

Testosterone as a Mediator of Muscle Tissue Growth

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INTRODUCTION

Gaining muscle tissue can be an extremely complex process. Individuals want to know what exercises maximize growth, how to order those exercises, and what the correct split is for their current level of training. Often times it helps to take a step back and analyze models which attempt to explain muscle growth. One of the more simplistic explanations is demonstrated graphically in figure 1.0.

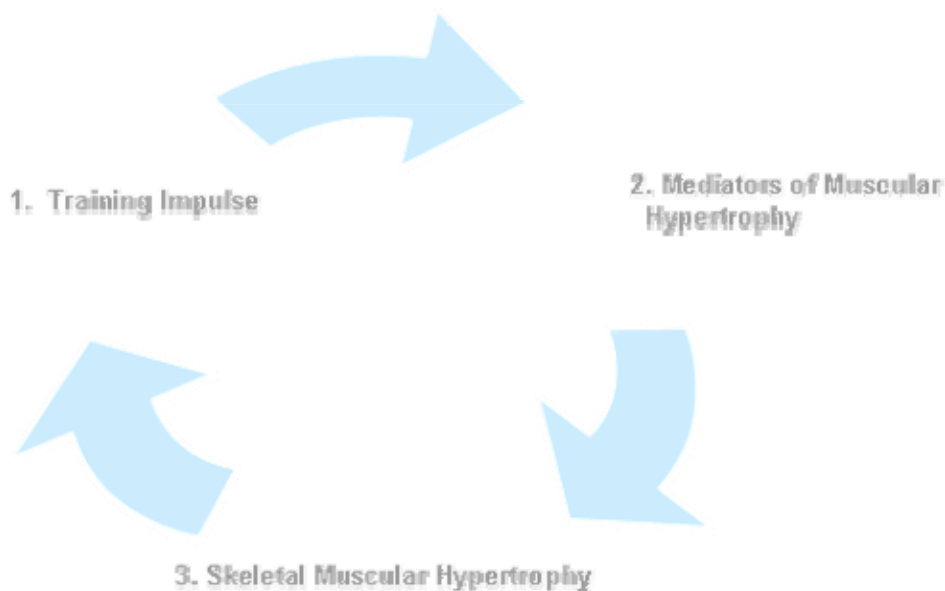


Figure 1.0 Muscular Hypertrophy

In this model we see that the training impulse, or stimulus provided through exercise can result in skeletal muscular growth. However, what is also apparent is that the training impulse may operate indirectly through what are known as “mediators.” One of the more famous substances which increases in response to exercise, and is strongly suggested to stimulate or mediate muscle tissue growth and strength is the hormone **testosterone**. It is the intent of the following paper to provide the reader with a working knowledge of what acute factors, such as exercise intensity, and exercise choice have on changes in testosterone levels. The paper will also explain how testosterone effects muscle tissue growth, and how testosterone changes chronically (over long periods) to training. Finally, athletes need to be aware of what the effects of aerobic exercise are on testosterone concentrations, especially for the bodybuilder whose endurance training has elevated during periods of dieting.

WHAT IS TESTOSTERONE AND HOW IS IT CONTROLLED?

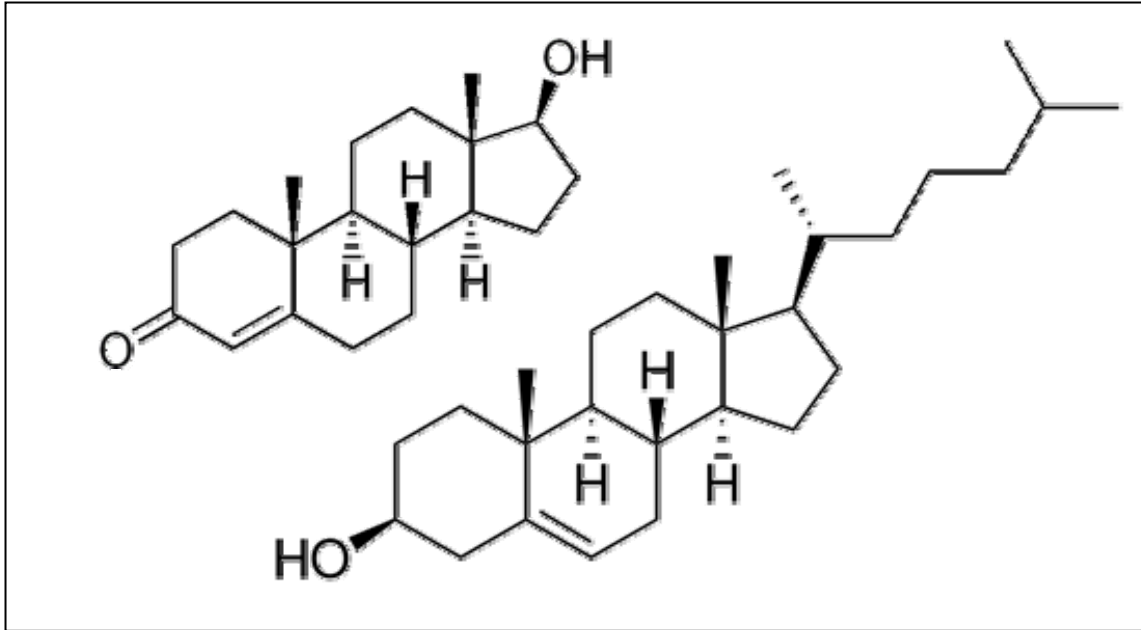


Figure 2.0 Basic structure of (A) testosterone and (B) cholesterol.

Testosterone is an anabolic, androgenic steroid hormone. It is a hormone because it is distributed to bodily tissues via the blood stream. It is critical to distinguish between its 'anabolic' and 'androgenic' properties. The anabolic characteristics are what bodybuilders are interested in, and refer to testosterone's capacity to increase muscle tissue, while its androgenic properties refer to the hormones capacity to stimulate secondary sex characteristics in males (e.g. deepening of voice, body hair). Finally, as with other steroid hormones testosterone is derived from cholesterol and comprised of a four carbon ring backbone.

In males the majority of testosterone is derived from the testes in specialized cells known as the interstitial cells of leydig. Control of testosterone release begins in the brain at the site of the hypothalamas (for more information see Wilson, G. 2006 <http://www.abcbodybuilding.com/exercisestress2.php>), which releases gonadotrophin releasing hormone (the testes are male gonads, hence the name), which travels directly to the anterior pituitary gland where it stimulates luteinizing hormone (LH) release into the blood stream. Luteinizing hormone then stimulates production and release of testosterone from the testes as depicted in figure 3.

