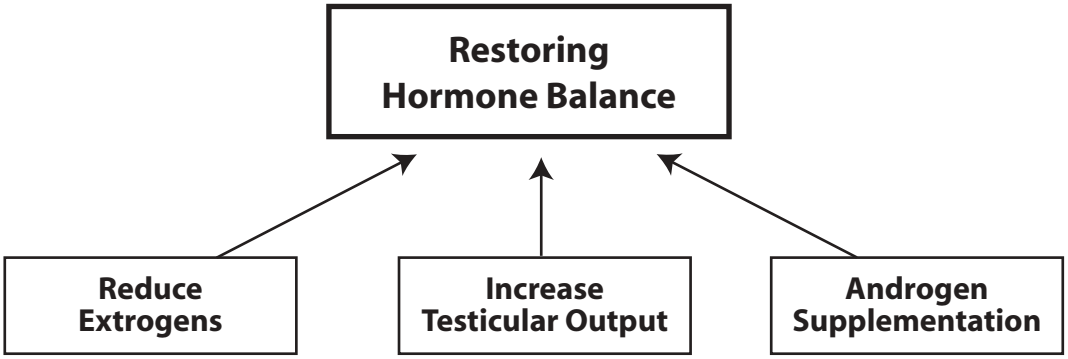
TREATMENT OPTIONS FOR ANDROPAUSE

Bruce Biundo, R.Ph.
P.C.C.A. Pharmacy Consulting Department
March 7, 2002

Andropause is a condition of hormonal imbalance, and may be related to declining levels of testosterone, elevated levels of estrogens, or a mixture of both. After proper diagnosis, including screening of testosterone and estrogen levels, therapy has been shown to be dramatically effective in relieving symptoms of andropause and restoring drive, health, potency and a sense of renewed vitality.



We will consider restoring hormone balance as our overall goal, and consider the following ways this may be accomplished: 1 - Reduce estrogen levels; 2 - Increase testicular output of testosterone; and 3 - Androgen supplements: pro hormone supplements and testosterone supplements.

1. Reduce Estrogen Levels

When estrogen (estradiol primarily, but also estrone) levels are elevated, there are several options that can be considered to lower them, while increasing testosterone levels at the same time. The simplest, least invasive steps are careful dieting to lose weight and exercise programs.

Nutritional supplements, such as elemental zinc (50 to 100mg per day) and Vitamin C (1Gm per day), may be useful as aromatase inhibitors, agents that slow down the system responsible for converting testosterone to estradiol, and androstenedione to estrone. Another interesting aromatase inhibitor is chrysin, a bioflavonoid that has been sold without a prescription in tablet and capsule form for oral use. Because studies have shown chrysin to be poorly absorbed when taken orally, it has been recommended for topical administration in doses ranging from 100mg to 200mg daily.

Remember that SHBG (sex hormone binding globulin) keeps testosterone in storage as opposed to being free and readily available at the cell receptor sites. Because estrogen elevation contributes to the elevation of SHBG, and therefore, binds more testosterone to the inactive state, agents that lower estrogen are believed to make

free testosterone, the active form, more abundant.

2. Increase Testicular Output

Increasing testicular output of testosterone may be the desired option in the case of secondary hypogonadism, in which the testes may be fully intact, but are not receiving proper signals to secrete testosterone. The signal hormones FSH (follicle-stimulating hormone), and especially LH (Leutenizing Hormone) may be mimicked by HCG (Chorionic Gonadatrophin); an injection of HCG can often reactivate the testicular secretion of testosterone. Dosage requirements vary from patient to patient, with some responding to a singular injection of 500 units, while others requiring that dose three to five times a week. For some men, this may be a very effective way of restoring testosterone to physiologic levels, with less likelihood of suppression of the body's own production.

3. Androgen Supplementation

Pro Hormone Supplementation

Pro Hormones are precursor hormones; they do not necessarily have much direct androgenic activity, but rely on the body for conversion to more active hormones. Probably the best known of these pro hormones is androstenedione; others commonly used are dehydroepiandrostenedione (DHEA), pregnenolone, progesterone and androstenediol. These agents are considered food supplements, and often can be purchased without a prescription.

Like other hormones, these pro hormones have relatively low oral bioavailability, and may be more active when given in a topical application. The comparison between androstenedione and androstenediol is interesting; while both serve as immediate precursors to testosterone, androstenedione also is a direct precursor to estrone. Thus, androstenediol may be a more attractive and efficient pro hormone, as it does not show a direct estrone pathway.

