Hormone Replacement Therapy in Men

In the last chapter we reviewed menopause, that 'life change' our mothers, grandmothers, wives and daughters are subjected to in their lifetimes. However, not many people are familiar with the male menopause called *Andropause.* This is a relatively new term in the medical and lay literature to define what happens to a man, as he ages, in relation to testosterone, the predominant male hormone. Andropause also involves a number of other hormonal, physiological, chemical and psychosocial changes, but our discussion will focus on testosterone replacement. There is still some disagreement within the medical community as to whether this condition (and therefore treatment) actually exists. In this simple review, we will take the 'in favor of' side and limit our discussion to the symptoms and treatment of Andropause in relation to hormone replacement therapy, specifically testosterone. It is of interest that a number of ancient peoples including Indians, Greeks and Egyptians were aware that extracts of animal testes could be used to promote virility, potency and vigor in men. Also of note, testosterone was the first hormone to be discovered; yet its overall role is still not completely defined.

Andropause is a natural reduction of androgens levels in the aging male. Andropause is similar to menopause in women without the obvious onset like the cessation of menstruation. The decreased levels of androgens may lead to distressing signs and symptoms for some men. The signs of Andropause are loss of muscle mass, osteopenia, dry skin, insulin resistance and visceral obesity. Other symptoms include tiredness, fatigue, mood change (depression), irritability, and sexual dysfunction including decreased libido, erectile dysfunction, and an overall decreased quality of life.

So the next logical question is: *Does testosterone decrease with age?* A number of studies have shown that it does.[11-14] Bio-available testosterone and total testosterone can actually start decreasing in men's middle to late twenties!

The incidence and prevalence of Andropause is increasing in the aging male population. In 2004, an estimated 2-4 million American men had Andropause and only 5% of these men were treated.[16] In 2002, the Massachusetts Male Aging

Study[17] estimated an incidence of 481,000 new cases of androgen deficiency per year. The study was a large population-based random-samples cohort using 1709 men, ages 40 -70, investigating the age-related trends of androgen levels in this age group.

Most men, however, begin to experience deleterious changes in their bodies somewhere between the ages of 30 and 55. In the past, we attributed it to "growing old". A lot of information now points to changes in the levels of hormones that the body produces that help influence these changes. That is not to say that keeping the hormone levels at their youthful peak will prevent aging, but that some of the subjective and objective changes we see with aging may be related to this natural decrease in circulating hormones. Unlike changes females undergo at the start of and during menopause, such as the ceasing of menstruation, the symptoms of Andropause tend to come on slower and more gradual. These signs and symptoms are quite impressive and are listed in Table 8-1.

Testosterone levels begin to decrease for a number of reasons. These include a decrease in the number of cells that produce testosterone, and an increase in a protein called sex hormone binding globulin (SHBG), resulting in greater binding of testosterone with less of the free or 'active' testosterone available for the body's use.

There is also a higher relative amount of estrogen, the predominant female hormone, with less testosterone being produced. This can be caused by an increase in aromatase activity (the hormone that converts testosterone to estrogen) partly due to the increase in fat that occurs with 'normal' aging, as fatty tissue contains more aromatase activity than lean tissue. Alteration in liver function, zinc deficiencies and / or vitamin C deficiencies, obesity, and overuse of alcohol also add to the problem. A number of drug-induced estrogen imbalances can occur and the ingestion of estrogen-enhanced food or environmental substances also contributes to the rise. This increase in estrogen can cause a change in fat distribution, a decrease in lean mass, breast development, and an enlarged prostate.

TABLE 8-1: Symptoms Associated with a Decrease in Testosterone

Fatigue	Nervousness, anxiety, and irritability
Poor sleep quality or insomnia	Aches and pains
Body fat gain, particularly abdominal weight gain	Bone deterioration
Lean muscle deterioration and loss of strength	Hair loss
Decreased libido (sex drive)	Wrinkling and drying of the skin
Erectile dysfunction and reduced potency and/or penile size	Memory problems
Decreased ejaculatory force and volume	Depression
Reduced motivation	Increased apathy

Other effects of aging that we see include increasing amounts of heart disease, type II diabetes, dementia, and other age related conditions. While all of these have other, causative factors including diet, activity level, etc., the steady decline of testosterone is implicated as well [1 – 10].

As early as 1944, data indicated a correlation between the above-mentioned symptoms and hormonal changes [15]. Men also experience psychosocial symptoms as they enter this stage of their lives. These range from death of family members, in particular their parents, to work place and life goal opportunities decreasing. Retirement becomes imminent. Friends and acquaintances develop diseases. These psychosocial events can add to the depression and reduced motivation experienced with a decrease in testosterone levels. These issues are very important not only to realize but also to equate with one's ability to handle them, and I have found that testosterone replacement aids men during this time in their lives.

Many men experience mild versions of Andropause and, just as in the case with some women, some go through 'the change' totally unscathed.

