

Andropause: New Perspectives



“Some experts say that about 25 percent of men go through andropause, the male version of menopause, in which levels of testosterone drop significantly with age.”¹ That statement appeared in an article posted on the Web by Harvard Medical School’s Consumer Health Information. Since that percentage is considerably higher than the estimated (by various sources) 4 to 5 million of men in andropause, those involved in men’s health need to find out what is really happening. This article follows others published in the *International Journal of Pharmaceutical Compounding (IJPC)* on andropause over the past four years.²⁻⁵ For example, in the November/December 2000 issue of *IJPC*, an article discussed the basic concepts of the decline of testosterone in men and the ways quality of life and good health could be enhanced by normalized hormone levels.² In that same issue, another article stated that testosterone gels are effective when properly used and that by monitoring the levels of androgens and estrogens the physician could determine the efficacy of the treatment.³ In the September/October 2001 issue of *IJPC*, an article concluded that a variety of hormones, prohormones and metabolic modifiers are available for the treatment of male hormone imbalance.⁴ Also, in the July/August 2002 issue of *IJPC*, an article concluded that “as knowledgeable and accessible healthcare professionals, pharmacists are in a unique position to collaborate with physicians to help men toward the goal of better health.”⁵

Research continues to emerge. Recently, an Internet search for the keyword *andropause* revealed 143 articles that were listed on PubMed’s website, a service of the National Library of Medicine. This is nearly double the number found two years ago. The same keyword found nearly 43,000 hits on Google’s website. However, it is clear that, while there is a great deal of interest and new information continues to be published, some of the information reflects caution and controversy. In this article, our goal is to shed light on some of the poorly understood aspects of andropause, comment on existing concerns and offer some alternative ways to achieve hormonal balance.

Bruce Biundo, BS, RPh
Professional Compounding
Centers of America
Houston, Texas

What Constitutes Andropause?

Normal testosterone levels in men range widely, with a low end of 300 ng/dL and a high of 1050 ng/dL for serum total testosterone. Not all men operate happily in the same range; some men may require levels in the upper range to feel well, while others can be quite content on the lower end of the range. According to Dr. Malcom Carruthers, author of *Maximizing Manhood*, “the threshold at which the onset of symptoms occurs shows great variability.”⁶ Carruthers further stated that “each man may have his own ‘reference range’ for several endocrine variables, including androgens.”⁶ Dr. Robert Tan used the term *relative hypogonadism* in reference to this concept, which has also been described by other clinicians.⁷⁻⁸ Understanding that a man can be clinically hypogonadal while having

testosterone levels that are low but within range can contribute significantly to patient care. Laboratory values are helpful in diagnosing andropause, but those values should be combined with a history and physical examination as well as an evaluation of symptoms as listed on the androgen deficiency in aging males (ADAM) questionnaire.⁹

The Role of Estradiol and Estrone

Estradiol and estrone are the so-called female hormones. The primary source of estradiol is the aromatization of testosterone; estrone comes primarily from the aromatization of the adrenal hormone androstenedione. One might expect that, with the decline of the source hormone testosterone, we would see the same with estradiol. Instead, we see estradiol levels remaining fairly constant, which is the result of increased

aromatization because of increased body fat—primarily subcutaneous abdominal fat.¹⁰ Thus, we see a change in the androgen/estrogen ratio, mainly because of increased fat deposits that are commonly associated with the aging process. The role of estrogens in men has been studied in some detail in recent years. Estrogens in men play a vital role in the regulation of gonadotropin feedback, a number of brain functions, bone maturation, regulation of bone resorption and lipid metabolism. Estrogens are also an important factor in determining men’s level of sexual interest.¹⁰⁻¹¹

While the normal serum levels of estradiol are very low compared with testosterone (2–3 ng/dL versus 300–1050 ng/dL), the levels are deceiving because much of the activity of estradiol occurs as a result of peripheral formation (acting locally), and this does not show up in serum levels.¹⁰ A critical consideration in monitoring the androgen/estrogen balance is that changes in the ratio that favor estradiol may have adverse effects on the prostate.¹¹