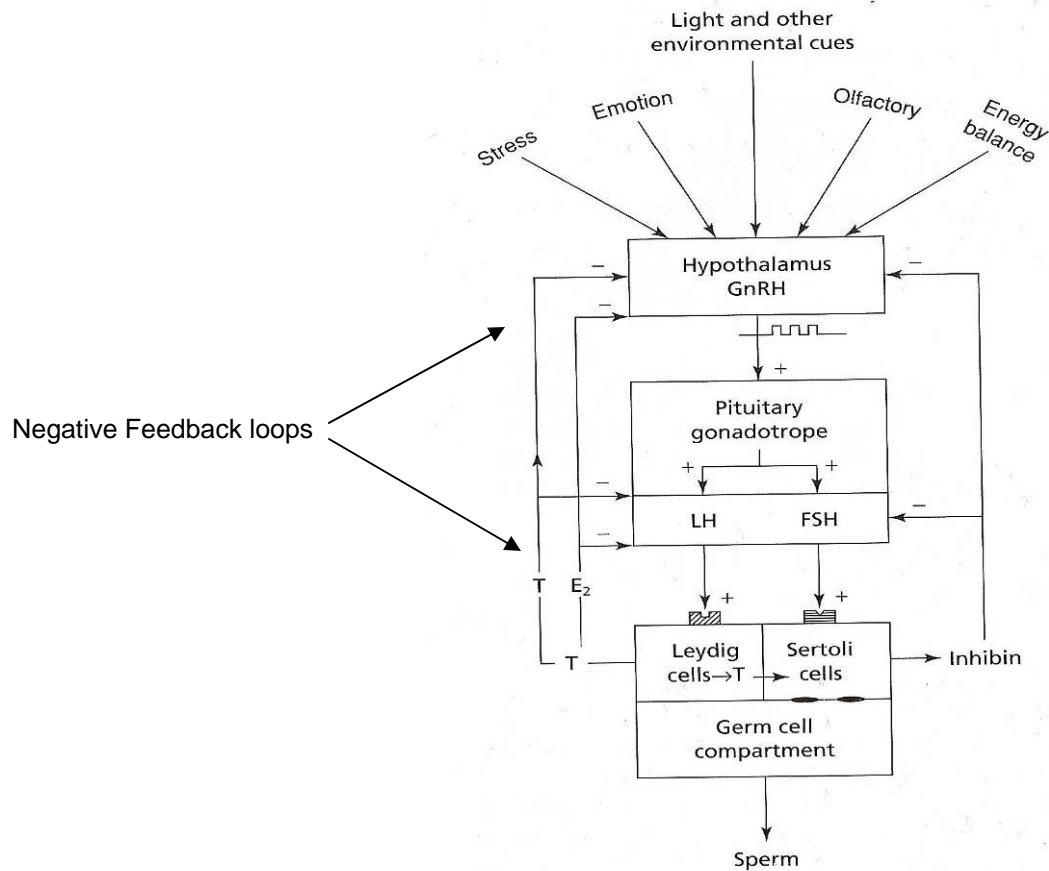


Figure 3.0 Regulation of testosterone. Adapted from Bhasin (2006)

From figure 3 you can deduce a number of implications. First testosterone can be increased by a number of mechanisms including emotion, energy balance, and stress. Coincidentally exercise can serve as a stressor, change our affective (emotional) state, and drastically alter energy balance. The figure also depicts that testosterone is controlled via a negative feedback loop. This means that an increase in testosterone may be sensed by the hypothalamus, and anterior pituitary gland which decreases release of gonadotrophin releasing hormone, and luteinizing hormone, respectively. You will also note that testosterone can be converted to estrogen (E2 in figure), which also serves to decrease the stimulators of testosterone. These will be discussed throughout the paper.

One final comment is in regards to sex differences in testosterone. In females testosterone is 20 times lower than in males, and is primarily synthesized and released from the adrenal glands.

EFFECTS OF TESTOSTERONE ON MUSCLE MASS AND PERFORMANCE

The use of testosterone can be traced to at least as far as the ancient Olympic games in 1776 BC, where some competitors would actually consume the testes of bulls! It was also known in the earlier part of last century that castration resulted in a loss of muscle tissue, strength, as well as a number of secondary sex

characteristics. However, it was not until recently when extremely controlled and highly valid experimentation with testosterone has been examined. A beautifully study which illustrates the effects of testosterone was conducted by Bhasin and colleagues (1996). These investigators administered testosterone to experienced weight lifters such that resting concentrations increased 4.6 fold. They also had the weight lifters enter into a group that either trained for the 10 week testosterone ingestion or not train. The results of the experiment can be seen in figure 4.0

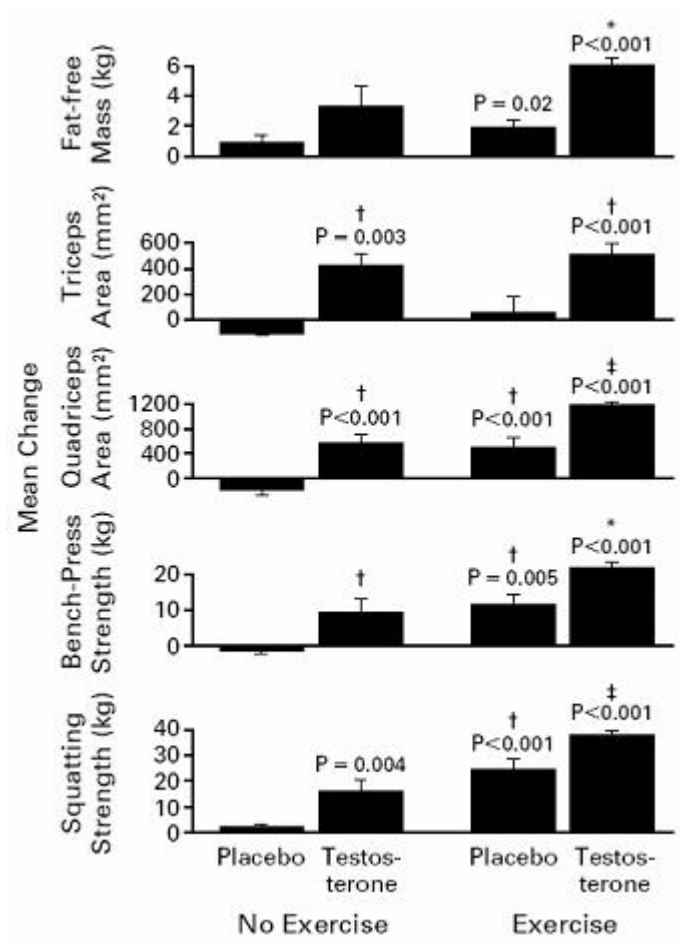


Figure 4.0 The effects of a 4.6 fold increase in testosterone on strength and muscle mass. Adapted from Bhasin et al. (1996)

