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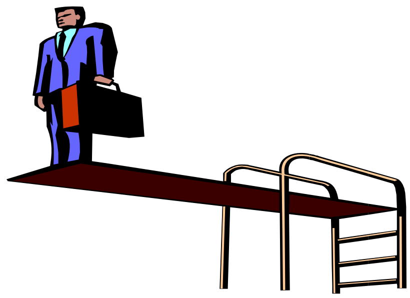
Cogita Ante Salis



"LOOK BEFORE YOU LEAP"

Greetings, the following question is reviewed in this issue:

#1 Should Athletes employ interventions to raise anabolic hormones (with special attention to *testosterone*)?

Introduction

Training preparation should always include interventions to enhance natural physiological function but avoid any protocol that compromises health from excessive production of anabolic hormones. Governing athletic agencies list several potentially harmful banned substances that when injected or orally dosed increase blood-carrying capacity, cellular metabolism, or muscle growth rate gains respectively. The use of anabolic-banned substances is both unethical, immoral, and opposes the rules of fair play. That such practices may increase the risk of a life-threatening disorder from chronic exposure, shortening the quality if and length of life is the conclusion of this edition. As you read this issue, consider the outcome from both exogenous and endogenous increases in the anabolic hormone profile, which testosterone presents to determine if you come to the same conclusion, as did I.

Sincerely,

Dr. Bill Misner Ph.D.

human Growth Hormone (hGH) and **Testosterone (Te)**, two anabolic hormones, (when released) increase the rate of muscle growth recovery following exercise stress events. As each hormone increases, the rate of muscle growth gain contributes to greater torque output capabilities when the stressed muscle is adequately rested. Immediately following a 3-hour high-aerobic exercise event, levels of hGH may increase to as high as 1500% above pre-exercise baseline. A natural healthy intervention for accommodate this hormone's contribution is to replace exercise-depleted metabolites by consuming 200-350 calories of 3-parts carbohydrate to 1-part protein (Glutamine-enhanced Whey Protein Isolates or Soy Protein Isolates) immediately following the workout event. Since the majority of nearly 85% of bioavailable hGH is released during sleep, taking a nap after exercise naturally safely accelerates hGH levels available for improved anabolic recovery. However, hGH has a negative feedback loop; when levels reach a certain zenith, the body exerts shutdown mechanisms to reduce hGH release. After a Zenith (high) in this anabolic hormone, a nadir (low) in hGH occurs, and then gradually normal levels are released in response to a number of regulatory signals between hormone sensory agents between muscle, blood, and hormone parent-releasing glands. Doing back-to-back prolonged workouts will reduce muscle growth advantages from exercise-induced hGH release, because the body requires around 3 days rest or "easy" workouts in order to replenish glycogen stores and lean muscle mass amino acids cannibalized during the prolonged or intense workout session. The more glycogen is depleted from daily exercise, the less muscle growth hormones will be released to rebound muscle growth to accommodate load.

SHOULD ATHLETES TAKE SUBSTANCES TO INCREASE TESTOSTERONE?

Since anabolic testosterone levels decrease as a result of exercise to fatigue training, and catabolic hormones increase at a greater rate, why raise or not raise the anabolic testosterone levels to enhance recovery? A negative feedback loop results in response to elevation in testosterone, which further depresses testosterone and its anabolic donor properties for anabolic muscle growth. When this happens, testosterone is depressed longer than elevation in the beneficial hormone increases initially released. This is illustrated from the pathway showing the male reproductive axis, hypothalamic GnRH secretion drives pituitary gonadotropin release:

LUTENIZING HORMONE

↓

TESTICULAR LEYDIG CELLS STIMULATED

↓

TIME-DELAYED
OUTPUT
SEX-STEROID HORMONES

↓

GONADAL SEX STEROIDS FEEDBACK

↓

RESTRAIN GNRH-GONADOTROPE SECRETION

↓

INCREASE IN ↑ TESTOSTERONE & DIHYDROTESTOSTERONE (DHT)
SUPPRESSES LH RELEASE IN HEALTHY MEN OR PATIENTS WITH GONADAL FAILURE

🡇

ESTROGEN EXCESS REPRESSES GONADOTROPIN SECRETION
NONSTEROIDAL ANTAGONISTS OF THE ESTROGEN OR ANDROGEN RECEPTOR MODERATELY AUGMENT LH AND FSH SECRETION

This pathway demonstrates that if testosterone levels are elevated above norms, the body over-reacts somewhat by prolonging biochemistry to reducing elevated testosterone as a hormone monitoring homeostasis survival action. Typically, exogenous-induced ***TESTOSTERONE 4-8 WEEKS WILL BE FOLLOWED BY 8-12 WEEKS OF SEVERELY DEPRESSED LEVELS***, so that the overall anabolic effect is actually less than what would have been released over the total time period had the subject not induced an exogenous dose intervention. Testosterone Undecanoate (TU) is a weak testosterone prescription dose injected to resolve hypogonadal disorder. Figure 2 illustrates how injected prescription TU effects testosterone levels through a treatment and time period post-dose:

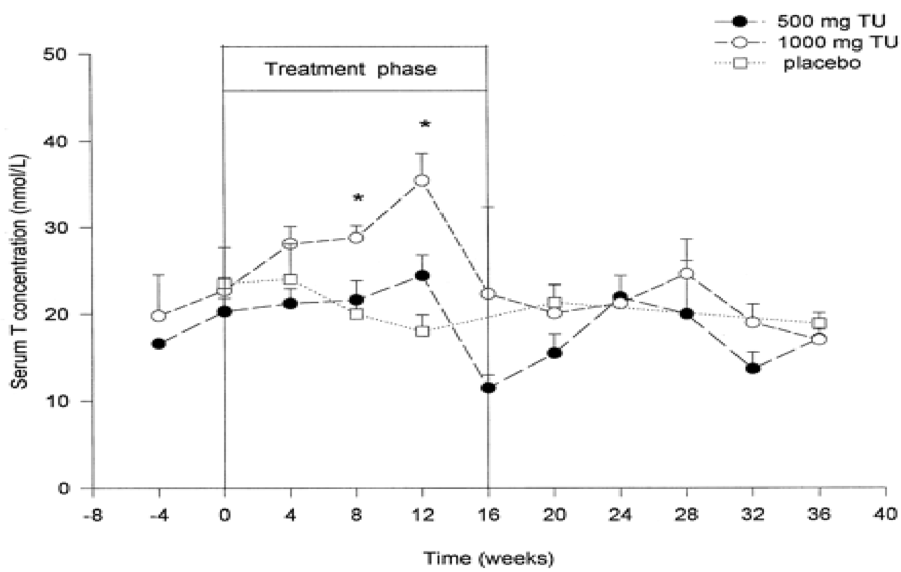


Figure 2. Mean serum T levels at nadir (mean ± SEM) in each treatment dose group and in the placebo group during baseline, treatment, and recovery periods. *Asterisks* indicate a significant difference in the higher dose group compared with the lower dose and placebo groups ($P < 0.05$).

