Testosterone—
A Critical Hormone for Men and Women

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MEN AND TESTOSTERONE
Testosterone is a hormone that has been intimately tied throughout time to a man's virility and sexuality. It is the major steroid hormone of the testicles. However, testosterone is much more than just a sex hormone. With testosterone receptor sites in the brain and heart, and in fact throughout the entire body, testosterone plays a critical role in maintaining a healthy immune system, insuring proper heart function, regulating mood and cognition, controlling blood sugars, regulating healthy cholesterol levels, controlling blood pressure, preventing heart attacks and even reducing the risk for prostate cancer.

Testosterone production in the male begins when the pituitary gland, located deep inside the brain, secretes lutenizing hormone (LH), which in turn stimulates the Leydig cells in the testicles to produce testosterone. It is estimated that men are born with 700 million Leydig cells and they begin losing 6 million each year after their 20th birthday. In spite of these losses, studies have found that testosterone levels peak in men at about age 30. After this, testosterone levels begin declining an average of 2 percent a year.

Declines in testosterone production are due to several factors besides decreases in Leydig cell numbers. Diminished testicular response to pituitary signals that initiate testosterone production and a poor coordination of the release of these pituitary signals play the most important role in testosterone decline. Another reason for testosterone decline is because most of the testosterone that is secreted into the bloodstream attaches to a protein called sex hormone binding globulin (SHBG). Testosterone that is not bound to SHBG is called free testosterone and it is only in this form that testosterone can exert its powerful effects on all of the body's cells. An increase of SHBG occurs in many men as they age, especially if they are obese. As SHBG levels increase the amount of testosterone that is available to act on cells diminishes even further.

These age-related declines in total and free testosterone levels in men are associated with easily identifiable, classic signs and symptoms called andropause. Andropause can cause significant problems that include negative attitudes about life in general, a loss of focus and drive, a questioning of one's values and accomplishments, loss of goals and directions in life, decreased libido, depression and even cognitive impairments. Declines in sex drive, frequency of sexual thoughts and erectile dysfunction are additional problems that are directly related to falling levels of free testosterone and these can have a profoundly negative impact on the male psyche and relationships.

Physical changes also occur and are characterized by thinning hair, a decline in lean muscle tissue and an increase in body fat (particular abdominal and pectoral fat). As muscle mass declines, strength declines and risk for falls and fractures increases. A decrease in bone mass is another major problem associated with declining levels of testosterone.

Osteoporosis is not just a woman's disease—up to 30 percent of men aged 60 and
over become osteoporotic. One out of every six men will fracture a hip at some point in their life as a result of decreased bone density. Declines in stamina and exertional performance are also a direct result of inadequate levels of testosterone, as are declines in mental skills, concentration and memory.

Testosterone can be converted, by enzymes, into other hormones. One of these enzymes is called 5-alpha reductase. It is found in especially high concentrations in the prostate gland where it converts testosterone into dihydrotestosterone (DHT). Another enzyme, called aromatase, is found in skin, brain, fat and bone. Aromatase converts testosterone into estradiol, the human form of estrogen. As men age, more of the testosterone they produce is converted into estradiol. When there is too much estradiol, it competes with testosterone and negative consequences develop. These include prostate cancer, heart disease and stroke. Abnormal increases of estradiol are caused by excess amounts of aromatase enzyme, impaired liver function (often caused by excessive alcohol or certain drug interactions), obesity (which increases aromatase enzyme), and zinc deficiency (zinc is a natural aromatase enzyme inhibitor). In addition to declining levels of testosterone and increasing levels of estradiol, growth hormone, thyroid hormone and dehydroepiandrosterone (DHEA) levels fall during andropause. As these levels decline, profound changes occur with growth and metabolism that affect men both physically and mentally and add to their testosterone deficiency problems.

Today the signs and symptoms of andropause should not be accepted as an inevitable consequence of the aging process. By utilizing bio-identical hormones and accurate monitoring techniques, replacement therapy is now possible. Hormone optimization programs offered by Age Management Medicine physicians have rapidly moved into the forefront of preventive medical care and have contributed greatly to the enhancement of quality of life as men and women age.