As can be seen in both exercising and non exercising conditions testosterone was able to increase overall muscle mass, the triceps, and quadriceps size, and increase both the squat and bench press. These results have been supported in numerous studies including in extremely advanced athletes (Alen et al., 1984). Further when testosterone is suppressed by as little as 10 %, the normal growth response to training is blunted (Kvorning et al. 2006)! And finally a recent study by Willoughby and colleagues (2004) found that 3 bouts of resistance training resulted in increased muscle fiber growth, and that this growth adaptation was paralleled by an increase in both testosterone and testosterone receptors (see below).

MECHANISMS OF TESTOSTERONE ACTION

So how exactly does testosterone work to increase strength and muscle tissue? This is a question that has been pondered for some time by the scientific community. One of the major hypotheses is that testosterone is able to directly stimulate protein synthesis. It is important to understand that testosterone operates at the nuclear level.

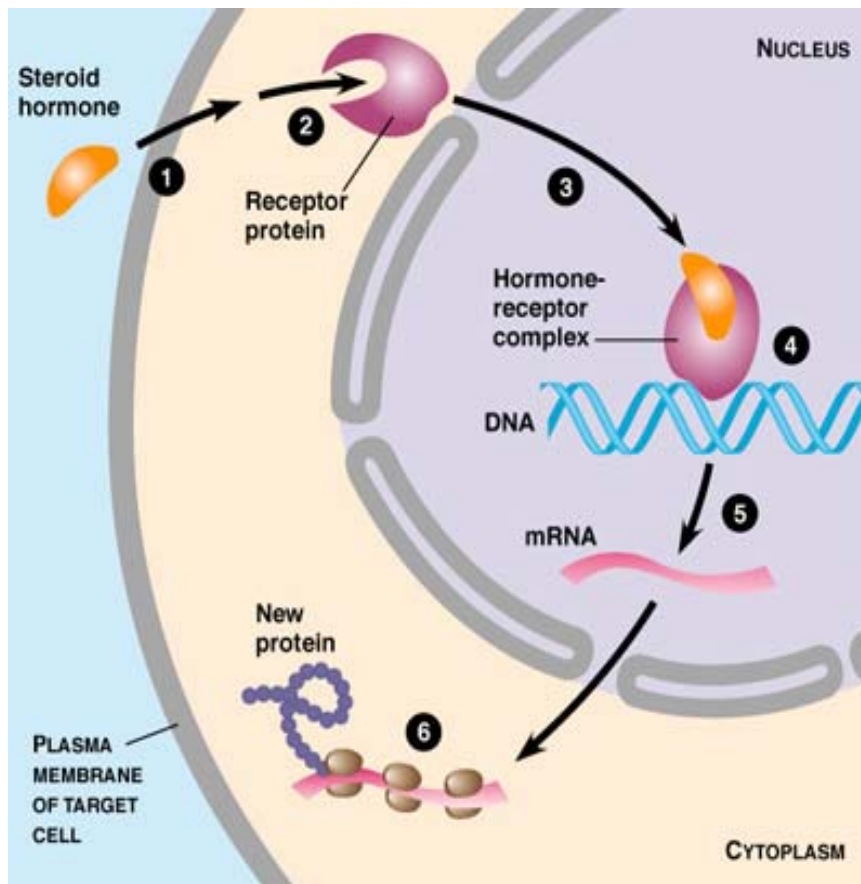


Figure 5.0 Inhibition of specific binding of cortisol to muscle cytosol glucocorticoid [3H] dexamethasone in adrenalectomized-castrated rats by the sex steroid hormone fluoxymesterone. Adapted from Mayer et al. (1975)

As can be seen in figure 5, testosterone or steroid hormones first diffuse or enter passively into a muscle cell, second they bind to a receptor on the nuclear membrane, which is then carried into the cell nucleus where testosterone stimulates DNA to transcribe or make instructions of a specific protein on a messenger molecule (mRNA). Finally, the mRNA is taken into the cytoplasm or cell environment where these instructions are used to construct new proteins, which ultimately increases the cell size. Research shows that when individuals train, that the effect of training on muscular growth is inhibited when testosterone is inhibited from binding to the nuclear receptor (Inoue et al. 1994)!

Testosterone is also a pro-hormone, meaning that it is converted to other hormones in the body including Dihydrotestosterone (DHT), by which testosterone indirectly exerts its androgenic effects, and to estrogen, which can actually increase bone density and quality, but in excess is associated with negative feedback, which lowers testosterone levels and fat accumulation (see figure 6.0).

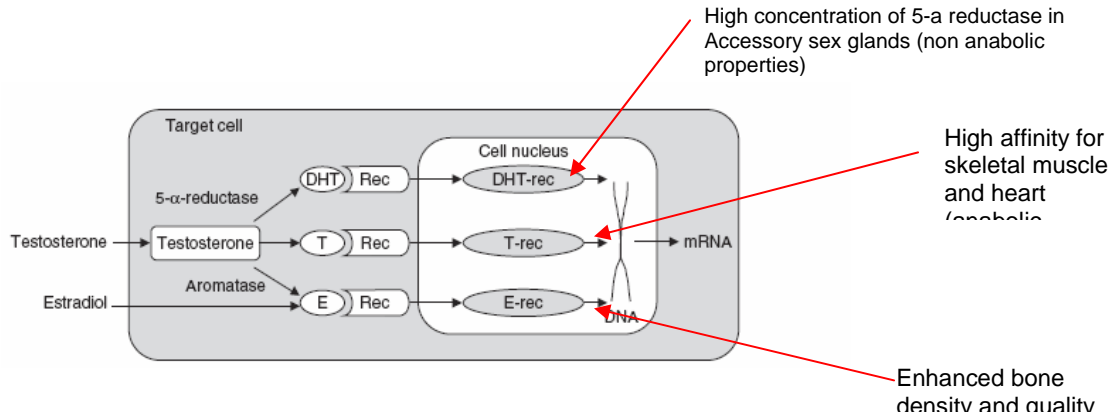


Figure 6.0 Testosterone's indirect effects through conversion to the estrogen known as estradiol and dihydrotestosterone. Adapted from Hartgen et al. (2004)

Ultimately athletes seek to enhance the androgenic properties of testosterone, while lowering aromatization and conversion to DHT. These latter topics will be discussed in future articles.