During administration of exogenous testosterone-enhancing TU, ***SPERM COUNTS DECREASED*** remarkably:

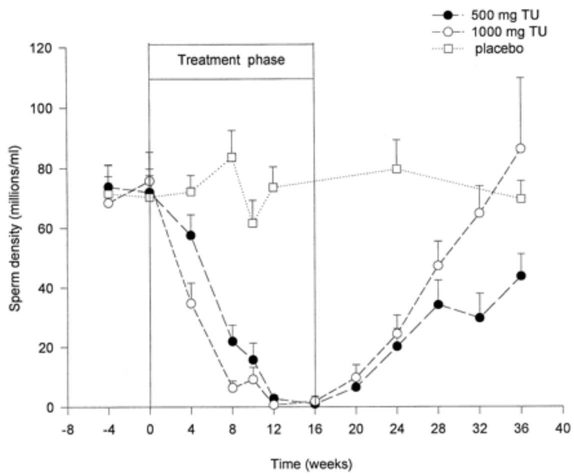


Figure 1. Mean spermatozoal concentrations during baseline, treatment, and recovery. Notice that testosterone was mildly increased sperm with exogenous influence of TU for 4 weeks, but was aggressively depressed for 32 weeks following peak values.

MALE TESTOSTERONE: THE POSITIVES VERSUS NEGATIVES

Testosterone is an anabolic steroid synthesized primarily by the Leydig cells in the testes in males, the ovaries in females, and adrenal glands in both sexes. Testosterone is synthesized from cholesterol, with androstenedione, androstenediol, dehydroepiandrosterone (DHEA), progesterone and pregnenolone acting as some of the intermediate substrates. Testosterone production is regulated by hormonal secretions from the hypothalamus and the pituitary gland in the brain. The process begins as the hypothalamus secretes gonadotropin-releasing hormone (GnRH) in generative pulses. In response to these steady intermittent bursts of **GnRH**, the pituitary gland releases luteinizing hormone (**LH**) and follicle-stimulating hormone (**FSH**), which act directly on the **testes**. FSH activates the Sertoli cells, which produce sperm (spermatogenesis). LH stimulates the Leydig cells to secrete testosterone in a daily rhythm characterized by peak levels in the morning and low levels in the evening. Once it reaches high levels, testosterone production generates negative loop feedback to the hypothalamus that downregulate LH release and diminish further testosterone production. **In this way, testosterone inhibits its own secretion.**

A HEALTHY FEEDBACK FUNCTIONING LOOP ENSURES STEADY SECRETION OF GONADOTROPINS, RESULTING IN RELATIVELY CONSTANT LEVELS OF TESTOSTERONE SECRETION BY THE TESTES:

Hypothalamus➔GnRH➔ Pituitary **Pituitary**

↓ **↓**

Luteinizing Hormone + Follicle-Stimulating Hormone (FSH)

↓ **↓**

Testes **Testes**

↓ **↓**

Leydig Cells **Sertoli Cells**

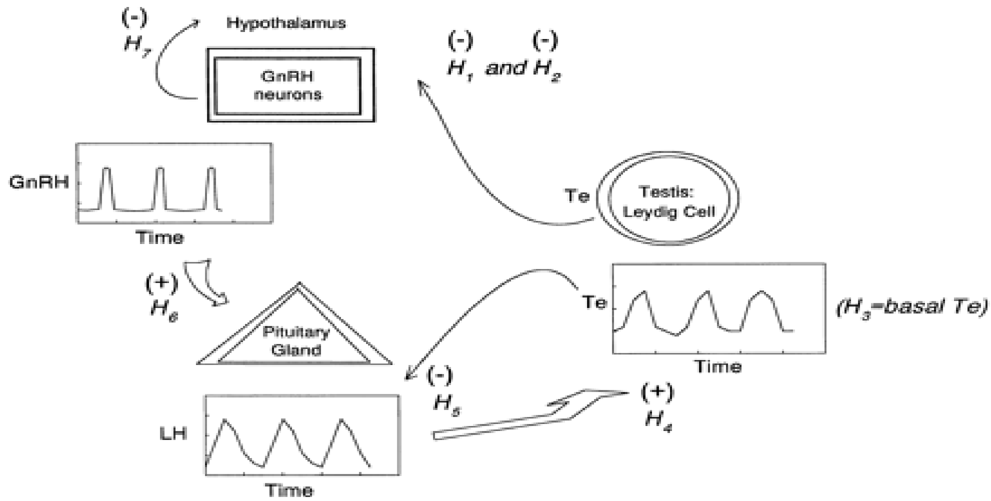
↓ **↓**

Testosterone +↑ **Sperm +↑**

Hypothalamus Downregulates LH -↓

Testosterone Inhibition -↓

LIKE MOST HORMONAL-CONTROL FEEDBACK MECHANISMS, THIS IS A CLOSED-LOOP SYSTEM, WHICH ALSO OPERATES IN THE OPPOSITE DIRECTION TO GUARD AGAINST DEFICIENCIES.



[Fig. 1.] Schematic illustration of time-delayed negative feedback (−) and positive feedforward (+) within human male gonadotropin-releasing hormone-luteinizing hormone-testosterone (GnRH-LH-Te) axis. Broad arrows, feedforward (+) stimulus-secretion linkages; narrow arrows, feedback (−) inhibition. "*H*" functions are developed further in section I and Fig. 2 and define dose-response relationships at each feedback interface within axis (see section VIII*A2*).

