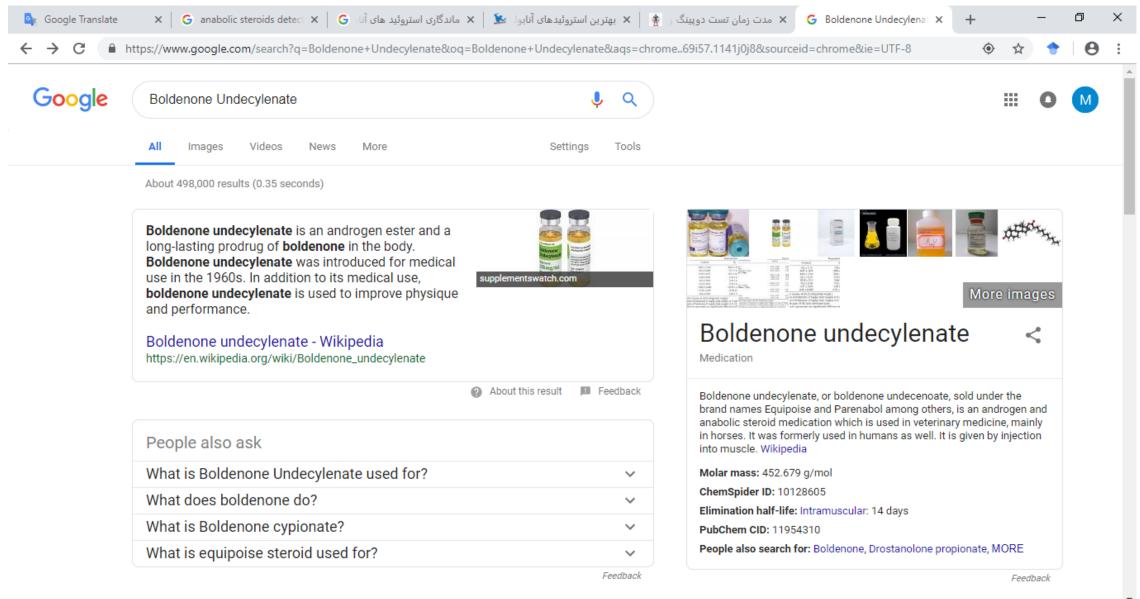
زمان تشخیص	نيمه عمر	نام جنریک	نام اختصاصی
۱۸ ماه	۱۵ روز	ناندرولون-دکوونات	Deca-Durabolin
۵ ماه	۱۵ روز	Boldenone Undecylenate	Equipoise
۳ هفته	۳ روز	دیستنوولون-پروپیونات	استرسون
۳ ماه	۸ روز	Drostanolone Enanthate	مسترون
۱۸ ماه	۵/۵ روز	تستوسترون-فنيل پروپيونات	NPP یا Durabolin
۳ ماه	۱۵ روز	۴ مخلوط استر است	Omnadren
۵ هفته	۶ روز	Trenbolone-Hexahydrobenzylcarbonate	پارابولان
۵ هفته	۱۰/۵ روز	henolone-Enanthateمت	انبار پريمو بلوان
۴-۳ ماه	۱۸ روز	۴ مخلوط استر است	Sustanon-250
۳ ماه	۱۲ روز	تستوسترون Cypionate	تستوسترون Cypionate
۳ ماه	۱۰/۵ روز	تستوسترون-Enanthate	تستوسترون-Enanthate
۳ هفته	۳ روز	تستوسترون-پروپيونات	تستوسترون-پروپيونات
۱-۲ روز	کمتر از ۲۴ ساعت	تستوسترون (بدون استرس)	تستوسترون سوسپانشن
۵ ماه	۳ روز	Trenbolone-Acetate	Trenbolone-Acetate

تزریقی ها

خوراکی

نام اختصاصی ن	نام جنریک	نیمه عمر	زمان تشخیص
آنادرول اک	اكسى متولون	کمتر از ۱۶ ساعت	۸ هفته
آنوار اک	اکساندرولون	۱۲ ساعت	۳ هفته
آندریول تس	تستوسترون	کمتر از ۱۲ ساعت	۵ هفته
е دیانابول	methandrostenolone	۸ ساعت	۶ هفته
هالوتستین فلر	فلوكسيمسترون	۸ ساعت	۸ هفته
پريمو بولان مت	متيونولون	۶ ساعت	۵ هفته
Proviron ما	ماستولون	۱۲ ساعت	۶ هفته
пе تورینابول	rchlorodehydromethyltestosterone	۱۶ ساعت	۶ هفته
وينسترول اس	استنزولول	۸ ساعت	٣ هفته