Testosterone May exert its effects through Insulin Like Growth Factor I

One of the major mechanisms that testosterone is suggested to increase protein synthesis and subsequent muscle growth is through the stimulation of satellite cell number and an increase in the actual binding of satellite cells to muscle fibers.

Briefly muscle fibers are long structures and therefore, have numerous nuclei. This is necessary as nuclei receive messages which allow muscle tissue to synthesize new proteins. As a muscle fiber grows it needs new nuclei to compensate for the extra proteins needed to maintain its new size. Satellite cells are cells which surround a muscle fiber, and when that muscle fiber is damaged they divide, elongate and fuse to the muscle fiber. As they fuse they 'donate' their nuclei to the fiber. What is interesting is that if they do not fuse to a muscle fiber then growth is stopped.

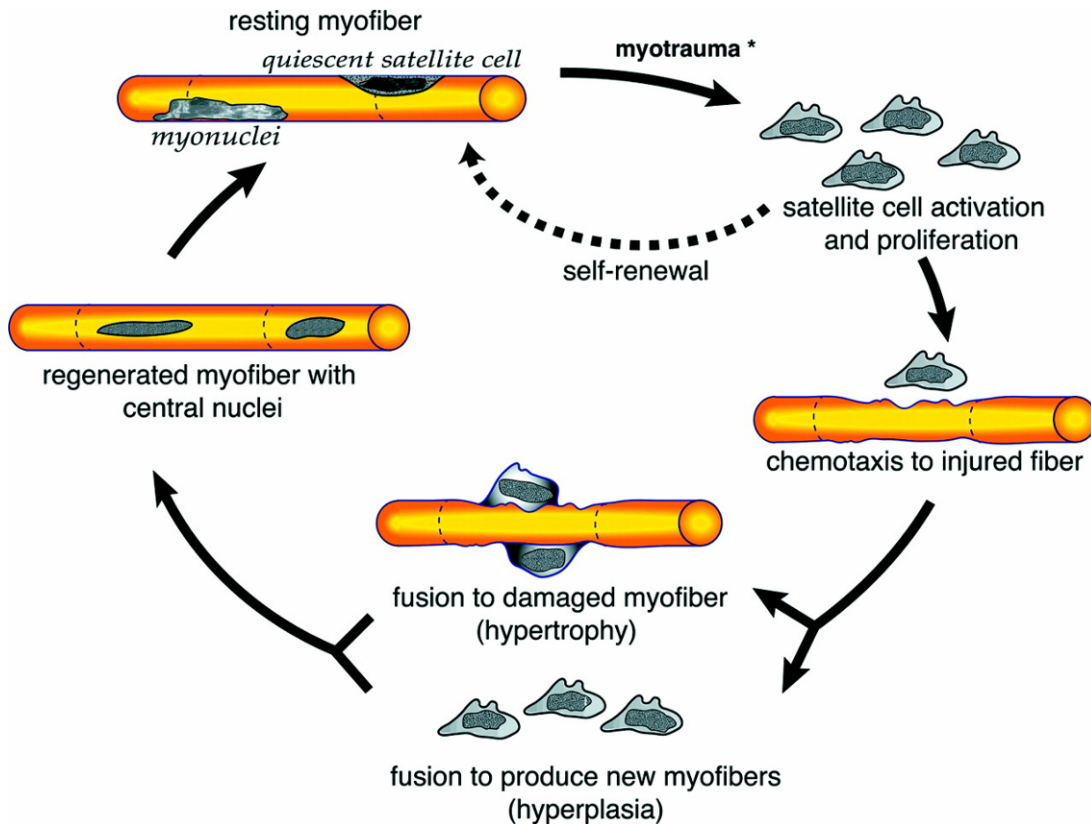


Figure 7.0 The role of satellite cells in muscle fiber repair in response to trauma. Adapted from Hawke et al. (2002)

Testosterone administration has been shown to increase both satellite cell number and fusion to a muscle fiber. It is uncertain how this occurs, but what is known is that when testosterone was administered to rat diaphragm muscles that insulin like growth factor-1 increased proportionally to the amount of testosterone administered (Lewis et al. 2002). IGF-1 is known to directly stimulate both protein synthesis and satellite cell division and fusion to muscle fibers (See Wilson, 2005 for a review). However, this suggestion was recently called into question by a 2007 study which found that suppression of testosterone during exercise did not lower IGF expression (). Future studies will need to continue to investigate how testosterone is increasing satellite cell number (Kvorning et al., 2006).

Testosterone May Inhibit Cortisol's Effects on Protein Breakdown

Cortisol is a hormone responsible for stimulating the breakdown of muscle tissue. However evidence suggests that testosterone actually blocks the binding of cortisol with its nuclear receptor. Studies clearly show this (Mayer et al. 1975), and in addition studies show that when cortisol is administered to muscle tissue that it lowers the muscle tissue's force, probably by increasing protein breakdown. However, this decrease in force is slowed drastically with testosterone administration (Van Balkom et al. 1998)

THE EFFECTS OF EXERCISE CHOICE AND EXERCISE INTENSITY ON TESTOSTERONE CONCENTRATIONS

Exercise choice

The choice of exercise appears to effect the testosterone increase to muscle tissue. For example Volek et al. (1997) investigated the effects of 5 sets of 10 repetitions of bench press Vs. 5 sets of 10 jump squats, with 2 minutes rest between sets in 12 resistance trained (≥ 1 year) men.