The role of estradiol on gonadotropin feedback is so vital that it invites commentary. Briefly, the hypothalamus sends out gonadotropin-releasing hormone (GNRH) as a messenger to the pituitary, which then sends out leutenizing hormone (LH) to the testes as a call to produce more testosterone, and follicle-stimulating hormone (FSH) as a messenger to increase spermatogenesis. Conversely, when the body has enough hormones there is a slow-down of production of GNRH and LH. This feedback system is mainly mediated by estrogens.¹² In fact one study, which further revealed that role of estradiol, showed that a controlled dose of a potent aromatase inhibitor, anastrozole, not only slowed down the production of estradiol significantly but also raised the levels of testosterone to the same extent.¹³ This gives credence to the concomitant use of testosterone and an aromatase inhibitor in preventing suppression of gonadotropins.¹²

The TOTAL Software Solution

Extemporaneous Rx Compounding Software

MOVE UP to ExtempX—
Ask about a FREE
data conversion

Extemp_{Rx}

**Everything you need...
right out of the box.**

Download
the DEMO today,
or call us for a
FREE CD

877.343.0229

Florida 727.906.4499

www.AppDC.com
info@AppDC.com

- The Top Rated all inclusive Windows based application for Compounders
- Maintain your formula library
- Print log sheets with prep instructions
- Fill Rx's and generate labels
- Calculate unit costs, par levels, reorder quantities—complete inventory control
- Generate dozens of useful reports
- Build pricing schemes and price quotes
- Mailing labels and Mail Merge letters

ExtempX is produced by Application Design Consultants, Inc.
We are a software company specializing in healthcare applications since 1987.

Involvement of Testosterone in Prostate Cancer

The involvement of testosterone in prostate cancer is a subject that has been the focus of much study and continues to be an area of concern. According to one prominent researcher, “epidemiological studies provide no clues that the levels of circulating androgen are correlated with or predict prostatic disease. Similarly, androgen replacement studies in men do not suggest that these men suffer in a higher degree from prostate disease than control subjects.”¹⁴ However, many concerned specialists now believe that a large, controlled study of older men is needed to arrive at a conclusion of safety.

Benign prostatic hyperplasia (BPH) is somewhat different. “Recent knowledge indicates that prostate development depends on the synergistic effect between androgens and estrogens.”¹¹ Therapy that reduces the levels of dihydrotestosterone is standard for BPH and often results in a lessening of symptoms and a reduction in the size of the prostate. (Recall the earlier statement concerning the adverse effects on the prostate of the changing androgen/estrogen balance.) Nutritional supplements have been widely studied for improved prostate health, and beneficial agents include vitamin E, selenium, lycopene, soy and omega-3 fatty acids.¹⁵

Therapeutic Options in the Treatment of Andropause

Our overall goal should be to enhance the health of the patient, both in the quality of life and long-term wellness. Achieving hormonal balance is at the heart of that therapy, and the most prevalent treatment is testosterone supplementation. In using topical gels or creams, we have found that dosage titration is important because the initial dose may need to be adjusted. Dr. Christopher Cutter found in his practice that some men showed initial elevations of testosterone levels from

topical gels, but then had declines after 3–4 weeks because of suppression of LH (endogenous suppression).¹⁶ At that point, the dose had to be increased in order to overcome suppression. We have found that buccal systems work, as evidenced by the arrival of the product Striant. While many are familiar with the limitations of traditional therapy with intramuscular injections of long-chain esters such as cypionate, there have been anecdotal reports of improved outcomes when dosing occurs on a weekly basis, rather than every 3 weeks. And, while it is not the most common therapy, testosterone implants (pellets) continue to have support from those who find that route to be dependable.

Nonsupplemental Therapy

While testosterone supplementation, frequently with the use of aromatase

inhibitors, is the most common form of therapy, it is not the only way in which we can help patients achieve hormonal balance and good health. Nonsupplemental ways to achieve hormonal balance include exercise, weight management, proper diet and stress management. Exercise and its effect on testosterone levels has been studied. Zmuda et al stated, “We conclude that short-term exercise produces a transient elevation in serum testosterone levels in elderly men.”¹⁷ Tremblay et al stated, “Androgens increased in response to exercise...”¹⁸ Additionally, the same kinds of comments were made about exercise increasing testosterone independently of LH and FSH secretion.¹² Proper diet for many would mean increasing lean protein as well as fruits and vegetables while decreasing carbohydrates. For others, it would be a simple directive—eat less.



Introducing IKA yellow line homogenizers, stirrers, and hot plates. Available **exclusively** through Spectrum Pharmacy Products.