WOMEN AND TESTOSTERONE
Testosterone may be well-known as a hormone that has been tied to a man’s virility and sexuality, but few realize that it is also a very important hormone for women. As women age, estradiol and progesterin levels begin falling as they enter menopause. Testosterone (produced in the ovaries and adrenal glands), thyroid hormone and growth hormone levels also decline during this time. As the levels of these key hormones diminish, profound degenerative changes begin occurring with growth and metabolism that affect the breasts, vagina, bones, blood vessels, gastrointestinal tract, urinary tract, cardiovascular system, skin, brain and energy levels.

We now know testosterone is critically important for a woman’s libido, sexual responsiveness, mood and generalized feelings of well-being. Women, like men, also need adequate testosterone levels for peak mental acuity and the maintenance of healthy bone density and muscle tissue. Maintaining bone density is absolutely critical for women. Unsupplemented women have a 50 percent chance of experiencing a pathological fracture of their hip or vertebra at some point in their life. This is a frightening statistic because a hip fracture carries with it a 25 percent six-month mortality rate and a 50 percent two-year mortality rate. Testosterone also plays a key role in the prevention of the accumulation of unwanted body fat, heart disease and loss of cognitive function in women. Testosterone replacement therapy is now recommended for women with suboptimal blood levels. Like men, women must have all of their hormones at optimal levels and be followed with laboratory studies on a regular basis after therapy is started.

TESTOSTERONE MEASUREMENT
Clinical signs and symptoms are important indicators that an individual needs testosterone replacement therapy. However, objective laboratory measures must be obtained to properly institute and manage therapy. These lab measurements are also necessary to rule out or address any accompanying medical problems. To adequately measure testosterone levels, both total and free testosterone studies should be obtained. The normal laboratory ranges for these is, ironically, the same for 20-year-olds and 70-year-olds.

Obviously, the 50-year span from age 20 through 70 with the same normal range is not a useful guide to determine optimal testosterone levels for older individuals. Typically there is a 70 percent decline from the more youthful levels to the levels typically seen after age 40, and this will produce most, if not all, of the problems associated with low testosterone levels described above. Yet a level this low does fall in this broad range and is declared “within the normal range” by today’s laboratory standards. A more accurate approach would be to use the upper third of the normal range for one’s age as the optimal or normal level.

The decision to institute testosterone replacement therapy should always be made in the context of other hormonal and laboratory studies. Prostate Specific Antigen (PSA) measurement and a digital rectal exam of all men must accompany testosterone blood levels at the time of the initial evaluation to screen for any preexisting prostate disease and they need to be followed at regular intervals. Other studies, such as thyroid hormones, growth hormone (hGH), lutenizing hormone (LH), dehydroepiandrosterone (DHEA), estradiol, progesterone, blood count, lipid profiles and other laboratory and metabolic markers (such as body composition and bone density) all play important roles in maximizing a testosterone replacement program in both men and women. Once therapy is initiated, follow up hormone levels, as well as other markers, must be monitored over time at regularly scheduled intervals by a well-trained physician to maximize success and assure safety.

TESTOSTERONE THERAPY
Any hormone therapy, including testosterone therapy, is very serious business and must be performed by physicians trained in hormonal modulation. Before any testosterone supplementation program is started, all key hormone levels must be evaluated and therapy should be based on the augmentation of all hormones with suboptimal levels. After the decision has been made to optimize hormone levels, the next step is to decide on the best means of administration.

The best method of testosterone delivery varies from individual to individual and is dependent upon several factors. Optimally, a testosterone delivery method should be clinically effective in correcting the signs and symptoms of testosterone decline and produce predictable and reproducible optimal levels of testosterone without increasing levels of other potentially harmful hormones. The fact that testosterone can be converted to estradiol by an aromatase enzyme is a serious concern for men because, in some, any intervention that raises testosterone levels will raise estradiol levels. With proper laboratory follow up, this is easily identified and corrected. The raising of serum levels of dihydrotestosterone (DHT) can also be clinically important in men. DHT, as discussed earlier, is the hormone associated with male pattern baldness and prostate enlargement. These do not become a problem if DHT levels are closely monitored and controlled.

Testosterone is available directly in injectable, topical, and implantable formulations, and may also be supplemented indirectly by the administration of human
chorionic gonadotropin (hCG). At present there are no recommended oral testosterone formulations in the United States for men. Testosterone pellets have been developed for men that can provide augmented serum testosterone levels for up to six months. Pellets, however, require a surgical procedure for implantation and removal, and once they are placed, they do not allow for altering dosages based on an individual’s testosterone blood levels.