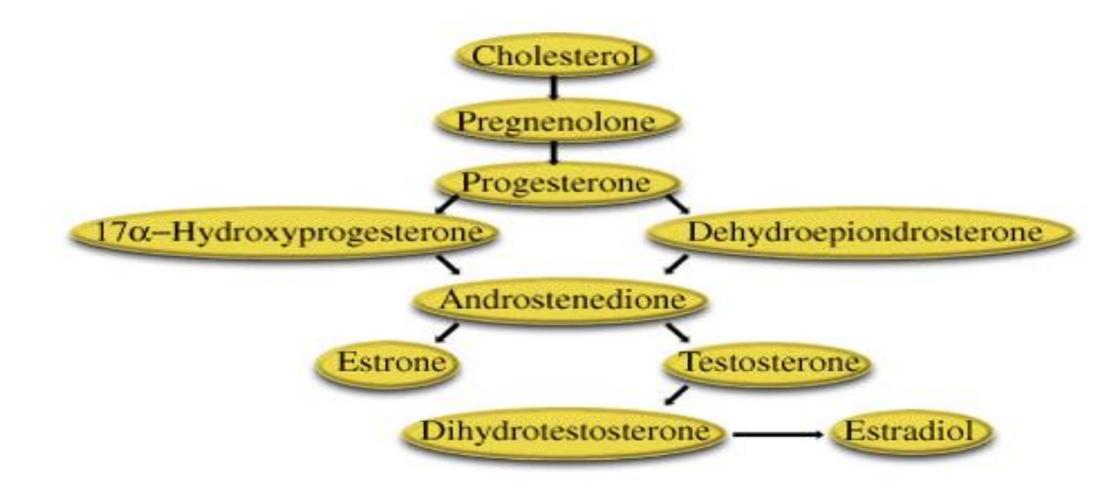


Anabolic Steroids Status in Sports

- Normal T:ET ratio 1.3:1
- Positive test result 6:1 or 4:1

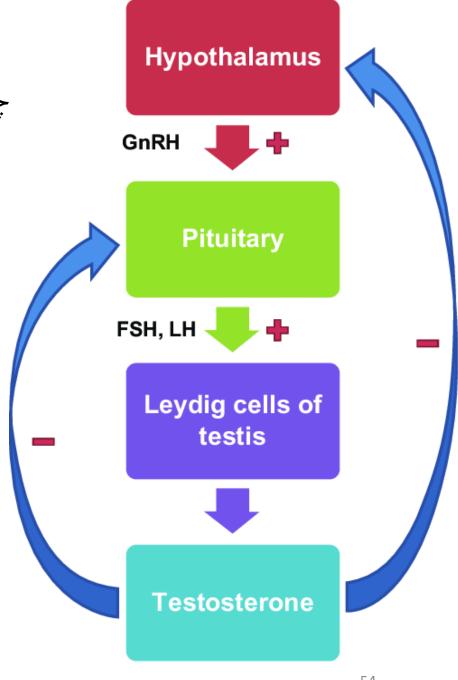
Steroid Chart

پیش سازهای تستوسترون



چرا پیش سازهای تستوسترون بهتر از خود تستوسترون هستند؟

- Only temporarily increases blood levels of testosterone, does not cause body to naturally produce testosterone.
- Has higher conversion rates to testosterone.
- Doesn't convert into estrogen.
- Does not convert into DHT (cause of balding).



Negative Side Effects

- Balding
- Acne
- Enlarged prostate
- Reduced sperm count
- Increased aggression
- Kidney & Liver damage
- Disrupt the menstrual cycle
- Decrease levels of HDL cholesterol

TABLE 15.3 Possible Health Consequences of Anabolic Steroid Use (Part 1)

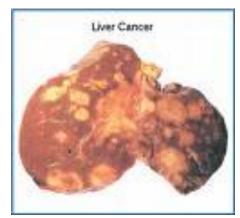
Category	Effects
Cardiovascular effects	Hypertension (high blood pressure)
	Increased blood clotting
	Increased red blood cells
	Decreased HDL cholesterol (the "good" kind of cholesterol)
Effects on the liver (particularly	Jaundice
from oral steroid use)	Peliosis hepatis (blood-filled cysts in the liver)
	Tumors
Effects on the skin and hair	Oily skin and scalp
	Severe acne
	Male pattern baldness
Growth effects	Growth stunting in adolescents due to premature epiphyseal closure