TESTOSTERONE EFFECTS ON BMI LEAN MUSCLE MASS & FAT MASS

This following research data demonstrates how testosterone increases within or near the natural physiological range can produce increases in muscle anabolism, LBM, and muscle strength similar to supraphysiological administration.

Variable, units (INCREASE - ↑ DECREASE - ↓)	**TESTOSTERONE**	**Placebo**
[1]**Total LBM, kg**	↑**4.2**	↓ **2.0**
[1]**Leg LBM, kg**	↑**1.6**	↓ **1.3**
[1]**Arm LBM, kg**	↑**1.6**	↓ **1.4**
[1]**Body fat, %**	↓ **3.6**	↑ **0.3**
[2]**Leg muscle volume, ml**	↑ **488**	↓ **96**
[3]**Bicep curl, kg 1 mo**	↑ **3.6**	↓ **0.5**
[3]**Bicep curl, kg 6 mo**	↑ **9.1**	↓ **0.9**

[3]Tricep extension, kg 1 mo	↑ 4.9	↑ 2.3
[3]Tricep extension, kg 6 mo	↑ 10.4	↓ 0.9
[3]Leg curl, kg 1 mo	↑ 5.5	↑1.8
[3]Leg curl, kg 6 mo	↑ 7.5	↔ 0.0
[3]Leg extension, kg 1 mo	↑ 6.5	↑4.5
[3]Leg extension, kg 6 mo	↑ 15.3	↔ 0.0
Isokinetic endurance knee extension, dominant leg, J 1 mo	↑ 2.3	↑3.4
Isokinetic endurance knee extension, dominant leg, J 6 mo	↑ 17.6	↑6.0

During the 6 mo of TE administration, some subjects experienced testosterone concentrations that exceeded the physiological; however, testosterone concentrations were consistently maintained above baseline values. This study indicates that these LBM and strength increases can be maintained over 6 months with careful dose adjustments that ensure primarily physiological testosterone levels. This study also demonstrates that the muscle's response to testosterone changes over the 6-month period of administration, indicating that alternative paradigms of testosterone administration (i.e., cyclic administration) can be of physiological benefit.[1]

Anabolic Levels of Free Testosterone (Te) During Endurance Exercise ↑↓

Exercise ***elevates testosterone*** initially, but levels ***dramatically decrease with exercise*** sessions that progress toward fatigue. Plasma testosterone increases significantly from a mean basal value of 5.4 ng per milliliter to a peak of 8.76 ng per mililiter 40 minutes after the start of a run, and remains elevated for the duration of the run. Thus resting testosterone levels (4.55 ng per mililiter) were reached by two hours after discontinuation of the exercise. The suggestion is that shorter workouts raise testosterone and peak right at 40 minutes. Continuing an endurance workout to fatigue severely reduces testosterone remarkably. Repeated prolonged efforts may therefore deprive the athlete of testosterone's performance-enhancing muscle rebuilding potential, reduce both rate of muscle growth and the pace rate dependant upon muscle torque output. The over-reaching, over-trained endurance "junky" can go all day long, but is unlikely to make it to the podium because of a lack of muscle mass torque output that cannot match the faster pace of others. It is wise therefore to both precede and follow prolonged training with rest days, easy days, or shorter faster sub 40-minute efforts. Let us examine this postulate further.

During an exercise-to-fatigue session (running for 85 minutes @ high aerobic pace 7 mph on treadmill), Total testosterone increased 131% above baseline to the 85-minute peak fatigue, while free testosterone decreased –7%. Free testosterone is the anabolic property of unbound muscle building testosterone and during exercise to fatigue efforts; free testosterone's anabolic muscle-building property decreases. During this same 85-minute exercise event, the catabolic hormones, cortisol and prolactin increased dramatically

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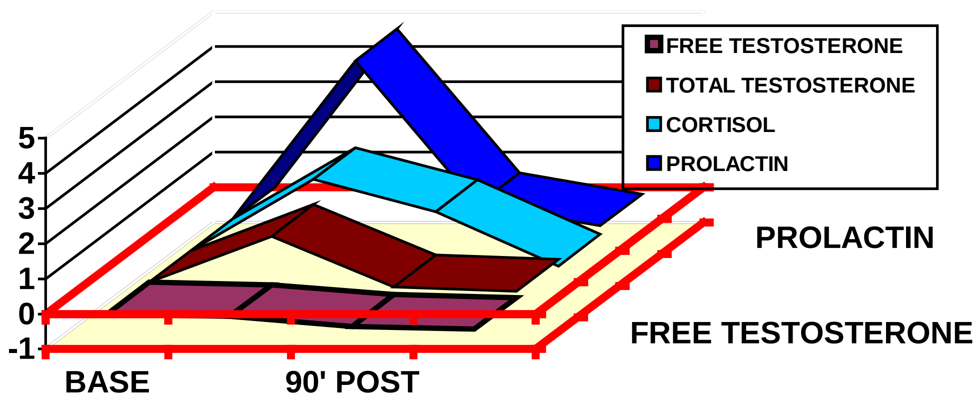
[1] ***Am J Physiol Endocrinol Metab*** **282: E601-E607, 2002 @: http://ajpendo.physiology.org/cgi/content/full/282/3/E601**

203% and 450%, respectively. For the 24 hours following an exercise-to-fatigue event, both free and total testosterone levels are less than at resting baseline, while elevated levels of catabolic cortisol and prolactin are elevated.