One method of treating the hormonal aspect of Andropause is similar to that for women, natural hormone replacement therapy. In my opinion, the future will

dictate hormone replacement therapy as commonly for men as it now does for women.

Hormones and therefore hormonal response are a very individual issue. Adequate time for adjustment and implementation are essential in finding an ideal amount not only to control symptoms associated with hormonal loss, but also to ensure optimal health.

There is no evidence that natural testosterone stimulates the development of prostate cancer and to my knowledge, there has been no relationship established between endogenous testosterone and benign prostate hyperplasia (BPH) and prostate cancer[16]. However, there IS a contraindication to natural testosterone replacement therapy *in the presence* of prostate cancer.

Testosterone deficiency has been implicated in accounting for a number of the symptoms listed in Table 8.1. Again, it is beyond the scope of this book to delve into great detail, but I would like to review a few more medically related examples:

Blood pressure[5]

In one study, researchers tested 1,132 men 30-79 years of age. Those with hypertension, categorically defined as systolic blood pressure (top number) greater than 160 mmHg and/or diastolic blood pressure (bottom number) greater than 95 mmHg, had significantly lower testosterone levels than non-hypertensive patients. This demonstrates an inverse relationship between testosterone and blood pressure (people with low testosterone had higher blood pressure).

Brain function[4]

Short-term testosterone supplementation improves spatial functions and verbal memory in healthy older men, according to a report published in the Journal of Neurology. Twenty-five healthy men, 50 to 80 years of age, received a 6-week course of weekly placebo or testosterone (100 mg) injections. Spatial memory, spatial ability and verbal memory were significantly improved in the testosterone

group compared to their baseline cognitive function and the cognitive function of the placebo group. This study also demonstrated an increase in estradiol (a type of estrogen) in the treatment group, and the researchers commented on the fact that it is difficult to tell if this hormone or the testosterone was responsible for the noted improvements.

Heart disease[3, 10]

One study demonstrated that a decrease in testosterone levels, with age, is associated with potentially unfavorable changes in blood lipids. Triglycerides, an independent risk factor for heart disease, were higher and HDL cholesterol (the good cholesterol) was lower.

Body Composition[1, 6, 8]

Studies have shown that testosterone treatment was followed by a decrease of visceral fat mass, as measured by computerized tomography (CT scan), without a change in body mass, subcutaneous fat mass or lean body mass. Other studies have demonstrated that men with increased abdominal obesity (yet another risk factor for cardiac disease) have lower testosterone levels than men without central obesity.

Other medical improvements with testosterone therapy include a decrease in insulin resistance, improved blood sugar, a decrease in serum cholesterol[6], increase in bone density[10] and sleep improvement[2].

Insulin Resistance

Testosterone is an important regulator in insulin sensitivity and low levels of testosterone have been observed in men with diabetes, metabolic syndrome, insulin resistance and coronary artery disease (CAD). A study with metabolic syndrome showed that men with testosterone levels in the lower third were 1.7-2.8 times more likely to have metabolic syndrome.[19,20] The association between low testosterone and insulin resistance is mediated by obesity and visceral

adipose tissue in non-diabetic men.[19] Another study found that testosterone levels and glycosylated hemoglobin levels are inversely related.[21] Low testosterone levels may be an independent risk factor for the development of diabetes and it has been shown that low ranges within the normal range of free and total testosterone were associated with diabetes, independent of adiposity.[22]

Improvements in the other Andropause symptoms mentioned (sex drive, depression, skin changes, etc.) also occur with testosterone replacement, as has been noted in a number of well-designed studies.

There are, of course, risks involved with therapeutic testosterone replacement (as with any medication) and these need to be discussed and reviewed on an individual basis with a physician trained in this area.

Most of the available evidence suggests that testosterone replacement is potentially beneficial to aging men, particularly in the areas of bone density and body composition. However, the amount and longevity of the beneficial effects are not yet known[10].

Table 8-2 is the St. Louis University Androgen Deficiency in Aging Male (ADAM)[18] Questionnaire. If you are male and after reading this chapter feel you may have andropause, fill out this questionnaire and take it to your physician or health care provider to discuss possible intervention.

Table 8-2: ADAM Questionnaire

St. Louis University Androgen Deficiency in Aging Male(ADAM)18 Questionnaire
A positive screen for hypogonadism includes a ‘‘Yes’’ response to numbers 1 and 7, or any other 3 questions.

1. Do you have a decrease in libido (sex drive)?
2. Do you have a lack of energy?
3. Do you have a decrease in strength and/or endurance?
4. Have you lost height?
5. Have you noticed a decreased enjoyment of life?
6. Are you sad and/or grumpy?
7. Are your erections less strong?
8. Have you noticed a recent deterioration in your ability to play sports?
9. Are you falling asleep after dinner?
10. Has there been a recent deterioration in your work performance?

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