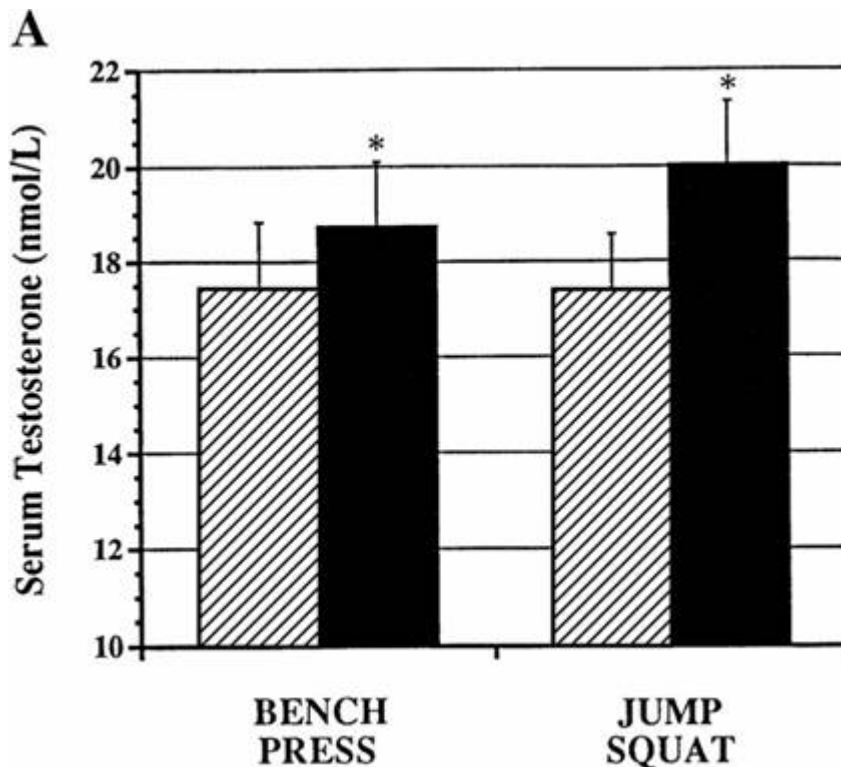


Figure 8.0 Adapted from Volek et al., 1997

As can be seen in figure 8, testosterone was raised higher following the jump squat (15 %) then the bench press (7%). This suggests that exercises which recruit the most substantial amounts of muscle tissue will optimize testosterone. It also reinforces the central tenants of exercise order principles. Generally compound movements should be performed before isolation. As testosterone is concerned, the larger exercise may raise testosterone levels and exert its effects on the smaller isolation type exercises. For example, if an athlete performs squats before biceps curls, the biceps may be exposed to higher levels of circulating testosterone.

Exercise Intensity

Intensity also effects testosterone increases. For example Raastad and colleagues had participants perform 3 sets of 3 repetitions each on back and front squats, and 3 sets of 6 repetitions on leg extensions. Now, they either performed the exercise at 100 % of their intensity or at 70 % intensity within the given repetition range. For example, if an individual could perform 100 pounds for 6 repetitions and not get another rep, that is 100 % intensity, whereas, if they were to perform 6 repetitions, at 70 % of their 6 RM, they may only work with 70 pounds. The results on testosterone increases is demonstrated in figure 9.0.

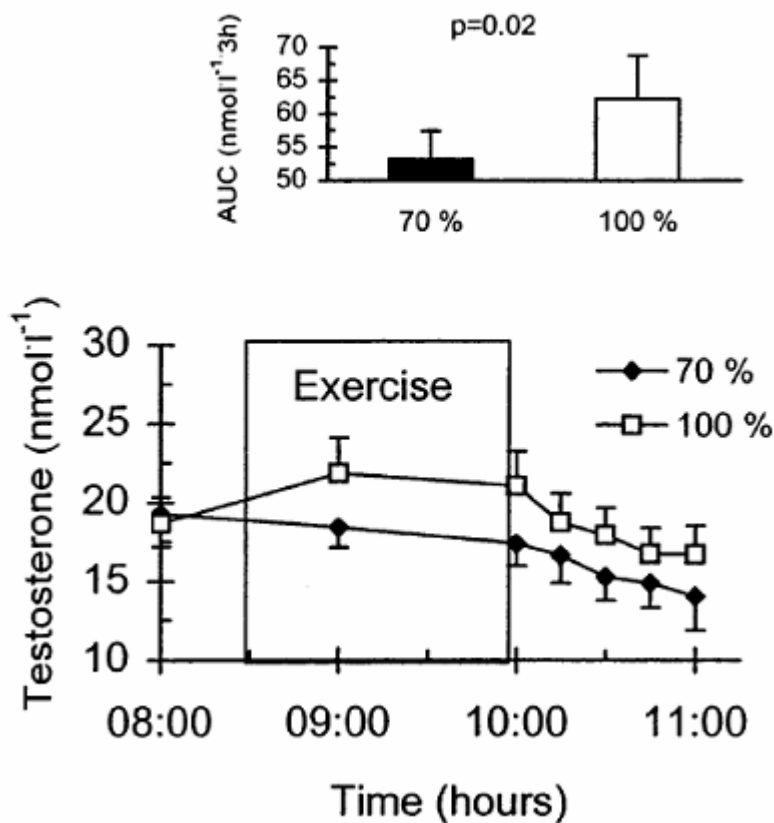


Figure 9.0 The effects of exercise intensity on testosterone increases.

As can be seen individuals who performed 6 repetitions at 100 % intensity had greater increases in testosterone than those who performed 6 repetitions at 70 % intensity. The take home message is that when an individual does not perform to failure, or close to failure within a given range, they will not elicit as great of a hormonal response to exercise.

There are a number of explanations that have been put forth for the results in the Rastaad study. They can be summarized as follows

1. Changes in Plasma Volume – When you exercise you lose fluid through both sweat and filtration. Filtration means that when your blood pressure increases you end up losing fluid to water surrounding your tissues known as interstitial fluid. The greater the exercise intensity, the higher the blood pressure and therefore the greater the fluid lost through filtration. When this occurs, the concentration of testosterone is increased, simply because less fluid equates to a more concentrated solution in terms of the hormone testosterone. This was able to explain 50 % of the differences between conditions

2. Changes in Blood Lactate – Studies indicate that lactic acid is able to directly increase testosterone secretion in the testes. As intensity increases lactic acid also increases.

3. Catecholamines (epinephrine and norepinephrine) – These rise with intensity. Also sympathetic neurons innervate the testes, and catecholamines stimulate testosterone secretion in vitro.

What is the optimal intensity and volume?

Volume is defined as total work done, and there appears to be a volume threshold for testosterone secretion. For example Schwab et al. (1993) found that 6-10 repetition sets in the squat lift did not increase testosterone until the fourth set suggesting that a volume threshold may exist.

Still in another study Hakinen and colleagues (1993) investigated the effects of intensity on testosterone increases by using two protocols. They used a 1 repetition maximum protocol for 20 sets of 1-RM squats, and compared this to 10 sets of 10 repetitions of squats. While large increases in testosterone were found in the 10 set condition, this was not found in the 20 set condition.