Hackney et al., (2005) measured Free Testosterone, Total Testosterone, Cortisol and Prolactin male hormone levels progression during fatigue to exhaustion endurance exercise in elite fit athletes as follows:

1. Fit (62.1 VO^2 Max mean)
2. Lean (8.8% body fat mean)
3. Age (24.6 mean years, max HR 195),
4. During glycogen-depletion exercise to fatigue 84.8 minutes mean @ 81-94% max Heart Rate range 157-183 mean
5. Post 90 minutes glycogen-depletion exercise to fatigue
6. Post 24 hours glycogen-depletion exercise to fatigue

These findings give some credence to the hypothesis suggesting a linkage between the persistent low resting testosterone found in endurance-trained runners and stress hormones responses to exercise. The following graphs show the approximate catabolic hormones (cortisol & prolactin) and anabolic testosterone levels (as total or free T) expressed from baseline at rest, at fatigue reached 85 minutes of aerobic exercise treadmill running to fatigue at 51-94% max heart rate (73% average HR) for 22 fit endurance athletes:



Both catabolic hormones prolactin and cortisol are produced at a higher rate during exercise and peak at higher levels than either free or total anabolic testosterone. Free testosterone the active anabolic actually decreases both during exercise and continues to below baseline values 24 hours after exercise. During exercise to fatigue workout 85 minutes, catabolic hormone values expressed are a dominant 24:1 ratio over anabolic testosterone levels.

What happens to hormones when prolonged endurance-training sessions are habitually repeated?

Hackney et al. (1989) reported a significant negative relationship between total testosterone and prolactin. In this study[2], resting blood samples were collected at 2-week intervals as subjects underwent an 8-week intensive training program (volume and intensity of training increased every 2 weeks). Over the 8-week training period, resting levels of prolactin increased significantly from pre-training values and testosterone concurrently decreased. While prolactin levels were similar to those observed in the present study at volitional fatigue, they reported/observed no such chronic elevation in prolactin. Levels in the present study, as noted, returned to normal pre-exercise values within 24 h of activity. It is proposed that the Hackney et al. (1989) study may be showing a cumulative effect (chronic exercise training) rather than the acute effect of a single exercise bout as was used in the present study. Therefore, the present data do not support the assumption by some researchers that acute exercise-induced increases in prolactin can be associated with decreases in testosterone. These researchers concluded that a negative (inhibitory) relationship between cortisol and prolactin and circulating levels of testosterone. The present findings suggest that a negative relationship exists between exercise-induced hypercortisolaemia and total testosterone levels but not for free testosterone levels. However, the exercise-induced hyperprolactinaemic states did not appear related to the subsequent changes in either form of testosterone.

The finding of this negative relationship (i.e., statistical) between cortisol and total testosterone following prolonged endurance exercise appears novel.

However, the present findings must be considered limited due to several factors:

(1) Because of the infrequent blood sampling protocol employed
(2) Because this design does not allow for a testing of a cause and effect mechanism
(3) The overall sample size was small

Nevertheless, it shows that some proposed assumptions about exercise stress hormone responses and testosterone changes are partially accurate. These findings give some credence to the hypothesis suggesting a linkage between the persistent low resting testosterone found in endurance-trained runners and stress hormones responses to exercise.

POSITIVES **HIGH➔NORMAL RANGE TESTOSTERONE (Te)**	***NEGATIVES*** **LOW OR EXCESS TESTOSTERONE (Te)**
Reduces Cardiovascular Disease	**Levels of free, unbound testosterone associated with an increased incidence of prostate cancer**
Reduces diabetes	**Elevated Te or Te imbalances often precede and may possibly trigger the metabolic dysregulation associated with**

	obesity, dysglycemia, hyperinsulinemia, diabetes, and heart disease.
Reduces harmful blood lipids	Elevated or imbalanced harmful blood lipids
Te grows healthy skin	Increased risk of skin acne
Te supports sound sleep	Increase risk of sleep apnea
	Reduced sperm count and infertility
	Increased risk of fluid retention
Reduces arthritis	Elevated arthritic symptoms
Reduces muscle wasting due to age	Elevated muscle mass loss
Increases immunity	Elevated or imbalances in immunity
Vasodilatition of arteries	Reduction of arterial blood flow
Reduces thyroid imbalances	Depressed or imbalanced Thyroid
Reduces stroke	Elevated risk of stroke
Increases rate of bone/muscle growth	Increases rate of bone/muscle loss
Improves mood and mental state	Depression
	Increased sweat rate
Healthy hair growth	Hair loss male pattern baldness
Testosterone lowers Body Mass Index by raising fat metabolism	Increases raise basal metabolic rate but shorten life span
Stress➔Hypercortisolism of endogenous or exogenous sources suppresses Te secretion by a direct action on the testis.	Elevated testosterone in men is associated with poor spatial awareness

TESTOSTERONE WEIGHING 55 STATEMENTS

1. Genetic physiology implicates testosterone and other sex hormones as measured differences in the **pituitary weight**: (1) Blacks (800 mg), (2) Whites (700 mg), and (3) Orientals (600 mg).
2. A **higher-than-normal levels of** ***prenatal testosterone levels*** increase in testosterone is believed to cause both *lefthandedness* and *homosexuality* in women, giving a more pronounced effect in women than in men.
3. **Highly trained male athletes, like their female counterparts, may have a deficiency of hypothalamic gonadotropin-releasing hormone**.
4. **A profound suppression of testosterone and sperm occur in men undergoing extremely intense physical training.**
5. ***OBESE WOMEN*** **with abdominal fat have increased percentage free testosterone** fraction and reduced sex hormone-binding globulin (SHBG) concentrations in peripheral blood, and several lines of evidence support the hypothesis that hyperinsulinemia and sex hormone abnormalities may be causally related. A significantly positive correlation between the degree of hyperandrogenism and that of hyperinsulinemia has been found in hyperandrogenized obese and non-obese women. Moreover, in vitro studies have

shown that insulin seems to act as an amplifier of luteinizing hormone (LH) effects by stimulating ovarian androgen synthesis. ***Thin women*** **have lower testosterone levels than do heavier obese women.**