TABLE 15.3 Possible Health Consequences of Anabolic Steroid Use (Part 2)

Category	Effects
Behavioral effects	Increased libido (sex drive)
	Increased irritability and aggressiveness
	Dependence
Specific effects on men	Testicular shrinkage
	Reduced sperm counts and possible infertility
	Prostate enlargement
	Gynecomastia (breast development)
Specific effects on women	Menstrual abnormalities
	Deepening of the voice
	Excessive hair growth, especially on the face
	Enlargement of the clitoris
	Decreased breast size

Anabolic Steroids Adverse Effects





- Accelerate the rate of premature baldness (male and female)
- Acne stimulates the sebaceous glands
- Liver damage (cancer) increased demand on liver as oral steroids are changed (increase bioavailability and stability)

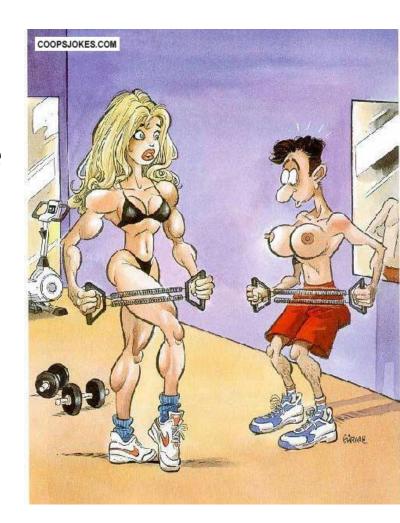
Anabolic Steroids Adverse Effects

- Tendon rupture has been linked to AS
- Stiffer and less elastic tendon
- No consistent AS –induced ultrastructural or biochemical alterations
- Probably tendon does not adapt as fast



Anabolic Steroids Gender Specific Effects

- Gynecomastia development of breast tissue in males
- Conversion of testosterone to estrogen by an aromatase enzyme



Anabolic Steroids Female-Specific Effects

- Increase in body hair
- Male-pattern baldness
- Deepening of voice (permanent)
- Enlarged clitoris (permanent)
- Temporary decrease in menstrual cycle
- Affect fetal development during pregnancy



Anabolic Steroids Behavioral Effects



- Controversial
- Mood swings
- Aggression (roid rage)
- Mania
- Depression
- Withdrawal
- Dependence

Steroid design issues

testosterone can be converted to estradiol by aromatase (aromatisation)

normal process, mediating testosterone effects on CNS

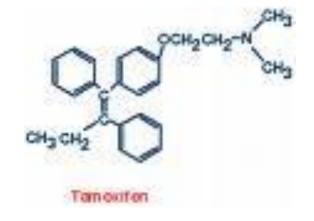
this has *feminising* effects - so is also to be avoided

Anabolic Steroids Adverse Effects

- Risk of mortality among chronic AS users repoted to be 4.6 times higher than non-AS users
- Weekly doses of 600 mg ot testosterone or its equivalent for cycles lasting less than 12 weeks appear to cause few side effects during scientific studies
- Rule: bigger the dose, the bigger the muscle, the bigger the problem

Minimization of Side Effects (during cycles and post cycle)

- Increase CV exercise to counter act effects on left ventricle
- Estrogen receptor modulators to reduce effect of aromatization of steroid hormones (tamoxifen) reduce gynecomastia





Post Cycle Therapy

- "Clomiphene or tamoxifen (Primary PCT drug)
 - Anastrozole aromatase inhibitor
 - 2. HCG restore hormonal balance
 - Human chorionic gonadotropin (**HCG**) is a hormone produced by the placenta after implantation.

Steroid design issues

- testosterone can be converted in some tissues to dihydrotestosterone (DHT) by 5α -reductase. This has androgenic effects so is to be avoided as want the anabolic effects (doesn't happen in skeletal muscle).
- Finasteride (Propecia) reduces the conversion of testosterone to DHT (high rate of alopecia)
 - این دارو در مواردی که استروئید به یک مشتق آندروژنیک تبدیل نمی شود بی فایده است.



Side effects: behavioural

addictive? to some extent -- users show:

withdrawal symptoms -- fatigue, depression, insomnia, restlessness, anorexia, decreased libido, dissatisfaction with body image, desire for more steroids(!)

but no big studies so don't know how common this is...

symptoms could be rare... or just unreported