Progesterone has a particularly interesting role in men: it is active in both the aromatase and 5-alpha reductase systems in reducing the conversion of testosterone to estradiol and to dihydrotestosterone, respectively. In low (5 to 10mg) daily topical doses, progesterone can be an important adjunct in andropause therapy.

Testosterone Supplementation

Now, we will discuss the therapy more familiar to patients and physicians - direct testosterone supplementation. For many men, this will be the treatment of choice- it is easily understood and, when properly administered, can be very effective in restoring testosterone levels. Prior to beginning testosterone therapy, the physician should administer an office examination that includes gathering usual laboratory values, such as those for cholesterol, CBC, hematocrit, PSA, testosterone (total and free are recommended), and estradiol. The baseline testosterone and estradiol numbers should be established so that, after therapy is undertaken, it will be very clear whether or not the patient's levels are moving in the desired direction.

DOSING FORMS

ORAL

This is an inefficient way of dosing because of the high first-pass effect, in which the liver converts most of the testosterone into inactive metabolites. Most researchers and experienced clinicians do not recommend oral dosing of testosterone, as doses as high as 400mg per day may be required to achieve physiologic levels by this route. Note: methyltestosterone has greater bio-availability by oral administration, but is not recommended because of its adverse side-effect profile, primarily involving liver toxicity.

INTRAMUSCULAR INJECTION

Giving testosterone by intramuscular injection is probably the most common form of dosing, and for some men, it seems to work well. However, a serious drawback is its erratic ratio of release. Although it is suggested to be dosed at a two- or three- week intervals, there is no controlled-release mechanism. Many men will experience the IM injection as a bolus dose, primarily achieving high testosterone levels in the first week, with noticeable declining effects beyond that. Worse, there is a heightened possibility of increasing estradiol conversion as the body cannot properly store the excess testosterone. Instead of reaching a more positive testosterone-estrogen ratio, the opposite effect sometimes occurs with gynecomastia as an occasional outcome.

There are three methods of dosing which clinicians find acceptable, effective, and less likely to cause side effects: topical, sublingual or buccal, and implant pellets. Each of these offers a gradual and constant means of raising testosterone levels.

TOPICAL

At this time, topical administration appears to be the most effective means of dosing testosterone - creams, lotions, and gels have been used with good results. We will focus on gels because more clinical information is available with this type of vehicle, and because compliance can be achieved and maintained with an easy-to-follow regimen. A suggested starting dose is 50mgs per day, using 2 mLs of a 2.5% carbomer-alcohol gel. Research has shown that application of topical testosterone to a surface area of approximately 2 inches by 2 inches produces greater absorption than when dosed to a smaller area. The larger surface area that 2 mLs require, compared with a more concentrated, smaller volume, is an important factor in restoring testosterone levels and maintaining them in a consistent manner. In addition to the carbomer-alcohol gel, topical applications can be successful using creams, lotions and transdermal vehicles. Studies have shown that a once-a-day application can be sufficient to elevate and maintain levels consistently in a gel that covers a larger than customary surface area, such as 2 mLs would offer. Because of individual differences in the way patients absorb testosterone, some men may require their daily dose divided into two applications.

SUBLINGUAL OR BUCCAL

Sublingually or buccally, testosterone is given three to four times a day for andropause therapy. While absorption is efficient and rapid (peak levels obtained after approximately 30 minutes), metabolism is also fairly quick, with peak levels returning to normal after 4 to 6 hours. Effective sublingual or buccal doses can range from 10 to 40mgs per day, with a suggested mid-range of 20 to 25mgs daily. While this is a relatively inexpensive and non-invasive method of dosing, the patient must understand his daily compliance of multiple dosing is necessary for him to obtain maximum benefit of the hormone.

IMPLANTABLE PELLETS

A method many physicians and patients find acceptable and effective is the use of implantable pellets. This is an office procedure that is relatively simple and offers a major compliance advantage: effectiveness can last from three to five months from a procedure, eliminating the compliance issue.

In summary, andropause is a common progression in the aging process. While men are affected to varying degrees and at different ages, virtually all experience effects of hormonal imbalance. By taking positive steps to restore normal balance, many men can regain vitality and zest for life and enjoy their mature years fully and healthily.

For more detailed information, contact the Pharmacy Consulting Department at P.C.C.A.