6. ***Obese Men*** **are characterized by reduced testosterone and SHBG concentrations with or without subnormal gonadotropin levels.** The underlying mechanisms leading to these abnormalities have not been clarified; although it has been suggested that hyperestrogenemia due to increased aromatizaton of androgens in the adipose tissue may play a role by interacting with gonadotropin regulation. ***Thin men*** **have higher testosterone levels than do heavier men.**
7. **Alcohol intake decreases circulating testosterone**.
8. Increases in Testosterone's downstream metabolite, ***dihydrotestosterone***, are how Te is *implicated in prostate cancer*, because it is the principal trophic hormone with testosterone that regulates growth and function of epithelial prostate tissue.
9. "**Blacks in the United States have the highest prostate cancer rate** *in the world and nearly twice that of whites.* The 2:1 black-to-white ratio in prostate cancer rates is already apparent at age 45 years, the age at which the earliest prostate cancer cases occur. Mean testosterone levels in blacks were 19% higher than in whites, and free testosterone levels were 21% higher. A 15% difference in circulating testosterone levels could readily explain a twofold difference in prostate cancer risk.
10. **Female fasting plasma glucose levels** *positively correlated with levels of the endogenous androgens dehydroepiandrosterone sulphate and free testosterone and negatively with sex-hormone-binding globulin across the whole range of glucose and hormone levels.* Mean dihydroepiandrosterone sulphate and free testosterone levels were 16% and 46% higher, respectively, and mean sex-hormone-binding globulin levels 27% lower in the top compared with the bottom quartile of fasting plasma glucose levels.
11. ***Testosterone excess*** **may retard the growth of structures involved in the immune system's efficacy.** Elevated testosterone effects are most marked heightening susceptibility to later *immune disorders*. It might be argued that this mechanism would lead to a higher rate of immune disorders in males. Testosterone suppresses the thymus even in adult life due thymic involution after puberty being more pronounced in males.
12. **Hand preference** is correlated with serum testosterone levels anomalous (Irregular) dominance (left-handers, mixed-handers, and right-handers with familial sinistrality) and was compared to subjects with standard dominance (right-handers without familial sinistrality). The mean serum testosterone levels were found to be significantly higher in subjects with anomalous dominance than those with standard dominance. It was concluded that the results are in accord with the testosterone hypothesis of cerebral lateralization.
13. **Right-handers (RH) had higher T concentrations** than left-handers (LH). This was also true within each sex independently. Males overall had much higher T concentrations than females. (mixed results)
14. **Summarized Te** results indicate that **LH of both sexes had significantly *lower salivary T concentrations than RH.***

15. Associations observed from **elevated testosterone** in individuals who were strongly left-handed were more likely to ***exhibit learning disorders*** (i.e., dyslexia and stuttering) and certain ***immune diseases*** (e.g., thyroid and bowel disorders) than those who were strongly right-handed. The authors suggest that the cause of the levels during development.
16. **High levels of testosterone produce left-handedness and learning disorders by *delaying the growth of the left hemisphere in utero*, and influence the maturation of *the immune system* by suppressing the thymus.**
17. ***Prenatal elevations in testosterone* may be related to the development of left-handedness.**
18. ***Learning disabilities* may be associated in part with abnormal testosterone levels.** Sex steroids have organizational effects upon neural tissue and that abnormal secretion during development may lead to functional anomalies. The presence of learning disabilities was significantly associated with higher salivary testosterone.
19. **Hypogonadal males *low testosterone present superior verbal scores and low scores on tests of spatial function, unlike normal males.***
20. ***Dark winter months* pineal gland activity suppresses both ovaries and testes, whereas in the summer it is inactive and sex hormone levels are higher.**
21. ***Males born in each of the six months beginning in September-February, the rate of nonrighthandedness was higher than that found in any of the other six months*, but no clear trend was observed for female births**
22. Before puberty the ***common immune disorders*** are the male-predominant allergies; after puberty the autoimmune disorders are generally, although not universally, female predominant. Testosterone in adult life acts to suppress autoimmunity, presumably by its effects on the thymus. The implication is therefore that the male is indeed more susceptible to autoimmune disorders but is protected by his own production of testosterone after puberty. High testosterone effect in utero increases susceptibility to immune disease, but after puberty it diminishes its expression. If this hypothesis is correct, then males subjected to high testosterone effect in utero, but who are hypogonadal after puberty, should have very high rates of autoimmune disease.
23. ***Antibodies binding to the hair follicles present a barrier to androgens.*** We have noted the lower rate of early male pattern baldness and sparse facial hair among the Japanese, resulting form insensitivity of the hair follicles to dihydrotestosterone. Do Europeans or Blacks with early gray hair also need to shave less frequently---that is, whether the immune protection against androgens also extends to facial hair?
24. **Testosterone origin & effects**: *Ovaries* produce some testosterone, though not as much as *testicles* do. They are exaggeratedly feminine in their behavior, with typically a special interest in babies, clothes, housekeeping, and romantic stories. Men with less than usual testosterone in their blood as adults---eunuchs, for example---are noted for their femininity of appearance and attitude. Men exposed to less than usual testosterone as embryos---for example, the sons of diabetic women who took female hormones during pregnancy---are shy, unassertive, and effeminate. Men with too much testosterone are pugnacious. Women whose

mothers were injected with progesterone in the 1950's (to avert miscarriage) later described themselves as having been tomboys when young; progesterone is not unlike testosterone in its effects. Girls who were born with an unusual condition called either adrenogenital syndrome or congenital adrenal hyperplasia are equally tomboyish. The body is masculinized by testosterone from the testicles at puberty, whatever its womb experience. But not the mind. The mind is immune to testosterone unless it was exposed to a sufficient concentration (relative to female hormones) in the womb.