An oral preparation that is useful for helping normalize testosterone levels in women is DHEA. Men do not convert DHEA into meaningful levels of testosterone, but many women do. A good first step in improving testosterone levels in women is to optimize DHEA levels and then recheck testosterone levels after five to seven weeks. If testosterone levels have not increased, direct testosterone therapy can be started at that time.

Testosterone for use in men is available in a formulation that provides a long biological effect time and can be purchased by prescription in a low cost, easily self-injectable form. A dosage interval of once a week works very well. Delivering testosterone in this way has a 100 percent success rate in providing every cell with usable hormone. It is also easy to control precisely the dosage of testosterone and manage the results by following levels over time at regular intervals. This is the supplementation of choice for men whose testicles are no longer able to produce testosterone in adequate amounts.

Testosterone formulations are also available for topical placement, which allows testosterone to be absorbed through the skin. Testosterone cream is the therapy of choice for raising testosterone levels in women. There is only limited application for topical testosterone in men because this method can produce elevated serum levels of DHT. The very small amounts of testosterone cream required to raise testosterone levels in women have not been associated with any problems. Testosterone patches are available by prescription for men but have been associated with problems including inability to achieve adequate serum testosterone levels and local reactions from the adhesive. Mild to moderate reactions occur in as many as 50 percent of men using some formulations of the skin patch. Patches have also been shown in studies to produce a 30–50 percent failure rate in clinical applications.

An interesting new way of increasing testosterone levels in men has been achieved through the use of human chorionic gonadotropin (hCG). The hCG is a hormone that is able to bind to luteinizing hormone (LH) receptors with the same binding affinity as LH. Administration of hCG can, therefore, mimic the same effect as LH and increase testosterone production by stimulating Leydig cells in the testicles. In men who still have a functional LH/testosterone control loop, testosterone production with hCG is the most physiologic method and is not associated with the testicular atrophy that can occasionally happen with direct testosterone administration. The preferred method of administering hCG is to give self-administered subcutaneous doses with a tiny insulin syringe twice weekly. With normal aging, the testicles will at some point stop responding to the LH and hCG signals. If testosterone levels do not rise in a patient receiving hCG after six weeks, we know the “disconnect” between the testicles and the pituitary gland has occurred and direct testosterone supplementation is the preferred route.*

Once a hormonal augmentation program is initiated, laboratory markers which include hormone blood levels, should be followed at regularly scheduled intervals and therapy must be adjusted accordingly if an endocrine supplementation program is to be safe and effective. Physicians specifically trained and certified in Age Management Medicine are best suited to oversee such programs.

CONCLUSION

Hormonal balance plays a huge role in determining the overall health and well-being of both men and women. Today age-related hormone deficiencies and imbalances are correctable and optimal hormone balances that place individuals in the upper percentiles of their normal hormone ranges can be safely achieved when performed by a competent physician specifically trained and certified in Age Management Medicine. Men, women and their loved ones need not suffer the consequences of a mid-life crisis. There is definitely hope. It is now within our power to make the rest of our lives the best of our lives.

References are available on request.


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About Cenegenics

Cenegenics Medical Institute is the largest and most experienced Age Management Medicine Practice in the world with patients from every state in the United States and several countries, 25 percent of whom are physicians and their families. Cenegenics consistently receives regional, national and international media exposure and has been the featured expert in the media, including USA Today, Wall Street Journal, ABC’s “20/20,” and CBS’s “48 Hours.”

Cenegenics Physician Training Programs

Through the joint sponsorship of the Cenegenics Medical Institute and the Foundation for Care Management, Cenegenics provides American Medical Association PRA Level 4 Classification Tutorial Training in Age Management Medicine for physicians with a maximum of 50 Category 1 Continuing Medical Education (CME) Credits. Cenegenics also sponsors an Institutional Review Board (IRB) Research Protocol for Age Management Medicine with University affiliation. In addition, Cenegenics has the highest rating for a privately held entity with Dun & Bradstreet, Inc. because of their business ethics. For further background information, including biographies of their physicians, management team, and medical advisory board, please visit www.Cenegenics.com.