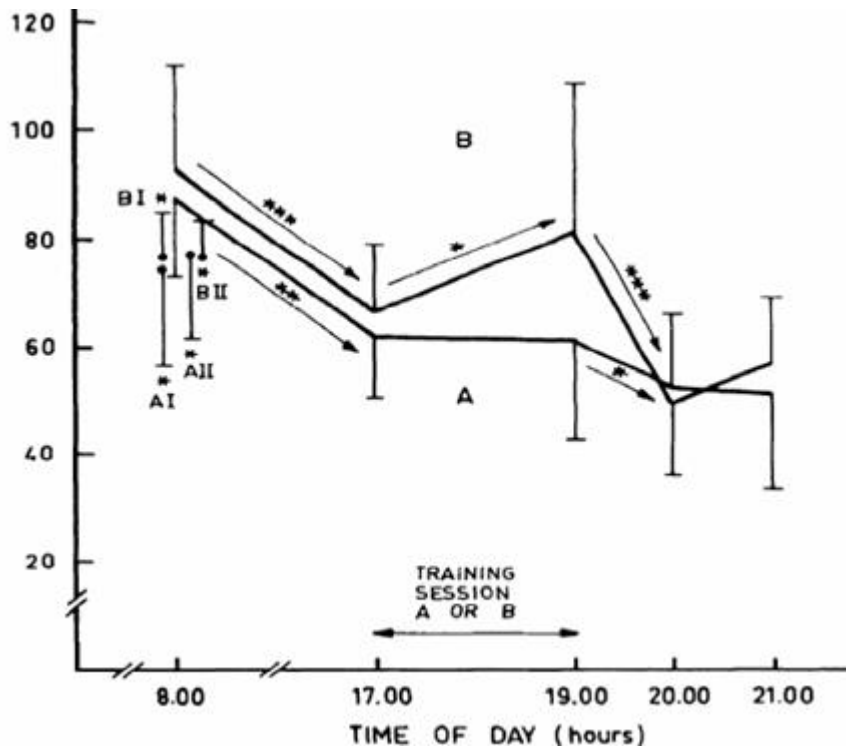


Figure 10.0 Comparison of 20 sets of 1 RM vs 10 sets of 10 RM on testosterone increases. Adapted from Hakkinen et al. 1993

This leads to the conclusion that moderate intensity (8-12 repetitions), high volume exercise leads to greater increases in testosterone than low volume, maximal intensity exercise.

PRE CONDITIONING EFFECTS OF TESTOSTERONE

Testosterone appears to augment power activities and activities with high force output. For example, work from Bosco and colleagues (1988) with 97 high level athletes, found that the highest values of testosterone were for jumping performance in sprinters, while the lowest values were in cross-country skiers, and intermediate values were found in soccer players. They (Bosco et al., 1996) also found that testosterone was directly related to both the height in the countermovement vertical jump and average sprinting speed. What is most fascinating is that actual increases in testosterone concentrations in a maximal continuous vertical jumping test for 60 seconds in professional soccer players was directly correlated with average power output ($r = 0.61$) and jumping height ($r = 0.66$). Finally other studies have shown that during judo and tennis that those who win have higher levels of testosterone than losers on average.

But why is testosterone related to running speed, and power output, and even winning? Viru and Viru (2005) suggest that changes in testosterone concentration provide a short-term preconditioning effect on athletes by influencing the central

nervous system. The result is “tuning” of the motor centers of the central nervous system for explosive performance. In other words it prepares the nervous system to operate at its maximum capacity!

The practical application here concerns athletes warm ups. Because of fluid volume shifts, athletes can increase testosterone in their warm ups by as little as 3-6 explosive jumps and therefore, augment the testosterone response. The second application is found in pre competition tapering strategies, as well as in pre competition dieting strategies.

What we currently know is that by tapering prior to an event, which means that the athlete systematically lowers volume, that their testosterone levels increase (refer to [Wilson & Wilson, 2005](#)). This rise in testosterone may explain partly why athletes speed of movement and force output increase. Pre competition dieting will be discussed in the ensuing paragraphs.

Effects of Testosterone on Endurance Performance

Testosterone has been suggested to possibly increase endurance performance as it has the capacity to increase red blood cell formation. However, an extensive review by Hartgen et al. (2004) found that endurance performance was not increased in 8 studies investigating endurance performance during endurance training, and that only two studies have reported an increase in aerobic capacity. However these two studies were conducted in strength athletes. Therefore, it appears that in already trained endurance athletes testosterone does not affect performance.

Response of Testosterone to Endurance Training

One question bodybuilders and strength athletes are concerned with, is whether or not endurance training or a high amount of aerobic training can lower testosterone concentrations. The answer is that at very high volumes of running testosterone decreases linearly as aerobic exercise increases. This can be seen in figure 11.