25. ***You need some testosterone*** **= normal aggressive behavior**---zero levels after castration, and down it usually goes; quadruple it (the sort of range generated in weight lifters abusing anabolic steroids), and aggression typically increases. But anywhere from roughly 20 percent of normal to twice normal and it's all the same; the brain can't distinguish among this wide range of basically normal values.
26. ***Androgens reduce nitrogen excretion*** in many species and *promote growth of muscle*. The uptake of glucose and glycogen synthesis in muscle is androgen-dependent. *Men who have the genes for pattern baldness do not lose head hair unless they have circulating androgens. Androgens increases sweat secretion rates.*
27. **Dietary Choices influence hormones:** Carnivores in general have relatively large adrenal glands in terms of body weight; Herbivores in general have thyroid glands relatively large in terms of body weight. ***Testosterone declines* among men who were briefly switched from western higher fat diets to *vegetarian diets.***
28. **Dietary Choices influence hormones*:*** *Males consuming less dietary fat but increase unsaturated fatty acids tend to reduce serum concentrations of androstenedione, testosterone and free testosterone.* Changing the composition of the diet can at least partly modify testosterone activity in plasma.
29. **Dietary Choices influence hormones: *Caucasians* excreted significantly higher levels of individual and total androgenic ketosteroids than did** Chinese. To distinguish genetic from environmental/dietary factors as a cause of these differences, we compared Chinese men living in Pennsylvania and a similar group living in Beijing, China. We detected a reduction in testosterone production rates and total plasma testosterone and sex hormone-binding levels, but not in testosterone This suggests that environmental/dietary, but not genetic, factors influence androgen production and explain the differences between Caucasian and Chinese men.
30. ***Exercise effects hormones***: Endurance human runners have greatly larger thyroid glands, and significantly larger adrenal glands and consequently greater hormone output than do rhesus monkeys and chimpanzees.
31. ***Starvation, high temperature, and high altitude reduces sperm life span to shorter-lived than normal or aspermia.***
32. ***Stress* reduces testosterone levels in men**.
33. **Health-enhancing normal levels of testosterone (total, free, and bioavailable) are *higher for Asians born in Asia* versus *Asians born in North America*, whereas levels of SHBG and DHT were similar in both groups. On the other**

hand, not healthy DHT: testosterone ratio was lower in Asians born in Asia compared to those born in North America.

34. **AMERICAN TESTOSTERONE LEVELS (by influence of lifestyle factors)**
    #1 Chinese & Japanese
    #2 African-Americans
    #3 Africans
    #4 Whites
35. **Benign prostate condition shows a significantly higher DHT: testosterone ratio DHT: testosterone ratio = *prostate cancer incidence rates highest in*:**
    #1 African-Americans
    #2 white-Americans
    #3 Asian-Americans
36. ***Heavy alcohol use may increase estrone production and, thus, increase conversion of androgens to estrogens.***
37. **TESTOSTERONE** *levels are elevated in "winners"* and relatively repressed in "losers."
38. **TESTOSTERONE IS ELEVATED IN *AM*.**
39. ***LESS TESTOSTERONE LENGTHENS LIFESPAN*** (Castrated tomcats live longer than their intact male counterparts, and so do human castrates.
40. ***TESTOSTERONE RAISES BMR 5% MALES SHORTENING LENGTH OF LIFE*** **(one known effect of testosterone is to raise the resting metabolic rate of males by approximately 5 percent as compared to females. Effectively, this means that the male biochemical "engine" is running about one-twentieth faster all the time than is that of a woman, perhaps explaining why it wears out sooner.**
41. ***TESTOSTERONE INCREASES IN BASAL METABOLISM & LOWERS BODY MASS INDEX*** **Women carry 20-25% of their body weight in the form of fat, men on average have only 10-12%. Although women on average have about twice as much fat as men, they nevertheless weigh on average almost 20-25% LESS than men.**
42. ***Musical talent*** *is related to left-handedness and to anomalous dominance*; **immune vulnerability was found in female musicians, and in subjects with reversed dominance for language functions as well as in male left-handers, independently of musical talent.** Creative musical behavior, musical intelligence, and spatial ability were investigated in relation to salivary testosterone (T). In a cross-sectional study with 117 adults and in an 8-yr longitudinal study with 120 adolescents, composers, instrumentalists, and nonmusicians of both sexes were compared by analyses of variance. ***Results indicate that an optimal T range may exist for the expression of creative musical behavior. This range may be at the bottom of normal male T range and at the top of normal female T range.***
43. ***Male composers attained significantly lower mean testosterone values*** *than male instrumentalists and male nonmusicians*; ***female composers had significantly higher mean testosterone values*** *than female instrumentalists and female nonmusicians.* **Musical composers of both sexes were physiologically highly androgynous=(female gonads but male-like characteristics of glands)**

44. ***Acute increases in serum cortisol levels (STRESS) induce a rapid decrease in circulating Te concentrations.*** In men, over 95% or circulating T is derived from the Leydig cells of the testis.
45. **Dominance patterns in right-handed men with right-eye preference**, *the difference in skill between hands is directly related to serum testosterone, but there was not a significant relationship between these parameters in women with right-eye preference.*
46. ***Testosterone seems to be advantageous for the male brain***, but detrimental for the female brain with regard to skilled movements. Moreover, testosterone seems to create a more asymmetrical brain in men, and a more symmetrical brain in women
47. ***Male testosterone could account for fact that they get Alzheimer's less frequently than women***, since much of a man's circulating testosterone is converted to estrogen in the brain and since men's testosterone levels do not decline with age like women's natural estrogen levels.
48. ***Women had whole BRAIN glucose metabolic rates that were 19% higher*** than those of men. All neuroanatomical structures surveyed showed significant female greater than male rates, with no particular regions being outstanding. **The higher cerebral glucose metabolic rates we observed in women may have been *related to the effects of the high estrogen levels*** that can obtain in the phase of the menstrual cycle during which we tested our female subjects.
49. **Elevation of circulating cortisol resulting from insulin-induced hypoglycemia or the administration of hydrocortisone was followed by a rapid decrease in serum T levels, without accompanying changes in LH or PRL. These findings suggest that *this adrenal-testicular axis may have biological implications on the reproductive adaptation to stress. Hypercortisolism of endogenous or exogenous sources suppresses T secretion by a direct action on the testis.***
50. **When *plasma hormone levels undergo rapid and large oscillations*, a single random sample is likely to yield a result *Testosterone=68% of the time*, *FSH=54% of the time, and LH-=30% of the time*, respectively within *+/-20%* of the true mean value only.**
51. **Testosterone levels correlated with right-hand skill on a modified version of the Annett pegboard: right-handed men showed a positive correlation between serum testosterone level and right-hand skill, while right-handed women showed a negative correlation*. This would suggest that high testosterone levels are associated with increased right-hand skill in men, but with decreased right-hand skill in women. These findings generally show that increased serum testosterone is associated with increased right-handed performance in men, but not in women.***
52. ***Testosterone has also been implicated in influencing the size of specific areas of the corpus callosum.*** Lower levels of androgens lead to less axon elimination in specific areas of the brain, apparently resulting in specific patterns of functional asymmetry. ***Left-handed men have a larger isthmus of the corpus callosum than right-handed men.***
53. ***Te levels correlated positively with spatial relations and negatively with performance on verbal-sequential tasks.*** **One interpretation of these findings is**

that, across sexes, there may be a nonmonotonic relationship between T (or its metabolites, which have not been measured directly in any of these studies) and spatial performance, with optimal performance occurring in the middle range of T values, closer to the lower end of the normal range of T for young adult males.