SPECTRUM
PHARMACY PRODUCTS

800.791.3210

www.spectrumrx.com



Weight management is always important. In the case of andropausal men, with less weight there is less fat and thus less aromatization to estradiol. Treatment of obese men with testosterone was associated with a decrease of visceral fat tissue mass, a rise in insulin sensitivity and a decrease in insulin resistance. On the other hand, weight loss is associated with an increase of serum levels of testosterone and a decrease of serum levels of estradiol.¹² Exercise, weight management and a healthy diet should result in less fat, more muscle and better hormone balance, and better health is achieved in a more holistic manner. Finally, stress management is important because increased cortisol levels are associated with decreased testosterone.

Conclusion

In summary, hormonal balance is important for men to achieve maximal

health. While supplementing testosterone and attempting to keep estrogens under control is useful, other means of obtaining hormonal balance should be encouraged.

References

- [No author listed.] Harvard Medical School's Consumer Health Information. [Aetna Intellihealth's Website]. Available at: <http://www.intelihealth.com/IH/ihtlH/EMIHC274/8124/24788/2962>. Accessed October 15, 2003.
- Biundo B, Shippen E. Testosterone deficiency in men: New treatments for andropause. *IJPC* 2000; 4(6): 429-431.
- Cutter C. Compounded testosterone gels: A guide for clinicians and pharmacists. *IJPC* 2000; 4(6): 432-437.
- Biundo B. Treating andropause: Prohormones and hormone metabolic modifiers. *IJPC* 2001; 5(5): 351-353.
- Biundo B. Establishing an andropause practice. *IJPC* 2002; 6(4): 259-261.
- Carruthers M. A multifactorial approach to understanding andropause. *J Sex Reprod Med* 2001; 1(2): 69-74.
- Tan RS. Andropause: Introducing the concept of "relative hypogonadism" in aging males. *Int J Impot Res* 2002; 14(4): 319.
- Namey TC. Hypogonadism and Andropause: Diagnosis, Consequences and Treatment. Presented at: The Men's Health Seminar at the Professional Compounding Centers of America; June 2003; Houston, TX.
- Morley JE, Perry HM. Androgen deficiency in aging men. *Med Clin North Am* 1999; 83(5): 1279-1289, vii.
- Vermeulen A, Kaufman JM, Goemaere S et al. Estradiol in elderly men. *Aging Male* 2002; 5(2): 98-102.
- Gooren LJ, Toorians AW. Significance of estrogens in male (patho)physiology. *Ann Endocrinol* 2003; 64(2): 126-135.
- Nieschlag E, Behre HM, eds. *Testosterone: Action, Deficiency, Substitution*. 2nd ed. Heidelberg/New York, NY: Springer; 1998: 115, 430.
- Mauras N, O'Brien KO, Hayes V et al. Estrogen suppression in males: Metabolic effects. *Clin Endo Metab* 2000; 85: 2370-2377.
- Gooren L. Androgen deficiency in the aging male: Benefits and risks of androgen supplementation. *Steroid Biochem Mol Biol* 2003; 85(2-5): 349-355.
- Biundo B. Nutraceuticals as Preventive Medicine in Aging Men's Health. In: *Aging Men's Health: A Case Based Approach*. New York, NY: Thieme Medical Publishing; 2004.
- Cutter CB. Compounded percutaneous testosterone gel: Use and effects in hypogonadal men. *J Am Board Fam Pract* 2001; 14(1): 22-32.
- Zmuda JM, Thompson PD, Winters SJ. Exercise increases serum testosterone and sex hormone-binding globulin levels in older men. *Metabolism* 1996; 45(8): 935-939.
- Tremblay MS, Copeland JL, Van Helder W. Effect of training status and exercise mode on endogenous steroid hormones in males. *J Appl Physiol* 2003; 96: 531.

WHEN IT COMES TO OINTMENTS, CREAMS AND GELS.

We're NUMBER ONE because Gallipot is more innovative and resourceful when it comes to topical delivery systems.

We offer the most complete line of bases and vehicles for all your compounded dosage forms. Take our POLOX[®] Gel mixed with LIPOL[™] for example, the quick and easy topical drug delivery system.

Our goal is to assist you with all your compounding. Call today and see for yourself why we are number one.

GALLIPOT
The Art Of Compounding
1-800-423-6967

www.gallipot.com

Address correspondence to: Bruce Biundo, BS, RPh, Professional Compounding Centers of America, 9901 S. Wilcrest, Houston, TX 77099. E-mail: bbiundo@pccarx.com ■