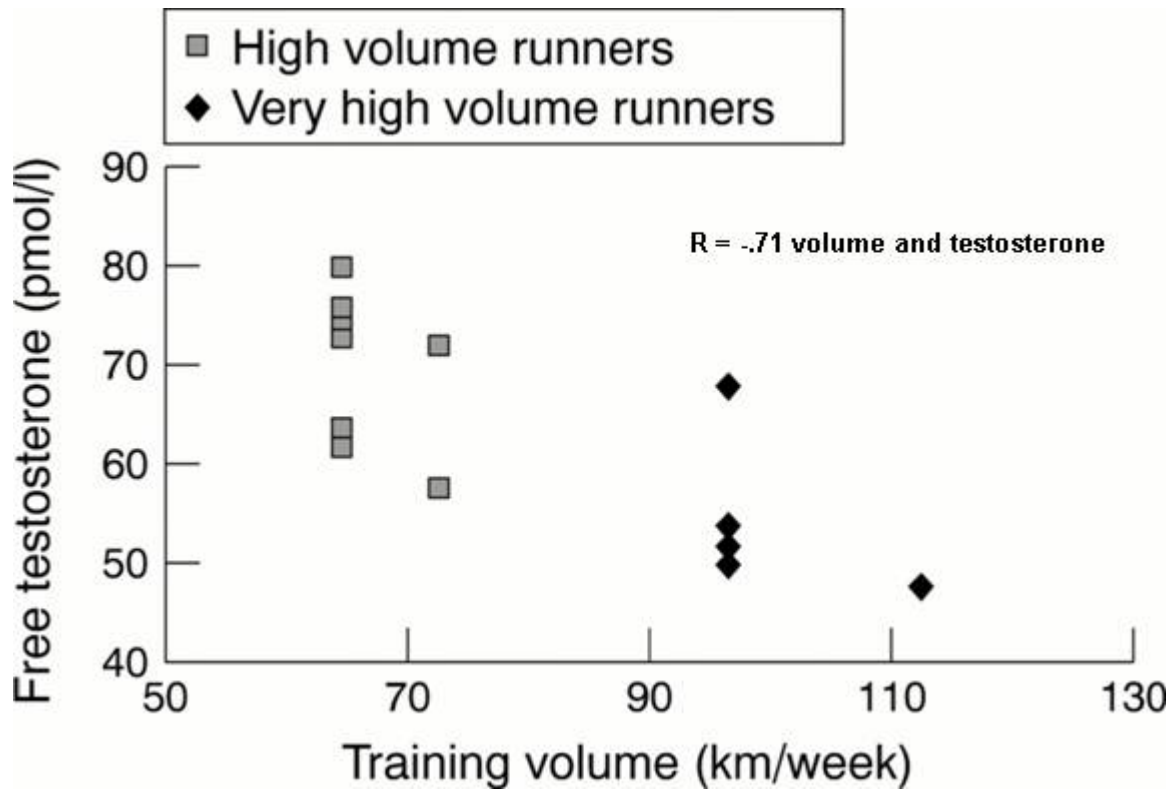


Figure 11.0 Free testosterone concentrations in (a) high volume runners (64–80 km a week), and (b) very high volume runners (more than 95 km a week), Adapted from Mackelye et al 2000

However in studies with moderate to low volume endurance exercise corresponding to 15-20 miles weekly there is not change in testosterone (Frost, 1992).

The question is why do super high volumes lower testosterone concentrations?

Energetic Deficit Hypothesis of Lowered Testosterone Concentrations in Endurance Training

In a famous experiment conducted by Keys and colleagues in the 40s, known simply as "The Minnesota Experiment" 32 young men consumed 1600 calories daily to create a caloric deficit. The results of the experiment are seen in figure 12.0

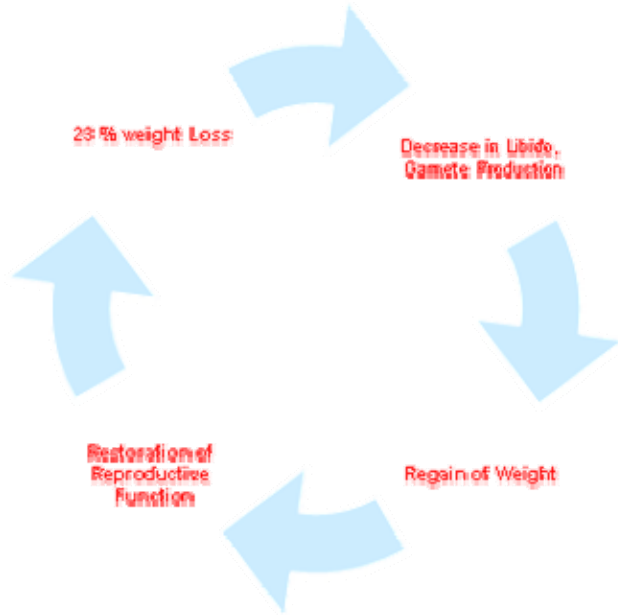


Figure 12.0 Results of the Minnesota Experiment

As can be seen, a 23 % weight loss led to decreased libido, and gamete production, while a regain in weight restored reproductive function. Because testosterone effects these functions it is hypothesized that the caloric restriction lowered testosterone.

Extensive research has continued to confirm that weight loss and body composition changes resulting from under nutrition are associated with reduced gonadotropin secretion and subsequent testosterone concentrations (Kraemer and Rogol, 2005).

This was summed by an excellent study by Cameron

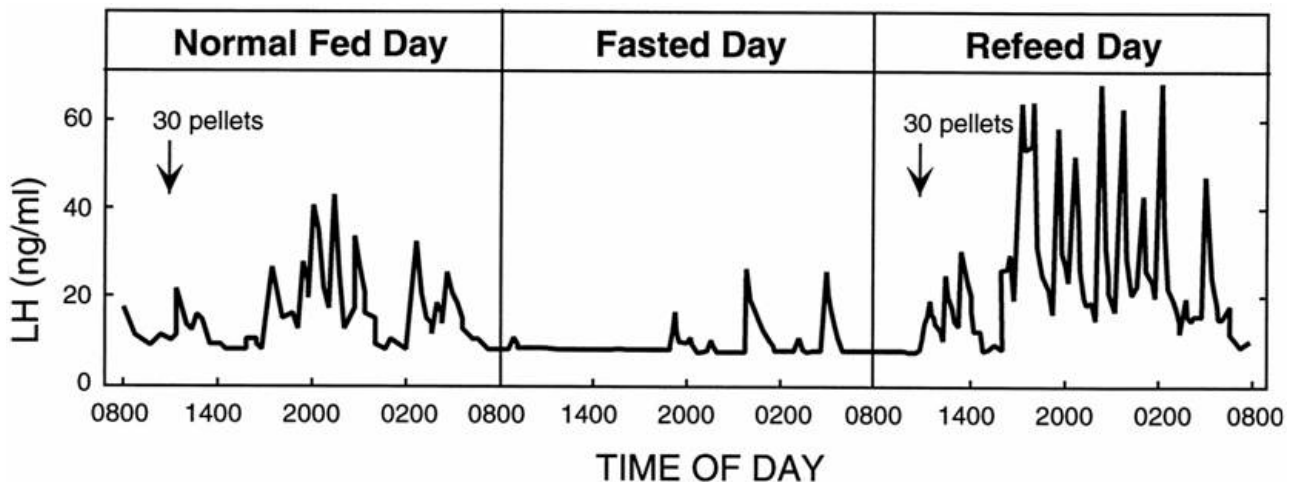


Figure. 13.0 Patterns of LH secretion in a rhesus monkey on a normal day of feeding, during a day of fasting, and during refeeding. Adapted From Cameron et al. (1995)

As can be seen, luteinizing hormone (LH) which stimulates testosterone production was lowered during fasting and increased with refeeding! This has led to the

energetic deficit hypothesis, which suggests that caloric deficits lower testosterone secretion.

Mechanism Linking Energetic Deficit and Testosterone Decreases

The mechanism appears to be related to plasma leptin levels. Leptin is a hormone which is secreted by fat tissue, which is increased with body fat increases, and also generally by increasing food intake. When calories are lowered leptin lowers with it. It appears that as leptin increases so does testosterone and as it lowers, again so does testosterone. Below is a figure from an excellent study, which shows that when individuals fast both leptin and luteinizing hormone lowers, but when they fast and are administered leptin the decrease in luteinizing hormone is eliminated!