54. **Testosterone (Te) may play a significant role in the development of the corpus callosum (CC). A significant positive correlation between Te concentration and cross-sectional area of the posterior body of the CC was found.** **The results of this study are *consistent with the notion that Te, at an earlier stage in development, may play a significant role in modulating cortical/callosal architecture in humans.***
55. ***Higher Testosterone (T) in males is associated with relatively poorer spatial performance. Testosterone supplementation in androgen-deficient, older men results in selective enhancement in spatial-constructional abilities, but not in performance on other cognitive tasks.***

WHAT ENHANCES OR INHIBITS TESTOSTERONE AND SHOULD ENDURANCE ATHLETES ESPECIALLY MALES ATTEMPT TO RAISE LEVELS?

(ENDOGENOUS PATHWAY: Luteinizing Hormone (LH) stimulates the production of Testosterone by the Leydig Cells of the Testicles.

MALE average Testosterone is only 7 mg daily.
FEMALE average Testosterone is only 0.3 mg daily.

MALES get their higher testosterone from testes, yet equal amounts are manufactured by the adrenal glands in both males and females.

FEMALES: Small (but biologically significant) quantities of testosterone are manufactured by the female ovaries up until menopause. Ovary-manufactured testosterone contributes to female sexual desire. After menopause approximately 35% of females have reduced sexual desire due to the cessation of testosterone production by the ovaries (the other 65% manufacture enough testosterone in their adrenal glands to sustain their sexual desire).

CIRCADIAN CYCLIC RHYTHM INFLUENCES TESTOSTERONE
Testosterone production also has a monthly cycle but there is no clear evidence regarding the time of the month for peaks and troughs. Testosterone production presents a DAILY CYCLE. Male peak testosterone levels occur from 6-8 AM with highest levels at 8:00AM, while the lowest levels occur between 6-10 PM with absolute lowest levels at 8:00 PM. The differences between peak and trough production of testosterone are large (up to 1/3 of total serum testosterone). Testosterone is not produced within the body in a totally continuous manner; hence production may vary subject to a circadian rhythm:

MEN in the northern hemisphere, the lowest levels of testosterone occur in January to April/the highest levels of testosterone occur in July to October (peaking from 8 September to 23 October)
MEN in the southern Hemisphere, lowest testosterone levels would occur in July to October/ highest Testosterone levels would occur in January to April.
WOMEN (I speculate have similar responses though no research confirms.)

TESTOSTERONE LABORATORY REFERENCE VALUES (Males: free testosterone) The following free testosterone levels are regarded as normal for males aged 20-49 (values differ between different laboratories). We use free salivary specimen sample by ZRT Labs and recommend 90% or more of max normal range pr 180-210 pg/ml free testosterone for a competitive athlete during training.

NORMAL REF RANGE	OPTIMAL RANGE
12.4-40.0 pg/mL (LabCorp)	26-40 pg/mL
34-194 pg/mL (SmithKline)	128-194 pg/mL
50-210 pg/mL (Quest Labs)	138-210 pg/mL

From a small sample taken from athletes during training, the ranges were between 42-63% of the max normal reference range or 27-47%; this is too low for optimal (90% or above desired) anabolic strength gain during training.

DIET INFLUENCES TESTOSTERONE

[1] HIGH INTAKE OF DIETARY PROTEINS increases levels of (free, unbound) Testosterone versus LOW INTAKE OF DIETARY PROTEINS decreases Testosterone by increasing levels of Sex Hormone Binding Globulin (SHBG) which binds to testosterone causing it to be unavailable to its receptors; conversely high intake of dietary proteins lowers SHBG levels which causes more free, unbound testosterone to become available for binding to testosterone's receptors. Normally, 1%-3% of endogenous testosterone is in its free, unbound state, while 44% is bound to Sex Hormone Binding Globulin (SHBG) and 54% is bound to albumin and other endogenous proteins (testosterone that is albumin-bound is available for tissue uptake; approximately 56% of the body's testosterone is readily available for uptake into tissues.) A LOW PROTEIN DIET DOES NOT SUPPORT ANABOLIC PRODUCTION OF TESTOSTERONE.

[2] REDUCED DIETARY FAT intake from 40%===>25% (dietary fats as a % of total diet) results in an average -15% decrease in "Free" testosterone. Researchers determined that dietary fats should comprise 25%-30% of total calorie intake in order to maintain optimal testosterone production. A LOW FAT DIET DOES NOT SUPPORT ANABOLIC PRODUCTION OF TESTOSTERONE.

[3] SATURATED FATTY ACIDS increase endogenous testosterone levels. Supplemental superunsaturated fatty acids (SUFAs) stimulate the leydig cells of the testicles to synthesize testosterone.

[4] ISOFLAVONES such as DAIDZEIN (extract soybeans) increased in serum testosterone (and beta-endorphin) in castrated rats. The same results were obtained in chickens given total SOY ISOFLAVONES. VELVET BEANS are reported to increase testosterone.

[5] OATS are claimed to stimulate the release of testosterone from its "bound" state (with sex hormone binding globulin (SHBG)) to its "free" state.

[6] GARLIC increases testosterone levels (due to the Diallyl Disulfide content of garlic increasing luteinizing hormone (LH) levels.

SUPPLEMENTS INFLUENCE TESTOSTERONE LEVELS

[1] ACETYL-L-CARNITINE (ALC) increases plasma testosterone levels (via its influence on acetylcholine neurotransmission in the striatal cortex of the brain).

[2] MELATONIN prevents the age-related decline in Testosterone production. A 1995 study demonstrated that nightly supplementation of melatonin to rats prevented age-related decline in testosterone production. Melatonin supplemented rats had nearly 300% the level of testosterone compared with rats that didn’t receive melatonin. Conversely, one study has demonstrated that supplemental ~~HIGH DOSE===>MELATONIN INHIBITS the production of Testosterone~~ - However, LOW DOSAGE LEVELS OF MELATONIN (up to 3 mg per day) do not appear to interfere with testosterone production. Males produce testosterone over a 24-hour cycle - the highest levels occur in the morning. Testosterone production and release occurs high-quality during sleep, meaning that sleep deprivation leads to lower or lower quality testosterone.

[3] BETA-SITOSTEROL inhibit the conversion of testosterone to dihydrotestosterone and estradiol (by inhibiting the 5-alpha reductase and aromatase enzymes)

[4] BORON increases serum testosterone levels - Boron does not raise testosterone to higher than normal physiological values but does appear to restore testosterone levels in older males to levels that they had in their 20's and 30's.

[5] POTASSIUM helps to REGULATE plasma testosterone levels (Potassium deficiency can lead to sub-optimal plasma testosterone levels. Potassium is high in whole plant foods such as fruits and vegetables.

[6] ZINC & SELENIUM are essential cofactors for the endogenous production of testosterone and supplemental zinc increases testosterone levels that are depleted AS A RESULT OF ZINC DEFICIENCY. Zinc also inhibits the conversion of testosterone to dihydrotestosterone (by inhibiting the 5-alpha reductase enzyme that catalyzes this conversion). Low Testosterone levels (in males) can occur as a result of SELENIUM DEFICIENCY.

[7] VITAMIN A helps to regulate plasma testosterone levels (vitamin A deficiency can lead to sub-optimal plasma testosterone levels).

[8] FENUGREEK SEEDS may increase testosterone levels (steroid saponins in fenugreek seeds stimulate the release of luteinizing hormone which in turn stimulates the production of testosterone).

[9] ~~KOREAN GINSENG~~ increases the body's endogenous production of testosterone.

[10] ~~HORNY GOAT WEED & MACA~~ are "claimed" to increase testosterone levels.

[11] NETTLE inhibits the binding of testosterone to Sex Hormone Binding Globulin (SHBG), resulting in lower levels of "bound" testosterone and higher levels of "free" testosterone (this occurs from Nettle binding to SHBG in place of testosterone).

[12] SAW PALMETTO inhibits the conversion of testosterone to Dihydrotestosterone (DHT). Increasing DHT is a factor in reduced or irregular urinary flow and benign prostate hyperplasia in males over 40.

[13] ~~TRIBULUS TERRESTRIS~~ is claimed to increase production of luteinizing hormone, which causes the testes to release more testosterone. Tribulus terrestris is speculated to enhance the conversion of androstenedione to testosterone (although androstenedione is the immediate precursor of testosterone, it is speculated that this conversion occurs under the influence of luteinizing hormone. Research suggests that daily intake of 750 mg of tribulus terrestris results in an increase in free testosterone levels of 30% (only in males) within five days.

[14] ROYAL JELLY is claimed to contain testosterone.

COMMENT: The following thoughts represent a personal opinion[3]. I do not recommend #'s 9, 10, and 13 above.
Natural testosterone increases that occur up to 90-100% of normal free testosterone reference range are typical, as a result of strength training and supportive dietary

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interventions that supply fats and protein quality and quantity, included with adequate rest and recovery periods. Too much exercise may inhibit the positive effects testosterone potentially presents.
DIET should be high protein, say 1.7-2.0 grams protein per kilogram body weight and at least 25-30% fat including meat-sources saturated fat, which supports the body's natural production of testosterone. Without such a caloric admixture, the body will not have the building blocks with which to manufacture testosterone. This means that during low fat, low protein, vegetarian diet intake, the testosterone levels will be predictably lower than with the opposite type of diet. Oats, velvet beans, soy isoflavones or soy protein isolates and garlic should be a staple of the vegetarian diet if testosterone release is supported.

SUPPLEMENTS taken increase testosterone or reduce aromatizing harmful side effects are saw palmetto, nettle extract, fenugreek seeds, low-dose melatonin, and acetyl-l-carnitine taken during strength training and recovery phase. Deficiency in minerals may reduce testosterone levels, but there is no need to increase minerals above the optimum daily allowance dose. Premium Insurance Caps provides each of the minerals at this dose in each 14-capsule packet. ***I do not recommend stimulating free Testosterone levels above 210 pg/ml or above 5% of normal maximum reference range.***

SPECIAL PRECAUTIONS: Immediately following a testosterone-reducing, glycogen-depletion exercise session, dietary intake of carbohydrates for replenishing depleted glycogen stores and glutamine-enhanced highly biologically-available proteins to rebuild cannibalized lean muscle mass safely and rationally supports natural the desired natural anabolic testosterone rebound in athletes. The natural anabolic property of human Growth Hormone (hGH) and testosterone (Te) present profound dynamic pathways for improving muscle growth as it relates to torque output potential, without which, performance gains will only occur at a lesser rate. Given the unpredictable nature of negative feedback hormone loops, it is concluded that athletes should avoid the temptation to boost performance by exogenous prohormone interventions. Even boosting a good hormone will predictably result in severe feedback loop depression accordingly. Exogenous stimulation of testosterone or growth hormone release above normal reference range may activate a cascade of hormone changes, which the body sees it must regulate in order to survive. The gains from raising a hormone above this regulated level are temporal and potentially harmful in athletes. Optimal regulation of survival by keeping homeostasis (balance) relationship between hormone levels and their effects in anabolic and catabolic straits are best left alone. During strength training, recuperative rest, recovery, diet and a few of the "safe" supplements for supporting anabolic high normal reference range Te may be advised including salivary free-Te hormone testing to responsibly monitor normal reference range values. Remember this for a 1-month increase in Te, 8 weeks may be required before normal natural levels return. What is elevated for only a few weeks requires around 8 times more time to return to normal natural levels.

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103. Excerpts: Testosterone pathways, by permission courtesy of In-Tele-Health 2002 (Hyperhealth Pro CD-ROM)

ADDITIONAL WEBSITE REFERENCES:

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http://www.gsdl.com/home/assessments/malehormone/appguide/references.html

Testosterone, Estrogen, and Related Hormones parts 1, 2, 3 @
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