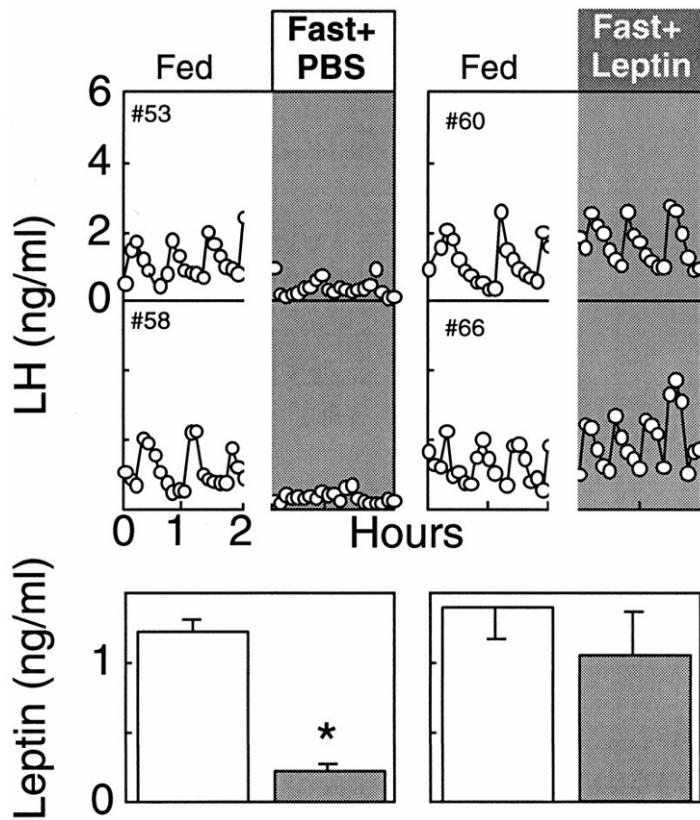
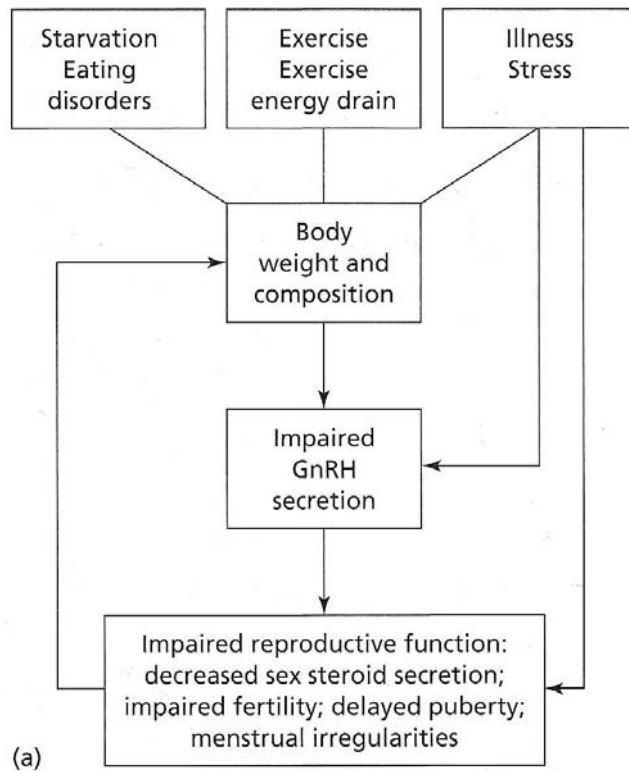


Figure 14.0 Patterns of LH secretion in adult female rats during a 48-h fast in the absence (left) or presence (right) of leptin replacement throughout fasting. (Adapted from Nagatani et al. 1998)

And this has generalized to numerous studies. Kraemer and Rogol provide an excellent model for how Leptin's effects are elicited



Here you can see that starvation, or energy drains associated with exercise can lead to caloric deficits, and impaired gonadotrophin releasing hormone and ultimately testosterone production and everything it stimulates. Leptin is thought to exert its effects by at least two mechanisms

1. Directly stimulating Luteinizing hormone
2. Inhibiting neuropeptide Y, which is a hormone which inhibits gonadotrophin releasing hormone.

The take home message is that aerobic exercise will lower testosterone to the extent that it creates a caloric deficit. It is simply important for the athlete to realize that combined dieting and cardio will stimulate these effects. Possible counter measures include calorie cycling, as well as carbohydrate cycling as leptin appears to increase in response to carbohydrates.

CHRONIC ADAPTATIONS TO TESTOSTERONE

Two key studies summarize what we know about chronic adaptations to testosterone. The first is by Hakkinen et al. (1985).

- Hakkinen et al. (1985) investigated the effects of jumping and strength training at 60-80% of 1-RM over 24 weeks.

8 weeks – Testosterone levels increased and cortisol decreased

16 weeks – Testosterone and cortisol decreased

24 weeks – Both hormones returned to baseline values

By this data it appears that early in a training program that testosterone increases but by the end of the program it returns to baseline.

In the second study Hakkinen et al. (1988) investigated the effects of 24 months of training in elite weight trainers. In these elite athletes he found that testosterone was increased after 24 months of training.

But what is the difference between these two groups? Kraemer (1996) summarizes by postulating that heavy training results in hormonal changes. However, it is possible that when the stimulus becomes inadequate that these changes disappear. Similarly Viru and Viru (2005) suggest that a decrease in hormonal changes **may indicate the need to further increase the training stimulus.**

In summary testosterone appears to increase in response to training, but if the training stimulus becomes inadequate then it will fall to baseline. This leads to the need to periodize training so as to avoid stagnation and accommodation.

SUMMARY AND CONCLUSIONS

The goal of this paper was to provide the reader with a sound and solid understanding of testosterone and how exercise affects it. This will allow for future articles which further cover a number of variables associated with testosterone.

In summary this paper found that testosterone is a powerful hormone capable of stimulating increased muscle tissue, strength, and neural output. It is increased maximally with moderate intensity and relatively high volume exercises using compound movements. It is not maximized in those who slack off and perform under their max efforts. This also applies to chronic training. When individuals allow their program to become stagnant, testosterone levels will decrease. Cardiovascular training and diet also affect testosterone. To the extent that the greater the caloric deficit, the greater the decrease in testosterone. This may be partly countered by caloric cycling.

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